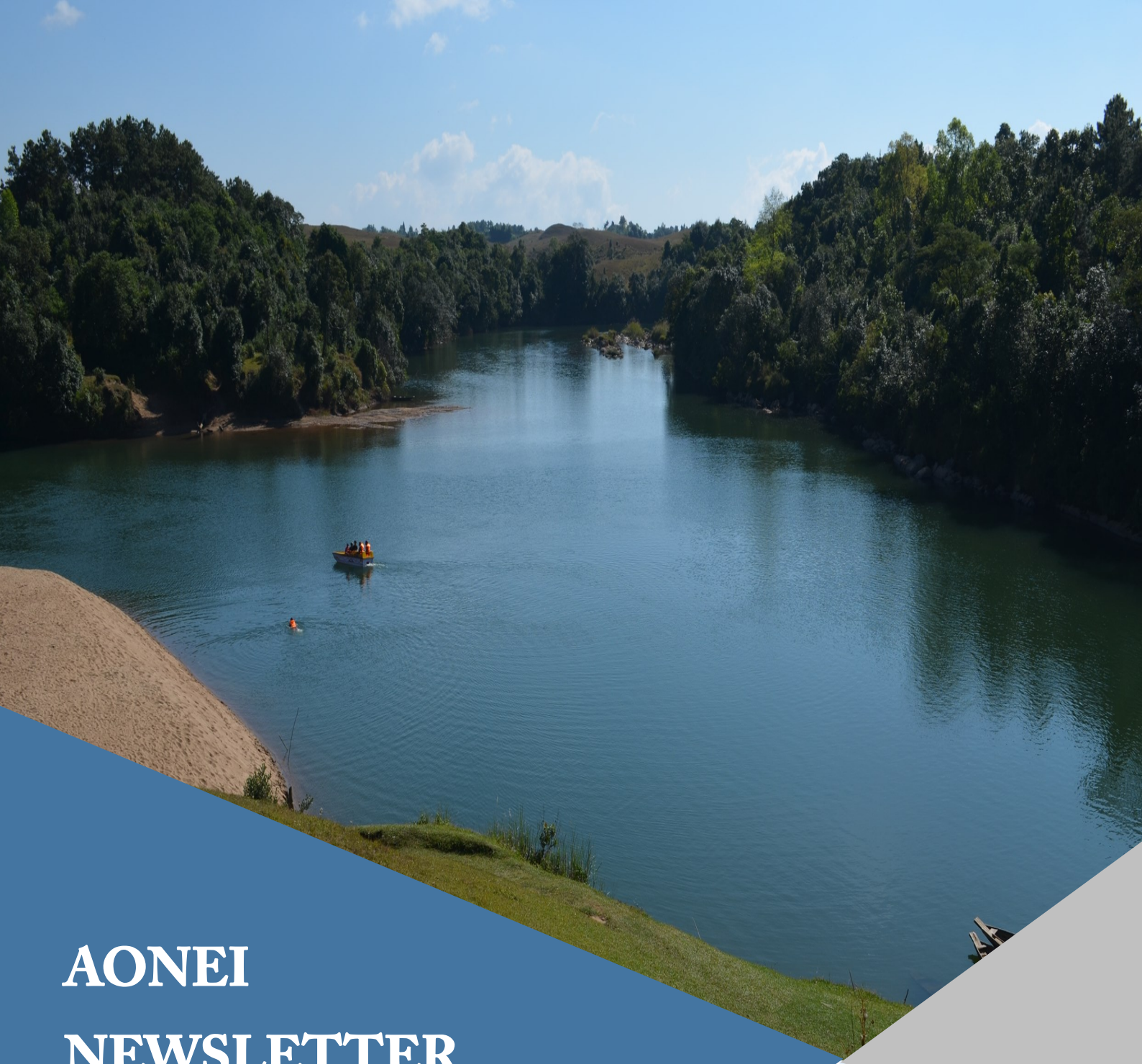


AONEI NEWSLETTER

DARPAN – A reflection of AONEI activities

Volume 1; Issue 5 : January 2019

Inside this issue :

Editor's note

Its my pleasure to greet you all through the 5th issue of this newsletter. The Northeast Region of India is gaining importance and we need to enable the improvement of healthcare in this region. Even the 'Look East Policy' of the government has been changed to 'Act East Policy', wherein greater cooperation with the other countries in this region is envisaged. While this opens up a lot of potential for medical tourism, we are still struggling with the provision of cancer care to our own countrymen, and need to do our part in improving cancer care.

The purpose of this newsletter is not only to inform all our members of the activities of the association, but also to update ourselves on the changing management protocols for the cancers common to this region. Relevant topics have been reviewed by authors who understand the needs and limitations of Northeast India. Also, we have published some original work done by youngsters of the region.

In 2018, we had our annual meeting at Guwahati in February and two mid-term CMEs- on Gynaecological cancers at Shillong in July and Gall bladder/Ovarian Cancers at Dibrugarh in September. The reports and pictures of these events are published in this issue.

It was heartening to see the promptness which the contributors have shown this year, and I wish to thank them for the same. Special thanks to Christopher Zorammuana and Marina H L Laskor (MBBS students) for the creativity displayed in designing this newsletter, and to Vikas Jagtap for his support.

Caleb Harris

Editor and website in-charge

Associate Prof. Surgical Oncology,

NEIGRIHMS, Shillong

Cover photo : Nongkhnum river island, Meghalaya (PC : Dr. B. Nongrum)

Time to demote 'convenient standard': Weekly cisplatin besieged!

Dr.Avinash Vijaykumar Pandey, M.D., D. M.(Med. Onco.)
Asst. Professor and Head (Incharge),
Department of Medical Oncology,
State Cancer Institute/RCC,
I.G.I.M.S,Patna, Bihar

Dr. Avinash Pandey is a young and dynamic oncologist, who after completing his M.D. in Radiotherapy, went on to train in Medical Oncology from Tata Memorial Centre, Mumbai. He is dynamic and has built the department of Medical Oncology at his institute, where he performed the first bone marrow transplant. He loves reading and writes on a wide range of issues.

In India, incidence of oral cavity cancer is among the highest in the World with 16.4 and 10.6 per 100000 population, in men and women respectively.[1] Unlike in Western countries, where oropharyngeal carcinoma is racing far ahead compared to oral cavity cancer, riding on the wave of HPV infection, in India Oral cavity carcinoma continues to rise alarmingly as use of tobacco, areca nut, gutkha, pan masala and betal quid are still rampant and thrive unabated.[1] Only one-fifth of oral cavity cancer present with operable disease while majority suffer inferior outcomes due to advanced unresectable disease.[2] Upfront radical surgery followed by adjuvant radiotherapy with or without concurrent high dose three weekly cisplatin, as per high risk features mainly perinodal extension and margin positivity is the current standard accepted therapy with level I evidence.[3]

Two large phase III randomised controlled clinical trials paved the way to use high dose three weekly cisplatin 100mg/m^2 on day 1,22 and 49 concurrent with radiotherapy in post operative high risk oral cavity cancer resulting in improved loco-regional control and survival. Bernier et al., in one of the first randomised control trial compared adjuvant radiotherapy with or without three weekly cisplatin is postoperative head neck squamous cell carcinoma.[4] Use of cisplatin not only decreased local failures, improved progression free survival, but also increased overall survival at 5 years from 40% to 53%significantly, compared to radiotherapy alone. Albeit, this benefit came at the cost of doubling of severe grade 3 mucositis (41% versus 20%) and worsening of severe myelosuppression. However, two-third of patients received two full cycles of high dose cisplatin, while 49% manage to receive all prescribed three cycles successfully. Long term results of another similar RTOG9501/Intergroup Phase III randomised trial, continues to demonstrate reduced local failures , (33% versus 21%,p=0.02) and improved disease free survival (12.3 versus 18.4%,p=0.05) at 1o years of follow up favouring concurrent high dose three weekly cisplatin over post operative radiotherapy alone.[5] This also consolidated the rationale of using concurrent cisplatin, only in high risk postoperative pathological features such as perinodal extension and positive margin, while excluding only nodal positivity as selection criteria for using cisplatin with radiotherapy.

Despite above robust evidence favouring three weekly high dose cisplatin, weekly cisplatin was widely adopted, especially

in limited resource countries citing lesser toxicity, ease of administration, better tolerances, better radiosensitization and less chemoresistance as competing arguments. Major academic centres in India have relied on the 'backbone' of weekly low dose concurrent csiplatin as radio-sensitizer to post operative radiotherapy in oral cavity cancer. Gupta et al in a retrospective review of 264 patients justified weekly cisplatin 30 mg/m2 as preferred candidate for optimum regime for concurrent chemoradiotherapy with 5 year local control of 57% and acceptable grade III mucositis (29%) with two-third of patients receiving planned dose of cisplatin.[6] Moreover, in subsequent prospective trials, researchers from same institute continued weekly cisplatin 30mg/m2 as control arm in concurrent chemotherapy for comparing outcomes with accelerated hyperfractioned radiotherapy and conventional radiotherapy.[7,8] Sarbani et al, showed better loco regional control (49% versus 32% at 5 year, p=0.049) favouring concurrent chemoradiotherapy.[7] Another premier Indian institute used 40mg/m2 of weekly cisplatin in Phase II randomised trial comparing chemoradiotherapy versus radiotherapy alone in predominantly oropharngeal carcinoma in definitive setting. They demonstrated better locoregional control and overall survival albeit with 40% patients receiving weekly cisplatin requiring admission for grade III mucositis.[9]

To settle the debate it was prudent to conduct randomised control trial comparing high dose three weekly cisplatin versus weekly low dose cisplatin along with radiotherapy in high risk postoperative oral cavity carcinoma, especially in India ,where oral cavity carcinoma is major health care problem. Recently, Noronha et al reported one of the largest randomized non-inferiority Phase III trial of concurrent weekly cisplatin 30 mg/m2 versus once every 3 weeks cisplatin 100 mg/m2 (high dose) for definitive and adjuvant chemoradiotherapy for stage III and IV HNSCC.[10] The majority of the 300 randomly assigned patients had oral cavity squamous cell carcinoma and received treatment in the adjuvant setting (92.7% in the weekly arm v 93.3% in the high-dose arm). Completion of planned treatment was achieved in 94% in the high-dose arm and in 88.7% in the weekly arm. The trial demonstrated a significant difference in the 2-year locoregional control rate, the primary end point: 58.5% in the weekly arm and 73.1% in the high-dose arm (P 5 .014; HR, 1.76 [95% CI, 1.11 to 2.79]) after a median follow-up of 22 months. The progression-free survival (PFS) results favoured the high-dose arm, but there were no significant differences in PFS or overall survival. This should reasonably settle the debate in favour of using 100mg/m2 every 3weeks concurrent with radiotherapy as new standard of choice for at least all oral cavity post operative chemoradiation.

It is however, interesting to note that a survey conducted among Indian oncologists after above results were published to acknowledge the pattern of cisplatin use in concurrent setting with radiotherapy in common community practice demonstrated significant bias still favouring weekly low dose cisplatin. Goyal et al in above survey illustrated that weekly cisplatin schedule (87.9%) triumphs over three weekly cisplatin100 mg/m2 (8.9%) as most favourable choice in community practice. Majority of respondents were radiation oncologists (63.8%), in private oncology setup (47.9%) and relatively young in practice (44%).[11] Better tolerance (59.5%) of weekly cisplatin was most common reason cited for preference. More interesting was to acknowledge that when it comes to choice between dose of weekly cisplatin, only 25% of responders mentioned 30mg/m2 weekly, while 60% preferred 40mg/m2 weekly schedule. As inferiority of 30mg/m^2 of cisplatin to high dose three weekly cisplatin was comprehensibly achieved by Noronha et al, for those still sceptical and wondering whether 40mg/m2

could withstand the formidable challenge for three weekly concurrent cisplatin, will have to eagerly await outcomes of two randomised clinical trial addressing above question.

Concrete and decisive action needs to be taken urgently in order to promulgate the role of high dose 100mg/m2 cisplatin three weekly as choice of schedule of cisplatin over weekly cisplatin among Indian oncologists as one of the largest clinical randomised trial conducted in India, upholds the old 'gold standard'. This also hold true that the 'perceived' ease of administration and 'limited' resources should not take precedence over better loco regional control and possibly survival, for which radical change in psyche is merited and clinical lethargy needs to be amended for better patient outcomes.

References

1. Chaturvedi AK, Anderson WF, Lortet-Tieulent J, Curado MP, Ferlay J, Franceschi S, Rosenberg PS, Bray F, Gillison ML. Worldwide trends in incidence rates for oral cavity and oropharyngeal cancers. Journal of clinical oncology. 2013 Dec 20;31(36):4550.

2. Sankaranarayanan R. Oral cancer in India: an epidemiologic and clinical review. Oral surgery, oral medicine, oral pathology. 1990 Mar 1;69(3):325-30.

3. National Comprehensive Cancer Network: NCCN Clinical Practice Guidelines in Oncology, NCCN Evidence Blocks: Head and neck cancers version 2.2017.https://www.nccn.org/professionals/ physician_gls/pdf/head-and-neck.pdf

4. Bernier J, Domenge C, Ozsahin M, Matuszewska K, Lefèbvre JL, Greiner RH, Giralt J, Maingon P, Rolland F, Bolla M, Cognetti F. Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. New England Journal of Medicine. 2004 May 6;350(19):1945-52

5. Cooper JS, Zhang Q, Pajak TF, Forastiere AA, Jacobs J, Saxman SB, Kish JA, Kim HE, Cmelak AJ, Rotman M, Lustig R. Long-term follow-up of the RTOG 9501/intergroup phase III trial: postoperative concurrent radiation therapy and chemotherapy in high-risk squamous cell carcinoma of the head and neck. International Journal of Radiation Oncology* Biology* Physics. 2012 Dec 1;84(5):1198-205

6. Gupta T, Agarwal JP, Ghosh-Laskar S, Parikh PM, D'Cruz AK, Dinshaw KA. Radical radiotherapy with concurrent weekly cisplatin in loco-regionally advanced squamous cell carcinoma of the head and neck: a single-institution experience. Head & neck oncology. 2009 Dec;1(1):17.

7. Ghosh–Laskar S, Kalyani N, Gupta T, Budrukkar A, Murthy V, Sengar M, Chaukar D, Pai P, Chaturvedi P, D'cruz A, Agarwal J. Conventional radiotherapy versus concurrent chemoradiotherapy versus accelerated radiotherapy in locoregionally advanced carcinoma of head and neck: Results of a prospective randomized trial. Head & neck. 2016 Feb;38(2):202-7.

8. Laskar SG, Chaukar D, Deshpande M, Chatterjee A, Hawaldar RW, Chakraborty S, Sharma S, Agarwal JP, Gupta T, Budrukkar AN, Murthy V. Phase III randomized trial of surgery followed by conventional radiotherapy (5 fr/Wk) (Arm A) vs concurrent chemoradiotherapy (Arm B) vs accelerated radiotherapy (6fr/Wk)(Arm C) in locally advanced, stage III and IV, resectable, squamous cell carcinoma of oral cavity-oral cavity adjuvant therapy (OCAT): Final results (NCT00193843).

9. Sharma A, Mohanti BK, Thakar A, Bahadur S, Bhasker S. Concomitant chemoradiation versus radical radiotherapy in advanced squamous cell carcinoma of oropharynx and nasopharynx using weekly cisplatin: a phase II randomized trial. Annals of oncology. 2010 Apr 28;21(11):2272-7.

10. Noronha V, Joshi A, Patil VM, Agarwal J, Ghosh-Laskar S, Budrukkar A, Murthy V, Gupta T, D'Cruz AK, Banavali S, Pai PS. Once-a-week versus once-every-3-weeks cisplatin chemoradiation for locally advanced head and neck cancer: a phase III randomized noninferiority trial. Journal of Clinical Oncology. 2017 Dec 8;36(11):1064-72.

11. Goyal G, Patil VM, Noronha V, Joshi A, Khaddar S, Kakkar S, Pruthy R, Parikh P, Prabhash K. Once-a-week versus once-every-3-weeks cisplatin in patients receiving chemoradiation for locally advanced head-and-neck cancer: A survey of practice in India. Cancer Research, Statistics, and Treatment. 2018 Jan 1;1(1):63.

CLINICAL IMPORTANCE OF SYNCHRONOUS COLORECTAL CANCER: A CASE REPORT

Dr. Gaurav Das
M.S., MCh, Assistant Professor, Surgical Oncology
Dr. B. Borooah Cancer Institute, Guwahati

BACKGROUND:

The presence of multiple tumours in the colon is an uncommonly encountered clinical scenario. The importance of a comprehensive endoscopic and radiological evaluation of colonic tumours cannot be over-emphasized.

CASE PRESENTATION:

A 53 year old gentleman was evaluated for the complaints of pain abdomen and weight loss of 6 months duration. He had received 3 blood transfusions for anemia during this period. His performance status was good(ECOG 1) and clinical examination was unremarkable. Imaging with contrast CT scan showed asymmetric wall thickening in the ascending colon with pericolonic fat stranding and enlarged pericolic nodes. Colonoscopy showed an ulcerated obstructive growth occluding the lumen at the region of transverse colon beyond which the scope could not be negotiated. Biopsy showed adenocarcinoma grade 1. Serum CEA was 7.46 ng/dl. At laparotomy, there was no evidence of metastatic disease. Two separate tumors were appreciated, one in the ascending colon and another one in the mid-transverse colon, separated by a distance of about 10 cms. Extended right hemicolectomy with complete mesocolic excision and central vascular ligation was done. The patient had an uneventful recovery and was discharged on post-operative day 6. At grossing, three separate tumours were identified. The final histopathology report showed three tumours, with dimensions 7 cm × 5.5 cm × 2 cm, 7 cm × 4.5 cm × 2.5 cm and 6.5 cm × 5 cm × 3 cm, the first two tumours being located in the ascending colon, separated by a distance of 1 cm and the last one was located in the transverse colon 7 cm distal to the second tumour. All three were well-differentiated adenocarcinomas with infiltration to the muscularis propria and pericolonic tissues but intact visceral peritoneum. Lymphovascular and perineural invasion were not seen. All the 15 nodes dissected were free of tumour. The final pathological stage was pT3N0M0 stage group IIA (AJCC 8).

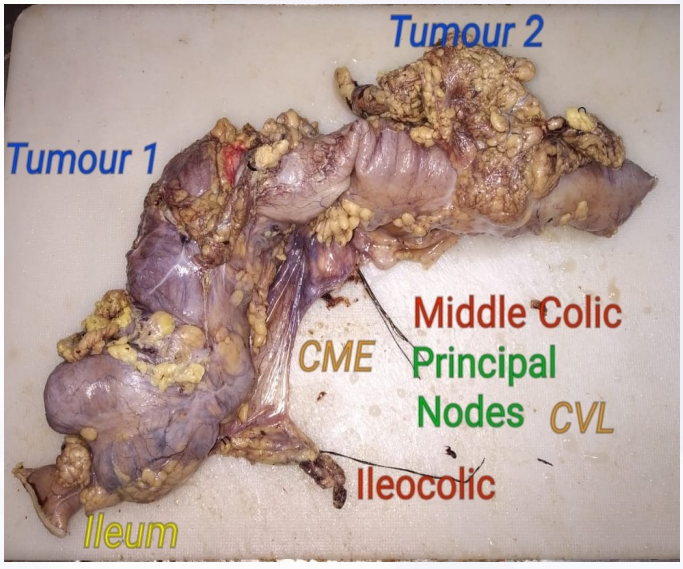


Figure 1: Specimen with two tumours felt on palpation, one in ascending colon and another in the transverse colon

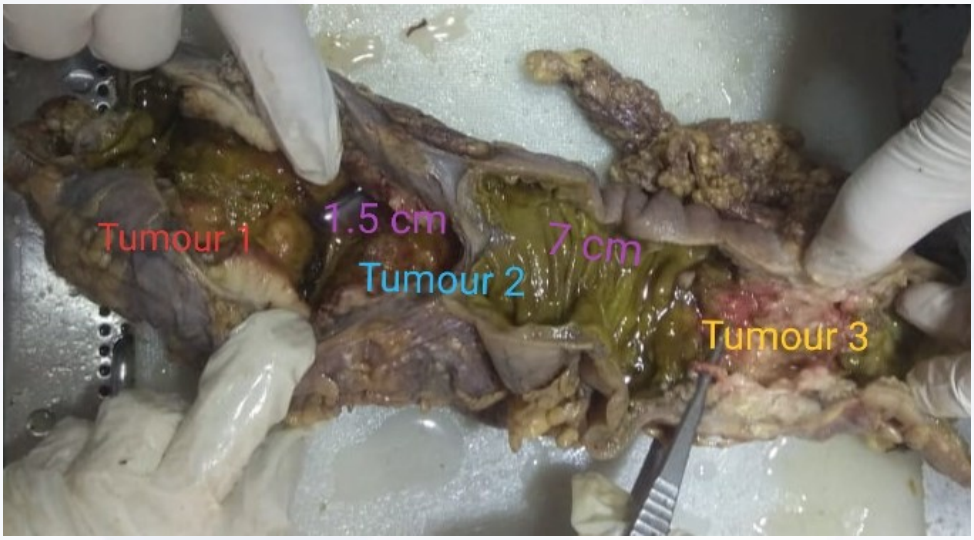


Figure 2: Cut open specimen showing three tumours. The first and the second one are separated by 1.5 cm of normal mucosa and the second and the third one are separated by 7 cm of normal mucosa.

DISCUSSION:

In India, the age adjusted incidence rates (AAR) for colon cancer are 4.4 and 3.9 per 100,000 among men and women respectively. Women of Nagaland (5.2) and Aizawl (4.5) have the highest incidence rates of colonic cancers in India[1].

The colonic mucosa has a large surface area. High and low penetrance genetic variants as well as environmental exposures can affect this large field and lead to several foci of colorectal cancer which may manifest simultaneously or over time. The development of two or more different tumours in the colon is called multiple primary colorectal cancer (MPCRC); when they are diagnosed at the same time, it is called synchronous colorectal cancer (SCRC) and when diagnosed later (after 6 months), is termed metachronous colorectal cancer (MCRC)[2].

The Warren and Gates criteria[3] for SCRC include: a) each tumour must present a definite picture of malignancy; b) each tumour must be distinct; c) the probability of one being a metastasis of the other must be excluded; d) the synchronous lesions must be diagnosed simultaneously or within 6 months of the initial diagnosis.

The incidence of synchronous colorectal cancers (SCRC) ranges between 1.1 and 8.1%. It has a male to female ratio of 1.8:1.Well-established risk factors include familial CRC syndromes and ulcerative colitis but these predisposing factors account for slightly more than 10% cases of SCRC[4].

Majority of the patients with SCRC have two tumours, but upto 7 synchronous cancers have been reported. The most advanced cancer is designated as the index cancer and the less advanced cancers (with lower T stage) are considered as concurrent lesions. If two or more lesions have identical T stage, the largest lesion is designated as the index cancer. The location of the index and concurrent lesions is important since it has surgical implications.

There is no consensus on the relationship between age and the incidence of SCRCs with disparities seen among studies. Concurrent adenomas are significantly higher in patients with SCRCs than in solitary cancer, reported as 34.1% and 19.1% respectively in one study. This emphasizes the preponderance of the adenoma-carcinoma sequence in SCRCs. Various authors have reported on a high incidence of microsatellite instability (MSI) among SCRCs as compared to solitary lesions, with incidence as high as 32%. Epigenetics has a major role in the carcinogenesis of sporadic SCRC. 31% to 62% of SCRCs have loss of MLH1 protein expression

because of hypermethylation of the promoter region[2].

Alcohol consumption has been associated with a relative risk of 6.8 compared to non-drinkers. It is hypothesized that alcohol may render the entire colorectal mucosa unstable, making it more susceptible to malignant changes. Other environmental factors that cause damage to the colonic mucosa (eg: smoking and eating foods cooked at high temperatures) may be responsible for SCRC[5].

In the management of multiple tumours, intraoperative palpation has been found to be insensitive with more than 50% failure rate in detecting lesions of SCRCs[6]. Hence, a pre-operative complete colonoscopic evaluation is mandatory unless there is an obstructive tumour where the study of the proximal bowel is hindered. In such cases, the use of intra-operative colonoscopy, if available, is recommended. If pre-operative colonoscopic evaluation is incomplete, the follow up colonoscopy is to be scheduled at 3 to 6 months of the definitive surgery. CT colonography (virtual colonoscopy) is of value in patients where colonoscopy is incomplete, for a pre-operative assessment[7].

Some authors have suggested a total or subtotal colectomy or total proctocolectomy, reasoning that missed synchronous lesions may result in repeated surgery. Others favour a more conservative policy with multiple segmental resections aimed to preserve normal colon. There is no consensus on doing a total colectomy or proctocolectomy as is done in proven cases of HNPCC or FAP, if either the right or the left colon is only involved.

In our patient, there are no other high risk features (according to high risk features listed by NCCN). An elevated preoperative CEA level is the only poor prognostic factor according to CAP criteria. The immunochemistry results for MSI are awaited. The presence of a MSI-H phenotype in the setting of a stage IIA colon cancer will mean that the patient is unlikely to derive a significant benefit from a 5FU/LV based adjuvant chemotherapy regimen.

Colonoscopic evaluation in our patient had been done upto the obstructive, most distal lesion and no other mucosal abnormality was noted. With an extended right hemicolectomy, the entire non- visualized colon has been removed. The follow up for the left colon will include a colonoscopy at 1 year. If this is normal, the next colonoscopy will be at 3 years and subsequently every 5 years. Clinical examination every 3 months for the first 2 years, then every 6 months for the next 3 years and then annually will be done. At every visit, serum CEA will be checked till 5 years of follow up. A chest X ray and a CT scan of the abdomen will be done annually for 5 years.

SCRCs have similar stage-wise survival when compared to solitary tumours even though there are authors who have shown better survival and others who have suggested poorer prognosis.

Significance of SCRCs:

1. Multiple tumours provide a good model to examine common molecular alterations and a potential field effect.

2. It provides an opportunity to study the efficacy of prophylactic actions like chemoprevention

3. There is a real chance of missing concurrent lesions that will necessitate repeat surgery

4. In the revised Bethesda guidelines, the presence of synchronous or metachronous colorectal cancers is an indication for screening for HNPCC. MSI testing has to be done.

LEARNING POINTS:

1. Pre-operative complete colonoscopy is mandatory in the evaluation of colorectal cancer, unless there is an obstructive tumour.

2. Multiple colonic tumours is an indication for testing for MSI.

REFERENCES:

1. NCRP (2013) Three-year report of the population based cancer registries- 2009-2011. National cancer registry programme, Indian council of medical research (ICMR), Bangalore, India, 2013.

2. Pajares JA, Perea J. Multiple primary colorectal cancer: Individual or familial predisposition? World J Gastrointest Oncol 2015; 7(12): 434-444

3. Warren S, Gates O: Carcinoma of ceruminous gland. Am J Pathol 1941; 17: 821–826.3.

4. Kato et al. Clinical characteristics of synchronous colorectal cancers in Japan World Journal of Surgical Oncology (2016) 14:272

5. Jun Yang *et al.* Synchronous Colorectal Cancers: A Review of Clinical Features, Diagnosis, Treatment, and Prognosis. Dig Surg 2011; 28:379–385

6. Arenas RB, Fichera A, Mhoon D, Michelassi F: Incidence and therapeutic implications of synchronous colonic pathology in colorectal adenocarcinoma. Surgery 1997; 122: 706– 709, discussion 709–710.

7. Neerincx M *et al.* Colonic work up after incomplete colonoscopy. Endoscopy 2010; 42: 730-735

Role of adjuvant Radiotherapy in Resectable Gastric Cancer

Dr. Rubu Sunku [1], *Dr. Partho P Medhi* [2]

[1] *TRIHMS, Naharlagun, Arunachal Pradesh*

[2] *BBCI, Guwahati, Assam*

BACKGROUND:

Gastric cancer has very high incidence as well as mortality worldwide. Following surgery in gastric cancer, the rate of locoregional recurrence is very high. Although increase in extent and improvement in quality of surgery has decreased the failure rate, the modality of adjuvant treatment still remains under debate. Several trials such as INT-0116, MAGIC, ARTIST, FLOT4 etc, has shown the benefit of chemotherapy/ chemoradiotherapy, but controversy remains regarding the role of post-operative radiotherapy and optimum timing and agent of chemotherapy. Here we review the role of radiotherapy in post-operative gastric cancer in the era of D2 lymphadenectomy and discuss the result of various landmark trials.

INTRODUCTION:

Gastric cancer is 3rd most common cause of cancer mortality worldwide according to GLOBACON 2018 (1). There is a wide variation in incidence rate among different regions of the world, with a very high incidence in Asian countries such as Japan, Korea and China. In India, North-Eastern region of the country records a very high incidence of stomach cancer, being 3rd most common site of cancer among men (2). Treatment methodology of stomach cancer still varies among oncologists and between Western and Asian countries. The standard surgery in gastric cancer in

high volume centres such as in Japan and South Korea, includes routine D2 lymph nodal dissection, which gives better survival than D1 or lesser lymphadenectomy[3]. Locoregional recurrence after surgery is as high as 15% to 45%, depending upon quality of surgery, which rationalizes the requirement of adjuvant radiotherapy[4].

CURRENT SCENARIO IN TREATMENT OF GASTRIC CANCER :

Surgery remains the main modality of curative treatment, but general practice of surgical resection in stomach cancer varies between Western and Asian country. Debate on extent of surgical resection persisted for several decades. Dutch Gastric Cancer trial and UK Medical Research Council failed to show any added benefit of survival in D2 resected group, but this failure was attributed to high post op morbidity and mortality [5,6]. The 15 years follow up of the Dutch trial showed improved survival in D2 resected group [7]. A phase II trial by Degeuli showed that pancreas preserving D2 resection is safe and beneficial, even when performed by surgeons in the Western world, with sufficient training [8]. After these trials, surgical resection with D2 lymphadenectomy is accepted as standard and recommended surgery in resectable gastric cancer. But in practice, D2 lymphadenectomy is not yet uniformly performed outside some east Asian countries as seen in large database analysis by National Cancer Database Analysis and hence NCCN recommends gastric resection with D1 or modified D2 lymph node dissection with goal of examining $\geq$ 15 lymph nodes [9,10].

MAGIC trial in 2006 established the role of perioperative chemotherapy in gastric and lower esophageal adenocarcinoma. Perioperative chemotherapy with Epirubicin, Cisplatin and 5FU (ECF) in MAGIC trial improved 5 year survival from 23% to 36%, but none of the patients had complete pathological response, despite which the same chemotherapy was continued postoperatively [11]. Recently, FLOT4 trial showed that perioperative chemotherapy with 5FU, Leucovorin, Oxaliplatin and Docetaxel improve 3 years survival to 57% from 48% seen in the ECF/ECX group [12]. Further study of targeted therapy such as Trastuzumab in ToGA trial and Lapatinib in MAGIC B trial will increase the scope of systemic therapy in gastric cancer. But as of now, none of the chemotherapy regimen can be considered standard [13,14].

Role of adjuvant chemoradiotherapy in resectable gastric cancer was widely accepted after the South West Oncology Group's (SWOG) land mark (Intergoup – 0116) trial in 2001[15]. Patient receiving chemoradiotherapy had better 3 years survival of 50% as compared to 41% in surgery only group. Update after 10 years of follow up showed that locoregional recurrence was significantly reduced from 47% (local -8% and Regional 39%) in surgery only arm to 24% (local 2% and regional 22%) in chemoradiotherapy arm [16]. Since this study was done before D2 resection was accepted as standard surgery, most of the patients (90%) had less than D2 lymphadenectomy, and the observed benefit of radiotherapy was attributed to compensatory effect to poor surgery. SEERS Database analysis in 2014 and National Cancer Database analysis in 2017, analysed 21,472 patients and 3656 patients respectively. Both these retrospective data showed advantage of adding adjuvant radiotherapy, although patients included in these study had heterogeneity in terms of chemotherapy regimen used and the extent of surgery [9,17]. Is D2 resection sufficient to address the locoregional control in gastric cancer? Can the

benefit of radiotherapy be replaced by extensive D2 resection? This question has to be answered to achieve best possible outcome from intervention in patients suffering from gastric cancer.

TRIALS AND CURRENT CONTROVERSIES IN THE ROLE OF RADIOTHERAPY IN GASTRIC CANCER :

Lim et al in 2004 studied the pattern of recurrence in patients undergoing chemoradiotherapy after D2 lymphadenectomy [18]. In these patients, the local recurrence was 7% and regional recurrence was 12%, which is much lower than previously reported [4]. But it is difficult to say whether this result is only because of good surgery or whether radiation had any additive effect, because it was not randomized controlled study.

To compare the effect of adjuvant chemotherapy vs chemoradiotherapy in D2 resected gastric cancer, ARTIST trial was done in Samsung Medical Center, South Korea and published in 2012 [19]. This trial did not find any added benefit of Radiotherapy to adjuvant chemotherapy of Cisplatin and Capecitabine in resected gastric cancer. The two significant drawbacks of this study were the inclusion of large number of early stage disease and failure to reach planned event (planned 227 events from total 458 patients). Approximately 60% of the patients in both chemotherapy and chemoradiotherapy arm had stage IB and II disease, therefore they had better prognosis than advanced stage disease. This also could be the reason why at mean follow up of 53.2 months, only 127 of planned 227 events (recurrences or death) were reached.

A subgroup analysis in the study showed significant prolongation of survival in node positive gastric cancer in chemoradiotherapy arm. An Update of ARTIST trial was published in 2015 after 7 years of follow up, which showed a significant difference in pattern of relapse [20]. Locoregional relapse was more frequent in chemotherapy arm (13%) as compared to chemoradiotherapy arm (7%), but no difference in distant metastasis. In chemoradiotherapy arm, 3 year disease free survival (DFS) was better among node-positive disease (72% in chemotherapy vs 76% in chemoradiotherapy arm; p = .04) and intestinal gastric cancer (83% in chemotherapy vs 94% in chemoradiotherapy arm; p = .01). Also, a trend toward improvement in DFS was seen among the patients with advanced stage. Even after 7 years of mean follow up, only 141 of planned 227 events were reached, therefore no change was seen in overall survival from previous report. From this landmark ARTIST trial, it is reported that treatment compliance and safety profile of chemotherapy and chemoradiotherapy is comparable and there are subsets of patients who benefited from addition of radiation to adjuvant chemotherapy. Since this benefit was seen in subgroup analysis only, therefore ARTIST II was initiated to verify this difference in lymph node positive gastric cancer [21].

Following results of SWOG/Intergroup 0116 trial in US and MAGIC trial in UK, adjuvant chemoradiotherapy became recommended treatment in completely resected gastric cancer in North America while perioperative chemotherapy is considered in curative treatment of gastric cancer in Europe. To compare these two standard treatments, Chemotherapy versus chemoradiotherapy after surgery and preoperative chemotherapy for resectable gastric cancer (CRITICS) trial was carried out by Dutch Cancer Society, the result of which was published in April 2018 [22]. In this study, after randomization all the patients were given preoperative chemotherapy with epirubicin, cisplatin/oxaliplatin and capecitabine, after which patients were taken up for surgery. After surgery,

only around 50% (180/392 in chemotherapy arm and 197/389 in chemoradiotherapy arm) completed the planned adjuvant treatment due to unresectable primary tumor, toxicity, death, poor general health and refusal to continue treatment. Although this study showed similar survival between the two arms, the result should be interpreted with caution, because only 60% of randomized patients could be included in this study.

Considering the high patient dropout after surgery and inability to completely administer planned treatment, preoperative chemoradiotherapy is an appealing alternate modality, which needs to be explored. A phase II trial done by Ajani et al proved the feasibility, safety and post-operative pathological complete response of >20% in patients who received neoadjuvant chemoradiotherapy[23]. Following this, a Phase III Trial Of Preoperative therapy for Gastric and Esophagogastric junction AdenocaRcinoma Trial (TOPGEAR) is being carried out, which is an international intergroup collaborated trial including Trans-Tasmanian Radiation Oncology Group (TROG), European Organization for Research and Treatment of Cancer (EORTC), National Cancer Institute (NCI) clinical trial group and led by Australasia Gastro-intestinal Trial group (AGITG) [24].

Ongoing trials such as ARTIST II trial, which is studying the role of chemoradiotherapy in post—operative lymph node positive D2 resected gastric cancer and TOPGEAR trial studying the role of preoperative chemoradiotherapy will hopefully clarify the controversy regarding the role of radiotherapy in gastric cancer [21,24].

COMPLEXITY OF POST-OPERATIVE RADIOTHERAPY IN STOMACH CANCER:

Gastric cancer is a challenging site to plan and administer radiotherapy due to following reasons –

1. Deficiency of surrounding bony landmark and fixed musculature, unlike the cancer of head and neck or pelvic region;
2. Internal motion due to bowel gas, food and peristalsis makes stomach very mobile, therefore limiting the efficacy of external immobilization device.
3. Diaphragmatic movement with respiration.
4. Planning is more challenging in post-operative cases due to distortion of anatomy.

In all the landmark trials, except in CRITICS, Antero-posterior parallel opposed 2D X ray planning was used for radiotherapy administration. Tumor bed was irradiated in all patients in INT - 0116 trial, but in ARTIST trial, tumor bed was irradiated in only T4 disease [15,19]. In CRITICS trial, all participating institute had to use 3D conformal treatment, maintaining a strict CT based delineation protocol. Jansen et al studied the interobserver variability in Clinical Target Volume (CTV) delineation among the 10 participating institutes in CRITICS trial [25]. When CTV and PTV delineation of different institutes were compared, a significant interobserver variability was seen in the index case with largest difference in cranial and caudal edge [25]. In conformal CT scan-based treatment, delineation of lymphatic target is done by tracing the blood vessels supplying the stomach [26]. Training and routine use of reference guidelines will decrease this interobserver variability in target volume [27]. Use of Surgical Clips in delineating target volume in pancreatic and hepatobiliary cancer has shown to improve accuracy [28]. In INT-0116 trial, surgical clips were used for tumor bed definition in some patients, therefore feasibility of using surgical clips to define tumor bed in post-operative radiation can be considered in gastric cancer [15]. Anatomy of stomach and volume of tumor can be better defined before surgery, due to

which pre-operative radiotherapy is an option, which should be explored and compared.

Efficacy of radiotherapy in gastric cancer, either in adjuvant and neoadjuvant setup can be studied only in presence of high degree of precision and accuracy. With advance in radiotherapy technology, need for improving the quality and quality assurance in radiotherapy technique cannot be over- emphasized.

Conclusion:

Adjuvant Radiotherapy in resectable gastric cancer improves outcome in patients who undergo D0 or D1 lymph node dissections except in very early stage, as shown by Intergroup-0116 trial and large database analyses by SEERS and National Cancer Database.

Role of radiotherapy following D2 lymphadenectomy in resectable gastric cancer remains controversial. More studies on the subgroup of patients with lymph node positive, intestinal histology and advanced stage disease is needed to conclusively define the utility of radiotherapy in gastric cancer, in adjuvant as well as in neoadjuvant setting.

References:

1. Bray F. Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A et al. Global Cancer Statistics 2018: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA CANCER J CLIN 2018; 68:394–424.
2. A Report on Cancer Burden in North-Eastern region of India 2017. National Centre for Disease Informatics and Research. Indian Council of Medical Research.
3. Degiuli M, De Manzoni G, Di Leo A, D'Ugo D, Galasso E, Marrelli D et al. Gastric Cancer: Current status of Lymph Node Dissection. WJG 2016; 22: 2875 – 93.
4. Lim DH. Postoperative Adjuvant Radiotherapy for Patients with Gastric Adenocarcinoma. J Gastric Cancer 2012;12(4):205-209
5. Hartgrink HH, van de Velde CJ, Putter H, et al. Extended lymph node dissection for gastric cancer: who may benefit? Final results of the randomized Dutch gastric cancer group trial. J Clin Oncol 2004; 22: 2069–77
6. Cuschieri A, Weeden S, Fielding J, et al. Patient survival after D1 and D2 resections for gastric cancer: long-term results of the MRC randomized surgical trial. Surgical Co-operative Group Br J Cancer 1999; 79: 1522–30.
7. Ilfet Songun, Hein Putter, Elma Meershoek-Klein Kranenbarg, Mitsuru Sasako, Cornelis J H van de Velde. Surgical treatment of gastric cancer: 15-year follow-up results of the randomised nationwide Dutch D1D2 trial. Lancet Oncol 2010; 11: 439–49.
8. Degiuli M, Sasako M, Ponti A, Calvo F. Survival results of a multicentre phase II study to evaluate D2 gastrectomy for gastric cancer. Br J Cancer 2004; 90: 1727–32.
9. Priscilla K Stumpf, Arya Amini, Bernard L Jones, Mathew Koshy, David J Sher, Christopher H Lieu et al. Adjuvant Radiotherapy Improves Overall Survival in Patients With Resected Gastric Adenocarcinoma: A National Cancer Data Base Analysis. Cancer 2017; 3402-3409.
10. NCCN Clinical Practise Guideline in Oncology. Gastric Cancer. NCCN Evidence Block. Version 2.2018.
11. Cunningham D, Allum WH, Stenning SP, Thompson JN, Van de Velde CJ, Nicolson M, Scarffe JH, Lofts FJ, Falk SJ, Iveson TJ, Smith DB, Langley RE, Verma M, Weeden S, Chua YJ. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med 2006; 355:11-20.
12. Al-Batran SE, Homann N, Schmalemberg H, et al. Perioperative chemotherapy with docetaxel, oxaliplatin, and fluorouracil/ leucovorin (FLOT) versus epirubicin, cisplatin, and fluorouracil or capecitabine (ECF/ECX) for resectable gastric or gastroesophageal junction (GEJ) adenocarcinoma (FLOT4-AIO): a multicenter, randomized phase 3 trial. *J Clin Oncol*. 2017;35(suppl; abstr 4004).
13. Bang YJ, Van Cutsem E, Feyereislova A, Chung HC, Shen L, Sawaki A, Lordick F, Ohtsu A, Omuro Y, Satoh T, Aprile G,

Kulikov E, Hill J, Lehle M, Rüschoff J, Kang YK. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. Lancet 2010; 376: 687-697

14. Audrey H Choi, Joseph Kim, Joseph Chao. Perioperative chemotherapy for resectable gastric cancer: MAGIC and beyond. World J Gastroenterol 2015 June 28; 21(24): 7343-7348

15. MacDonald JS, Smalley SR, Benedetti J, Hundahl SA, Estes NC, Stemmermann GN et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. N Engl J Med;345:725-30.

16, Stephen R. Smalley, Jacqueline K. Benedetti, Daniel G. Haller, Scott A. Hundahl, Norman C. Estes, Jaffer A. Ajani, Leonard L. Gunderson, Bryan Goldman, James A. Martenson, J. Milburn Jessup. Updated Analysis of SWOG-Directed Intergroup Study 0116:A Phase III Trial of Adjuvant Radiochemotherapy Versus Observation After Curative Gastric Cancer Resection. J Clin Oncol 30:2327-2333.

17, Steven Seyedin, Pin-Chieh Wang, Quan Zhang, Percy Lee. Benefit of Adjuvant Chemoradiotherapy for Gastric Adenocarcinoma: A SEER Population Analysis. Gastrointest Cancer Res 2014;7:82–90.

18. DH Lim, DY Kim, MK Kang, YI Kim,WK Kang, CK Park, S Kim, JH Noh, JWJoh, SH Choi, TS Sohn et al. Patterns of failure in gastric carcinoma after D2 gastrectomy and chemoradiotherapy: a radiation oncologist's view. British Journal of Cancer (2004) 91, 11 – 17.

19. Lee J, Lim DH, Kim S, Park SH, Park YS, Lim HY et al. Phase III Trial Camparing Capecitabine plus Cisplatin Versus Capeciatbine Plus Cisplatin with Concurrent Capecitabine Radiotherapy in Completely resected Gastric Cancer with D2 Lymph Node Dissection: The Artist Trial. J Clin Oncol 2012;30:268-73.

20. Park SH, Sohn TS, Lee J, Lim DH, Hong ME, Kyoung-Mee Kim, Insuk Sohn, Sin Ho Jung et al. Phase III Trial to Compare Adjuvant Chemotherapy With Capecitabine and Cisplatin Versus Concurrent Chemoradiotherapy in Gastric Cancer: Final Report of the Adjuvant Chemoradiotherapy in Stomach Tumors Trial, Including Survival and Subset Analyses. J Clin Oncol 2015;33: 3130-36.

21. Se Hoon Park, Su Jin Lee, Seung Tae Kim, Jeeyun, Joon Oh Park, Young Suk Park et al. Multicenter phase III trial of adjuvant chemoradiotherapy in stomach tumors 2 (ARTIST 2). J Clin Oncol 2017;33 (suppl)

22. Cats A, Jasen EPM, Grieken NCT, Sikarska K, Lind P, Nordsmark M, Kranenbarg EM et al. Chemotherapy Verus Chemoradiotherapy after surgery and preoperative chemotherapy for resectable gastric cancer (CRITICS): an international,open label, randomised phase 3 trial. Lancet Oncol 2018;19: 616-28.

23. Jaffer A. Ajani, Kathryn Winter, Gordon S. Okawara, John H. Donohue, Peter W.T. Pisters, Christopher H. Crane, John F. Greskovich, P. Rani Anne, Jeffrey D. Bradley, Christopher Willett, Tyvin A. Rich. Phase II Trial of Preoperative Chemoradiation in Patients With Localized Gastric Adenocarcinoma (RTOG 9904): Quality of Combined Modality Therapy and Pathologic Response. J Clin Oncol 24:3953-3958

24. Leong T, Smithers BM, Haustermans K, Michael M, Gebski V, Miller D, Zalcberg J, Boussioutas A, Findlay M, O'Connell RL, Verghis J, Willis D, Kron T, Crain M, Murray WK, Lordick F, Swallow C, Darling G, Simes J, Wong R. TOPGEAR: A randomised phase III trial of perioperative ECF chemotherapy versus preoperative chemoradiation plus perioperative ECF chemotherapy for resectable gastric cancer (an international, intergroup trial of the AGITG/TROG/EORTC/NCIC CTG). BMC Cancer (2015) 15:532. DOI 10.1186

25. Edwin P.M Jansen, Jasper Nijkamp, Michael Gubanski, Pehr A.R.M Lind, Marcel Verheij et al. Interobserver variation of clinical target volume delineation in gastric cancer. Int. J. Rad Oncol Biol. Phys., Vol. 77, No. 4, pp. 1166–1170, 2010.

26. Yu Haijun, Wu Qiuji, Fu Zhenming, Huang Yong, Liao Zhengkai, Xie Conghua, Zhou Yunfeng, Zhong Yahua. A new approach to delineating lymph node target volumes for post-operative radiotherapy in gastric cancer: A phase II trial. Radiotherapy and Oncology 2015;116:245-251.

27. Onal C, Mustafa C, Guler O, Dolek Y, Ozcok S. The role of delineation education programs for improving interobserver variability in target volume delineation in gastric cancer. Br J Radiol 2017; 90: 20160826.

28. Jin Suk Bae, Dong Hyun Kim, Won Taek Kim, Yong Ho Kim, Dahl Park, Yong Kan Ki. The role of surgical clips in the evaluation of interfractional uncertainty for treatment of hepatobiliary and pancreatic cancer with postoperative radiotherapy. Radiat Oncol J 2017;35(1):65-70.

RADIOLIGAND THERANOSTICS IN METASTATIC CASTRATION - RESISTANT PROSTATE CANCER

Dr. Sandeep Taparia
D.N.B. (Nuclear Medicine)
Consultant in Nuclear Medicine, Guwahati

It is estimated that there will be almost 1.3 million new cases of prostate cancer and 359,000 associated deaths worldwide in 2018, ranking as the second most frequent cancer and the fifth leading cause of cancer death in men (1). With an aging population, more men are being diagnosed with prostate cancer. Prostate cancer incidence in recent decades has been heavily influenced by the diagnosis of latent cancers either by PSA testing of asymptomatic individuals or by the detection of latent cancer in tissue removed during prostatectomy.

Prostate cancer is an ideal target for the development of targeted radionuclide therapy because of the frequent occurrence of multi-focal disseminated disease when it recurs after treatment of disease initially thought to have been confined to the prostate gland or even at presentation in patients with advanced disease.

What is PSM, targeted imaging and targeted therapy?

PSMA is a 750 amino acid type II transmembrane glycoprotein. It is thought to have multiple cellular functions, acting as an enzyme involved in nutrient. Over 90% of prostate cancers over-express prostate specific membrane antigen (PSMA) and these tumour cells may be accurately targeted for diagnosis by ^{68}Ga-PSMA-positron emission tomography/computed tomography (^{68}Ga-PSMA-PET/CT) imaging. Apart from the significantly higher diagnostic sensitivity that 68Ga-PSMA PET/CT offers, it also constitutes the therapeutic armamentarium, complementing the 177Lutetium-PSMA [2] and more recently the 225Actinium-PSMA [3], theranostic pairs, both currently being investigated for the therapy of metastatic castrate resistant prostate cancer (mCRPC). Castration-resistant prostate cancer (CRPC) is defined by disease progression despite castrated levels of testosterone, and may present as either a continuous rise in serum prostate-specific antigen (PSA) levels, the progression of pre-existing disease, and/or the appearance of new metastases [4].

Ge-68/Ga-68 generator is used to produce positron-emitting radionuclide Ga-68. The parent isotope Ge -68 has a half-life of 270.95 days. Gallium-68 (with a half-life of only 67.71 minutes, difficult to transport) can be easily eluted from the generator any time at the site of application. PSMA ligand comes as cold kit, which is labelled with Ga-68 for imaging under PET CT machine.

177Lutetium and 225Actinium are beta and alpha emitters, labelled with PSMA, and are used for therapeutic application. Since 2013, an increasing number of centres worldwide have begun employing radioligand therapy (RLT) using 177Lu-PSMA [5].

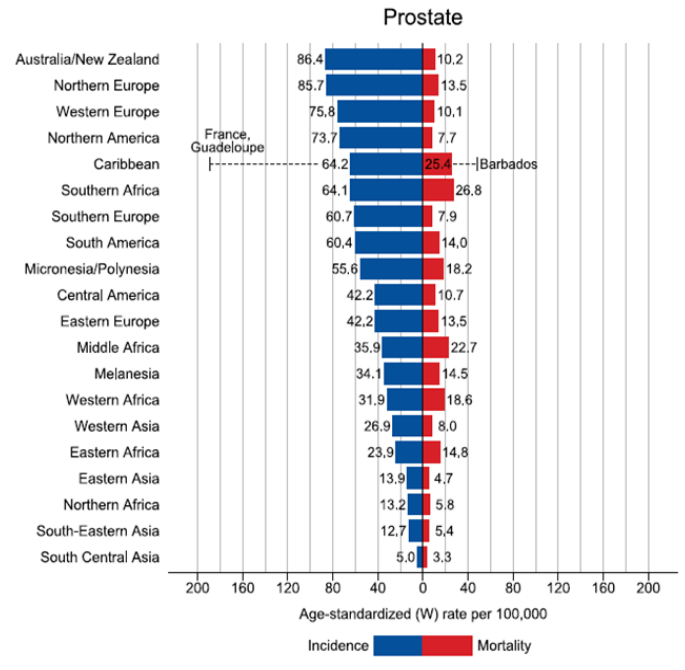


Figure 11: Bar Chart of Region-Specific Incidences and Mortality Age-Standardised Rates for Cancers of the Prostate in 2018. Rates are shown in descending order of the world (W) age-standardised rate, and the highest national age-standardised rates for incidence and mortality are superimposed. Source: GLOBOCON 2018

Indications for RLT:

The current essential inclusion criteria, as stated in the 2016 consensus recommendations of the German Society of Nuclear Medicine [6]:

1) Histologically detected prostate carcinomas;

2) Non-resectable metastases;

3) Tumour progression under guidelines therapy;

4) Detected PSMA expression of the tumour;

5) Reasonable haematological function (leukocyte count > 2.0 × 109/L, thrombocyte > 75 × 109/L);

6) Normal or slightly decreased renal function (creatinine < 2 x the upper standard limit);

7) Sufficient liver function (aspartate aminotransferase [AST] or alanine aminotransferase [ALT] < 5 x the upper standard limit); and

8) Six-week interval with myelosuppressive therapy.

Response rate:

Up to 80% of patients with mCRPC will have a treatment response to 177Lu-PSMA shown by any PSA decline [7, 8-10]. Studies using 177Lu-PSMA-617 and 177Lu-PSMA-I&T have observed a reduction in PSA levels by 50% or more in 32–60% of patients. Moreover, 47% of patients have experienced a stable disease [7, 8-10]. The median OS was significantly longer for patients who showed a PSA decline after the first cycle compared to patients without a PSA decline (68 versus 33 weeks respectively) [11].

Toxicity:

No grade 3–4 acute loss of renal function was detected, and this was in line with the German multicentre study with a very small probability of haematotoxicity and transient xerostomia or hypogeusia occurred in 4–37% of patients [12].

Discussion:

Ga68-PSMA PET/CT has a potential to be one stop diagnostic modality of choice for initial staging of prostatic carcinoma with high sensitivity and PPV for the localization of primary and detection of distant metastases.

Ga68-PSMA PET examination identifies higher proportion of loco-regional metastases than conventional imaging and is better than bone scintigraphy for localization of skeletal metastases.

177Lu- and 225Ac-based PSMA-targeted therapies are new and effective therapeutic agents, which seem to prolong survival in patients with advanced mCRPC pretreated with chemotherapy, aberaterone and/or enzalutamide. Lu-PSMA has shown high response rates, a low toxicity profile, and improved quality-of-life parameters especially in men with pain.

References:

1. Cancer J Clin. 2018;68:394-424. © 2018 American Cancer Society.
2. Fendler, W.P.; Rahbar, K.; Herrmann, K.; Kratochwil, C.; Eiber, M. (177)Lu-PSMA Radioligand Therapy for Prostate Cancer. J. Nucl. Med. 2017, 58, 1196–1200.
3. Kratochwil, C.; Bruchertseifer, F.; Rathke, H.; Bronzel, M.; Apostolidis, C.; Weichert, W.; Haberkorn, U.; Giesel, F.L.; Morgenstern, A. Targeted α-Therapy of Metastatic Castration-Resistant Prostate Cancer with (225)Ac-PSMA-617: Dosimetry Estimate and Empiric Dose Finding. J. Nucl. Med. 2017, 58, 1624–1631.
4. Saad F, Chi KN, Finelli A, et al. The 2015 CUA-CUOG guidelines for the management of castration-resistant prostate cancer (CRPC). Can Urol Assoc J. 2015;9:90–6.
5. Ahmadzadehfar H, Rahbar K, Kurpig S, et al. Early side effects and first results of radioligand therapy with (177) Lu-DKFZ-617 PSMA of castrate-resistant metastatic prostate cancer: a two-centre study. EJNMMI Res. 2015;5:114.
6. Fendler WP, Kratochwil C, Ahmadzadehfar H, et al. 177Lu-PSMA-617 therapy, dosimetry and follow-up in patients with metastatic castration-resistant prostate cancer. Nuklearmedizin. 2016;55:123–8.
7. Ahmadzadehfar H, Rahbar K, Kurpig S, et al. Early side effects and first results of radioligand therapy with (177) Lu-DKFZ-617 PSMA of castrate-resistant metastatic prostate cancer: a two-centre study. EJNMMI Res. 2015;5:114.
8. Kratochwil C, Giesel FL, Stefanova M, et al. PSMA-targeted radionuclide therapy of metastatic castration-resistant prostate Cancer with 177Lu-labeledPSMA-617. J Nucl Med. 2016;57:1170–6.
9. Fendler WP, Reinhardt S, Ilhan H, et al. Preliminary experience with dosimetry, response and patient reported outcome after 177Lu-PSMA-617 therapy for metastatic castration-resistant prostate cancer. Oncotarget. 2017;8:3581–90.
10. Heck MM, Retz M, D'Alessandria C, et al. Systemic Radioligand therapy with (177)Lu labeled prostate specific membrane antigen ligand for imaging and therapy in patients with metastatic castration resistant prostate Cancer. J Urol. 2016;196:382–91.
11. Ahmadzadehfar H, Wegen S, Yordanova A, et al. Overall survival and response pattern of castration-resistant metastatic prostate cancer to multiple cycles of radioligand therapy using [177Lu]Lu-PSMA-617. Eur J Nucl Med Mol Imaging. 2017;44:1448–54.
12. Rahbar K, Ahmadzadehfar H, Kratochwil C, et al. German multicenter study investigating 177Lu-PSMA-617 Radioligand therapy in advanced prostate cancer patients. J Nucl Med. 2017;58:85–90.

Cutaneous Metastasis of Ovarian Carcinoma : A Case Report

Dr. Megha Nandwani(Resident), Dr. D. Barmon(Professor)
Department of Gynae Oncology
Dr. B Borooah Cancer Institute, Guwahati, Assam.

Introduction:

Ovarian malignancy is a common cancer of the female genital tract. The age adjusted incidence of ovarian cancer in Kamrup Urban district of Assam, India, for 2010-14 was 9.17 [1]. According to the American National Cancer Registry of 2012, there were a total of 22,280 cases of ovarian cancer.[2] The mortality rate of the same was high with a recurrence rate of around 65 to 75 %. The highest rate of recurrence is seen in the peritoneal cavity.[3] Metastasis to the skin is not commonly seen with cancers of internal organs. A very few cases have been reported in the past where ovarian cancers have shown spread to the skin. Hu SC et al from Taiwanese Medical Center reported cutaneous metastases in 1.02% of malignancies.[4] Carcinoma breast showed the maximum rates of these metastasis and the most common histopathology was adenocarcinoma.

Case Report:

A 50 year old lady presented with abdominal pain , distension and a skin lesion over right loin of 3 month duration. Patient was postmenopausal since 5 years, with one live child. On examination, patient's general condition was good with WHO performance status of 1. Systemic examination including abdominal examination was normal. While the per speculum examination was normal, on per vaginal examination, uterus was bulky with fullness in the right fornix. CT scan of whole abdomen showed right ovarian mass of 4*6 cms with minimal ascites and peritoneal disease and CA 125 was elevated. FNAC from ovarian mass and skin biopsy from the cutaneous lesion showed features of adenocarcinoma. After discussing the case in multidisciplinary tumor board meeting, patient was given 3 cycles of neoadjuvant chemotherapy (Paclitaxel and Carboplatin). Due to logistical reasons, patient could not be taken up for surgery. So further 3 cycles of chemotherapy was adminstered. Partial response to chemotherapy was seen. Patient was then taken up for interval debulking surgery. Total abdominal hysterectomy with bilateral salpingo-oopherectomty with total omentectomy and pelvic peritonectomy was performed, along with wide local excision of the cutaneous lesion. R-0 resection was achieved.

Patient has been on follow up for 6 months and is free of disease.

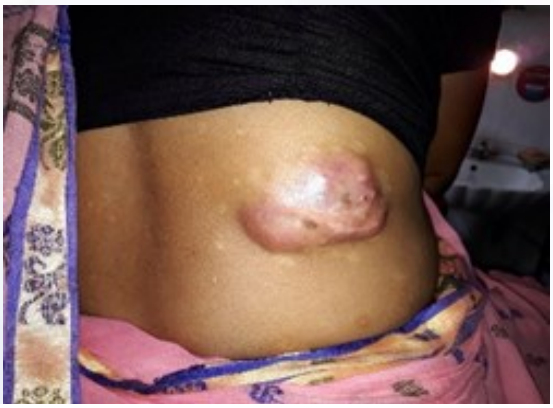


Image 1: Initial presentation of the patient.

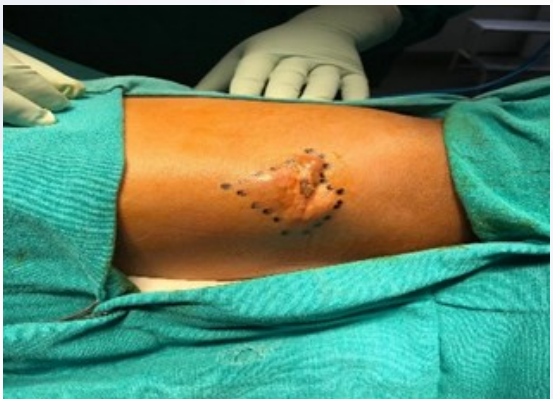


Image 2: Response after NACT

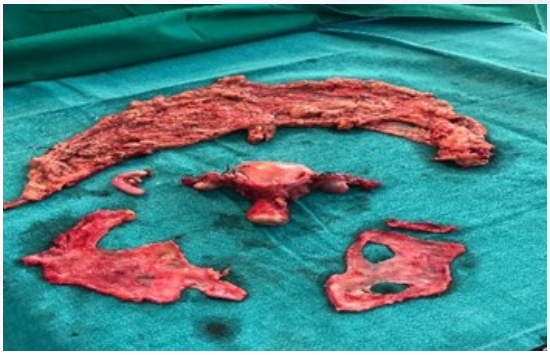


Image 3: Total abdominal hysterectomy with BSO and omentectomy with lateral peritonectomy

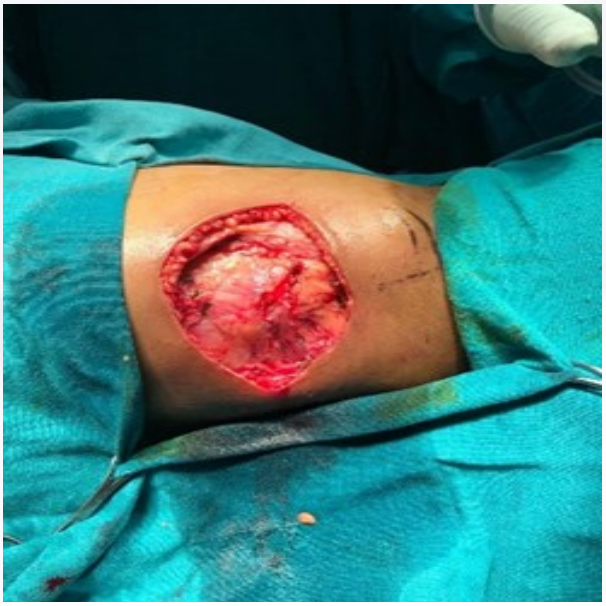


Image 4: Defect following wide local excision of skin lesion

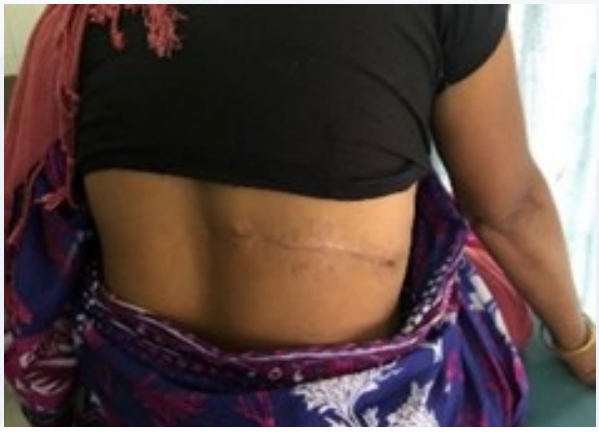


Image5: Present condition of the patient.

Discussion:

Metastasis to the skin is not a common occurrence in ovarian carcinomas and usually they portend a poor prognosis. Yilmaz Z et al reported a case of cancer ovary with metastatic recurrence to the skin. This patient expired within 4 months of this recurrence.[5] While the skin lesion was seen at recurrence, in our case, the lesion was seen at initial presentation. Senem Demirici et al also reported cutaneous metastasis in carcinoma of ovary. Their patient was a 43 year old lady who underwent palliative radiotherapy for the management of the metaststic lesion. The patient survived for 7 months.[6] H. Woopen et al used immunotherapy with catumaxomab for the management of skin metastasis. The treatment was given intraperitoneally and response studied.[7]

Several presentations of metastatic carcinoma from ovaries have been reported. Abbas O et al reported a perforating lesion of the skin in a case of ovarian adenocarcinoma.[8] Antonio AM et al from Portugal reported skin metastasis on nasal dermis in ovarian cancer[9]. Kim MK et al reported papillary adenocarcinoma of ovary metastatizing to the upper part of both lower limbs along with the inguinal region.[10] In comparison, our patient presented with metastasis to the loin region and was treated by radical intent, with chemotherapy and surgery.

Conclusion:

Epithelial ovarian cancers rarely metastasize to skin. The management of these lesions largely depends on the site and accessibility of the lesions. Radical treatment can be offered to these patients depending on the presentation and response to chemotherapy.

References:-

1. D Barman, JD Sharma, D Barmon, AC Kataki, A Sharma, M Kalita. Epidemiology of gynaecological cancers in Kamrup Urban District cancer registry. Indian Journal of Cancer. 2017;54(1):388-391.
2. Siegel R., Naishadham D., Jemal A. Cancer statistics, 2012. CA Cancer J. Clin. 2012;62(1):10–29.
3. Christine D, Craig, David A, Iglesias, Jack Watkins, Robert L Coleman , Larry Kilgore, and Pedro T. Ramirez. Extensive cutaneous metastases of ovarian cancer after prolonged response to liposomal doxorubicin. Gynecol Oncol Case Rep.. 2013 Aug; 5: 64–66
4. Hu SC, Chen GS, Wu CS, Chai CY, Chen WT, Lan CC. Rates of cutaneous metastases from different internal malignancies: experience from a Taiwanese medical center. J Am Acad Dermatol. 2009 Mar;60(3):379-87.
5. Yilmaz Z, Bese T, Demirkiran F: Skin metastasis in ovarian carcinoma. Int J Gynecol Cancer. 2001, 16 (Suppl 1): 414-418.
6. Demirci S, Yavas F, Ozsaran Z, et al. Palliative radiotherapy for the skin metastasis of ovarian cancer: a case report and review of the literature. Med Oncol. 2010;27(3):628–31.
7. Woopen H, Sehouli J (2009) Current and future options in the treatment of malignant ascites in ovarian cancer. Anticancer Res 29:3353–3359
8. Abbas O, Salem Z, Haddad F, Kibbi AG. Perforating cutaneous metastasis from an ovarian adenocarcinoma. J Cutan Pathol. 2010;37:e53-6.
9. Antonio AM, Alves JV, Goulao J, et al. Ovarian carcinoma presenting as cutaneous nasal metastasis. An Bras Dermatol 2016;91(5 suppl 1):101–4
10. Kim MK, Kim SH, Lee YY, Choi CH, Kim TJ, Lee JW, et al. Metastatic skin lesions on lower extremities in a patient with recurrent serous papillary ovarian carcinoma: a case report and literature review. Cancer Res Treat. 2012;44:142

8TH EDITION OF AJCC HEAD AND NECK CANCER STAGING SYSTEM: WHAT'S NEW?

Dr. Shashank Bansal[1], Dr. Gautam Sarma[2]
1) Post Graduate Student, Department of Radiation Oncology
2) Assistant Professor, Department of Radiation Oncology
Dr. B Borooah Cancer Institute Guwahati, Assam

Head and Neck Cancers are one of the commonest malignancies encountered in Indian patients. North-eastern states have the highest incidence compared to any other part of the country. According to NCRP- PBCR reports of 2012-14, the highest Age Adjusted Incidence Rates (AAR's) of Nasopharyngeal cancer are from Nagaland (15.7), Tongue cancer (11.7), Hypopharyngeal cancer (22.2) and Laryngeal cancer from East Khasi Hills (10.8)[1].

The American Joint committee on Cancer (AJCC) has significantly modified the Head and Neck cancer staging system in its 8th Edition[2] and is applicable from 1st January 2018. This updated version has incorporated various important prognostic factors [HPV positivity, Depth of Invasion (DOI), Extra Nodal Extension (ENE)], which directly affect patient's survival. **T0 has been excluded from staging of all sites except for Nasopharyngeal cancer, Salivary gland tumour and HPV+ Oropharyngeal cancer.**

Oropharyngeal cancers: 7th edition did not have separate staging system for HPV+ and HPV- oropharyngeal cancers. Patients having HPV+ oropharyngeal cancers are highly responsive to treatment and carry an excellent prognosis[3]. Therefore, it has been separately staged in 8th edition.

For HPV + tumours, there is no change in T1-3 category. T4a and T4b stage has now been clubbed together under stage T4 and described as tumour with invasion of the larynx, extrinsic muscles of the tongue, medial pterygoid muscle, hard palate, mandible and beyond.

Clinical nodal staging has also been modified- N0 is absence of lymph node (LN) involvement, N1 is one or more ipsilateral LN involvement; all <6 cm, N2 is contralateral or bilateral LN involvement; none > 6cm, N3 defined as LN > 6cm. Stage grouping has also been modified; stage I is T0-2, N0-1, stage II is T0-2, N2 or T3, N0-2 stage III is T0-4, N3 or T4 N0-2 and stage IV is for metastatic disease (Any T, Any N M1).

- **T stage: - T4a and T4b Clubbed together to T4.**
- **N stage: - ENE not considered, No Further subdivision of N2 and N3**

Stage: - T0-2, N1 is stage I and T0-2, N2 or T3, N0-2 is stage II, whereas N3 disease is Stage III, while in previous staging if node is positive (N1), it directly goes to Stage III.

For HPV- Oropharyngeal cancers "T" category has not changed. In Nodal category, N3 have been further classified as N3a (at least one LN >6cm and no ENE) and N3b (presence of overt clinical evidence of ENE, irrespective of number, size and laterality of pathologic LN). Pathologic nodal staging of 8th edition now classifies single LN < 3cm with ENE as N2a, whereas single LN > 3cm with ENE is classified as N3b.

T stage: - No change
N stage: - N3 is divided into N3a and N3b.
Stage: - No change

Nasopharyngeal cancers: In 8th Edition, a few changes have been made in both "T" and "N" staging of nasopharyngeal cancers. While in 7th edition T2 was defined as tumour involving parapharyngeal space, 8th edition now defines T2 as tumour involving parapharyngeal space,

medial pterygoid, lateral pterygoid and prevertebral muscles. The previous T4 criteria of involvement of masticator and infratemporal space has been replaced in 8th edition by a specific description of soft tissue involvement beyond the lateral surface of the lateral pterygoid muscle and parotid gland to avoid ambiguity. N3a(node >6 cm) and N3b (Suprclavicular node) nodal staging has been merged into single category N3, which is described as involvement of lower neck defined by nodal extension below the caudal border of the cricoid cartilage. Stage grouping is also modified with previous stage IVa (T4, N0-2, M0) and IVb (T Any, N3, M0) has been merged into single stage IVa. Previous Stage IVc (Any T, Any N, M1) is now stage IV b.

- **T stage: - T2 and T4 definition has been revised.**
- **N stage: - N3a and N3b have been clubbed to form N3.**

Stage: - Previous stage IVa and IVb has been clubbed to form Stage IVa and Previous stage IVc is now stage IVb.

Oral Cavity Cancer: Substantial changes have been done in "T" category and now clinical and pathologic depth of invasion is used in indicating the "T" Category. T1 is tumour <2 cm, DOI <5mm, T2 is tumour <2cm, DOI >5 mm and <10mm or >2cm but <4cm, <10mm DOI and T3 is tumour >4 cm or any tumour with DOI >10mm. In T4 category, extrinsic muscle of tongue involvement is not considered now, since it is a feature of DOI. Nodal staging is same as for HPV- oropharyngeal carcinoma.

T stage: - Apart from Tumour size, Depth of Invasion is also used to define T stage

N stage: - similar to N staging for HPV(Neg.) Oropharyngeal cancers.

Staging: - No change

In 8th edition of AJCC staging system, Extra Nodal Extension (ENE) and Depth of Invasion (DOI) significantly impact the tumour staging, few salient points are discussed below:

Extra Nodal Extension (ENE): Clinically it is diagnosed by the presence of Matted LN mass, involvement of overlying skin, adjacent soft tissue or clinical signs of cranial nerve or brachial plexus, sympathetic chain or phrenic nerve invasion. Radiologically it is suspected when there is indistinct nodal margin, irregular nodal capsular enhancement, or infiltration into the adjacent fat or muscle. Pathologically Microscopic ENE (ENEmi) is defined as <2mm microscopic involvement and Macroscopic ENE (ENEma) is defined as >2mm extension beyond the nodal capsule or extracapsular extension visible to naked eye. It is important that only ENEma is considered as ENE positive and ENEmi is considered ENE negative.

ENEmi: - <2mm microscopic extracapsular extension

ENEma: - >2mm/ Macroscopic extracapsular extension.

Depth of Invasion (DOI): Thickness of tumour is measured from top of the tumour to the deepest tumour cell. Depth of invasion is the assessment of invasiveness of carcinoma regardless of any exophytic component. DOI is measured first by finding the horizon of basement membrane of squamous mucosa, a perpendicular "plumb" line is drawn from this

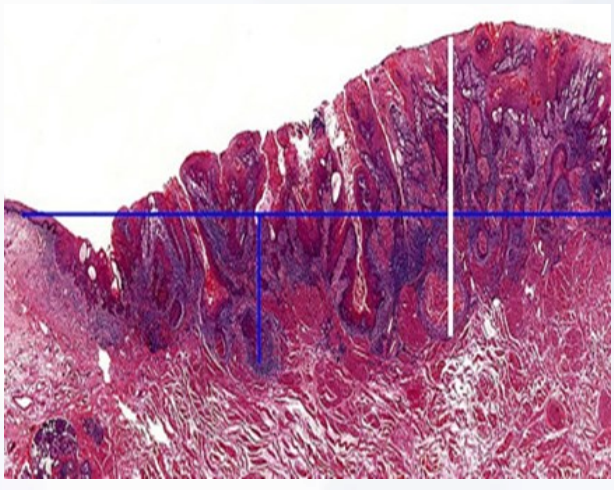


Fig: The white bar represents maximum tumor thickness, which here is greater than the depth of invasion (blue bar)

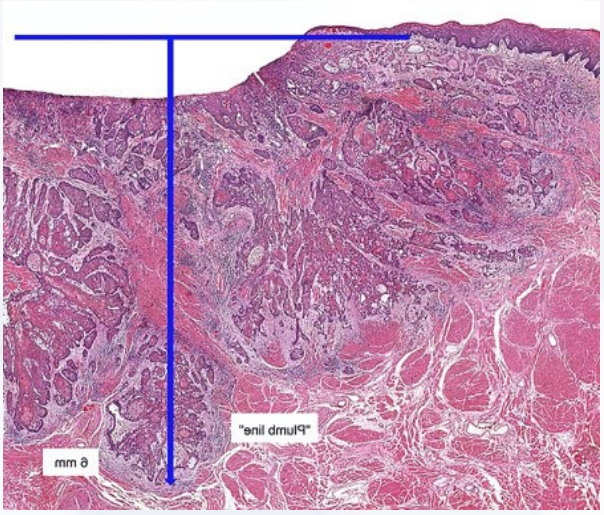


Fig: Depth of Invasion in an Ulcerated Carcinoma. Notice how "tumor thickness" would be deceptively thinner than depth of invasion.

Courtesy:- William M. Lydiatt et al, Head and Neck Cancers —Major Changes in the American Joint Committee on Cancer Eighth Edition Cancer Staging Manual; CA CANCER J CLIN 2017;67:122–137

horizon to deepest part of tumour, which represent depth of Invasion.

In conclusion, we can say that, 8th edition provides more accurate and reasonable prediction of survival for newly diagnosed Head and Neck Cancers, as it has considered the prognostic factors (HPV positivity, ENE and DOI), which directly impact the treatment and patient survival.

References

1) NCRP (2016) three-year report of the population based cancer registries-2012-2014. National cancer registry program, Indian council of Medical research (ICMR), Bangalore, India, 2016.

2) Amin MB, Edge SB, Greene FL, et al, eds. AJCC Cancer Staging Manual,8th ed. New York: Springer; 2017.

3) Chaturvedi AK, Engels EA, Pfeiffer RM, et al. Hu man papillomavirus and rising oro-pharyngeal cancer incidence in the United States. J Clin Oncol. 2011; 29:4294-4301.

COLLISION TUMOUR IN HEAD NECK ONCOLOGY : A RARE CASE REPORT

Dr Hemish Kania

**Dr Aditya Joshipura*

**Fellow in Surgical Oncology, Gujarat Cancer Research Institute , Ahmedabad*

***Assistant Professor Head Neck Oncology, Gujarat Cancer Research Institute , Ahmedabad*

Keywords: laryngeal squamous cell carcinoma, papillary thyroid carcinoma, collision tumor, giant cell tumour larynx.

Introduction:

Although double cancers in the upper aerodigestive tract mucosa are not uncommon (1–6), collision tumors that are composed of a papillary thyroid carcinoma and a laryngeal giant cell tumour are rare. The term 'collision tumor' refers to the coexistence of two histologically distinct malignant tumors within the same mass.

There are case reports of the Collision Tumour composed of papillary thyroid carcinoma with laryngeal squamous cell carcinoma. However, even isolated presentation of giant cell tumour of the larynx is very rare and only 8 cases hav been reported.

Giant cell tumors of the larynx (GCTL) are extremely rare benign tumors arising in the osteocartilaginous tissue of the larynx. The majority of the tumors reported in the literature arise from the thyroid cartilage (thyroid cartilage: 80%, cricoid cartilage: 15%, epiglottis: 5%) and have predilection for male (M:F =10:1), with the mean age at the presentation of 40 years.[2] The site of origin has been localized to the thyroid or cricoid

cartilage that has undergone endochondral ossification. The common signs and symptoms are palpable neck mass, hoarseness, airway obstruction, and dysphagia. Other symptoms include sore throat, chronic sinusitis, voice loss, and ear pain. There is no definitive association with smoking, heavy alcohol use, or radiation exposure. The duration of symptoms ranges from 1 to 9 months.[2] GCTLs seem to behave less aggressively than their long bone counterparts. Although there are not sufficient numbers of cases and follow-up to accurately predict future biologic behavior of these lesions, GCTL appear to be, to date in all reported cases, non-metastasizing lesions. Complete surgical resection is adequate for local control in all the reported cases. Radiation therapy and/or chemotherapy are not a necessary adjunct in the treatment of these laryngeal tumors. This paper reports the case of a 55-year-old male who presented with a collision tumor in the neck.

Written informed consent was obtained from the patient.

CASE REPORT:

A 55 year old male presented with complaints of bilateral neck swelling since 6 months, difficulty in swallowing since 2 months and change in voice since 15 days . He had history of using tobacco products, both smokeless and smoked, for over ten years.

A single, hard, midline mass 4*4*2 cm size, fixed to the underlying structures and free from the skin was seen. On Direct Laryngoscopy(DL), there was a bulky growth involving left Pyriform fossa , ary epiglottic fold , true and false vocal cord anterior and posterior commissure, lateral and posterior hypopharyngeal wall. The Contrast Enhanced Computerised Tomography(CT) scan of the neck revealed a mass lesion of left ary epiglottic fold and pyriform fossa involving the laryngeal surface of epiglottis, true and false vocal cord with obliteration of left paraglottic fat space. The posterior commissure was involved and the lesion was seen to involve the hypopharyngeal wall. The lamina of the thyroid cartilage was involved. Both lobes of the thyroid gland were enlarged, of size 46*30mm and 38*22mm. Multiple enlarged necrotic nodes were present in levels 2,3,4,5 bilaterally.

Patient underwent Total Laryngectomy with Total thyroidectomy and bilateral Lateral neck dissection with the hypopharynx being augmented using a Pectoralis Major Myocutaneous patch. Intraoperatively, a large mass with extensions as suggested by the imaging was seen, with both lobes of thyroid being enlarged. The thyroid mass was distinct apart from the laryngeal mass. Also, another separate lesion of size 2*2 cm was found on left postero-lateral wall of the hypopharynx. The patient had an uneventful recovery, but for transient post-operative hypocalcemia.

Histopathology report was suggestive of a giant cell tumour involving left pyriform sinus, extending to the thyroid cartilage. The tumors showed no connection to the surface epithelium and arose in sites of ossification. The tumors had an expansile, infiltrative growth and consisted of numerous multinucleated osteoclast-like giant cells within a cellular stroma composed of plump, oval mononuclear cells. Of interest was that the nuclei of the giant cells were similar to the nuclei of the stromal cells. Second tumour was of papillary carcinoma of infiltrating both lobes, isthmus, capsule and surrounding structures. The interventing tissue between Giant cell tumour of Larnyx and Papillary carcinoma was free of tumour. The separate hypopharyngeal lesion was free of tumor. Two of the twenty nodes dissected from the right side of the neck showed metastatic tumor deposits, while all the nodes on the left side were free of tumour.

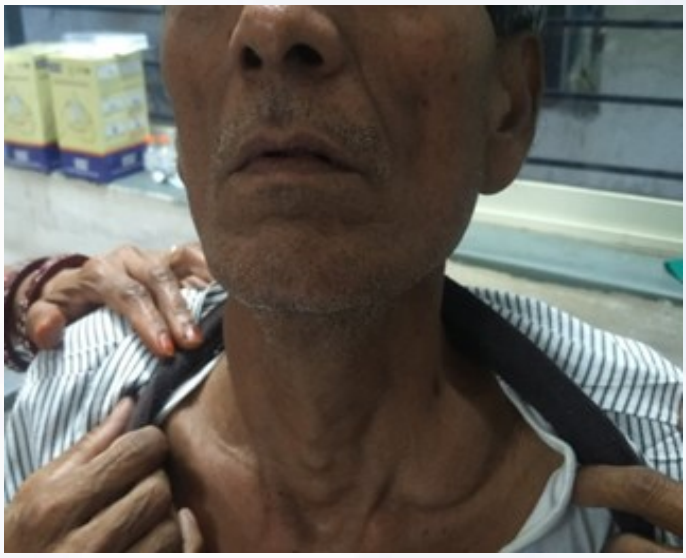
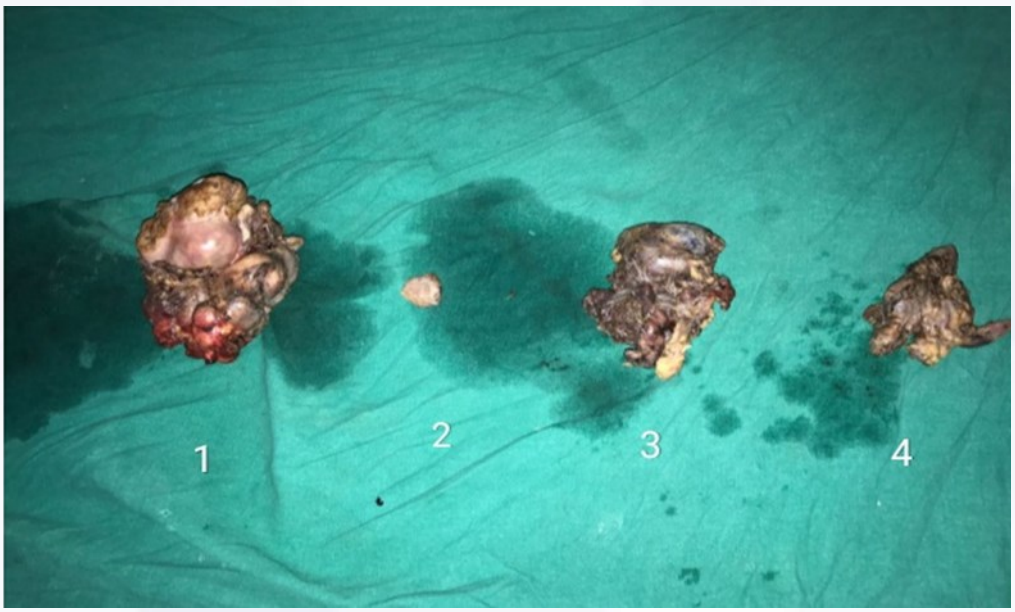


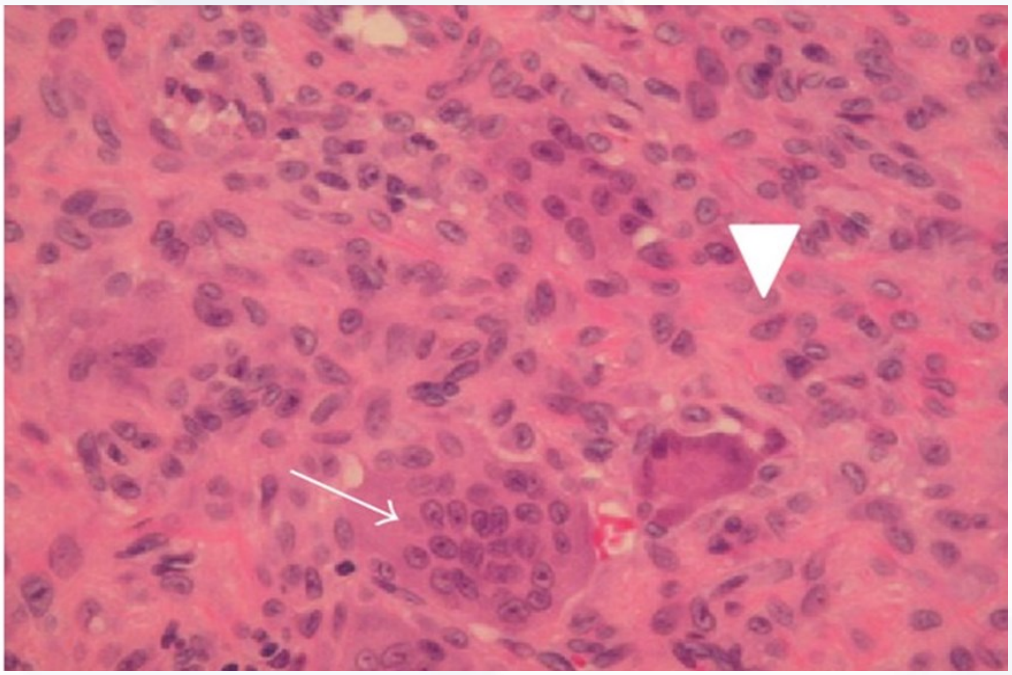
Figure 1: Clinical picture



1.Giant cell tumour of larynx along with the papillary carcinoma thyroid specimen

2. Posterior Pharyngeal Wall

3, 4. Right and Left Neck Nodes



Histological examination demonstrates the cellular mononuclear eosinophilic stromal component (arrowhead) and multinucleated osteoclast -like giant cells (arrow) scattered throughout the lesions in an intermediate power field.

After the patient recovered, he was referred for radioactive iodine scan in view of nodal involvement thyroid. Informed consent was obtained from the patient for this publication.

Discussion

In multiple primary cancers, each tumor is malignant and is of an independent pathological type(6). Multiple primary cancers may be double (i.e. two primary cancers) or triple (i.e. three primary cancers) cancers. Collision carcinomas are a special type of multiple primary tumors, which are difficult to diagnose prior to a surgical resection due to a lack of characteristic clinical features. In this patient, the mass presented as a submucosal lesion. The initial findings indicated a thyroid tumor that was invaded by a laryngeal tumor or a laryngeal tumor that was invaded by a thyroid tumor.

We initially thought it to be a papillary carcinoma thyroid that was invading the laryngeal cartilage. Tracheal invasion has been more extensively studied and characterized due to its greater frequency relative to laryngeal involvement. A widely cited staging system by Shin and colleagues is based on the depth of tracheal invasion. Stage I disease invades through the capsule of the thyroid gland and abuts but does not invade the external perichondrium of the trachea. Stage II disease invades into the cartilage or causes cartilage destruction. Stage III disease extends into the lamina propria of the tracheal mucosa with no elevation or penetration of the mucosa. Stage IV disease is full-thickness invasion with expansion of the tracheal mucosa that is visible

bronchoscopically as a bulge or an ulcerated mass

True giant cell tumors of the larynx (GCTL) are quite rare, and only individual case reports are documented in literature. Eight cases of GCTL were identified in the Otorhinolaryngic Pathology Tumor Registry between 1966 and 2000.

Collision tumors may be located anywhere in the body. A collision tumor of the breast has been described (7), as has an intracranial collision metastasis (8). Similar to the present case, a collision tumor of a papillary thyroid carcinoma and a laryngeal squamous cell carcinoma has been previously reported (9). In that patient, however, the metastatic lymph nodes were derived from both primary thyroid papillary carcinoma and laryngeal squamous cell carcinoma, with one lymph node showing metastases from the two. In the present patient, the metastatic lymph nodes were all derived from the primary thyroid papillary carcinoma. Since the other reported collision tumor had a squamous carcinoma component, he received both adjuvant radiotherapy and ^{131}I adjuvant treatment, whereas the patient of the present study underwent only ^{131}Itherapy.

Due to the rarity of collision tumors of the head and neck, it is difficult to determine their etiology. Two hypotheses have been suggested. The first suggests that the two primary tumors developed in the same location by chance, perhaps due to radiation. The second hypothesis suggests that the presence of the first tumor alters the microenvironment, allowing the second, adjacent tumor to develop. The present patient and the earlier study patient were diagnosed with a collision tumor of a papillary thyroid carcinoma and a laryngeal squamous cell carcinoma (10), and the tumors were extremely large. Probably, had these patients felt uncomfortable and sought treatment earlier, they may not have developed collision tumors.

The therapy for multiple primary cancers should consist of a combination of the treatments that are normally used for each focus. Since few patients with these tumors undergo a pre-operative histological diagnosis, there may be differences in the post-operative patient management. A collision carcinoma is a special type of multiple primary carcinoma. Thus, en bloc resection of the two inter-infiltrating tumors should be performed. GCTL are rare tumors that can cause significant airway obstruction. Complete surgical resection yields excellent outcomes without the need for any adjuvant therapy.

Conclusion:

As collision tumors of the head and neck are rare, it is very difficult to obtain a pre-operative diagnosis. The therapy for a collision tumor should consist of a combination of the treatments that are normally used for each focus.

References:

1. Esposito ED, Bevilacqua L, Guadagno MT. Multiple primary malignant neoplasm in patients with laryngeal carcinoma. J Surg Oncol. 2000;74:83–86. [PubMed]
2. Wang CP, Lee YC, Yang TL, Lou PJ, Ko JY. Application of unsedated transnasal esophagogastroduodenoscopy in the diagnosis of hypopharyngeal cancer. Head Neck. 2009;31:153–157. [PubMed]
3. Wang CP, Lee YC, Lou PJ, Yang TL, Chen TC, Huang CC, Ko JY. Unsedated transnasal esophagogastroduodenoscopy for the evaluation of dysphagia following treatment for previous primary head neck cancer. Oral Oncol. 2009;45:615–620. [PubMed]
4. Lin ZM, Chang YL, Lee CY, Wang CP, Hsiao TY. Simultaneous typical carcinoid tumour of the larynx and occult papillary thyroid carcinoma. J Laryngol Otol. 2008;122:93–96. [PubMed]
5. Brandwein-Gensler M, Urken M, Wang B. Collision tumor of the thyroid: a case report of metastatic liposarcoma plus papillary thyroid carcinoma. Head Neck. 2004;26:637–641. [PubMed]
6. Warren S, Gates O. Multiple primary malignant tumors: a survey of the literature and a statistical study. Am J Cancer. 1932;16:1358–1414.
7. Jacobson AS, Wenig BM, Urken ML. Collision tumor of the thyroid and larynx: a patient with papillary thyroid carcinoma colliding with laryngeal squamous cell carcinoma. Thyroid. 2008;18:1325–1328. [PubMed]
8. Cheung KJ, Tam W, Chuang E, Osborne MP. Concurrent invasive ductal carcinoma and chronic lymphocytic leukemia manifesting as a collision tumor in breast. Breast J. 2007;13:413–417. [PubMed]
9. Palka KT, Lebow RL, Weaver KD, Kressin MK. Intracranial collision metastases of small-cell lung cancer and malignant melanoma. J Clin Oncol. 2008;26:2042–2046. [PubMed]
10. XIN WANG, XIANG-YAN CUI, **NING FANG, WEI-LUN CHEN, HONG YU, and WEI** Papillary thyroid carcinoma and laryngeal squamous cell carcinoma manifesting as a collision tumor of the neck: A case report **[pmc/articles/PMC3834194]**

Pledge for Life

Dr. Caleb Harris
M.Ch.(Surgical Oncology)
Associate Professor and HOD,
Department of Surgical Oncology, NEIGRIHMS, Shillong

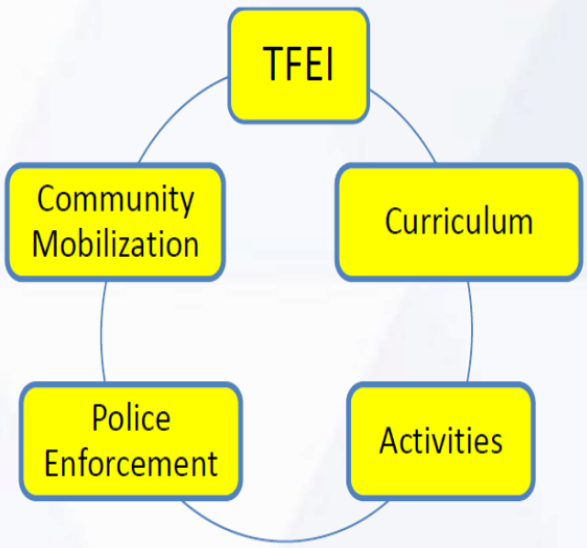
Tobacco is a major killer in our country and the world, and major efforts are on to curb the use of this highly addictive substance. While increasing the taxes has been effective to a great extent, the cost of tobacco products, especially the smokeless forms are still inexpensive, largely due to the fact that most of these are produced by the unorganized sector. However, the quit rate among smokers has been a dismal 3 to 4%. Hence the ideal strategy would be to ensure new users aren't added to the pool of tobacco users.

Since the life expectancy of tobacco users is reduced, the strategy of the industry is to target new users, who are invariably the adolescents. Hence, we should target this group to raise awareness on the ill-effects of tobacco, thereby enabling them to make the right choices.

While we do have laws to protect youngsters from this menace, it is the enforcement which is found to be lacking and this is where we can engage the society into meaningful action. The Cigarettes and Other Tobacco Products (Prohibition of Advertisement and Regulation of Trade and Commerce, Production, Supply and Distribution) Act, 2003 or COTPA, 2003, not only prohibits the sale of tobacco products to minors and but also bans the sale within 100 metres of educational institutions. This act also says that owners of public places like restaurants, malls, cinema, etc. should put up displays saying that it is a 'No Smoking Zone'.

The Tobacco Free Educational Institution (TFEI) is an initiative of the Sambandh Health Foundation along with other partner organisations. This initiative strives to enforce the provisions of COTPA such as proper signage in educational institutions and ensuring that tobacco products are not sold in the vicinity of the institution. Also, no staff of the school can use tobacco inside the premises and the principal/ headmaster declares that the institution is tobacco - free.

Children are involved in activities that encourage them to take up leadership against the use of tobacco. They are administered pledges that reinforce the stand that they need to take against tobacco. Also, various competitions are held to raise awareness and evince interest. This also has a positive effect on parents and other family members who are addicted to tobacco.



While extra-curricular activities can generate interest, once things are made mandatory, everyone will read about the ill - effects of tobacco. The school education authorities are requested to include this in the curriculum right from 5th standard, so as to make students aware early in life.

Sensitisation workshops are being held to enable the police to understand the magnitude of this problem and the need to enforce the provisions of COTPA. This is especially important in ensuring that tobacco is not sold within 100 metres of the institution.

Youth and other community groups have been tapped into, to involve the society. If the community at large understands the gravity of the situation, there is increased participation. Organisations like the National Service Scheme (NSS) are being involved in this initiative.

Sambandh Health Foundation has been able to ensure compliance of over 3.5 lakh schools. By partnering with the Assam School Education Department, over 14 lakh children have taken a pledge against tobacco-a pledge for life; the curriculum changes will be effected from the year 2020 in Assam.

We as oncologists of the Northeast Region can help by partnering with Sambandh and other organisations in making each of the 7 sisters (and a brother) of this region truly tobacco free, by preventing the next generation from being lured into this evil by the schemes of the tobacco industry.

GATS 2 HIGHLIGHTS FOR MEGHALAYA

- 53.7% of men, 9.5% of women and 31.6% of all adults smoke tobacco.
- 11.6% of men, 29.1% of women and 20.3% of all adults currently use smokeless tobacco.
- 59.8% of men, 34.2% of women and 47.0% of all adults either smoke tobacco and/or use smokeless tobacco.
- From GATS 1 to GATS 2, there has been a significance decrease in the prevalence of smoking by 4.1 percentage points and smokeless tobacco use by 7.9 percentage points. The prevalence of any tobacco use has decreased significantly from 55.2% in GATS 1 to 47.0% in GATS 2.
- Cigarettes and *bidi* are the most commonly used tobacco products. 23.4% of adults smoke cigarettes and 17.2% smoke *bidi*.
- The prevalence of tobacco use among person aged 15-17 has decreased from 26.4% in GATS 1 to 12.6% in GATS 2.
- The mean age at initiation of tobacco use has increased from 17.0 years in GATS 1 to 17.5% in GATS 2.
- 28.3% of adults were exposed to second-hand smoke at any public place.
- 52.9% of cigarette smokers and 45.4% of *bidi* smokers thought of quitting smoking because of warning label. 45.7% of smokeless tobacco users thought of quitting smokeless tobacco use because of warning label.


XIII
Annual Conference
of
Association of Oncologists
of North-East India
Theme: Tobacco Related Cancer
9th & 10th February, 2018


CME : Gynaecological Oncology


Enforcement as a catalyst
XIII
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of North-East India
Theme: Tobacco Related Cancer

REPORTS


RICOH


XIII
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North-East India
Tobacco Related Cancer

SECRETARY'S REPORT

Dr. Vikas Jagtap
Associate Professor & HOD, Department of Radiotherapy, NEIGRIHMS, Shillong

Dear all,

AONEI has been achieving milestones every year. With more than 110 members, AONEI is one of the largest association of oncologists in North East India. The main focus of AONEI-academic enrichment, is very well executed by regular CME & Conferences wherein cancers which are common to this region are discussed. There is a conscious effort to not only discuss, but also encourage people to change practice in accordance with current evidence.

The academic activities in the past two years were the Annual conference at BBCI-Guwahati (Feb 2018), CME on Esophageal & Hypopharyngeal Cancers at Shillong (Jun 2017), CME on Gynecological Cancers at Shillong (July 2018) & also CME at Dibrugarh on Palliative care, Gall Bladder and Ovarian Cancer (Sep 2018). For the successful academic interactions AONEI collaborated with other institutes & scientific bodies like NEIGRIHMS (Shillong), BBCI (Guwahati), Association of Radiation Oncologists of India – North East Chapter (AROI –NE), Shillong Obstetrics and Gynecological (SOGS), Indian Association of Surgical Oncologists (IASO), Dibrugarh Surgeons & Physicians Association, Palliative care groups etc.

AONEI is sincerely thankful to all the entire regional & national faculty and members who have made this endeavor a success by sharing their knowledge and precious time. However, though our AONEI members have been actively involved, through other organizations, in social activities like health camps and cancer awareness activities, no event was conducted under the banner of AONEI. I hope that in coming years this important activity would also be taken up by the association.

The AONEI newsletter (Darpan) which was started a few years ago, has grown leaps and bounds, showcasing work done in this region and has been a platform for the members, students and trainees to present their achievements, work (original research, reviews, case reports etc.) and has been a huge success.

This year the Annual Conference is being held at Kohima (Nagaland - 2nd – 3rd Feb 2019). I wish to see you all with the same energy and enthusiasm to enable the association to reach greater heights.

Long live AONEI.

Dr. Vikas Jagtap

(Associate Professor & Head, Radiation Oncology, NEIGRIHMS – Shillong)
Secretary – AONEI

XIIITH ANNUAL CONFERENCE OF AONEI, GUWAHATI

The 13th Annual Conference was organized by Dr B. Borooah Cancer Institute on 9th and 10th February 2018, at Dr B. Borooah Cancer Institute, Guwahati. The organizing chairman was Dr. J. D. Sarma while Dr. Ashok Kumar Das was the organizing secretary. In view of the high use of tobacco in North East India, the theme of the conference was **'Tobacco Related Cancer'**.

The conference started with three pre-conference workshops- Pathology Workshop on Immunohistochemistry, Radiotherapy Workshop on Radiotherapy Planning, and an Anti - tobacco Media Sensitizing Workshop, in line with the theme of the conference. Dr Vishal Rao, an Anti - Tobacco activist from HCG Bangalore was the resource person and he elaborated on the concept of 'Voice of Tobacco Victims'. Dr Arundhuti Deka, Nodal Officer of the Assam State Tobacco Control Cell also participated in the workshop. Media persons from both the print and electronic media attended the workshop and they were briefed about the tobacco menace in North East India and the huge burden of Tobacco Related cancer.

The conference was inaugurated by Dr. Prasant Mathur, Director, NCDIR Bangalore along with Dr. Amal Kataki, Director, Dr. B. Borooah Cancer Institute, Guwahati. Dr. Mathur also moderated a panel discussion on 'Cancer Burden in North East India'. Participants from Assam, Meghalaya, Manipur, and Nagaland participated in the discussion.

The scientific session on Lung cancer included a talk by Dr P. S. Roy on targeted therapy in lung cancer, followed by a panel discussion covering all the practical aspects of lung cancer management. This was moderated by Dr. Caleb Harris, Surgical Oncologist from NEIGRIHMS. Dr Ravi Kannan from Cachar Cancer Hospital then spoke on Gall Bladder cancer. The General Body meeting which followed was attended by around 40 members.

Day two began with award paper session in the morning. Dr Subhalaksmi Saikia from Dr B. Borooah Cancer Institute was awarded the 1st prize for her presentation on Nasopharyngeal Cancer, while Dr Shreeram from RIMS, Imphal bagged the second prize.

The Panel discussions on ovarian and esophageal cancers were moderated by Dr Jadunath Buragohain and Dr. Arvind Krishnamurthy (Cancer Institute, Chennai) respectively. These were very interactive, with active participation from all the delegates. Dr. D. C. Goswami then talked on 'Palliative Care in

Dr. Pankaj Chaturvedi delivering the oration

A pre-conference workshop in progress

North East India' and Dr. Kuddush Ahmed on 'Near Total Laryngectomy'.

The AONEI Oration was awarded to Dr Pankaj Chaturvedi from Tata Memorial Hospital, Mumbai. He spoke on 'Tobacco Related Cancer', emphasizing on the need for doctors to not only offer care for cancer, but also actively involve in primary prevention of cancers.

Dr. Gauri Kappor from RGCI, New Delhi talked on 'Pediatric ALL' while Dr Siddharth Laskar, Senior Radiation Oncologist from Tata Memorial Hospital, Mumbai gave an 'Overview of Pediatric Solid Tumor'. The last session included a guest lecture by Dr Bishwajyoti Hazarika from New Delhi on 'Paradigm shift in the management of thyroid cancer', followed by a panel discussion on oral cancer which was moderated by Dr Ritesh Tapkire from Cachar Cancer Hospital, Silchar.

The conference was attended by 122 participants, a good number being post graduate students from the Medical Collages and trainees. It was heartening to note that there were 23 scientific poster presentations in the conference.

A panel discussion on esophageal cancer

Mid -Term CME at Dibrugarh

AONEI mid term CME was organized by Assam Medical College, Dibrugarh, in association with Associations of Physicians and Surgery , Pratishruti Cancer and Palliative Trust on 29th September at Hotel Garden Treat, Dibrugarh.The Organizing Chairperson was Prof. Hiranya Kr Goswami, Principal, AMCH and Organizing secretaries were Dr Gayatri Gogoi and Dr Ramesh Saharia. It was inaugurated by Dr Bhabani Chaliha, a renowned gynaecologist of the city. Prominent personalities like Pranay Bordoloi, Executive editor of Prag News Channel and Lohit Deka, Director, All India Radio, Dibrugarh, attended the inaugural session. Dr AC Kataki and Dr Dinesh Ch Goswami spoke on Community Oncology and Pallliative care respectively followed by interactive sesssion with cancer patients and their family members.

The main scientific sessions were on ovarian and gallbladder cancers. Dr Avinash Pandey, Medical Oncologist from Patna was the faculty, besides AONEI members. The sessions covered all the practical aspects of the two selected cancers which are common in women in the region. Around 100 participants attended, including the faculty, post-graduate students and practicing clinicians.

Mid-term CME on Gynaecological Cancers at Shillong

AONEI successfully conducted the "Mid-term CME on Gynecological Oncology" on 21st July 2018 at Hotel Pinewood, Shillong (Meghalaya). The CME was conducted in association with Shillong Obstetrics & Gynaecological Society (SOGS) & Association of Radiation Oncologists of India - North East Zonal Chapter (NE-AROI). Three most common gynaecological cancer i.e. Cervix, Endometrium and Ovary were taken up for the academic program.

Chief Guest Prof (Dr). Noor Topno (Medical Superintendent - NEIGRIHMS) inaugurated the program and praised AONEI for conducting such activities in North East India. Faculty from North East and other parts of India participated for the enlightment of delegates. Dr. Amita Maheshwari (Mumbai), Dr. Neha Kumar (Delhi), Dr. Tanweer Shahid (Kolkata), Dr. Suman Mallick (Kolkata) & Dr. P Mohpatra (Kolkata) were amongst the invited faculty. Dr. Jadunath Borgohain, Dr. Poulome Mukherjee, Dr. Caleb Harris, Dr. Debabrata Barmon & Dr. Umesh Das from AONEI also participated as faculty for the programme.

Dr. Indrani roy (President, SOGS) & Dr. W Mawlong (Secretary, SOGS) worked for the success of the program, and ensured participation of a very good number of practicing gynaecologists and Obs &Gynae trainees from Shillong. There was very good interaction by the participants, especially in the panel discussions, which helped clarify common doubts in patient care. The '*Debate on Treatment of Cervical Cancer-Ray v/s Knife'*, while keeping the participants enthralled, also helped in simplifying treatment decisions for this cancer.

The event was graced by Prof (Dr). A C Kataki (Director, BBCI) & Prof (Dr). A K Kalita (President, AONEI) & Dr. Shyam Tsering (Secretary – NE-AROI) amongst others and the presence of these seniors enriched the event. More than 80 participants with their academic involvement made the CME a grand success.

Dr. Vikas Jagtap
Secretary AONEI

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CORRESPONDENCE:

Dr. Vikas Jagtap, Secretary; drvikasj@yahoo.co.in, aonei_secretary@aonei.in

Dr. Caleb Harris, Editor and Website in-charge; calebhar@gmail.com

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