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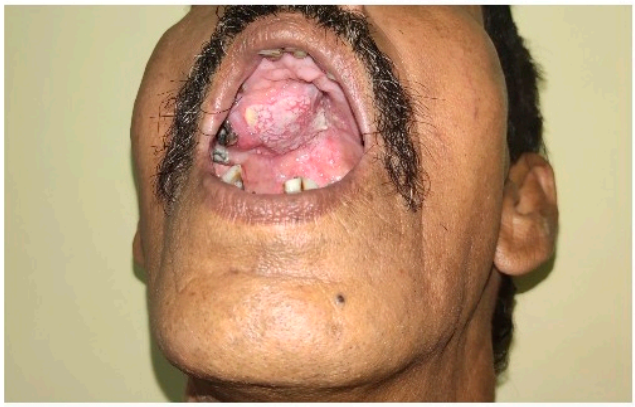
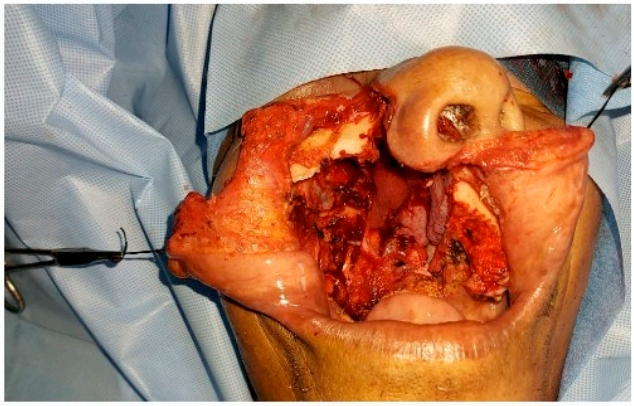
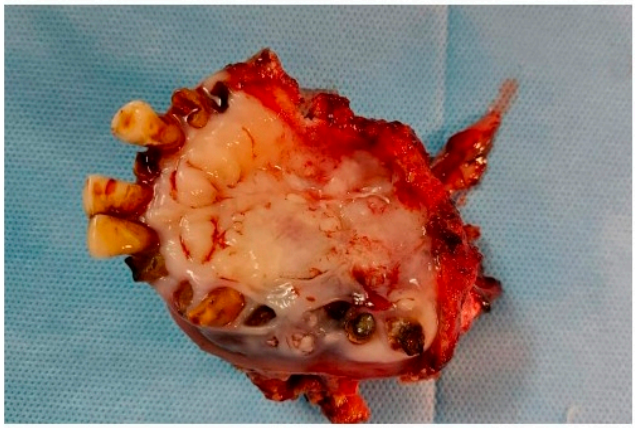
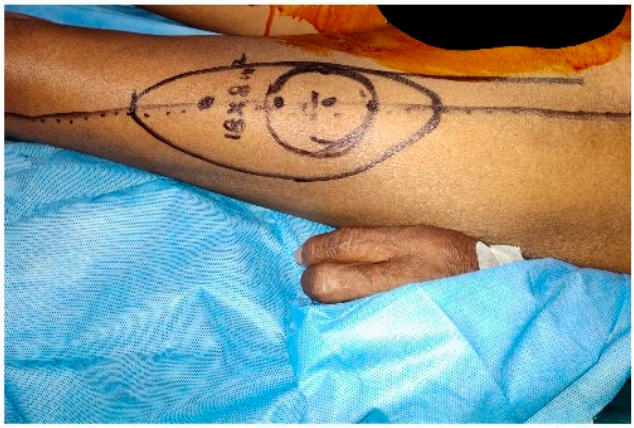
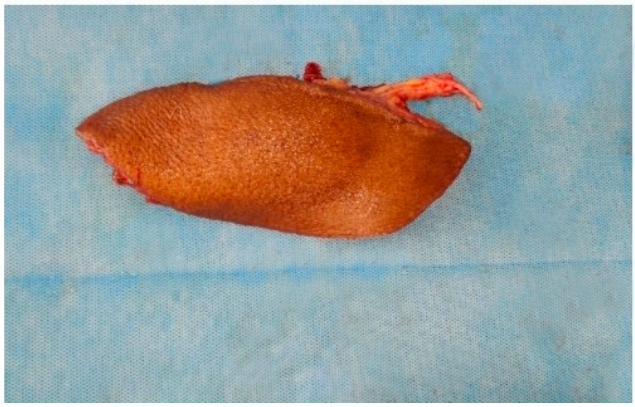
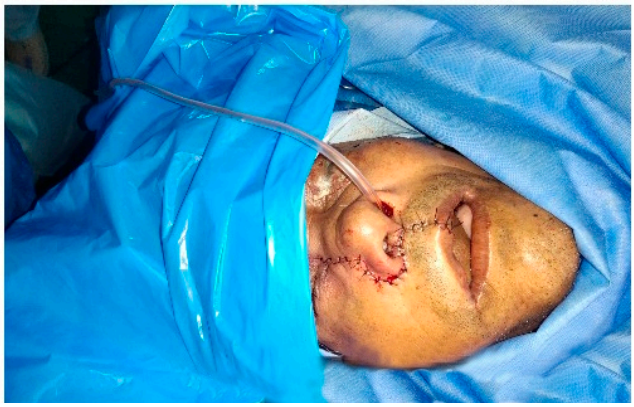
BBCI EDGE

Special Issue : **Head and Neck Oncology**

A Science Magazine

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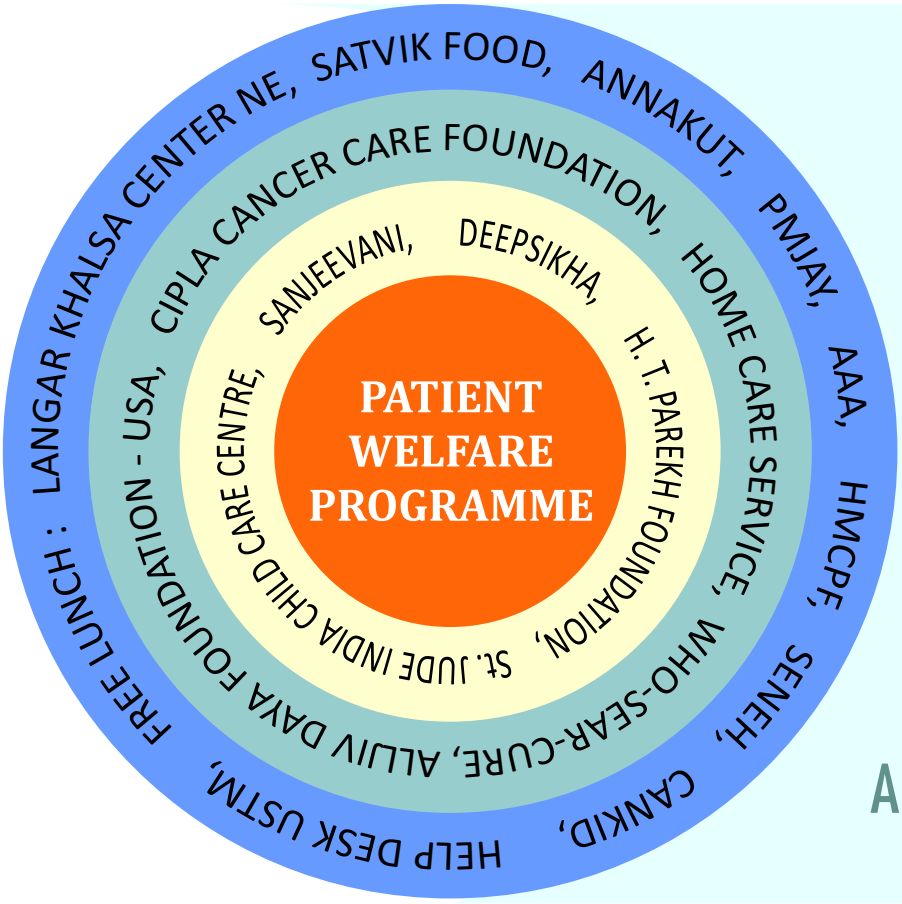

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Director's Note

Dr A C Kataki
Director,
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The first issue of BBCI EDGE- *A Science Magazine* met with immense praise from all corners and being a highly optimistic person, I envision the continued success of this initiative. This second issue contains articles which will definitely engage its readership just like the last occasion. A lot have transpired since the beginning of this effort and the institute has taken up the task of pursuing academic brilliance with utmost sincerity and in the same vein, I am happy to announce that we will be taking one step further with our Journal named *Annals of Oncology Research and Therapy (AORT),* the first issue of which will come out in the year 2021. However, BBCI EDGE will continue surging ahead in its course of breaking boundaries. My best wishes are always with the Editor and his team and all the young and experienced researchers, clinicians and academician of the region. I appreciate the contributions of the revered guest authors from across the country!

Editorial

Dr. Gaurav Das, MS, MCh
Associate Professor
Deptt. of Surgical Oncology, BBCI
Editor, BBCI EDGE

I have been tremendously encouraged by the positive feedback received for the inaugural issue of BBCI EDGE – *A Science Magazine* that we managed to bring out in the unbelievable year that it was, year 2020! It was a learning phase in this job and continues to be so when I am doing this for the second time with this July 2021 issue. In the meanwhile, the coronavirus pandemic dies down after a second wave with the advent of a massive vaccination campaign where our nation heads the way. This gives us a renewed impetus and we will definitely steer this drive in the positive direction.

The Department of Head and Neck Oncology, under the capable leadership of Prof. Tashnin Rahman and the active involvement of Dr. Kaberi Kakati, has done a commendable job of making this issue *a Head and Neck Oncology Special*. The readers will enjoy having a glimpse of the work being done in this department through the various articles penned down with contributions from the entire team. I would also like to thank Dr. Vikas Jagtap, a former faculty at BBCI and now working at NEIGRIHMS Shillong, for getting involved with this cause.

I am indebted to all other contributors and especially so because they have been ever so forthcoming with ideas and advice. A surgical oncologist from our region at IRCH AIIMS Dr. Jyoutishman Saikia, who continues to work with Prof. SVS Deo, has shared an article on cytoreductive surgery and hyperthermic intraperitoneal chemotherapy and I believe this will enrich our understanding on the subject matter.

Lastly, Mr. Ph. Surachandra Singha deserves all the credit for the arduous job of realizing this concerted effort as a well-organized print issue.

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Review Article

Radiotherapy in Nasopharyngeal Carcinoma from 2D to 3D

Vikas K. Jagtap

Department of Radiation Oncology
NEIGRIHMS, Shillong

INTRODUCTION

Nasopharyngeal carcinoma is very distinct from other head and neck cancers; it is very aggressive locoregionally and has a high risk of distant metastasis. Nasopharyngeal carcinoma occurs in specific geographical location globally. In India, its prevalence is highest in the North-eastern region of our country, specifically Nagaland, which leads the list.[1] Unlike other head and neck cancers, surgery is rarely done after the 1950s because of difficulty in surgical exposure because of anatomical location, proximity to critical structures, inability to achieve adequate surgical margins. Surgical intervention is only done to acquire a biopsy or as a salvage therapy for persistent or recurrent disease. Radiotherapy with or without concurrent chemotherapy is the single most important local therapy to achieve sufficiently reasonable local control with minimal toxicity in nasopharyngeal carcinoma (NPC).

ERA OF 2D RADIOTHERAPY

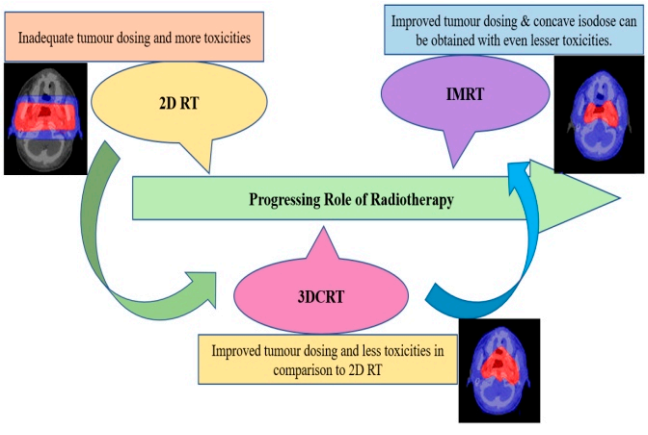
Initially, 2D radiotherapy approaches were employed in two phases to deliver doses up to 60 Gy.[2] Later on, when newer radiotherapy delivery techniques were introduced it was found that with 2D conventional plans, the tumour dose coverage is not adequate, and the toxicities were also higher.[3,4] 5-year survival rates with 2D radiotherapy are mentioned in Table 1 below.

Table 1: Showing survival rates by T and N stage after conventional radiotherapy .[5]

Author	Year	Time period	Local control rate by T stage (%)				Survival rate by N stage (%)			
			T1	T2	T3	T4	N0	N1	N2	N3
Hoppe et al.	1976	5yr	76	68	55	0	78	70	42	39
Wang et al.	1990	5 yr	60	48	27	29	60	42		32

ERA OF 3D RADIOTHERAPY

With the advent of 3D conformal radiotherapy, the dose delivery to tumour improved, and tumour underdosing was reduced with 3D plans in comparison to 2D plans and mean tumour dose increased.[6] Jen et al. for the first time demonstrated improved event-free survival with 3D conformal therapy in comparison to 2D radiotherapy for stage III (80% vs 56%) and stage IV (82% vs 33%) disease. Xerostomia at three years was also significantly low with 3D conformal radiotherapy.[7]



From the beginning of 21st century, a significant shift occurred with the wide use of IMRT for the treatment of nasopharyngeal cancer, which enabled radiation oncologist to obtain concave isodose, helped in reduction of toxicities and also enabled them to increase the total delivered dose. The first evidence of the benefit of using IMRT was shown by *Sultanem K et al*.[8] in their study loco-regional control at 21 months was 100 per cent and four-year overall survival was 94%. They concluded that the coverage with IMRT is excellent, dose to GTV is significantly higher in comparison to other techniques and dose to the critical organs was also lesser. Later on, with the increased use of IMRT in the other centers, and they also reported better loco-regional control and overall survival with the use of IMRT. A few studies are mentioned below in the Table 2.

Table 2: Showing Local control rates and Overall survival rates in patients of Ca Nasopharynx treated with IMRT with or without chemotherapy.[9]

Study	Year	Stage	N	Time point	Local control	Overall survival
Xiao et al.	2011	III-IVa	81	5 yr	95	75
Su etal.	2012	I-IIb	198	5yr	97	NA
Sun et al.	2014	I-IVb	868	5yr	92	NA
Setton et al.	2016	I-IVb	177	5yr	83	74
Wu et al.	2017	I-IVb	614	10yr	89	73

As it is evident from the above table that IMRT not only provided better coverage but also improved the local control rates and the overall survival rates.[10] Ca Nasopharynx is the only site in the body where radiation delivery by IMRT is proven to increase local control and overall survival when compared to 2D radiotherapy, this is difference is not noted anywhere in any subsite other than nasopharynx. Meticulous attention to every single step in the RT process is important, particularly when using an increasingly conformal technique. The first fundamental step is accurate delineation of the gross tumor extent. Fusion of magnetic resonance images with planning computed tomography is indicated. Positron emission tomography is being increasingly used, not only for better detection of distant metastases, but also for depiction of locoregional tumor metabolic activity for supplementary information .[11]

NEWER TECHNIQUES OF RADIOTHERAPY

With further advancement in radiotherapy interest has grown up and researchers are exploring the role of Stereotactic radiosurgery and stereotactic radiotherapy in this subset of patients. Till now the SRS in definite settings is used to boost the primary if residual disease persists after definitive EBRT or for Re-irradiation of primary on recurrence [12]. There are no definitive guidelines regarding dose and fractionation schedule in both indications. Few studies which show encouraging results are mentioned below in Table 3:

Table 3: Results of patients treated with SRS boost after EBRT in definitive setting. [11]

Study	Patients	Treatment	Follow-up	Outcomes
Hara et al. 2008	n = 82, stage IIA-IVb 85% w/concurrent Cisplatin chemotherapy during EBRT	EBRT to 66Gy + single fx SRS boost Boost 2–6 weeks post-EBRT (reimaged prior to boost) Boost: Median 11 Gy (range 7–15 Gy) × 1 fx Dose Rx to 80% IDL	40 months	98% 5-year LC 69% 5-year OS Late toxicity: Carotid aneurysm (1%), temporal lobe necrosis (12%)
Yamazaki et al. 2014	n = 25, stage IIA–IVb Majority w/ Concurrent cisplatin or 5FU chemotherapy during EBRT	EBRT to 50Gy (median) in 1.8–2Gy/fx + SBRT boost Boost: 5Gy × 3fx (median) Dose Rx to 80% IDL	28 months	71% 5-year LC 70% 5-year OS Late toxicity: G2 ulcerations, >G3, fistula (8%)
Bakst et al. 2011	n = 25	Dose painting EBRT w/ chemotherapy 2.34 Gy × 30 fx PTV = GTV + 1 cm	33 months	91% 3-year LC 89% 3-year OS Late toxicity: 12% temporal lobe necrosis

There is wide variation in published studies with regard to dose, fraction size, prescribed IDL, use of concurrent chemotherapy, and volume irradiated. Results are promising; however, there remains a relatively high rate of grade 3/4 toxicity, including some grade 5.

CONCLUSION

local control and overall survival are excellent with the use of conformal radiotherapy techniques. It's the only site where radiotherapy with IMRT has a survival advantage in comparison to 2D radiotherapy. Newer techniques like SRS/SRT are being explored to achieve better results with lesser toxicities.

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Original Article

A retrospective review of elective neck dissection versus neck observation in N0 oral cancer: a single institution experience from the North East India

Tashnin Rahman[1], Nizara Baishya[2] Kaberi Kakati[1], Kishore Das[1], Anupam Das[1], Ashok Das[1], Rajjyoti Das[1], Manigreeva Krishnatreya[2]

1. *Head and Neck Oncology Department, BBCI Guwahati*
2. *Cancer Registry and Epidemiology, BBCI Guwahati*

INTRODUCTION

Oral cancer accounts for 2%–4% of all cancer cases worldwide. But the prevalence of oral cancer is much higher in the South East Asian countries, accounting for around 45% in India.[1] This high prevalence is attributed to the consumption of tobacco. OSCC is the most common malignant neoplasm of the oral cavity with a high potential to metastasize even in the early stage. Nodal metastasis is the most significant prognostic factor in OSCC. The management of early-stage OSCC (cT1/2N0) can be divided into two protocols: surgery and radiation therapy. However, management of neck in clinically N0 early OSCC is still controversial when surgery is advocated first, as to whether END should be performed simultaneously with primary site resection or neck observation.[2, 3] It has been reported that 30% of oral cancer patients with clinically N0 neck harbour occult metastases, depending on the size and site of the primary tumour and the histological diagnostic methods. [4] The greatest challenge faced by head and neck oncologists is the correct identification of that subset of patients who do not have cervical nodal micro metastases and may not require END. Clinical palpation of the neck is grossly inadequate for assessment of cervical nodes and radio diagnosis lacks considerable power to detect occult neck metastasis making the non-invasive neck staging methods limited to a maximum accuracy of76%.[5] Occult metastases are defined as lymph nodes metastases that are not detected initially by neck palpation and imaging examination, but they are detected by histological examination after neck dissection, or they are presented as delayed regional recurrence, if they were untreated. [6, 7] In this retrospective study, we report our experience in the treatment of 291patients with early OSCC by comparing the survival outcomes between END and neck observed group (OG).

MATERIALS AND METHODS

From 1st January 2010 to 31st December 2015, a total of 685 patients with early stage OSCC were diagnosed in the Head and Neck Oncology Department of Dr B Borooah Cancer Institute in Guwahati, India. Patients' medical records were retrospectively reviewed for clinical and demographic parameters. Two hundred ninety-one patients with early-stage oral cancer were included in this retrospective study. Staging was performed according to the criteria for oral cancer developed by the American Joint Committee on Cancer (AJCC) 8th Edition. The present study has been approved by the Institutional review board.

Patients follow up were being done by going through the hospital revisit records, telephonic calls and home visits. All patients were followed up for at least 5 years.

The inclusion criteria

1) The primary lesions of the tongue, buccal mucosa, floor of the mouth, or upper and lower alveolus.
2) Clinically N0 neck: both on physical and

radiological examination.
3) Histologically confirmed OSCC.

The exclusion criteria

1) Patients with previous history of head and neck treatment (surgery, radiotherapy, or chemotherapy)
2) Patients with various co morbid conditions or reluctant to undergo surgery.
3) Patients with synchronous primary tumours.

Treatment

Among the 291 patients, 243 patients were managed with END and in 48 patients neck was not addressed, which was the observed group (OG). In the END group, wide local excision of primary tumour performed simultaneously with END and reconstruction was done where appropriate to cover the defect. Neck specimens were sent to the pathologist after proper labeling to identify the potential occult metastases. Postoperative adjuvant radiotherapy (RT) was scheduled within 4–6 weeks after surgery, if patients had a pathologically positive lymph node. In the OG, patients were treated only with local excision of primary tumour and were then kept under observation with close follow-up by proper counseling.

Follow-up

For the END group, follow-up was done every 1 ½ months for the first 1 year followed by 3 months for 2 years, and then, every 3 or 6 months later. For the OG group, the follow-up interval was suggested to be 1–3 months for the first 3 years, and then, 3 or 6 months later. Ultrasonography, CT scan or MRI was performed as a routine radiological examination(s) every 6 months for the OG and 6 months to 1 year for the END group.

Statistical methods

Data were analyzed using IBM SPSS advanced statistics version 20 (SPSS Inc., Chicago, IL). The overall survival (OS) was calculated from the date of surgery to the date of the last follow-up or death. Disease free survival (DFS) was calculated from date of surgery to the time the patient survives without any signs or symptoms of the cancer. Survival analysis was done using Kaplan-Meier method and comparison between two survival curves was done using log-rank test. $P<0.05$ was considered significant.

RESULTS

Of the 291 patients, 201 were males and 90 were females. The age ranges from 26 to 83 years with a median of 58 years. The most common sites involved were the buccal mucosa (BM) 150 (52%) followed by tongue in 78 patients (27%) and lower alveolus 33 patients (11%). 243 patients underwent END and 48 patients were kept under close observation following wide local excision of the primary. Incidence of occult metastasis in clinical N0 neck was found to be 25%. The most common site of occult nodal metastasis in relation to site was the tongue which accounts for 47% followed by buccal mucosa which was 39%. The Kaplan Meier survival curves showed that the 5-year OS was 56.8% [Figure1a] and the disease free survival (DFS) was 54.9% [Figure 1b]. The 5-yearDFS difference between the pathological N0 and N+ve neck were 68.9% and 28.2%, respectively($P=0.0001$) [Figure 2]. The5-yearDFS between the END versus OG was 63.7% versus 52.1% ($P= 0.047$) [Figure3].

DISCUSSION

According to the NCCN guidelines, Observation of neck and Elective Neck Dissection are the two main treatment strategies for the neck in patients with early-stage Oral Cancer. But, it's still a matter of debate. Kligerman *et al*. demonstrated that patients who underwent END had a significantly higher 3-year disease-free survival rate than those who did not.[8]D'Cruz et al enrolled 500 patients with early-stage OSCC in their study and found that the therapeutic neck dissection group had higher 3-year OS and disease-free survival rates than the observed group.[9] Because of the high incidence of occult metastases in patients with early-stage OSCC, which ranges from 8.2% to 46.3% some surgeons advocate END.[10,11] In our present study, the incidence of occult metastasis was 25%. However, in those patients without occult metastasis, neck observation policy is followed by some, because it avoids overtreatment of the neck, and once regional recurrence is detected during follow-up, therapeutic neck dissection can be performed at that time.[12]Earlier, it was believed that nearly 2/3rd of patients would be exposed to the morbidity of a neck dissection unnecessarily. [13] In the study by D'Cruz et al, majority (85.3%) of patients had tongue cancer. [9] In our present study, buccal mucosa (52%) was most common site followed by tongue (27%). However, most common

site for occult metastasis in the present study was in tongue cancers (47%).

In recent times, both the policies are practiced in different centres around the world. The proponents of END have put forwarded the argument that neck dissection can lead to a better disease control and improve the survival with acceptable surgical morbidity. [14] END also provides the better pathological staging of the disease and prognostication, and help in deciding the need for adjuvant treatment. [15]Our study has shown that, there is drastic reduction in the 5-year DFS in pathological N+ve neck (28.2%) in comparison with N0 neck (68.9%). Thus, there was a large difference in survival once there is nodal metastasis. One of significant findings from the present study has revealed the better 5-year DFS in patients who underwent END, i.e. 63.7% in compared to 52.1% in observed group. A review paper recommended sentinel lymph node biopsy can be an alternative diagnostic strategy to evaluate cT1-T2N0 early oral cancer. [16] However, application of sentinel lymph node biopsy must not be confused with treatment strategy, which is neck dissection.

Study Limitations

The major limitation of the present study is lack of randomization in each group, as it was a retrospective review of records. Furthermore, small number of patients in the OG compared to END group makes it difficult to draw head to head comparison.

In conclusion, metastasis to neck nodes significantly lowered the disease free survival in patients with clinical N0 oral cancer. Elective neck dissection should be considered in patients with oral squamous carcinoma with N0 neck rather than observation only, weighing in benefits and harms, like long-term physical complications of neck dissection.

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Original Article

A study of the pattern of neck node metastasis in squamous cell carcinoma of oral cavity in relation with depth of invasion

T. Kanato T., Kishore Das, T. Rahman, A.K. Das, R.J.Das, A. Das, K. Kakati

Head and Neck Oncology Department, BBCI, Guwahati

INTRODUCTION

Squamous cell carcinoma of oral cavity is the most common head and neck malignancy. The incidence varies worldwide with India and south East Asia showing highest rates. The global incidence is estimated to be 275,000 new cases per year .[1] Tobacco and alcohol consumption remain the most dominant etiologic factors in oral cancer in India.[2]

Surgery is the treatment of choice in management of oral cancer and the most significant prognostic factor in the treatment of patients with oral squamous cell carcinoma is the cervical lymph node status, as even a single lymph node metastasis may diminish survival and this may significantly change the postoperative course of treatment.[3,4,5] Therefore meticulous clearance of cervical lymph nodes plays a crucial part in thetreatment of oral cancer.

However, neck dissection is not without complications. In order to identify patients who are likely to have nodal metastases, several primary tumour factors like tumour differentiation, perineural invasion, lymphovascular invasion and tumour thickness have been studied. Presently it is well recognized that tumour thickness or depth of invasion is an important predictor of nodal metastases in oral cancer .[6,7]

One of the important changes in the 8th edition of the American Joint Committee on Cancer (AJCC) staging system for oral cavity squamous cell carcinoma (OSCC) is the addition of depth of invasion (DOI) as a modifier for the T category.[8] DOI is being measured histologically from the level of the basement membrane of the closest normal mucosa and dropping a "plumb line" to the deepest point of invasion .[9] The inclusion of DOI in the T category for oral cavity cancer may improve prognostic performance of AJCC staging by predicting regional control and status of regional lymph nodes.

This study was conducted to determine the incidence of nodal metastases based on the depth of invasion and whether the indication for neck dissection differ for each sub-group thereby individualizing the need and extent of neck dissection. It will also boost up the current concepts and will provide useful information to decide the extent and type of neck dissection in squamous cell carcinoma of oral cavity in respect to its depth of invasion.

MATERIALS AND METHODS

It is a Prospective clinical study of patients with pathologically diagnosed oral squamous cell carcinoma that attend 'Head & Neck Surgery' OPD from April 2019 to March2020 and subsequently get operated for oral cancer and neck dissection at Department of Head and Neck Surgery, Dr B Borooah Cancer Institute (BBCI), Guwahati.

Inclusion Criteria

All the new cases who had not received treatment before, and operated for both primary and neck

dissection and given consent for study has been taken up for study.Cases were taken up only after they were histopathologicaly proven.

Exclusion Criteria

Cases who received treatment outside and re-operated, Residual / recurrent cases/second primary. Those cases where neck has been operated before for other disease, post NACT or RT.

A total of 110 patients who gave valid consent and who fulfilled the inclusion and exclusion criteria were taken up for the study.Descriptive statistical analysis was used to represent the data.Data was analysed using IBM SPSS software version 21.0 with the guide of medical statistician. Data was summarized in the form of proportions, frequency tables and bar for categorical variables.Investigations conducted on patient were routine investigation for general anaesthesia, upper gastro intestinal endoscopy (UGI-E) to rule out second primary, Chest X ray, USG neck, CECT scan or MRI, FNAC, Punch Biopsy, HPE of surgical specimen.

Clinical features including age, sex, tumour location, histological grade and clinical stagewere evaluated and their relationships to clinical metastasis were determined. All the operable cases were included irrespective of their nodal status. None of the patients had distant metastasis detectable at the time of surgery. Tumours were staged according tothe American Joint Committee on Cancer, 8th edition.Surgery to remove the tumor consisted of a wide excision using the transoral, transmandibular, or pull-through approach depending on the location and size of the tumour and repair with local,pedicle or free flap. Neck dissection was performed simultaneously with tumour resection in all cases. MRND was done in clinicallyneck node positive patients and selective neck dissection was done in clinically node negative patients. If tumour was crossing the midline then bilateral neck dissection was done. Specimens were sent for histopathology examination in separate container after marking each level of neck node.Postoperative radiotherapy $\pm$ Chemotherapy were given to those patients who had close/positive margins with cervical metastasis depend on post-operative histopathology report. Depth of Invasion (DOI) was defined as according to the eighth edition of the AJCC staging manual.DOI was measured using the basement membrane of the adjacent normal epithelium, creating a line perpendicular to this horizontal, and measuring to the deepest point of tumour invasion in millimetres.

All the participants were informed about the nature of the study and those who agreed to participate were asked to sign the informed consent form. Participants were informed that they could withdraw from the study at any point of time. The study was carried out only after obtaining approval from the Institutional Ethical Committee (IEC), Dr B Borooah Cancer Institute, Guwahati.

RESULTS AND OBSERVATIONS

One hundred and ten patients of Squamous cell carcinoma of oral cavity, who came to Dr B Borooah Cancer institute were included and analysed in this study. The age of the patients ranges from 31to 75 years. The youngest was 31 years and eldest was 75 years with the mean age of 54.1 years. Out of 110 patients, there were 61 males comprising of 55.5% and 49 females comprising of 44.5% of patients.

The site of tumour location in the patients were-Lip: 2(1.8%),Buccal Mucosa:61(55.5%), RMT: 3 (2.7%), Hard Palate: 1(0.9%), Oral Tongue: 13(11.8%), Lower Alveolus: 25(22.7%) and Upper Alveolus: 5 (4.5%).

Out of 110 patients, 70 patients (63.6%) has no nodal metastasis, 12(10.9%) had metastasis in level 1B, 7(6.4%) patients had metastasis in level IIA, 6(5.5%) had metastasis in IA & IB, 11(10.0%) has metastasis in IB & IIA, 4(3.6%) had metastasis in IB, IIA & III. The incidence of isolated neck metastases to level IA, IV & V is 0%. Patients having metastases levels IA, IV & V were usually accompanied by metastases to other levels of neck node [table 1, Fig 1].

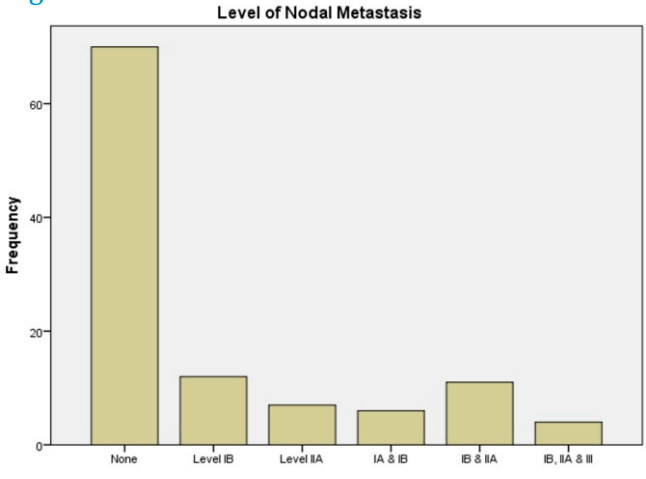
Table - 1

Level of Nodal Metastasis		
Level	**Frequency**	**Percent (%)**
None	70	63.6
IB	12	10.9
IIA	7	6.4
IA & IB	6	5.5
IB & IIA	11	10.0
IB, IIA & III	4	3.6
Total	110	100.0

Table - 2

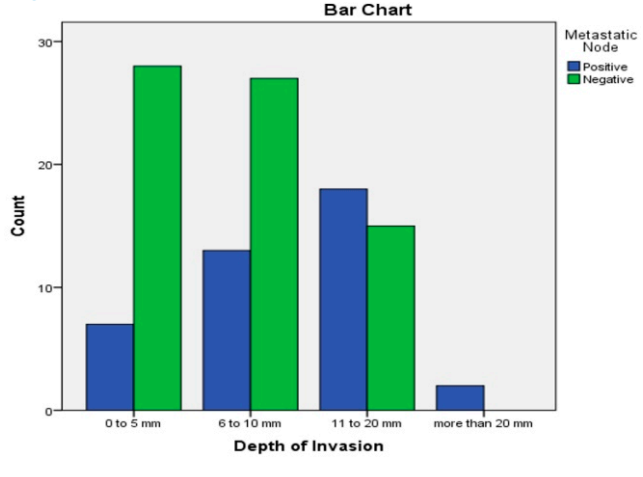
Depth of Invasion * Metastatic Node Crosstabulation			
Depth of Invasion	Metastatic Node		Total
	Positive	Negative	
0 to 5mm	7	28	35
6 to 10mm	13	27	40
11 to 20mm	18	15	33
more than 20mm	2	0	2
Total	40	70	110

Figure - 1



In the depth of invasion from 0 to 5 mm there were 35 patients out of whom 7 had positive nodal metastasis and 28 were negative for nodal metastasis. In 6 to 10 mm there were 40 patients out of whom 13 had positive nodal metastasis and 27 were negative. In 11 to 20 mm group there were 33 patients out of whom 18 had positive nodal metastasis and 15 were negative. In the group of more than 20 mm there were 2 patients and both positive for nodal metastasis [table 2, fig 2].

Figure - 2



When percentage of nodal metastasis is evaluate in each group separately. In the depth of invasion of more than 20mm there was 100% positive for metastatic node followed by 11 to 20mm which has 54.55%. In 6 to 10mm group, it has 32.5% for positive node and in the group of 0 to 5mm there is 20% positive for metastatic node [table 3].

Table - 3

DOI	Total	Positive (%)	Negative (%)
< 5 mm	35 (100%)	7 (20%)	28 (80%)
6mm to 10mm	40 (100%)	13 (32.5%)	27 (67.5%)
11mm to 20 mm	33 (100%)	18 (54.55%)	15 (45.45%)
>20 mm	2 (100%)	2 (100%)	0 (0%)

DISCUSSION

Neck disease is a poor prognostic indicator in squamous cell carcinoma of oral cavity. It decreases survival by 50% [10] and it is challenging to predict preoperatively which patients may harbour occult nodal metastasis. Squamous cell carcinoma is a three-dimensional composite of superficial, exophytic, and invasive growth. Numerous studies, including meta-analyses and literature reviews composed predominantly of retrospective studies, include different DOI cut-offs to evaluate the risk of neck metastasis. The DOI is defined as the distance from the normal mucosal surface to the point of deepest tumor invasion, which was used in this study .[9]

Various primary tumour factors have been studied in relation to the development of nodal metastases. One of the earliest factors studied was tumour size, which has formed the basis of the AJCC tumour (T) classification. However, it has become evident that tumour thickness or depth of invasion is also an important predictor of nodal metastases and independent predictor of survival in patient with squamous cell carcinoma of oral cavityand AJCC 8th Edition has included DOI in T classification .[11, 8] In our study we evaluate incidence of nodal metastasis according to its depth of invasion in Histopathological finding.

In this study, the highest numbers of patients were seen in the age group of 51 to 60 years with mean age 54.1 years. It comprises of 62 Male 55.5% and 49 females 44.5%. Tumour location is highest in Buccal Mucosa 61

(55.5%), followed by Lower Alveolus 25 (22.7%) and Oral Tongue 13 (11.8%). The incidence is higher in buccal mucosa and lower alveolus because most of our patients had habit of placing tobacco in lower gingival buccal sulcus.

Out of 110 patients, 70 patients (63.6%) were negative for nodal metastasis. The number of positivenodal metastasis is more in Level IB with 12 patients (10.9%), followed by IB & IIA 11(10.0%) and level IIA 7(6.4%). In IA& IB there were 6 patients (5.5%) and in 4 patients (3.6%) level IB, IIA & III were involved. The incidence of isolated neck metastases to level IA, IV& V is 0% and patients having metastases to this were usually accompanied by metastases to other levels.Similar result was found in the study byLi Y et al,[12] the number of positive areas in the IA, IB, IIA, IIB, III, IV and V levels was 2, 15, 12, 1, 4,0, and 0, respectively, their corresponding regional metastasis rates were 5.9%, 44.1%, 35.3%, 2.9%, 11.8%, 0% and 0%.

This study shows in the depth of invasion of more than 20mm, there is 100% positive for metastatic node followed by 11 to 20mm which has 54.55%. In 6 to 10mm group there is 32.5% for positive node and in 0 to 5mm group there is 20% positive for metastatic node. There is increasing pattern of nodal metastasis with increase in depth of invasion. So it shows a clear indication of neck dissection in advanced depth of invasion. However in this study there is 20% positive nodal metastasis even in ≤5 group which comes under T1 of AJCC 8th edition and the decision to go for neck dissection in this group of early disease may put a surgeon in dilemma to do or not to do. Further demarcation of depth of invasion in AJCC classification my need to ponder upon for this early disease.

In the earlier study as reported by Mohit-Tabatabai et al,[13] was found a tumour thickness of 1.5 mm as being critical for nodal metastases andFaisa et al[14] when incorporating depth of invasion, they found occult metastasis was 23% in tumors with DOI ≤5mm, 34% in tumors with DOI 6-10 mm and 53% in tumors with DOI >10 mm.

There is some limitation in this study as there is tissue shrinkage during formalin fixation and this may affect the exact measurements of tumour depth. Although this measurement of depth of invasion has been carried out postoperatively after the tumour had resected. Thetumour depth may provide usefulinformation in the intra or preoperative determination of the need for neck dissection. As there is no proper guideline in clinical evaluation of depth of invasion we use Histopathological depth of invasion.

Few studies have shown that tumour depth may also be obtained preoperatively by biopsy or imaging. Incisional biopsy or punch biopsy of frozen section specimens may correlate with tumourdepths in some selected casas. In the study by Iida at al[15] shows promising results by using intraoral ultrasound and MRI in oral tongue but it is not well applicable to other subsite of oral cavity.

However despite these limitations, the study provides local data that can help health care to develop guidelines for early detection and proper management of disease and to reduce development of recurrence and helps in further studies on the Depth of invasion and neck dissection.

CONCLUSION

Squamous cell carcinoma is the most common cancer of Head and Neck in North East India. It is more common in male with the mean age of 54.1 years and most of the patient usually comes in advanced stage of disease. Buccal mucosa and Lower alveolus is more commonly involved then other sub site of oral cavity because of placing tobacco in lower gingival buccal sulcus. Level IB is the most common site of metastasis in Oral cavity. Isolated metastasis at level IA, IV & V is rare in squamous cell carcinoma of oral cavity, however if present, other levels of node is usually involved.

This study shows the increase in incidence of nodal metastasis with increased depth of invasion. Nodal metastasis was found even in depth of invasion ≤ 5 mm with 20% and in 6 to 10mm with 32.5% as this group comes under T1 and T2 stage of 8th edition of TNM Classification and considering this an early disease doing a neck dissection may be a dilemma for surgeon. As there is evidence of nodal metastasis even in early stage of squamous cell carcinoma of oral cavity further demarcation of depth of invasion will be required.

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Original Article

Clinical presentation and pattern of nodal metastasis in upper gingivo-buccal cancer

Anil K Mathew, Tashnin Rahman, Ashok Kumar Das, Rajjyoti Das, Kishore Das, Anupam Das, Kaberi Kakati

Head and Neck Oncology Department, BBCI, Guwahati

INTRODUCTION

Oral cancer is the sixth most common malignancy in the world and the third most common in Southeast Asia. In India, Bhopal has the highest age adjusted incidence rates of 9.6 of 100,000 males for oral cancer. The prevalence varies with ethnicity, geographic distribution, and socio-economic differences.[1,2] The disproportionately higher prevalence of head and neck neoplasm in India may be due to the use of tobacco in various forms, alcohol abuse, poor oral hygiene, deficient diet or viral infections like human papilloma virus (HPV).The incidence is two to three times more frequent in men than women owing to increased tobacco and alcohol abuse.[3,4] Cancers of the superior gingival–buccal complex comprise cancers in the upper gingiva, including upper alveolar (ridge) mucosa (ICD-10; C03.0); the upper gingival–buccal sulcus or vestibule of the mouth (ICD-10; C06.1) and the upper part of the buccal mucosa (ICD-10; C06.0). Close proximity of these sites makes it difficult to localize the exact epi-centre of the disease because it often involves multiple adjacent sites and tumors arising in these sites have similar patterns of spread. Squamous cell carcinoma is the most common type of tumor encountered.[5,6]

Upper gingivo–buccal cancers are more aggressive than their lower gingivo– buccal counterparts, which have a comparatively better disease-free survival even in advanced stages.[7,8]

In this study we have tried to assess the clinical presentation of upper gingivobuccal complex cancer as well as its pattern of nodal metastasis.

METHODOLOGY

A prospective study including 98 patients were consideredas per statistical requirements and a descriptive analysis was used to represent the data. Chi-square test was used to evaluate the difference between the groups and T test will be used for continuous data analysis.

RESULTS AND OBSERVATIONS

Characteristics			
Age			
>50 years	60		
<50 years	38		
Men	54		
Women	44		
T Stage		**PAIN**	**TRISMUS**
T1	2	0/2	0/2
T2	8	1/8	0/8
T3	32	10/32	6/32
T4	56	56/56	56/56
N Stage			
N0	64		
N+	34		
STAGE GROUPING			
Stage 2	15		
Stage 3	30		
Stage 4			
Stage 4a	40		
Stage 4b	10		
Stage 4c	3		

GRADE OF DIFFERINATION			
WDSCCa	40		
MDSCCa	15		
PDSCCa	43		
TRISMUS	22		
TREATMENT			
Surgery	10		
Radiotherapy	22		
Chemotherapy	8		
Surgery + Radiotherapy	38		
Surgery+ RT+Chemotherapy	15		
Surgery + Chemotherapy	3		

98 patients were included in this study which satisfied the inclusion criteria of the study of which 54 were male and 44 were female patients. Sixty patients were above the age of 50 years while thirty patients were below the age of 50 years of age.

As per clinical and radiological assessment the patients were staged according to the AJCC 8th edition of Oral Cancer staging. Among the diagnosed 98 cases, forty of them were well differentiated, fifteen were moderately differentiated and forty three was poorly differentiated carcinoma.

The median age of presentation was fifty six years.

As per the TNM staging, fifteen were Stage II, thirty were Stage III, forty were stage IVA, ten were stage IVB and three were stage IVC

Considering the line of management as decided after the discussion in the Disease management group (DMG), ten patients were treated Surgery, twenty with radiotherapy, eight with chemotherapy. Forty patients received surgery followed after adjuvant RT, fifteen patients received Surgery followed by Radiotherapy and chemotherapy, three patients received Surgery followed by chemotherapy.

DISCUSSION

Common presenting symptoms of upper gingivo–buccal cancers are alveolar growth and trismus, resulting in relative inaccessibility of the area for proper evaluation.[9] This often makes early detection of these cancers difficult. Four-fifths of the patients in our study presented with T3 or T4 tumors, but only 38.6% of them had clinically or radiologically positive neck nodes. If we further examine histologically if there is tumor metastasis in these prominent nodes it's highly likely that the proportion can further reduce. This is noted in the study by Pathak KA .et al in which only 21% of the tumors had histologically positive nodes amongst their T3/T4 group of tumors. This suggests a late cervical metastasis usually after the tumor extends to vestibule, buccal mucosa or soft tissue of the cheek. However, nodal metastasis was seen in multiple nodes in 65% of upper gingival–buccal complex cancers compared with only 33% in lower gingival–buccal cancers. [10]

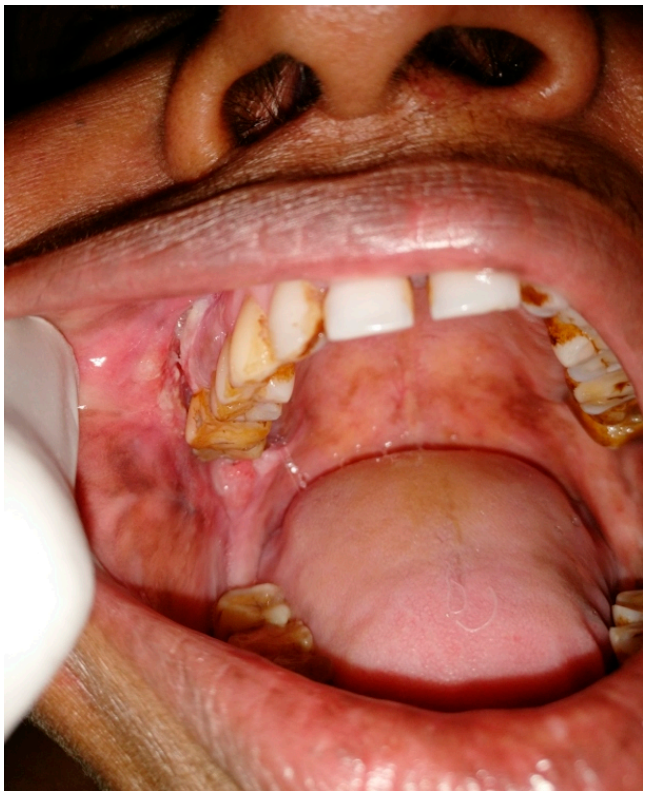
Owing to the thin layer of overlying soft tissue in the maxilla, SCC invasion of the adjacent bone can occur much sooner than SCC of the hard palate. A recent study has suggested that it is osteoclasts, rather than malignant keratinocytes, that are more important in facilitating entry of the tumor into bone and its progression thereafter. Ogura et al concluded that maxillary bone invasion was an indicator of cervical metastasis, because patients with bone invasion had a lower 5-year OS rate. Ebrahimi et al reported that bone invasion was an important predictive factor of oral cancer, and that the extent of bone invasion.

Lymphatic from the buccal aspect of the superior alveolar ridge drains to the submental and submandibular nodes. We noticed that though the incidence of neck nodes in Upper gingivobuccal cancers (UGBS) were less compared to lower gingivobuccal cancers (LGBS) , when the nodes were involved in UGBS it tends to present as multiple nodal level clinically than just a single nodal presentation.

Trismus is a clinical finding in advanced cases of UGBS. Cancers of the upper gingival buccal sulcus display a more aggressive behavior than their lower gingival buccal sulcus tumors, mainly due to the late presentation of the disease and early invasion of ITF.

When we assessed the grade of presentation it was predominantly poorly differentiated (43.87%), followed by well differentiated (40.8%) and moderately differentiated (16.13%).

Figure 1:



CONCLUSION

Upper GBS, hard palate and maxilla cancers are uncommon and are diagnosed at an advanced stage due to delay in presentation and ignorance of our population. They also present at an earlier age in our population due to consumption of smokeless tobacco and pan masala. Owing to rarity of the site of the disease, there are only a few case reports and case series discussing the management of these tumors. Most cancers are locally advanced, but surgery offers the best form of treatment. The role of NACT is not clear, but may be tried to downstage the disease in selected patients with borderline operable disease. However, generous margins should be taken post chemotherapy with concomitant neck dissection. Adjuvant radiotherapy is recommended in selected patients after surgery. Furthermore, patient counseling should be an integral part of treatment to ensure patient compliance and reducing the loss to follow-up.

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Original Article

Occurrence of contralateral lymph node metastasis in lateralized oral cavity cancer reaching the midline

A. Missong, T. Rahman, A. K. Das, R. J. Das, K. Das, A. Das, K. Kakati

Head and Neck Oncology Department, BBCI, Guwahati

INTRODUCTION

Squamous cell carcinoma of the oral cavity is one of the most common cancers worldwide, and represent thirty-six percent of head and neck cancers. Use of alcohol and tobacco products like cigarettes, smokeless tobacco and betel nut chewing are the most common risk factors for oral cancer. The squamous cell carcinoma of the oral cavity has a high incidence of lymph node metastasis and often bilateral because of the rich submucosal lymphatic plexus, that communicates freely crossing the midlin**e.** Several clinic-pathological factors might predispose to the development of contralateral neck node metastasis. These are location, midline extension and stage of the primary tumour, ipsilateral lymph node status, involvement of midline, degree of histological differentiation, depth of invasion, and lymphovascular and perineural invasion. Therefore squamous cell carcinoma of oral cavity reaching the midline warrants bilateral neck dissection.

METHODS

This study was conducted for a period of one year starting from April 2019 to March 2020 in the Department of Head and Neck Surgery, at Dr. Bhubaneswar Borooah Cancer Institute, Guwahati, Assam, a premier tertiary level cancer institute in the Northeast India. We properly evaluated all the cases with detail history, thorough clinical examination, investigation (biopsy, imaging as required). All patients who fulfilled the inclusion criteria were enrolled in the study after obtaining proper informed consent. After multidisciplinary tumour board discussion the patients underwent surgery with bilateral neck dissection with or without flap reconstruction. Staging of the disease was done as per AJCC 8th edition. Adjuvant treatment with radiotherapy or chemoradiotherapy was advised when indicated.

Analysis of the data was done using proper statistical methods with regards to-

1. Age and sex distribution of the patients.
2. Subsites involved.
3. TNM stage and CLNM.
4. Histological type.

Inclusion Criteria: Patients with lateralized oral cavity cancer reaching the midline, irrespective of nodal status, who underwent surgery with bilateral neck dissection with or without postoperative radiotherapy were included.

Exclusion Criteria: Recurrent or second primary cases, those cases who did not undergo bilateral neck dissection and those cases who refuse to take part in the study.

RESULTS AND OBSERVATIONS

Age distribution of the patients

Highest number of cases with oral cancer was seen in the age group 40-70 years. But younger age group patients were also seen.

Table 1: Incidence of oral cancer in different age group of patients

Age group (years)	No. Of cases (%)
0 -10	0 (0%)
11-20	0 (0%)
21-30	1 (2%)
31-40	6 (12%)
41-50	12 (24)
51-60	14 (28%)
61-70	15 (30%)
71-80	2 (4%)
81-90	0 (0%)
Total	50

Sex distribution of the patients

Cancer of the oral cavity is seen to affect males more than females with male: female ratio of 4:1 in the study group.

Table 2: Incidence of oral cancer according to sex.

Sex	No. Of cases	Percentage
Male	40	80%
Female	10	20%
Total	50	100%

Subsite distribution of the Patients and CLNM

Buccal mucosa was the commonest sub-site of oral cancer followed by tongue in the patients selected in the study.

Table 3: Subsite distribution of disease and CLNM

Subsite	Cases	CLNM+
Alveolus	9(18%)	1(2%)
Buccal mucosa	25(50%)	7(14)
Floor of mouth	1(2%)	0(0%)
Tongue	11(22%)	2(4%)
Retromolartrigone	0(0%)	0(0%)
Hard palate	2(4%)	0(0%)
Lip	2(4%)	0(0%)
Total	50(100%)	10(20%)

CLNM: contralateral lymph node metastasis

Histological types

Most of the cases were seen to have well differentiated squamous cell carcinoma (88 percent). In our study TNM stage of the disease rather than histological type was more associated with contralateral lymph node metastasis(CLNM).

Table 4: Histological distribution of tumour and CLNM

Histopathology	Number of cases	CLNM
Well differentiated squamous cell carcinoma	44(88%)	10(20%)
Moderately differentiated squamous cell carcinoma	5(10%)	0(0%)
Poorly differentiated carcinoma	1(2%)	0(0%)

TNM stage and CLNM

It is seen that TNM stage of the disease is an important factor that correlated with contralateral lymph node metastasis. Highest number of cotralateral lymph node metastasis was seen is patients with T4 and N3 disease.

Table 5 : TNM Stage of disease and contralateral lymph node involvement

Stage	Number of cases	Contralateral LN(+) %
T1	0(0%)	0%
T2	4(8%)	0%
T3	9(18%)	6%
T4	37(74%)	14%

Table 6 : Ipsilateral cervical lymph node status and CLNM

Ipsilateral cervical lymph node	Number of cases(%)	CLNM(%)
N0	54	0
N1	4	0
N2	18	4
N3	24	16
Total	50(100%)	20%

DISCUSSION

The oral squamous cell carcinoma has a high incidence of lymph node metastasis and often bilaterally due to the rich lymphatic drainage, that communicates freely crossing the middle line. The contralateral metastasis propagation can occur in the head and neck carcinoma

in different ways. First by crossing afferent lymphatic vessels tumour spread along the midline, when ipsilateral lymph nodes are widely involved and secondly in some anatomical regions which are located in the midline. The incidence of contralateral lymph node metastasis is variable in the literature. Kowalski et al.[1] found a rate of 36 percent of contralateral positive nodes after bilateral neck dissection. Kurita et al.[2] observed an incidence of contralateral lymph node metastasis in early oral tongue squamous cell carcinoma of 12.2%. Koo et al.[3] the overall rate of occult contralateral metastasis in oral squamous cell carcinoma was 11%, and the rate was 21% in cases of ipsilateral pathologic metastasis. Bier Laning et al.[4] the incidence was 10%.

Mukherji et al.[5] reported a similar finding. He also found that oral tongue and floor-of-mouth cancers had drainage to contralateral lymph nodes in up to 9% of cases. Lim et al.[6] detected contralateral occult metastases in only 4% cases in a series of early tongue carcinomas and did not recommend elective contralateral neck treatment. Gonzalez-Garcia et al.[7] in a large series of 315 patients with oral squamous cell carcinoma of the oral cavity, reported an incidence rate of 5.7% for contralateral lymph node metastasis. Oral cavity cancer with lateralized epicentre, which reaches the midline have a tendency for bilateral cervical lymph node metastasis. Several predictive factors have been seen to be correlated with the risk of contralateral lymph node metastasis. Apart from midline involvement, tumour stage, ipsilateral lymph node metastasis and extracapsular extension plays an important role in contralateral lymph node metastasis. Therefore in oral cavity cancer, even if lateralized primary, if the midline is involved contralateral neck dissection is warranted.

CONCLUSION

In the present study the contralateral lymph metastasis in oral cavity cancer involving the midline was seen to be 20 percent. Surgeons should take into account the specific individual risks, and potential benefits of elective neck treatment for contralateral neck although the morbidity associated with bilateral neck dissection should also be kept in mind.

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Original Article

Study of incidence of lymph node metastasis to submental node (level 1A) in oral cancer

Chanmiki Sayoo, Ashok Das, Raj Jyoti Das, Tashnin Rahman

Head and Neck Oncology Department, BBCI, Guwahati

INTRODUCTION

Cancer of oral cavity is one of the most common cancer worldwide.[1] It is an endemic cancer in several developing countries more so in those countries where betel nut and tobacco consumption is prevalent. In India it is among the top three types of cancer.[2] It is an established fact that in Oral Squamous Cell Carcinoma (OSCC) presence of lymph node metastasis is one of the most important prognostic factors related to survival, and several studies have shown there is a drastic decrease in survival in patients with positive neck node.[5,6] Metastasis to contralateral side of neck (CLNM) is also related to poor survival as shown by several studies.[5,6,7,8] The incidence of CLNM differ considerably among different institutions from 0.9% to 36%.[7,8,10,11] Incidence of submental node involvement may have some relation with contralateral node metastasis. In this study we retrospectively review the incidence of submental node involvement in oral cancer.

MATERIALS AND METHODS

In this study we retrospectively review the data of those patients with diagnosed squamous cell carcinoma oral cavity who underwent surgery at Dr B Borooah Cancer Institute during a period of one year, from January 2017 to December 2017. The post-operative biopsy report of the resected primary lesion and neck dissection specimen was reviewed and those who showed involvement of lymph node level 1a were taken in to consideration. These patients were then followed up for a period of two years and six monthsfor any contralateral lymph node metastasis. All patients were staged according to the American Joint Committee on Cancer (AJCC) staging 7th edition. Inclusion criteria were: previously untreated patients, histo-pathologically proven squamous cell carcinoma of oral cavity who underwent surgery as the primary treatment modality, consisting of resection of the primary lesion and neck dissection. Exclusion criteria were: tumor arising or crossing the midline (region between both the canines), tumor of floor of mouth, contralateral neck node positive and ipsilateral huge nodal disease (cN2c and cN3) and those patients in whom the post-operative biopsy report has no separate mention about the status of lymph node level 1a.

RESULTS

During a period of one year from January 2017 to December 2017, 302 patients underwent surgery in our hospital for oral cancer. When the exclusion criteria applied 200 patients were eligible for the study. The sample include 118 males and 82 females. Distribution of primary tumor according to sub-site and stages are shown in table 1 and table 2. Here lower gingivobuccal complex comprise of buccal mucosa, gingivobuccal sulcus and lower alveolar ridge mucosa. This sub site is included because it is very commonly seen in Indian cancer patients probably due to habit of tobacco consumption. All the patients received surgical resection of the primary tumor with neck dissection

and 224 patients received adjuvant therapy (196 patients received radiotherapy only and 28 received chemoradiation). Those who received radiation 26 of them received bilateral neck irradiation.

Table 1:

Subsite or oral cavity	No. of cases
Tongue	24
Floor of mouth	6
Buccal mucosa	21
Alveolus	23
RetromolarTrigone	19
Gingiva buccal sulcus	124
Hard palate	6

Table 2 :

Stage	No. of cases
T1	17
T2	45
T3	52
T4	86
N0	81
N1	58
N2	49
N3	12
M0	0
M1	0

Table 3 : Cases with submental node (level 1a) metastasis after post operative histo-pathological examination

Submental node status	Metastasis present	Non-metastatic
Number of cases	29 (14.5%)	171 (85.5%)

DISCUSSION

The pattern of lymphatic drainage of squamous cell carcinoma from the upper aerodigestive tract has been well described by Jatin Shah et al 1990. Lymph node in the neck were categorized into different level and sublevel. Cancer from the oral cavity predominantly drain into level I, II, III. Level Ia is a median region located between the anterior belly of the digastric muscle, which contain the submental node. The medial limit of level 1a is virtual as it is continuous with the contralateral 1a. Nodes in level Ia drain the skin of the chin, lower lip, anterior tongue and floor of mouth. These are predominantly midline structures, hence tumour arising from or reaching midline are excluded from this study. Level Ib nodes (submandibular nodes) received efferent lymphatics from the submentalnode (Level 1a)Hence, submental nodes being midline in location with bilateral drainage to submandibular nodes can act as a possible conduit for lymphatic drainage from the ipsilateral diseased involved node to the contralateral non-diseased, non-involved nodes.

These are: tumour crossing midline,[6,7] high nodal volume with extracapsular spread,[10] tumour arising in floor of mouth and base of tongue[7,8] multiple ipsilateral node involvement.[7,10] Hence, those patients or tumor characteristics which harbor any of these features were excluded. To our knowledge no study had compare the relation of submental node involvement with contralateral neck node metastasis.

The incidence of metastasis to level 1a as found in this study is 14.5% (29 patients) after removing the excluding criteria. Further study need to be evaluated for the correlation of contralateral neck metastasis with this incidence of submental node metastasis.

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Special Report

Skull base clinic : a new era in the dept of Head and Neck Surgical Oncology

K. Kakati, T. Rahman, A.K.Das, R.J.Das, K.Das, A. Das

Head and Neck Oncology Department, BBCI, Guwahati

The Dept. of Head and Neck Surgical Oncology of Dr. B. Borooah Cancer Institute has started its Skull Base Clinic from October, 2017. It had a modest beginning with the Head and Neck Surgeons of the Department and a Visiting Neurosurgeon where we used to discuss the treatment plans of the Sinonasal and Skull Base cases. Gradually, the Clinic grew and now it has turned into a Multidisciplinary clinic and has representatives from all disciplines like Radiation Oncology, Medical Oncology, Pathology, Radiology, Plastic Surgery apart from the Head and Neck Surgeons and the Neurosurgeon. The Clinic sits every Wednesday where we discuss all Skull Base cases and representatives from various fields give their inputs regarding further management so that such cases can be planned better. Till date, we have had around 120 such cases seen at our Clinic since October, 2017 which is quite a modest number considering the rarity of such tumors.

Mean age of our cases are 50yrs with a male –female ratio of 2: 1. We have had around 100 cases of Sinonasal and Anterior Skull base cases and 20 cases involving Lateral skull base.

In Anterior skull base tumors, majority of our cases presented as Stage IV disease (80%). Nodal metastases at presentation were reported to be 7.5%. Distant metastases were seen in 3 cases. Around 55% cases are of SCC histology, unlike other Head and Neck cancer cases where 95% are SCC. Various other histologies are also seen like Adenoid cystic CA, Sarcomas, Neuroendocrinetumors, Olfactory Neuroblastoma, Lymphomas with different clinical and biological behaviour. All these varied histologies offer a host of opportunities for research regarding IHC markers and molecular/genetic study to know the pathology better. Also, we have seen few cases of Skull base osteomyelitis which pose a diagnostic dilemma.

Table 1 : Histological distribution of Anterior skull base malignancies

Histologies	No. of cases (n)
Squamous cell carcinoma (SCC)	55
Adenoid cystic carcinoma (ACC)	12
Muco-epidermoid carcinoma	04
Adenocarcinoma	02
Esthesioneuroblastoma (ENB)	04
Sinonasal Undifferentiated carcinoma (SNUC)	02
Small cell carcinoma (SmCC)	02
Ewing's sarcoma	03
Rhabdomyosarcoma	02
Osteosarcoma	01
Chondrosarcoma	02
Angiosarcoma	01
Spindle cell sarcoma	01
Basal cell carcinoma (BCC)	02
Sebaceous gland carcinoma	01
Non-Hodgekin's Lymphoma	01
Neurofibroma	02
Skull Base osteomyelitis	03

In Lateral skull base malignancies, primary site to be involved was External auditory canal and Temporal bone which comprised 65% of our cases. Advanced parotid cancers and scalp tumors were also seen. Majority presented late with again around 80% cases coming as Stage IV disease. Various histologies are encountered apart from SCC.

Table 2 : Histological distribution of Lateral skull base malignancies

Histologies	No. of cases (n)
Squamous cell carcinoma (SCC)	11
Adenoid cystic carcinoma	03
Mucoepidermoid carcinoma	03
Basal cell carcinoma	01
Rhabdomyosarcoma	01
Myo-epithelial carcinoma	01

Histology is the most important determining factor in Skull Base Malignancies and along with the T-stage of the disease, both these factors dictate the treatment decision.

Around 60% cases have been treated with Curative intent with various treatment modalities like Surgery andnon surgical means like Chemotherapy, Chemoradiation, Neoadjuvant Chemotherapy followed by Surgery/ CTRT. Various surgical procedures were performed like Total maxillectomy with spheno-ethmoidectomy and pterygoid plate excision, Orbital exenteration with Temporalis muscle flap repair, Total parotidectomy with Lateral temporal bone resection, Total maxillectomy with Craniofacial resection. Big surgical defects are usually repaired with Free flap. Neo-adjuvant chemotherapy were given in 13 cases in view of orbit involvement, extensive soft tissue disease, chemosensitivetumor, tumor with highly metastatic propensitywith 7 cases showing partial/near total response. Orbit could be saved in 4 cases.

Although we are new in this field of Skull Base Surgery, nevertheless, we are making slow but steady progress and hope to continue offering greater and quality services to our patients.

Review Article

Anesthetic challenges in Head and Neck Surgery

Minoti Baruah

Associate Professor, Dept. of Anaesthesiology, Critical Care and Pain
Dr. B. Borooah Cancer Institute, Guwahati

Head and Neck cancers account for 30% of all cancers in India, of which 60-80% of patients present with advanced disease.[1] Surgery often forms a part of the multimodal approach to treat head and neck cancers. Administration of anesthesia for patients undergoing surgical procedures in the head and neck region is a unique challenge owing to the shared space, and airway difficulties due to disease or treatment sequelae.

AIRWAY

Ideally all available imaging should be jointly reviewed by the surgeon and anesthesiologist. The airway that was straightforward in a previous procedure might be grossly distorted due to progress of disease or as a result of treatment.

SEQUELAE OF HEAD AND NECK CANCER TREATMENT [2]

Radiotherapy

- Limited neck extension
- Temporomandibular joint ankylosis
- Osteoradionecrosis of mandible
- Hypothyroidism
- Baroreceptor damage
- Carotid artery stenosis
- Poor wound healing

Maxillectomy And Craniofacial Resection

- Difficult mask seal
- Difficult nasal access
- Temporalis contracture
- Temperomandibular joint pseudoankylosis

Tongue & Floor Of The Mouth Surgery

- Trismus
- Fixed immobile tongue
- Limited mandibular space
- Increased tongue: oral cavity ratio with flap reconstruction

Laryngeal Surgery

- Laryngeal stenosis
- Impaired swallowing
- Aspiration risk

Neck Dissection

- IX, X, XII nerve damage
- Impaired swallowing
- Aspiration risk
- Vocal cord palsy

Pre-operative evaluation should assess if

1) face mask ventilation would be possible following induction of GA
2) laryngoscopy and intubation are likely to be difficult

3) awake intubation would be a better technique
4) emergency front of neck access (FONA) is feasible.

A coordinated team effort with clear channel of communication is the key to successful airway management. In head and neck cancer airway difficulty is expected and should have an 'airway management strategy' for timely and sequential implementation of back up plans. Possibility of intubation after induction or 'awake intubation' for safety needs to be determined. If difficulty in bag and mask ventilation or intubation has been experienced before, awake intubation would be the preferred option. Awake intubation offers advantage of a patent airway, exchange of gases, and presence of reflexes to safeguard against aspiration. Patients having significant obstruction where awake fibreoptic intubation is not feasible are candidates for awake tracheostomy.

Direct laryngoscopy should be performed with appropriate positioning, using appropriately sized and configured blade, with the patient being adequately preoxygenated and having received sufficient neuro-muscular blockade. If direct laryngoscopy fails, it should be communicated to the team and back-up plans initiated. There is no evidence that videolaryngoscopes reduce the number of attempts at intubation or the incidence of hypoxia, especially after D/L has failed. [3]

Rescue oxygenation may be initiated with face mask, supraglottic airways or surgical airway. Insertion and placement of supraglottic airway is often difficult and at times near impossible in patients with trismus, oropharyngeal lesions and after radiotherapy.[4]

Trans nasal high flow rapid insufflation ventilatory exchange (THRIVE) provides for apneic oxygenation, continuous positive airway pressure, and flow dependent dead space flushing. It is useful in maintaining oxygen saturation and prolonging the apneic window in attempts to secure the airway.[5]

ANAESTHETIC MANAGEMENT

Most head and neck procedures are done in the supine position with a 15-20 degree head up tilt which improves venous drainage.

Access being limited, long tubing both for ventilation and vascular lines are needed. Frequent disconnections may result due to the length and shared space, mandating secure fixation and regular monitoring. Eyes should be protected by tapes in all cases and saline soaked eye pads in laser procedures. Temperature measurement is needed to avoid overheating as only head and neck area is exposed.

Induced hypotension should be avoided in patients with autonomic neuropathy, chronic hypertension, and those with known coronary or cerebral atherosclerosis, susceptible to ischemia.

Dexamethasone or Hydrocortisone is often given to reduce airway oedema.

Oral intubation is the preferred route for lesions within the maxilla, nose and paranasal sinuses, while naso-tracheal intubation is preferred in oral cancers. Submental intubation is an absolute contraindication in cancer surgery because of the risk of creating an orocutaneous fistula. [2]

In **free flap transfers** both skin and core bladder temperatures are measured to ensure that the core periphery gradient is less than 1.5. The aim in such cases is to maintain hyperdynamic circulation with increased cardiac output, peripheral vasodilation and normothermia to maximize flap perfusion.[2] Haematocrit is maintained at 30-35% to improve oxygen transfer and red cell velocity.[2] Norepinephrine with its vasoconstrictor effect is avoided while dobutamine with inodialator effect is preferred. Exposure and handling of flap causes vasoconstriction, an increase in mean arterial pressure using adrenaline infusion may assist perfusion.[6]

Sickle cell disease and polycythemia are absolute contraindications for free flap transfers asflap failure rate is high from microcirculatory sludging and hypercoagubility.[2] In patients with collagen vascular disease incidence of anastomotic thrombosis is high and may be co-related to the high incidence of active vasculitis[2].

Laser surgery in the aerodigestive tract needs special consideration, with techniques varying from no tubes where larynx is anesthetised with blocks or topical

agents, intravenous induction agents are used and anesthesia maintained with TIVA, oxygen is provided with nasal catheter or THRIVE, jet ventilation is preferred when neuromuscular blocking agents are used. Conventional tubes when used, a size or two smaller is chosen as they need to be protected by wrapping spirally with aluminum or copper tape, the cuff is inflated with saline not air. Saline soaked gauze should be kept between the cuff and vocal cords. A variety of specialized laser resistant tubes are available. If a laser fire does occur tube should be disconnected from gas source immediately. Steroids, humidification of inhaled gases, tracheostomy and prolonged ventilation may be needed depending on severity of burn injury.

In **parotid surgery** preservation of the facial nerve is paramount and nerve monitoring is used to prevent iatrogenic injury.

For **thyroid surgeries** patients with thyroxine secreting tumours should be medically euthyriod prior to being taken up for surgery. Intubation with a reinforced tube is recommended[2]. FONA may not be feasible in a large goiter. Where compression of the trachea is suspected a smaller sized tube is preferred. Intubation should aim at bypassing the compression. EMG is recommended to identify the recurrent laryngeal nerve.

Laryngeal cancer sufferers frequently have cardiac and respiratory comorbidities. Anemia, malnutrition and alcohol dependency are frequent associates. Preoxygenation with high flow nasal catheter provides continuous positive airway pressure. If HFNO is not available, oxygenation through conventional nasal cannula during efforts to secure the tube (NODESAT) maximizes oxygenation. Early FONA is best avoided to facilitate lower tracheotome made later in a planned total laryngectomy[7].

Extubation for all head and neck patients is preferably with the head raised to atleast 30 degree if not in the upright position. Full reversal of neuromuscular blockade and adequate oxygenation is essential prior to attempting extubation. For patients at a risk of airway obstruction a planned tracheostomy or delayed extubation are safer options. Most patients tolerate a nasal tube post operatively remarkably well.

Postoperative care includes pain management, pain in the head and neck region is moderate and well managed with paracetamol and opiates only being added when necessary.

New tracheostomies produce increased secretion, irritation and cough. Humidified oxygen, nebulization with 4% lignocaine and saline alleviate symptoms. Staff need to be suitably trained for tracheostomy care. Aim of care for free flaps is maintenance of normotension, normothermia, with regular monitoring of the flap for adequate filling. Hematocrit needs to be maintained at 30-35%. Low molecular weight heparin is administered for thrombo-prophylaxis.

Respiratory distress in the post operative period is specially challenging, primary plan of intubation may not be possible or may fail. Personnel and equipment for surgical access should be at hand.[4]

CONCLUSION

Head and neck cancer surgery needs targeted anesthetic management with awareness of the procedure and extra vigilance owing to the shared space with the surgical team. Most head and neck surgeries are a life changing experience for the patient and requires close coordination between the surgical and anesthetic team.

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Review Article

A review of paediatric anaesthesia in a tertiary cancer care centre : current techniques, challenges and what lies ahead

Marie Ninu

Assistant Professor, Dept. of Anaesthesiology, Critical Care and Pain
Dr. B. Borooah Cancer Institute, Guwahati

"No child should die in the dawn of life"
– Danny Thomas, founder of St. Jude Children's Hospital

INTRODUCTION

Cancer is a well-recognised killer disease that doesn't spare anyone whether they belong to a high-or-low income socioeconomic group,or whether they are of a paediatric or geriatric age group.

It is one of the leading causes of morbidity and mortality worldwide with 8.2 million cancer deaths in the year 2012.[1] Approximately, 215,000 cancers are diagnosed per year in those younger than 15 years with an estimated 80,000 cancer related deaths in this group.[2]

In India, although there is a higher proportion of childhood cancer relative to the developed world,it has not received adequate priority in health care. This is becausecancer causes about only 2%of all childhood deaths.[3]

In recent years, the developed world has seen a tremendous progress in the treatment of childhood cancer with a 5-year survival rate of 75-79% overall.[4] In India, this number drastically decreases to about 37-40%.[5]

However,in tertiary institutes like the Tata Memorial Hospital Mumbai, outcomes similar to the developed world have been observed.[6]

Role of an anaesthesiologist in the management of paediatric cancers

An anaesthesiologist is an essential member of the entire team caring for the child diagnosed with cancer. He/ she is a part of a multimodal team which includes paediatrician, medical oncologist, surgical oncologist, radiotherapist, nutritionist, etc.

Phases where an anaesthesiologist is involved in childhood cancers:

1. **Diagnosis**

   Diagnosis of cancer is made not just by history and clinical examination but also by a myriad of investigations.Radiological diagnostic procedures like CT and MRI imaging, ultrasonography, invasive procedures like endoscopy, FNAC, biopsy, bone marrow aspiration, lumbar puncture, etc. can be painful and stressful for younger children. Here the anaesthesiologist plays a unique and fundamental role in the management of the child by alleviating the anxiety and pain during such procedures.

   In our institute, almost all children coming for such diagnostic procedures are sedated using commonly available drugs like midazolam, ketamine and propofol in a safe,titrated and monitored manner. The same standards and guidelines for general anaesthesia are also applied to sedation which include preoperative preparation, fasting, monitoring, and postoperative care.

   Challenges faced by the anaesthesiologist areexclusive to out-of-operating room

procedureswhich includeairway management, monitoring, ventilation, oxygen supply, etc. because of lack of or accessibility to equipment and logistical problems.

Minimum Workup Required for Common Paediatric Malignancies to Assess Primary Tumour and Potential Metastases.[7]

	Bone Marrow Aspirate/Biopsy*	Chest X-ray	CT Scan*	MRI*	Bone Scan	CSF Analysis*	Specific Markers	Other Tests
Leukemia	Yes	Yes				Yes		
Non-Hodgkin lymphoma	Yes	Yes	Yes		Yes	Yes		
Hodgkin disease	Yes	Yes	Yes		Yes			Gallium scan*
CNS tumors				Yes		Yes		
Neuroblastoma	Yes		Yes		Yes		VMA, HVA	MIBG scan*
Wilm's tumor		Yes	Yes					
Rhabdomyosarcoma	Yes	Yes	Yes		Yes	Yes (for parameningeal tumours only)		
Osteosarcoma		Yes	Yes (of chest)	Yes (for primary tumours)	Yes			
Ewing sarcoma	Yes	Yes	Yes (of chest)	Yes (for primary tumours)	Yes			
Germ cell tumors		Yes	Yes	Consider MRI of brain			AFP, HCG	
Liver tumors		yes	Yes				AFP	
Retinoblastoma	+/-		Yes (if MRI not available)	Yes (of brain)	+/-	Yes		Retinoblastoma gene analysis

**procedures generally requiring anaesthesia services in paediatric age-group*

2. Treatment

The anaesthesiologist plays a leading role in the care of a child posted for oncologic surgery. Right from the pre-anaesthetic check up to the post recovery room, the child is managed by the directions given by the anaesthesiologistin conjunction with that of paediatricians and surgeons.

Pre-anaesthetic check-up

Children with cancer may present with associated congenital anomalies including congenital heart disease, which need specific consultation and evaluation preoperatively.

Recent URTI in children increases the risk of desaturation, breath holding, laryngospasm, bronchospasm, and coughing during both induction and recovery. The decision to anaesthetize or postpone depends upon various factors on a case by case basis.[12]

Most children are treated with chemotherapy and radiotherapypreoperatively and these modalities, although highly effective, are not without their own side effects. Chemotherapy, radiotherapy, steroids and haematopoietic stem cell transplantation (HSCT) all have a negative effect on immune system which may predispose

the child to perioperative infections.[7] Appropriate investigations and relevant measures where possible must be taken.

Common complications associated with cancer chemotherapy agents[8]

System toxicity	Chemotherapeutic agents
Cardiac toxicity	Busulphan, cisplatin, cyclophosphamide, daunorubucin, 5-fluorouracil
Pulmonarytoxicity	Methotrexate, bleomycin, busulphan, cyclophosphamide, cytarabine, carmustine
Renal toxicity	Methotrexate, L-asparginase, carboplatin, ifosfamide, mitomycin-C
Hepatic toxicity	Actinomycin D, methotrexate, androgens, L-asparginase, busulphan, cisplatinum, azathioprine
CNS toxicity	Methotrexate, cisplatin, interferon, hydroxyurea, procarbazine, vincristine
SIADH secretion	Cyclophosphamide, vincristine

Fasting: Compared to adults, paediatric fasting gastric contents are of larger volume and of lower pH. Overall, 1 in 2000 children develop perioperative pulmonary aspiration with 80% of these occurring during induction of anaesthesia. Preoperative fasting is usually advised for 2hours for clear fluids, 4 hours for breast milk, 6 hours for formula feeds and solids.

Radiation therapy

It is crucial that children receiving radiotherapy remain completely immobile to establish correct localization of the treatment. Therefore, a sedative or general anaesthetic is often required, especially in the younger child. Older children may tolerate the treatment awake with suitable preparation.

Intra-operative challenges

Separation anxiety faced by children may be allayed with oral midazolam or fentanyl lollipop given before induction.

Iv access can be amajor challenge in children. Blind techniques may have to be employed at the saphenous vein, medial cubital vein and dorsal hand vein. In emergency situations, intraosseous access may be done using an 18G needle in the tibia.[11]

Invasive procedures like central venous catheter or arterial line insertion is usually doneonly after the induction of GA. Use of ultrasound has greatly reduced the complications associated with these procedures.

The same monitoring standards must be applied in paediatric cases with use of appropriate sized cuffs and strict temperature monitoring.

Airway management: in addition to their anatomic features (large head, tongue, short neck, narrow nasal passages, cephalad larynx)[12], children with cancer may present with a difficult airway due to large tumours of the head and neck, retinoblastoma, neuroblastoma, radiation-induced airway distortion or post chemoradiotherapy mucositis. Appropriate equipment for the difficult airway must be kept in hand at all times.

Respiratory aspects: Due to their pliable ribs, increased chest wall compliance, smaller airways, and less number of alveoli, children have a reduced FRC.Children have twice the oxygen consumption of adults, hence they have limited reserve during apnoea which deters from the use of rapid sequence induction.

Cardiovascular aspects: The paediatric autonomic nervous system is parasympathetic dominant and children frequently respond to noxious stimuli with bradycardia.[11]

Pain: Pain canhave a psychological and emotional impact on the child in addition to the physical effect. Common analgesics usedin children include acetaminophen, diclofenac and ketorolac.Opioids may be used with caution in children due to their impaired clearance. Intravenous Tramadol 1mg/kg iv and fentanyl 1-2 mcg/kg iv are commonly used in the perioperative period.

Regional anaesthesia: most children less than 10 years of age do well with a regional anaesthetic technique especially since the advent of ultrasound has made it more safe. However, it is almost impossible to do a regional anaesthesia in children without sedation.Continuous epidural infusions at caudal, lumbar or thoracic levels and peripheral nerve blocks are safe and effective in children.

Fluid management: with their low body weight and body mass to surface area ratio, fluid management is of utmost importance in all children but especially in smaller age groups like infants and neonates. Usually an isotonic balanced salt solution is used. In neonates, a supplemental IV dextrose at the rate of 6 to 8 mg/kg/min may be warranted in prolonged fasting. All children <3 months old or with liver disease, sepsis, prolonged parenteral nutrition should have intraoperative glucose supplementation.

Blood loss: Physiological anaemia occurs between the 2nd to 3rd months of life.

Estimated blood volumes are around 100ml/kg for premature neonates, 90ml/kg for term neonates, 80ml/kg for infants, and 70 to 75ml/kg for small children. Using the **Maximum Allowable Blood Loss** formula, adequate blood and blood products replacement must be made.

MABL = EBV X (child's haematocrit – minimum accepted hematocrit)/ child's haematocrit[9]

Doses of blood products[7]

Blood product	Dose
Packed cells	4 ml/kg will raise Hb by 1 g/dl(desired Hb−actual Hb)×weight (kg)×3
Platelets	Children <15kg 10–20 ml/kg; children >15kg one apheresis unit (single donor)
Fresh-frozen plasma (FFP)	10–20 ml/kg
Cryoprecipitate	5 ml/kg

Temperature control: paediatric patients dissipate heat readily during anaesthesia due to their large body surface area, thin skin, and insufficient fat stores. Forced air warmers, heating lamps, warming blankets, fluid warmers and setting the OT temperature to 26ºC are some of the measures used to keep the child warm.

Deep tracheal extubation may be best for paediatric patients unless contraindicated. Post extubation complications like laryngospasm, stridor, coughing, apnoea may be seen in and must be recognized early and promptly corrected.

In the post anaesthesia care unit (PACU) and the ICU, the same levels of care must be maintained for the child with appropriate monitoring.Trained nursing and ancillary staff must be availableat all times.Appropriate doses of antibiotics, analgesics, and other postoperative medications must be calculated and given.

3. Follow up

A child followed up after oncologic therapymay need long term venous access for frequent blood tests and chemotherapy administration. Usually, the PICC or central line may get complicated by infections, thrombosis, leakage, dislodgement and may require placement of a new access in another site.[7] The anaesthetist may help in placement of difficult iv access with the help of ultrasound guidance.

Childhood cancer services in India are predominantly restricted to few tertiary care centres in few major cities. Being a developing nation, most cancers have an unpredictable outcome due to delay in consultation, advanced stage of presentation, delay in seeking treatment, limited supportive care during intensive treatment, treatment refusal and abandonment. For an anaesthesiologist, the challenges of paediatric anaesthesia become more complicated by the specific problems related to cancer.[8]

The way ahead:

Incorporation of best clinical practices in dealing with children, increasing knowledge of paediatric oncology, improving inter-departmental cooperation, forming disease-specific groups (DSG) for children with the various disciplines involved in caring for the child with cancer, will go a long way in creating an ecosystem for further improvement.

Training and enhancement of knowledge of all health care workers dealing with paediatric oncologic cases is essential.

Steps need to be taken to enhance or modify the present available resources (specific paediatric equipment) in our institute to cater to the paediatric patient.

We can definitely improve the paediatric cancer care by leaps and bounds if we work together in a systematic way.

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Review Article

Molecular genetics of soft tissue tumours

Argha Baruah, Anupam Sarma

Department of Onco-pathology
Dr. B. Borooah Cancer Institute, Guwahati

Soft tissue tumors are histologically diverse mesenchymal tumours and often pose significant challenges in rendering a definitive diagnosis and optimal therapy. Pathologists use a morphological pattern recognition approach along with individual cell morphology to analyze the histological information but due to considerable morphological overlap additional ancillary tests are required. Immunohistochemistry (IHC) is an important ancillary tool to aid in diagnosis because it can provide information about tumor histogenesis. Recently, considerable number of soft-tissue tumors are associated with recurrent chromosomal rearrangement which can help in sub classification and important in directing therapy.[1] Fusion genes resulting from chromosomal rearrangements including translocations, inversions, deletions and insertion or tandem duplications represent excellent markers for tumor classification. Since the first discovered translocation of t(11;22)(q24;q12) in Ewing sarcoma, cytogenetic studies are continuously advancing to specify distinct mesenchymal tumor entities. Here are few commonly altered genetic alterations common in soft tissue tumours.[2-4]

ADIPOCYTIC TUMOURS	TRANSLOCATION	FUSION GENE
1. Lipoma	12q15 rearrangements t(3;12)(q27–28;q13–15) -in 2/3rd cases 6p21 rearrangements	HMGA2
2. Lipoblastoma	8q11-13 rearrangements	PLAG1
3. Chondroid lipoma	t(11;16)(q13;p12-13)	C11orf95-MKL2 and MRTFB
4. Atypical lipomatous tumor/well differentiated liposarcoma	Amplification of 12q14-15 ± Co-amplified 1q21-25 sequences	MDM2 amplification ±CDK4 amplification
5. Dedifferentiated liposarcoma	Amplification of 12q14-15 ± Co-amplified 1p32, 6q23 and 6q25 sequences	MDM2 amplification ±CDK4 amplification
6. Myxoid/round cell liposarcoma	t(12;16)(q13;p11) t(12;22)(q13;q12)	FUS-DDIT3 , EWSR1-DDIT3

FIBROBLASTIC TUMOURS	TRANSLOCATION	FUSION GENE
1. Nodular fasciitis	t(17;22)(p13;q13.1)	MYH9-USP6
2. Soft tissue angiofibroma	t(5;8)(p15;q13)	AHRR-NCOA2
3. Desmoid-type fibromatosis	+8, +20 ,5q21-22 loss	APC inactivating mutations CTNNB1 mutations in 85% of sporadic lesions
4.Giant cell fibroblastoma	t(17;22)(q21.3;q13)	COL1A1-PDGFB
5.Dermatofibrosarcoma protuberans	t(17;22)(q21.3;q13) or r(17;22)	COL1A1-PDGFB
6. Solitary fibrous tumor	12q13 rearrangements	NAB2-STAT6

7. Inflammatory myofibroblastic tumor	Rearrangement involving 2p23	TPM3-ALK, TPM4-ALK, CLTC-ALK RANBP2-ALK.
8. Infantile fibrosarcoma	t(12;15)(p13;q25)	ETV6-NTRK3
9. Low Grade Fibromyxoid Sarcoma	t(7;16)(q33;p11)	FUS-CREB3L2
10. Sclerosing epithelioid fibrosarcoma	Deletions /copy neutral loss of heterozygosity at 11p,loss of 22	EWSR1-CREB3L1

VASCULAR TUMOURS	TRANSLOCATIONS	FUSION GENE
1.Epithelioid hemangioma	-	FOS or FOSB
2. Epithelioid hemangioendothelioma	t(1;3)(p36;q25) t(X;11)(p11.2;q13)	WWTR1-CAMTA1 YAP1-TFE3
3. Angiosarcoma of soft tissue	-	High-level amplification of MYC (8q24) is a consistent hallmark of radiation-induced, lymphedema-associated angiosarcoma

SKELETAL TUMOURS	TRANSLOCATIONS	FUSION GENE
1. Fetal rhabdomyoma		PTCH1 loss of function mutations in syndromic lesions
2. Alveolar rhabdomyosarcoma	t(2;13)(q35;q14) t(1;13)(p36;q14)	PAX3-FOXO1 PAX7-FOXO1
3.Spindle cell rhabdomyosarcoma	8q13 rearrangements	SRF-NCOA2 ,TEAD1-NCOA2 MYOD1p.Leu122Arg gene mutation

GASTROINTESTINAL STROMAL TUMOURS	TRANSLOCATIONS	FUSION GENE
Gastrointestinal stromal tumor	Monosomy or partial loss of 14 and/or 22 Deletions of 1p, 9p, 9q, 10, 11p, and 13q and gains/ amplifications on 5p, 3q, 8q, and 17q are associated with malignant behavior	KIT, PDGFRA

NERVE SHEATH TUMOURS	TRANSLOCATIONS	FUSION GENE
1.Schwannoma	Monosomy or partial loss of 22	NF2, SMARCB1
2. Neurofibroma	17q loss	NF1
3.Malignant peripheral nerve sheath tumor	17q loss 9p loss	NF1 (germline and somatic) CDKN2A
4.Malignant melanotic nerve sheath tumour	17q loss	PRKAR1A

SMOOTH MUSCLE TUMOURS	TRANSLOCATIONS	FUSION GENE
Benign metastasizing leiomyoma	6p21 rearrangement 19q and 22q terminal deletions	HMGA1

TUMOURS OF UNCERTAIN DIFFERENTIATION	TRANSLOCATIONS	FUSION GENE
1. Intramuscular myxoma	Point mutation of Exon 8 and 9	GNAS
2. Deep 'aggressive' angiomyxoma	12q13-15	HMGA2
3.Ossifying fibromyxoid tumor	6p21 or monosomy 22	PHF1 and/or TFE3
4.Synovial sarcoma	t(X;18)(p11.2;q11.2) t(X;20)(p11.2;q13.3)	SS18-SSX1 ,SS18-SSX2, SS18-SSX4 ,SS18L1-SSX1
5. Epithelioid sarcoma	22q11.2 anomalies + 8q, often as i(8)(q10)	SMARCB1
6. Alveolar soft part sarcoma	der(17)t(X;17)(p11;q25)	ASPSCR1-TFE3

7. Clear cell sarcoma of soft tissue	t(12;22)(q13;q12) t(2;22)(q33;q12)	EWSR1-ATF1 EWSR1-CREB1
8. Extraskeletal myxoid chondrosarcoma	t(9;22)(q22;q12) t(9;17)(q22;q11)	EWSR1-NR4A3, TAF15-NR4A3
9. NTRK rearranged spindle cell neoplasm	-	NTRK1,2,3
10. Extraskeletal Ewing sarcoma	t(11;22)(q24;q12) t(21;22)(q22;q12) t(7;22)(q22;q12) t(17;22)(q21;q12) t(2;22)(q36;q12) t(16;21)(p11;q22) t(2;16)(q36;p11)	EWSR1-FLI1 EWSR1-ERG EWSR1-ETV1 EWSR1-EIAF EWSR1-FEV FUS-ERG FUS-FEV
11. Desmoplastic small round cell tumor	t(11;22)(p13;q12)	EWSR1-WT1
12. PEComa	Deletion or loss of 16p	TSC2
13. Round cell sarcoma with EWSR1-non ETS fusions	inv(22)(q12q12) t(2;22)(q31;q12) t(20;22)(q13;q12) t(4;22)(q31;12) t(6;22)(p21;q12)	EWSR1-PATZ1 EWSR1-SP3 EWSR1-NFATC2 EWSR1-SMARCA5 EWSR1-POU5F1
14. CIC arranged sarcoma	t(4;19)(q35;q13) t(10;19)(q26.3;q13)	CIC-DUX4
15. Sarcoma with BCOR genetic	inv(X)(p11.2p11.4)	BCOR-CCNB3

Targeted therapy is a drug therapy that inhibits a 'target' in one of the cellular signaling pathways which must be measurable and involved in tumourigenesis, angiogenesis, progression and metastasis in cancer cells. Tyrosine kinase inhibitor imatinib has great historical significance as it was the first targeted therapy against STS gastrointestinal stromal tumor.

Following are the targeted therapy used in various soft tissue sarcoma's: [5,6]

Sarcoma	Targeted gene	Drug
Alveolar soft part sarcoma	VEGFR1-3	Cediranib
Inflammatory myofibroblastic tumour	ALK	Crizotinib
Epithelioid Sarcoma	EZH2	Tazemetostat
GIST	BCR-ABL, c-kit, PDGFR	Imatinib
Liposarcoma	CDK4/6	Palbociclib
NTRK rearranged spindle cell neoplasm	NTRK1,2,3	Larotrectinib
PEComa	mTOR	Sirolimus
Dermatofibrosarcoma protuberans	COL1A1–PDGF β	Imatinib mesylate

Advances in molecular pathology promises an exciting future of refined personalized care of patients with soft-tissue tumors.

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Case Report

Inflammatory myofibroblastic tumour – A case report with review of literature

Karma D. Bhutia

Department of Surgical Oncology
Dr. B. Borooah Cancer Institute, Guwahati

INTRODUCTION

Inflammatory myofibroblastic tumor (IMFT) is also known as an inflammatory pseudotumor or plasma cell granuloma. It is locally aggressive, often occurring in thoracic and abdominal cavities, where it may appear as infiltrative and lobulated appearance on imaging.

CASE REPORT

A one year old boy presented with a history of swelling in the right shoulder for 6 months with progressive increase in size. On clinical examination, the swelling was located in the intramuscular plane of the right upper arm anterolateral aspect, with a size of 8 cm in the craniocaudal direction and 5 cm in the transverse direction, with no skin involvement. Local imaging was done using contrast MRI under general anesthesia and then a corecut biopsy was done which showed histopathological features suggestive of spindle cell tumour. Wide excision of the tumour was done 2 cm margins all around, with labelling of the sides for orientation. The periosteum of the underlying humeral shaft was taken as deep margin. Frozen section of margins was negative for malignancy. Radio-opaque clips were placed to delineate the resection bed. Primary closure was achieved. The boy had an uneventful recovery and the wound healed along expected lines. The histopathology report of the surgical specimen showed a circumscribed and non-encapsulated white tan mass with whorled fleshy surface with focal areas of hemorrhage, of size 7.8 cm x 3.5 cm x 3 cm with features of spindle cells with an inflammatory infiltrate of lymphocytes, plasma cells, eosinophils and histiocytes and a background of abundant blood vessels suggestive of inflammatory myofibroblastic tumor (figure 1). Immuno-histochemical panel done showed positivity for vimentin and negative staining for CK, SMA, CD34 and desmin and Ki67 was 15%. It was a R0 resection. The patient was on regular follow up and recurrence-free for 20 months.

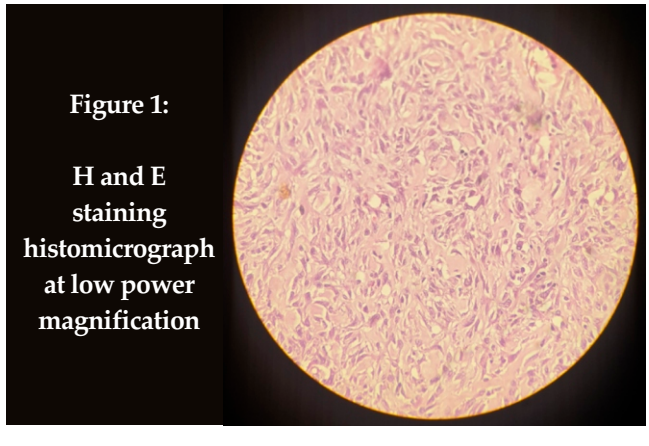

Figure 1:

H and E staining histomicrograph at low power magnification

DISCUSSION

Inflammatory myofibroblastic tumour (IMT) is a distinctive lesion composed of myofibroblastic spindle cells accompanied by an inflammatory infiltrate of plasma cells, lymphocytes and eosinophils. It occurs primarily in soft tissues and viscera of children and young adults. It is most frequently seen in first two decades of life with a female preponderance.[1] IMT can occur throughout the body, most common sites being the lung, mesentery and omentum. The clinical features

depend on the site of the tumor. A mass, fever, weight loss and pain are frequent complaints. In up to one third of patients, paraneoplastic syndrome occurs with fever, growth failure, malaise, weight loss, anemia, thrombocytosis, polyclonal hyperglobunemia and elevated erythrocyte sedimentation rate.[1] IMT is currently regarded as a neoplasm of intermediate biologic potential because of its tendency to locally recur and the fact that it does rarely metastasize.[2]

Its histology is heterogenous, with variable grouping of spindle, fibroblastic and inflammatory type cells. The variable appearance may result from the tumor's genetic heterogeneity. ALK rearrangements occur in 70% of patients (almost exclusively in patients below 40 years of age). However, this is not specific to IMT. Inflammatory components of the tumor do not have ALK rearrangement.

IMT shows strong diffuse cytoplasmic reactivity for vimentin. Reactivity for smooth muscle actin and muscle specific actin varies from a focal to diffuse pattern in the spindle cell cytoplasm and desmin is identified in many cases, Focal cytokeratin positivity is seen in one third of cases. Myogenin , myoglobin and S100 stainings are not seen.[3]

Extrapulmonary IMT has a recurrence rate of approximately 25% related to location, resectability and multinodularity. Less than 5% metastasize. Evidence suggests that combination of atypia, ganglion like cells, TP53 expression and aneuploidy may help to identify IMT with more aggressive potential.[4] Coffin CM et al[5] showed ALK-negative IMTs occurred in older patients (mean age 20.1) years, ALK reactivity was associated with local recurrence, but not distant metastasis, which was confined to ALK-negative lesions. Absent ALK expression was associated with a higher age overall, subtle histologic differences, and death from disease or distant metastases (in a younger subset). Other proliferative, apoptotic, and prognostic markers did not correlate well with morphology or outcome. Thus, ALK reactivity may be a favorable prognostic indicator in IMT and abdominopelvic IMTs recur more frequently (85%).

Even though there is a suggestion of an association of IMT with a gamut of infectious conditions like organizing pneumonia, mycobacterium avium intracellulare, corynebacterium equi, campylobacter jenuni, bacillus sphaericus, Epstein-Barr virus, E. coli or to other conditions like previous abdominalsurgery, trauma, ventricuoloperitoneal shunt, radiation therapy or steroid use, the exact mechanism remains unidentified.

Surgery is the treatment of choice. Regression and response to corticosteroid and non steroidal inflammatory agents have been noted in few cases. In case of unresectable tumor or metastatic or recurrence systemic therapy, anthracycline based or methotrexate and vinorelbine/vinblastine based regimen.[6] Crizotinib an ALK inhibitor has been recommended as a single agent treatment for advanced, inoperable IMTs.

CONCLUSION

There is a need to be well-versed with this histological variant of soft tissue tumour due to its unique set of characteristics and rare incidence.

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Review Article | Special Guest Article

Cytoreduction surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC)

Jyoutishman Saikia, SVS Deo

Department of Surgical Oncology
IRCH, AIIMS, New Delhi

INTRODUCTION

Tumors of the peritoneal cavity vary widely in their biology and present a unique challenge to oncologists. They may arise from the peritoneal cavity lining (primary peritoneal malignancies such as mesothelioma and serous carcinoma) or those that have secondarily spread to the peritoneum (secondary peritoneal malignancy). In developed countries an incidence rate of upto 3 per million has been reported for peritoneal mesothelioma.[1] Secondary isolated peritoneal spread is relatively common with ovarian and gastrointestinal malignancies, including colorectal, appendiceal, and gastric. Peritoneal carcinomatosis is of primary peritoneal origin in only 3% of the times; most often, it is the result of metastatic disease.

Historically, the only treatment for patients with peritoneal carcinomatosis was systemic chemotherapy with poor survival rates ranging from a few months (gastric cancer) to an year or more (ovarian cancer). In patients of colorectal cancer origin, western data suggests that median overall survival of patients with isolated peritoneal disease is around 16 months. This is considerably worse than those patients with isolated liver or lung metastases (19 months and 25 months respectively).[2] Surgery was considered only in cases of limited local disease or emergent situations like obstruction of bowel and perforation. However, in the last two decades our understanding of peritoneal disease has changed. The peritoneal cavity spread is increasingly being considered more as a locoregional disease rather than systemic spread. Accordingly, the application of cytoreductive surgery (CRS) seems to be logical treatment modality in these situations. But CRS in itself is considered as an intrinsically incomplete procedure due to possibility of leaving out microscopic tumor seedlings in the peritoneal cavity. To control this intraperitoneal chemotherapy has been attempted after completion of CRS. The synergism between heat and drugs has been well documented and this principle has been explored for controlling microscopic residual tumor seedlings following CRS.This treatment modality of hyperthermic intraperitoneal chemotherapy, popularly known as HIPEC, was introduced by the Netherlands Cancer Institute, became standardized nomenclature following the experts' consensus in Fourth International Workshop on Peritoneal Surface Malignancy[3] held in Madrid, 2004. The surgical expertise required for the CRS procedure; the experience, technical requirements, and infrastructure required to deliver intraoperative hipec; and the multidisciplinary team required to care for patients receiving those treatments have dictated that specialized centres be created for care delivery.[4,5,6]

CRS and HIPEC

The history and rationale

Cytoreductive surgery (CRS) is a complex procedure that comprises of peritonectomy procedures including resection of involved viscera as indicated, with the goal of removal of all macroscopically visible disease.[7] Following this the abdominal cavity is perfused with

heated chemotherapy to eradicate residual microscopic disease. A systematic approach towards comprehensive CRS was described in 1995 by Dr. Paul Sugarbaker, and that approach has generally been adopted.[8] The addition of HIPEC to CRS was first evaluated in the 1980s. The biologic rationale for intraperitoneal delivery was based on studies demonstrating a pharmacokinetic advantage because the peritoneal–plasma barrier allows for a high concentration gradient of chemotherapeutic drugs between the peritoneal cavity and the systemic circulation.[9] Also the blood drainage from the peritoneal cavity occurs through the portal system, providing a "first-pass" effect through the liver, reducing systemic toxicity and simultaneously increasing intrahepatic concentrations. The addition of hyperthermia is based on experimental evidence that malignant cells are more sensitive to the effects of hyperthermia in the range of 41°C to 43°C, resulting in accelerated cell death.[10] Besides this hyperthermia increases tissue penetration of the drug through the peritoneal membrane along with inhibition of repair mechanisms.[11] The depth of tissue penetration following heat ranges from 3 to 5mm in most studies, rationalising a 2.5mm tumor diameter to be the maximum that can be reliable killed following HIPEC.[12,13]

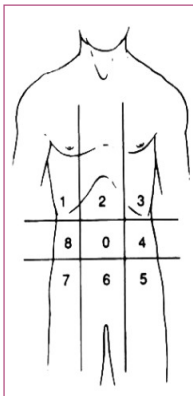
TECHNICAL ASPECTS

Cytoreductive surgery

Technical aspects of CRS begins with patient positioning. Most commonly patients are positioned in modified lithotomy or legs split apart for wider access to the perineum. After laparotomy the abdominal disease burden is assessed as per peritoneal cancer index (figure 1). Accordingly, a maximum PCI of 39 can be achieved after adding scores from all the 13 abdominal regions. The completeness of cytoreduction score (CC score) is labelled as CC=0(no visible residual disease), CC=1 (residual disease <2.5mm), CC=2 (residual disease 2.5mm to 2.5cm) and CC=3 (residual disease>2.5cm. The basic principles of CRS involve removal of all macroscopically visible disease or leaving residual disease not greater than 2.5mm.Common peritonectomy procedures are described in table 1.

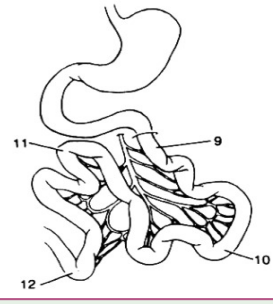
Figure 1 : Peritoneal caner index and abdominal regions.

Peritoneal Cancer Index



Regions	Lesion Size	Lesion Size Score
0 Central	—	LS 0 No tumour seen
1 Right Upper	—	LS 1 Tumour up to 0.5 cm
2 Epigastrium	—	LS 2 Tumour up to 5.0 cm
3 Left Upper	—	LS 3 Tumour > 5.0 cm or confluence.
4 Left Flank	—	
5 Left Lower	—	
6 Pelvis	—	
7 Right Lower	—	
8 Right Flank	—	
9 Upper Jejunum	—	
10 Lower Jejunum	—	
11 Upper Ileum	—	
12 Lower Ileum	—	

PCI ☐



0 Central
Greater omentum & Transverse Colon.
1 Right upper
Superior surface of the right lobe of the liver, undersurface of the right hemidiaphragm, right retrohepatic space.
2 Epigastrium
Epigastric fat pad, left lobe of the liver, lesser omentum, falciform ligament.
3 Left upper
Undersurface of the left hemidiaphragm, spleen, tail of pancres anterior and posterior surfaces of stomach.
4 Left flank
Descending colon, left abdominal gutter
5 Left Lower
Pelvic sidewall lateral to the sigmoid colon, sigmoid colon
6 Pelvis
Female internal genitalia with ovaries, tubes and uterus, bladder, Douglas pouch, rectosigmoid colon.
7 Right lower
Right pelvic sidewall, cecum, appendix
8 Right flank
Ascending colon, right abdominal gutter
9 Upper jejunum
Including both bowel and its mesentery
10 Lower jejunum
Including both bowel and its mesentery
11 Upper ileum
including both bowel and its mesentery
12 Lower ileum
Including both bowel and its mesentery

Table 1 : Peritonectomy Procedures

Peritonectomy procedures	Resections
Anterior parietal peritonectomy	Old abdominal incisions, umbilicus, epigastric fat pad
Right diaphragmatic peritonectomy	Glissons capsule deposits
Left diaphragmatic peritonectomy	Removal of the peritoneum covering Gerota's fascia and the adrenal gland (A splenectomy may added if involved)
Pelvic peritonectomy	Uterus, ovaries and rectosigmoid colon Urachus and anterior pelvic peritoneum are stripped from the bladder

Peritonectomy procedures	Resections
Omental bursectomy	Gall bladder and lesser omentum
Greater omentectomy	Greater omentum is elevated off of the transverse colon, and the superior and anterior transverse mesocolon is stripped
Additional resections	Mesenteric and serosal peritonectomies Visceral resections

Two methods of administration of HIPEC has been broadly described: the open method and the closed method.[14] Other methods appear to be a modification of these methods. Following CRS, in the open method (Coliseum technique) as described by Sugarbaker, a Tenckhoff catheter and four closed suction drains are placed (two in-flow and two out-flow) through the abdominal wall and made watertight with skin sutures. Skin edges of the abdominal incision are suspended up to a Thompson self-retaining retractor to create an open space in the abdominal cavity (figure 2). The abdominal wall edges were covered with a transparent adhesive film after suspending from the self-retaining Thomson retractors. In necessary situations the bowel can be manipulated via a small widow created through the adhesive film. The perfusate is being infused at 43-45°C with the help of a heat exchanger so that the intraperitoneal fluid is maintained at 41-43°C. Once the intraperitoneal temperature of the perfusate reaches 41.5°C, the HIPEC drug is added to the circuit and timer started. The duration of HIPEC varies depending on the drug andinstitute protocols but in general ranges from 30 minutes to 90 minutes in most studies. In bidirectional chemotherapy protocols (sometimes referred to as "HIPEC-plus"), the intravenous infusion of the appropriate drugs is started at this time point.While this open technique allows for an adequate drug distribution, it also carries the increased risk of exposure to operating room personnel along with heat dissipation problems. At our institute we also prefer this method. Another variation of the open technique is the use of a "peritoneal cavity expander" (PCE) used in Japan. The PCE is an acrylic cylinder containing in-flow and out-flow catheters that are secured over the wound. When filled with heated perfusate, the PCE can accommodate the small bowel, allowing it to float freely and be manually manipulated in the perfusate. After HIPEC is completed, the perfusate is drained and the PCE is removed. By using the expander, a more uniform distribution is theoretically achieved compared to a closed technique. The main disadvantage of the PCE technique is the risk of exposure to chemotherapy of the operating room personnel.

Figure 2 : The Coliseum technique

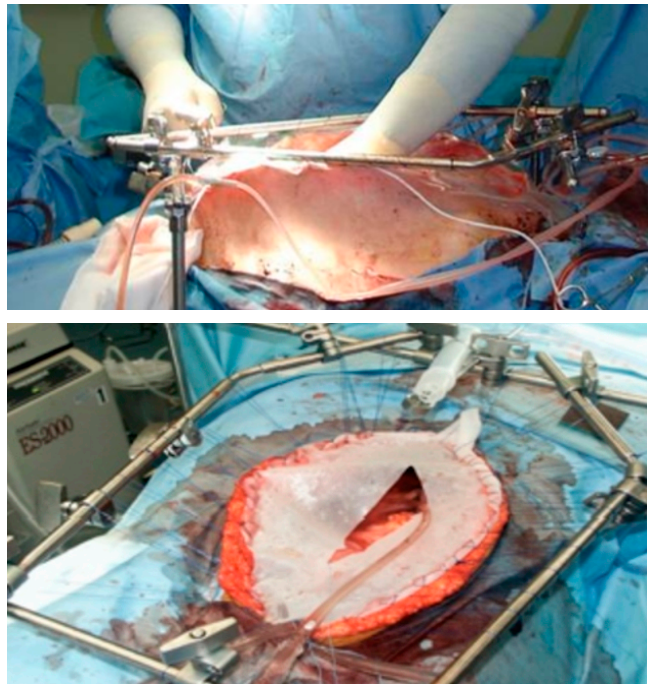


Figure 3 : The components of chemo-perfusion

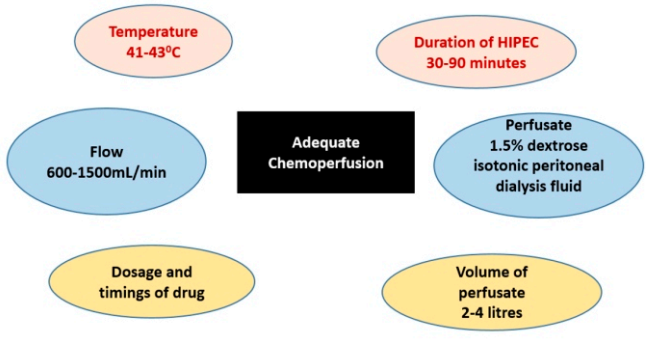
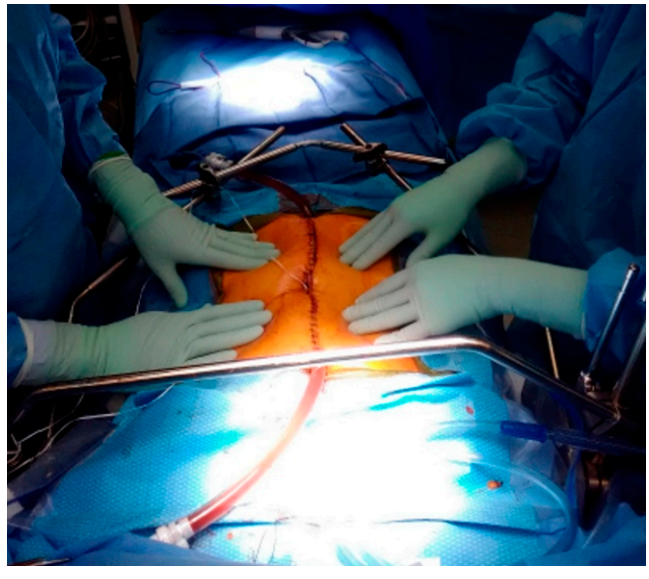


Figure 4 : Closed technique



In the closed technique catheters and temperature probes are placed in the same fashion but the laparotomy skin edges are sutured watertight so that perfusion is done in a closed circuit (figure 4). To promote uniform heat distribution the abdominal wall is manually agitated during the perfusion period. A larger volume of perfusate is generally needed to establish the circuit compared with the open technique. After perfusion, the abdomen is reopened and the perfusate is evacuated. A major advantage of the closed technique is the ability to rapidly achieve and maintain hyperthermia as there is minimal heat loss. In addition, there is minimal contact or aerosolized exposure of the operating room staff to the chemotherapy. The main disadvantage is the lack of uniform distribution of the chemotherapy and heat. This can be hazardous as heat has a narrow therapeutic index for tumoricidal activity and heat damage to the internal organs in areas of heat concentration. Some of the precautions while performing HIPEC include use of impervious gown, safety goggles, elbow length gloves and smoke evacuator.

Common chemotherapeutic regimens

Both single drug and drug combination regimens are currently in use. We prefer using a single drug for most of our patients. Among carrier solutions (perfusate), 1.5% dextrose isotonic peritoneal dialysis solution is the most widely employed.[15] Other options are crystalloids (normal saline or 5% dextrose in water). Heavy molecular weight starch (6% Hetastarch®) is used as a carrier solution for paclitaxel. Drug dose and the carrier solution volume were usually calculated based on body surface area, so that toxicity can be predictable. For a predictable effect of the drug, the concentration in peritoneal fluid instilled is important. The volume of perfusate to be used has been recommended to be around 1.5-2.0L/m2 by most authors.[16] HIPEC regimens using fixed doses (same dose for any patient), drug dosaging by volume of perfusate or by body weight are more prone to find untoward events. A 33% dose-reduction is recommended for patients over the age of 60, previously exposed to multiple lines of systemic chemotherapy, who needed GM-CSF rescue for febrile neutropenia while on systemic chemotherapy, history of renal toxicity or who have received radiation therapy to bone-marrow bearing regions. Common drug regimens include Mitomycin C for appendiceal malignancies, cisplatin for ovarian cancers and mesotheliomas, oxaliplatin for colorectal cancers.

EVIDENCES OF CRS/HIPEC

Ovarian Cancer

One of the first RCT in ovarian cancer was from Greece conducted in 120 patients with recurrent disease.[17] HIPEC drug used was a platinum analogue in sensitive cases. In resistant cases doxorubicin along with paclitaxel or mitomycin were used. The results of this study showed a significant improvement in OS and RFS among the treatment group with heated chemotherapy. However, in primary ovarian cancer staged III and IV, the randomised study by Kim et al found no difference in 5-year OS between the HIPEC and non-HIEC arms.[18] Lately in 2018, van Driel and team published the results of OVIHIPEC trial in patients with interval CRS. The probability of OS at 3 years was 62% vs 48% in the treatment and standard arms respectively.[19] In a health related quality of life analysis of this study, the authors observed that there was no negative impact following the addition of HIPEC to interval CRS.[20] With these evidences, HIPEC seems to be reasonable treatment line in ovarian cancers in interval and recurrent settings. The recently updated Canadian consensus guidelines also approved this after interval CRS.[21]

Colorectal cancer

The role of HIPEC in prevention of peritoneal carcinomatosis (PC) has been explored in details by two major RCTs. Among them, the results of the recently completed multicentre trial (COLOPEC) are interesting to note.[22] They included T4N0-2M0 stage or perforated colon cancer randomised to non-HIPEC or HIPEC using oxaliplatin. While out of 200 patients in the HIPEC arm, adjuvant HIPEC was performed only in 9%. In rest of the 91% patients HIPEC was offered within 5 to 8 weeks after primary tumor resection. In intention to treat analysis, the investigators could not find a peritoneal disease free survival at 18-months between the two groups. The authors further suggested to evaluate new regimens for HIPEC in in-vitro settings. The PROPHYLOCHIP study from France evaluated oxaliplatin based HIPEC in those with high risk of PC after 6 months of completion of adjuvant systemic therapy.[23] They observed that even when 52% of their patients had PC detected during second look surgery and underwent CRS and HIPEC, at 3-year follow up peritoneal cancer recurrence rate in the HIPEC arm

which was comparable to the surveillance arm (32% vs 33% respectively). Also there was no significant 3-year OS difference. However considering the risk of PM being high, the authors suggested strong peritoneal-centred surveillance in these high risk patients.

Other tumors

In advanced gastric cancer postoperative local recurrence and peritoneal metastasis are important factors that affect patient prognosis, with intraperitoneal metastasis being the most frequent outcome and cause of mortality in advanced gastric cancer. In these subgroup of patients, studies have shown that those with serosal invasion, neoadjuvant chemotherapy reduces intraperitoneal recurrence and metastasis, thus, increases the overall survival rate of patients.[24] In addition, hyperthermic intraperitoneal perfusion chemotherapy has been shown to effectively eliminate cancer cells that escape to the peritoneal cavity, thus, preventing peritoneal local recurrence and metastasis. Only level I evidence of HIPEC in gastric cancer PC comes from a small RCT of 68 patients while other studies were for prevention of PC in resected gastric cancer.

Appendiceal neoplasms with peritoneal spread, pseudomyxoma peritonei (PMP) are typically diagnosed between the ages of 40-55, and often found incidentally in patients undergoing laparotomy, laparoscopy, or imaging for other medical conditions. Due to its indolent nature and non-specific symptoms, most are found with advanced disease. The classical sign (jelly belly) is due to an increase in abdominal girth caused by an accumulation of gelatinous ascites.There are no randomised phase III data comparing either CRS alone or systemic chemotherapy to CRS plus HIPEC in PMP. Data is currently insufficient to recommend CRS and HIPEC, but given the limited alternative treatment options, many patients are still treated with this regimen.

Mesotheliomas are relatively rare tumors. Majority of them arise from pleura with only 7-30% arising from peritoneal surfaces. Due to this, studies in this disease remains very scarce. One of the largest retrospective studieswas from US analysing the National Cancer Data Base (NCDB.[25] Among the 1514 patients in the study 14% underwent CRS and HIPEC. The CRS with HIPEC group achieved a median survival of 61 months (5-year OS of 52%) which was higher than all the other arms of the study. Multiple poor prognostic factors were reported by the study which includes advanced age, male gender, uninsured/Medicaid insurance, and sarcomatoid/biphasic histology. Although the causation was unknown, the authors concluded that combined-modality management seems associated with the longest OS.

Complications:

The major complications were related to myelosupression, ileus and fistula. Most studies report a major morbidity (Clavien din do grade III-IV) of upto 15 to 30% and intraoperative mortality of 1 to 5%.

CONCLUSION

It is well established that the complexity of CRS/HIPEC is comparable to other complex oncologic operations with a similar safety profile. However, there is a significant learning curve in both technique and judgment.The learning curve for technical proficiency in CRS is reported in four studies and varies from 100 to 220 cases as reported by various studies.Considering the average volume of CRS/HIPEC at select high volume centres ranges from 24 to 123 cases per year, time to technical proficiency can take several years. A mentorship model has been demonstrated to reduce the learning curve for CRS/HIPEC regarding morbidity, mortality, and completeness of cytoreduction, and an essential step towards safety.

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Review Article

The impact of the COVID-19 Pandemic on the mental health of healthcare professionals and in general population

Anupam Sarma

Professor & Head, Department of Onco-Pathology Oncology
Dr. B. Borooah Cancer Institute, Guwahati

A novel corona virus (COVID-19) was identified as the source of infection for cases of life threatening pneumonia were reported in Wuhan, China in December 2019. The number of cases rapidly increased in Wuhan as well as other Chinese cities. Subsequently the corona virus has also been found in other parts of the world.[1] World Health Organization (WHO) declared COVID-19 outbreak a global pandemic on March 11, 2020. The emergence of corona virus disease 2019 (COVID-19) outbreak resulted in a situation of socio-economic crisis and psychological distress worldwide. Social activities have been restricted in most of the countries and almost all non essential individual movements were prohibited due to quarantine. The local health authorities received suddenly thousands of COVID-19 cases leading to spread of generalized fear and pervasive community anxiety which are typically associated with disease outbreaks and increased with the escalation of new cases together with inadequate, anxiety-provoking information which was provided by media. The psychological reactions to COVID-19 pandemic may vary from a panic behavior to pervasive feelings of hopelessness and desperation. Importantly, other health measures may be compromised by abnormally elevated anxiety. As the general population became increasingly exposed, anxiety provoking topics related to this emergence of the health and socio-economic crisis need to be rapidly identified leading to the onset of mental health problems. [2]

COVID-19 has spread rapidly to countries throughout the world. In the absence of a vaccine, and given the high degree of transmissibility and potential lethality of COVID-19, social and physical distancing, including avoiding crowding, the closure of non-essential services, stay at home orders, and movement restrictions, have been the main public health measures adopted to control the transmission of the virus. Despite the potential benefits of such measures, they might also have negative short and long term consequences for mental health. Such as financial loss and the socioeconomic distress that can result from quarantine may give rise to emergence of psychological disorders. So monitoring the mental health of younger and economically vulnerable individuals may be especially important. They also indicate the mental health of general public during the pandemic that might not only be affected by the direct health consequences of COVID-19, but also by the economic implications of the pandemic. [3]

The modern world in which all individuals are able to rapidly travel and communicate has been rarely forced to the current social isolation and restrictions which are linked to feelings of frustration and uncertainty. Social distancing and lockdown restrictions have been carried out first in China followed by in most European countries and other parts of world like in India where there is a tragic growth of the number of positive cases. Although government regulations are necessary to maintain social balance and guarantee the safety of all individuals, a direct strategy aimed to manage the psychosocial issues related to COVID-19 crisis and its

consequences in the community must be followed. Higher prevalence of subjects with psychological symptoms such as emotional disturbance, depression, stress, mood alterations, irritability, insomnia, fear, anger, anxiety, confusion, grief and emotional exhaustion among those who have been quarantined may be identified. There may be long-term behavioral changes like frequent hand washing and avoidance of crowds as well as a delayed return to normality even after many months after the quarantine. Thus, the quarantine period seems to have important and dysfunctional psychological consequences on the individual's mental health not only in the short-term but even in the long-term period. [4]

Those who have been exposed to the maximum risk of infection may develop pervasive fears about their health, worries to infect others and fear infecting family members. Social isolation related to restrictions and lockdown measures are linked to feelings of uncertainty for the future, fear of new and unknown infective agents resulting in abnormally increased anxiety. In this case first insomnia but later depression and post-traumatic stress may occur. In addition, anxiety and panic is closely associated with fatigue and reduced performance in healthcare workers while loneliness, lower social support, separation from loved ones, loss of freedom, uncertainty and boredom are directly related to anger, frustration and sufferings linked to quarantine restrictions. Cognitive functions and decision making are firstly impaired by hyper arousal and anxiety and later by disabling feelings of loneliness. In addition, social isolation and loneliness are also associated with alcohol and drug abuse, enhancing the risk of hopelessness and suicidal behavior in this specific context. [5]

There is increased risk of child maltreatment and domestic violence due to COVID-19 spread. One reason for this is that school closures force children to stay at home for longer durations, which may increase parenting stress. In India, all schools nationwide were temporarily closed starting from March 2020. There was a significant increase in parenting stress. Specifically addressing these issues through local and national policies may help in relieving parenting stress during this pandemic. Newer ideas could be obtained about effective coping methods that could be practiced at individual and household levels. It is possible that some families may find it difficult to implement such solutions due to their individual circumstances. These families will need additional support from governments and the private sector. [6]

The general population as well as most of the front-line health care workers became vulnerable to the emotional impact of COVID-19 infection due to both the pandemic and its consequences worldwide. Many psychological problems and important consequences in terms of mental health including stress, anxiety, depression, frustration, uncertainty during COVID-19 outbreak emerged progressively. Implementing community based strategies to support resilience and psychologically vulnerable individuals during the COVID-19 crisis is fundamental for any community. The impact on mental health due to fear and anxiety induced by the rapid spread of COVID-19 pandemic needs to be clearly recognized as a public health priority by both authorities and policy makers, who should rapidly adopt clear behavioral strategies to reduce the burden of disease and the mental health consequences of this outbreak.

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Special Report

A summary of major cancer surgery volume in a year of the pandemic

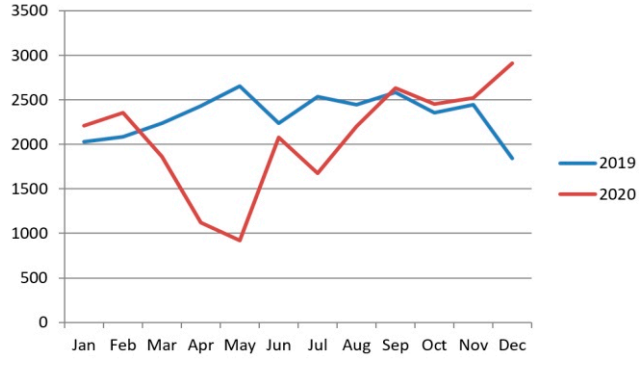
Gaurav Das

Department of Surgical Oncology
Dr. B. Borooah Cancer Institute, Guwahati

** This article was written before the onset of the second wave of COVID-19 pandemic. We will report about subsequent experiences in the next issue.*

The novel coronavirus disease 2019 (COVID19) pandemic affected the treatment of patients diagnosed with cancer and this included those who needed surgical intervention for the disease. Among the factors that disrupted the system included the fear and uncertainty associated with the pandemic in the initial period which encompassed both the patients and the care-givers, the enforced nation-wide lockdown and consequent hardships of travel and accommodation including financial strain, supply chain interruptions, the challenges of testing for novel coronavirus (SARS-CoV-2), the logistics of ensuring personal protection for health-care delivery personnel and the response of cancelling or delaying elective surgical procedures whenever deemed possible with use of alternate approaches. The surgical departments at Dr. B. Borooah Cancer Institute (BBCI) have come full circle as far as the surgical volume is concerned, with dwindling numbers observed at the beginning and the peak of the pandemic in the region and then a rapid return to the pre-COVID19 numbers as soon as an effective strategy against the pandemic was in place, right from in-house testing of pre-operative cases, isolation of confirmed COVID19 patients, appropriate use of personal protection equipment (PPE) and allaying of consternation regarding the pandemic with the passage of time.

Figure 1: Footfalls in the general surgical OPD.



Under the Department of Surgical Oncology, which addresses surgical management for malignancies apart from cancers of head and neck and gynaecological organs, a total of 779 major surgical procedures were performed in the year 2020, which is about 25% less than the preceding year (2019) but still more than the surgical volume in 2018 (**Table 1)**

Table 1: The year-wise total number of major surgical cases.

Year	Total number of major cases
2018	721
2019	1042
2020	779

A sheer drop in surgical volume was seen in the months of April and May, when the nation-wide lockdown was in force and the COVID19 case numbers were on the rise. However, by the month of September, the total number of major surgeries done was comparable to that of the previous year and was consistently more in the last quarter of the year, with the month of December recording the highest number of cases performed in one month. (**Table 2)**

Table 2: Month-wise break-up of the number of major surgeries.

Month	Year 2019	Year 2020
Jan	89	91
Feb	87	76
Mar	87	59
Apr	77	18
May	97	13
Jun	89	46
Jul	101	58
Aug	91	73
Sep	85	80
Oct	79	83
Nov	74	79
Dec	86	103
Total	1042	779

Surgeries for breast cancer were the most frequently done procedures (24.3% of total) and breast conservation surgery was performed in 28.7% patients. The use of oncoplastic procedures saw an increase compared to the preceding year. Definitive surgery for colorectal cancer accounted for 10.7% of the total surgical volume. Minimally invasive surgery (MIS) was used in 16.9% of these cases. A total of 41 patients with esophageal cancer underwent definitive surgical resection. Thoracoscopic mobilization was utilized in 46.3% of these surgeries.

It was seen that 39 patients with a diagnosis of a cancer of the gastrointestinal tract including the esophagus or the hepatobiliary system were found to be inoperable at the time of definitive surgery (17.9% of total). One of the contributing factors to this eventuality could be the time in the waiting period for surgery. This is a key area to address in the future and meticulous review of good quality, recent, appropriate and adequate pre-operative imaging will help in mitigating the problem.

Table 3: The various types of surgeries performed in the divisions of thoracic, GI, breast, musculoskeletal and urological oncology.

MAJOR SURGERY	Total number of cases
Breast cancer	
Mastectomy	129
BCS	52
ALND	8
Type I oncoplasty (*Round block, Batwing mastopexy, Grissoti and other mammaplasties*)	15
Type II oncoplasty (*mini-LD, AICAP, LICAP, TDAP*)	5
LD flap cover	5
TA flap cover	4
SLNB	16
Esophageal cancer	
VATS TTE	18
VATS converted to open TTE	1
Open TTE	18
LTA esophagogastrectomy	1
THE	3
Inoperable	6 (includes 4 OGJ tumours)
Other thoracic surgeries	
Lung lobectomy	2
Chest wall resection	3
Gastric cancer	
Distal gastrectomy	21
Total gastrectomy	7
Palliative gastrectomy	3
Inoperable	14
Colorectal cancer	
Open colectomies	39
Lap colectomies	8
Open LAR/ULAR/APR	23
Lap LAR/ULAR/APR	6
ELAPE	2
Pelvic exenteration	5
Inoperable rectal cancer	4
Small bowel malignancies	
Small bowel tumours resection	3
Pancreatic/ peri-ampullary tumours	
Whipple's procedure	8
Inoperable	5

Gallbladder disease/ cancer	
Radical cholecystectomy	14
Simple cholecystectomy	12
Inoperable	8
Hilar cholangiocarcinoma	
Inoperable	2
Resectable	0
Liver	
Left hepatectomy (for HCC)	1
Metastasectomy (for CRC)	1
Miscellaneous	
Palliative FJs and GJs	78
Diversion stomas	25
Stoma closures	4
Emergency laparotomies	9
Soft tissue sarcomas (STS)	
Excision of STS	13
Locoregional flaps (ALT, medial gastrocnemius)	2
Skin tumours	
Excision of skin tumours	11
SLNB (for melanoma)	1
Locoregional flaps (reverse sural, medial plantar, peroneus brevis)	3
Bone tumours	
Limb salvage surgery (total)	18
Total femur	2
Distal femur	8
Curettage/ excisions	4
Fibulectomy	1
Tibial shaft	1
Proximal humerus	1
Sacral chordoma	1
Rotationplasty	1
Bone grafting	1
Amputations (including fungating skin malignancies)	26
Genitourinary malignancies	
Radical nephrectomy	6
Partial nephrectomy	3
Radical cystectomy	4
Pelvic exenteration (for TCC prostate)	1
Adrenalectomy	1
Penectomies	12
SLNB (for carcinoma penis)	1
RPLND	1
Inguinal dissections (for penile cancer and skin cancers)	35

Miscellaneous	
Chemoports	20
Lap BSO	1

Special Report

COVID and its impact on Head and Neck cancer surgery

T Rahman, A K Das, Rajjyoti Das, Kishore Das, Anupam Das, Kaberi Kakati, Rupjyoti Das

Department of Head & Neck Oncology
Dr. B. Borooah Cancer Institute, Guwahati

** This article was written before the onset of the second wave of COVID-19 pandemic.*

The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) poses an unprecedented challenge to the global healthcare system , including the delivery of standard care to patients with cancer. Head and neck cancer (HNC) patients represented a major clinical challenge in treatment decision-making facing this highly contagious and potentially fatal infectious disease. As such, cancer patients are more vulnerable to SARS-Cov-2 infection and are more likely to develop severe and critical COVID-19 when infected thereby deteriorating their condition with high risk of mortality . Delivering timely HNC care is increasingly recognized as critical to achieving optimal oncologic outcomes and delayed treatment may increase the risk of disease progression and death for these patients.

Standard Operating Procedure(SOP) was formulated in our institute taking into account various factors so that the risk of COVID-19 transmission is reduced. Preoperative covid testing was mandatory for all patients and patients who turned positive after admission were shifted to covid isolation ward. Personal protection kits (PPE) (which included disposable shoe covers, gown, goggles, cap, mask, face shield and gloves) were used in every case especially at the beginning and the peak of the pandemic. There was a delay in elective surgical procedures during the pandemic and modality of treatment was changed from surgery to alternative methods like radiotherapy or chemotherapy especially in cases where further delay in initiation of treatment would have jeopardized the patient's condition and upstaged the disease.

The Department of Head and Neck Oncology witnessed a total of 444 major surgical procedures being performed in the year 2020 as compared to 800 such cases in 2019. Thus a 44.5% drop in the major surgical volume was seen in 2020 owing to the global pandemic.

Table 1: The year-wise total number of major surgical cases.

Year	Total number of major cases
January	800
February	444

There was a steep decline in the major surgical cases during the months of April and May due to the nationwide lockdown. The surgical volume started increasing gradually from June when the lockdown was relaxed to certain extent with limited restrictions. The tremendous impact of the covid pandemic is evident in the fact that though there was a rise in the surgical volume in the later part of the year 2020, month-wise surgical cases were still less than those in 2019.

Table 2: Month-wise break-up of the number of major surgeries.

Month	Year 2019	Year 2020
January	61	53
February	60	49
March	64	43
Apirl	65	4
May	80	5
June	70	26
July	72	28
August	69	39
September	66	44
October	64	58
November	65	43
December	64	52
Total	**800**	**444**

Like every year, Head and Neck Oncology Department recorded the highest number of surgeries for oral cancer in 2020 which included mandibulectomies, glossectomies, maxillectomies along with neck dissections. Reconstruction was performed with various local and pedicled flaps. Few cases with high-volume disease necessitated the use of free flaps for reconstruction whereas some cases turned inoperable at the time of definitive surgery. This can be attributed to the fact of long waiting period for surgery which eventually led to upstaging of the disease. Thyroidectomies, parotidectomies and laryngectomies were performed too but the number was much less than the preceding year.

Table 3: The various types of surgeries

TYPES OF SURGERY	TOTAL NUMBER OF CASES IN 2019	TOTAL NUMBER OF CASES IN 2020
Mandibulectomies		
Segmental	300	154
Marginal	117	31
Hemi	10	2
Upper Alveolectomy	150	38
Local and Pedicled Flaps		
PMMC	202	131
Nasolabial	44	33
Submental	14	23
Infrahyoid	19	6
Forehead	19	6
Deltopectoral	20	6
Bernard Burrow	25	10
Karapandzic	20	5
Tongue	15	1
Abbe Estlander	3	1
Neck Dissectons		
SOHND	170	120
EXTENDED SOHND	80	45
MRND	180	120
RND	55	18
EXTENDED RND	35	13
LND	35	21
CCC	20	9
Glossectomies		
Partial	40	5
Hemi	35	11
Subtotal	25	6
Maxillectomies		
Total	20	4
Subtotal	10	1
Infrastructure	40	17
Medial	4	1
Free flaps		
ALT	4	7
Free Fibula	5	5
FRAFF	10	9
Thyroidectomies		
Total	35	9
Hemi	20	5
Completion	11	3
Parotidectomies		
Total	11	6
Radical	6	2
Superficial	8	3
Laryngectomies		
Total	16	12
Miscellaneous		
Lateral Temporal Bone Resection	1	1
Orbital exenteration	6	1

A SURVEY ON COVID19 AMONG GENERAL PUBLIC

A random online survey was conducted by Dr. B Borooah Cancer Institute (BBCI) to understand the impact of corona virus disease-2019 (COVID-19) among the general public. The age of participants ranged from 21 years to 70 years. A total of 268 people participated in the online survey. Of them, vast majority 193 (72%) were from a city (Guwahati, Bengaluru, New Delhi, Gurugram, Hyderabad etc). And, 59 (22%) and 16 (6%) of respondents were from smaller towns and villages, respectively. The most common co-morbidity among survey participants was hypertension 38 (14.4%) followed by diabetes 26 (9.8%). It was seen that 76 (28.4%) survey participants were infected with COVID-19, and of them, 43 (56.5%) were infected in the year 2020 and 30 (39.4%) in 2021 (second wave). Strikingly, 3 (3.9%) of respondents were infected in both 2020 and 2021. Among the respondents who were infected with COVID-19, fever alone or in combination with body ache or cough 51(67.1%) was most common presenting symptom followed by loss of taste or smell in 47 (61.8%) respondents. Of all the COVD-19 patients, only one (1.3%) person required intensive care unit (ICU) admission and 11 (14.4%) required care in a hospital for their symptoms. Vast majority of respondents 60(78.9%) recovered in home isolation alone. Seven (9.2%) respondents were admitted in private hospitals. The cost of treatment in the private hospital ranged from rupees 30,000 to as high as 3-5 lakh. Among 20 (7.5%) of all the respondents, more than three family members were affected with COVID-19, and sadly, 92 (34.3%) respondents have lost a near and dear one due to COVID-19. Among the online survey participants, 229 (85.4%) persons have received the COVID-19 vaccine. Among the vaccinated, 163 (60.8%) were residents of city, 54 (20.1%) were from a town, and 12 (4.4%) were from village. Of all vaccinated,115 (50.2%) persons have received single dose and 114 (49.8%) have received both the doses. Of the vaccinated, 20 (8.7%) have been infected with COVID-19 and only one person (0.7%) required hospitalization. It was seen from the survey that 60.7% of respondents who have had COVID-19 are absolutely fit at present.

According to Dr. Amal Chandra Kataki, Director of BBCI, good public health messaging is required during a pandemic. From this survey, it was observed that 99 (36.9%) respondents faced difficulty in regular consultation and treatment of pre-existing diseases. Of all the respondents, 177 (66.0%) felt that lockdown has resulted in psycho-social issues among children and elders at their home. Furthermore, 135 (50.3%) respondents have faced financial hardship due to lockdown. The present and the earlier survey among health care workers, reveals that vaccines reduces need for hospitalization and protect from severe disease, further informed Dr. Kataki.

According to Dr. Manigreeva Krishnatreya, Medical Officer of BBCI, there should be a balance between mitigation of risk for COVID-19 and loss of livelihoods during pandemic. Also, we have noted that a significant proportion of respondents have faced difficulty in the treatment of hypertension, cancer etc., during the pandemic. The lateral integration of health care is the need of the hour during the pandemic, further said Dr. Krishnatreya.

Dr. B. Borooah Cancer Institute

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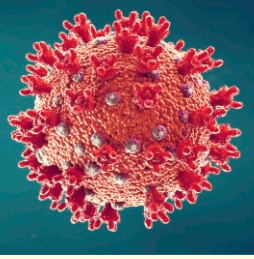

IMPACT OF COVID-19 INFECTION ON HEALTH CARE PROVIDERS

An online survey was conducted by Dr. B Borooah Cancer Institute (BBCI), Guwahati to determine the impact of Coronavirus disease 2019 (COVID-19) among doctors of North East (NE) India. A total of 146 doctors from across the NE region participated in the survey. The survey found that 43.8% of doctors were actively engaged in COVID-19 duty and the majority (59.6%) of the doctors who participated in the survey was specialist physicians. The age of doctors in the online interview ranged from 25 years to 71 years. Hypertension (34.2%) followed by diabetes (15.1%) were common comorbidities among interviewed doctors.

As per the online survey, 22.6% of doctors were infected with COVID-19 in 2020. Among doctors of the survey who were diagnosed with COVID-19, fever and body ache were most common symptoms, as seen in 61% of participants of the survey. Cough was present in 60% and breathing difficulty was present in 6% of doctors who were affected with COVID-19 last year. Among 146 participants of the online interview, 12 (8.2%) doctors required hospitalization for COVID-19 in 2020. Only 2.1% of doctors received convalescent plasma therapy and 4.1% received remdesivir (antiviral drug). None of doctors in the online survey required ventilator support due to critical symptoms of COVID-19. In 6% of doctors who participated in the online survey, more than 3 family members were affected with COVID-19. In around 14% of doctors, more than three family members suffered from COVID-19. It was observed that over 97% of doctors were vaccinated against COVID-19, and of them, 83% have received both the doses of the vaccine. Twenty (13.6%) doctors tested positive for COVID-19 even after receiving the vaccine. However, only one (0.7%) doctor required hospitalization in post vaccination COVID-19. This is miniscule compared to 8.2% who required hospitalization last year in the absence of vaccination. It was sad to note that 35% of interviewed doctors have lost a near and dear one due to COVID-19. It was heartening to observe that 90% of respondent doctors were determined to serve the people even after being fatigued from work for more than 1 year and 3 months. Only 10% of doctors were not sure whether they can continue to serve people like in pre-pandemic time because of the emotional and physical fatigue that has set in. Over 71% of doctors believe that we can overcome this crisis sooner than later. Only one doctor was having post COVID-19 complications and rest all were doing fine.

In another survey among healthcare workers of BBCI, it was observed that 23% suffered from COVID-19 last year and 6% of healthcare workers of the institute required hospitalization. Around 24% of healthcare worker's family members were affected with COVID-19. Among healthcare workers of BBCI, 86% have received the COVID-19 vaccine and 26% have received both doses of the vaccine.

According to Dr Amal Chandra Kataki, Director of BBCI, healthcare workers across the world have done a yeoman's job during the pandemic. It was challenging in many ways. First, the risk of becoming infected and then there was the possibility of infecting near and dear ones, especially elderly people in the family. Despite all the personal risks, healthcare workers continued to serve the needy patients in this difficult time and it is commendable. This survey is first of its kind, which will be useful for policymakers to understand actual needs of frontline workers and in order to execute further planning, further informed Dr Kataki.

We invite scientific articles from practicing oncologists, researchers, academicians and students of various disciplines of oncology and allied sciences for publication in coming issues.

Please send your contributions to the e-mail : das.drgaurav@gmail.com
We express our utmost gratitude for your support.

Thank you!

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editor : Dr. Gaurav Das
design : Surachandra Phuritsabam

das.drgaurav@gmail.com
bbci_info@yahoo.co.in
+91 99570 33199
99570 33212
www.bbcionline.org
www.bbcionline.in
A. K. Azad Road, Gopinath Nagar
Guwahati -781016, Assam, India

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