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Atypical Malignancies in Head and Neck- An Experience from a Tertiary Cancer Centre of Eastern India

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Abstract:-

- ***Introduction:***

Majority of malignancies in head and neck are of squamous cell carcinoma histology(90%). Malignancies of other pathological variants in head and neck are quite infrequent and hence lead to uncertainities in diagnosis, treatment and require needful research. Minor salivary gland tumours, lymphoma, mesenchymal tumours, melanoma and variants of squamous cell carcinomas come under this category.

- ***Materials and methods:***

A retrospective study was done of patients presenting with atypical malignancies of head and neck at a tertiary cancer centre of eastern India. They were analysed on basis of age, sex, histopathological variants, site of primary tumour, treatment received and its response.

- ***Results:***

Out of total 18 cases studied,mean age of presentation was 44.5 months. Male: Female ratio was 2:1.A wide spectrum of histopathological variants were found which included adenoid cystic carcinoma , sarcomatoid carcinoma, pleomorphic sarcoma, ewings sarcoma, rhabdomyosarcoma, eosinophillic granuloma, follicular dendritic cell sarcoma, malignant sweat gland tumour, sebaceous carcinoma, large cell carcinoma, undifferentiated carcinoma, peudotumor orbit and lipofibromatosis.11 patients underwent surgery and 12 patients received radiotherapy in definitive or adjuvant setting. Median follow-up period was 30 months.

- ***Conclusion:***

Atypical malignancies in head and neck region pose a diagnostic and therapeutic challenge due to paucity of relevant literature. The management is mainly guided by the histopathological variant and location of the malignancy. More research needs to be done in this regard and patients should be subjected to clinical trial whenever feasible.

***Keywords*:-** *Atypical Malignancies;Unusual Malignancies in Head and Neck; Rare Variants of Head and Neck Cancer.*

I. INTRODUCTION

Head and neck malignancies most commonly arise from the epithelial lining and hence are of squamous cell type(90%).[1] But atypical pathologies though unusual, do exist; which may be squamous cell variants or may arise from minor salivary glands, components of underlying stroma and mesenchymal tissue or secondaries from other primary malignancies.Unlike its squamous cell counterpart, atypical malignancies could remain unidentified on clinical and endoscopic examination as they usually present as submucosal masses without any mucosal change, unless in advanced stage[2].Hereby we are presenting our experience with these group of atypical head and neck malignancies, their management and response to therapy with relevant literature review.From management point of view, head and neck region can be broadly divided into four subsites such as: (1) orbit, (2)nasal cavity, paranasal sinus and nasopharynx, (3) oral cavity, oropharynx and salivary gland (4) hypopharynx, larynx and neck region. Our analysis and discussion will be based on malignancies in these subsites.

II. MATERIALS AND METHODS

A retrospective analysis was done from the hospital records of patients visiting during January 2013 to November 2018 at department of radiotherapy of a tertiary care centre in eastern India. Squamous cell carcinoma of head and neck region and lymphomas of cervical node region are two patient subgroups which were excluded from the study. All patients with histopathogically proven nonsquamous pathology of head and neck regionwere included in the study. The patients were analysed on basis of age, sex, histopathological variants,site of primary malignancy,treatment received and response thereof.

III. RESULTS

During this period a total number of 412 patients of head and neck cancers attended this department out of which 18 patients(4.37%) had atypical malignancies in head and neck region . Among them, 12 were male and 6 were female[Table-1]. Median age of presentation was 44.5 months (range being 15-70 years). Majority of patients (50% i.e. 9 patients) were in age group 40-59 years followed by 4 patients ≥ 60years. Based on location of malignant lesion, 8 cases (44.4%) were located in orbit, nasal cavity and PNS whereas 5 cases (27.78%) were in oral cavity, oropharynx and salivary gland. Histopathologically the cases showed a wide spectrum of myriad varieties such as adenoid cystic carcinoma (three

cases), sarcomatoid carcinoma (two cases), pleomorphic sarcoma, ewings sarcoma, rhabdomyosarcoma[Figure-1,Figure-2,Figure-3], eosinophillic granuloma, follicular dendritic cell sarcoma, malignant sweat gland tumor, sebaceous carcinoma, large cell carcinoma, undifferentiated carcinoma, peudotumor orbit and lipofibromatosis. 10 cases (55.5%) underwent upfront surgery followed by adjuvant treatment whereas 1 patient was operated after receiving neoadjuvant chemotherapy. Other cases (7 patients) were inoperable and were treated with radiotherapy and chemotherapy according to the stage and histopathology of the malignancy. 12 cases (66.67%) have received radiotherapy either in definitive or adjuvant setting in-totto. Median follow-up period was 30 months(ranging from 1 month to 70 months).Among these 18 patients, one patient has died during followup period; whereas three patients have shown recurrence of the disease. Among these three patients with recurrence, two were local recurrences which were managed with salvaged surgery whereas the other was locoregional recurrence with hard fixed node and is on metronomic therapy now.

IV. DISCUSSION

Squamous cell carcinoma constitute the majority of malignancies encountered in head and neck region.The staging and management of squamous cell carcinoma in head and neck is well established.However,extensive study regarding nonsquamous cell carcinoma and other atypical malignancies in head and neck is lacking.For discussion purpose, the whole head and neck can be divided into 4 subsites such as: (1) orbit, (2) nasal cavity, paranasal sinus, and nasopharynx, (3) oral cavity , oropharynx and salivary gland (4) hypopharynx, larynx and neck region.

- *Orbit:-*

Tumors arising in orbit can be benign (64%) or malignant (36%)[3]. These tumors can be broadly divided into tumors arising from bone and cartilageneous (osteoma, chondroma, aneurysmal bone cyst etc), vasculogenictumors (capillary and cavernous hemangioma, hemangiopericytoma etc), tumors of mesenchymal origin (rhabdomyosarcoma, lipoma, liposarcoma), tumors arising from neural structures and their coverings (schwannoma, optic nerve glioma), tumors of lacrimal apparatus, metastatic deposits and misselaneous tumors[4]. We have encountered three cases in this study of atypical neoplasms out of which two are lipofibromatosis and one is sebaceous carcinoma of eyelid.

- *Nasal Cavity , Paranasal Sinuses and Nasopharynx:-*

Cancers of the nasal cavity and paranasal sinuses are rare, comprising less than one percent of all human malignancies and only three percent of those arising in the head and neck[5]. The major histological types of malignancy arising in nasal cavity and paranasal sinuses include squamous cell carcinoma (46%), lymphoma (14%), adenocarcinoma (13%), and malignant melanoma (9%)[6]. However adenoid cystic carcinoma[7],sarcomas and undifferentiated carcinomas are considered as atypical presentations in this subsite. Patients generally present with a nasal mass and obstruction, midline facial swelling,nasal congestion and discharge or diplopia[8].Treatment options include surgery and radiotherapy.Radiotherapy may be given as a definitive treatment in inoperable cases or as adjuvant treatment in margin positive and high risk cases.We have encountered five cases of atypical malignancies in this subsite among which two were sarcoma(one ewings sarcoma and one rhabdomyosarcoma), one sinonasal carcinoma, one undifferentiated carcinoma of PNS and one adenoid cystic carcinoma. Among these three were male whereas two were female patients and the mean age of presentation was 37.8 yrs. Three patients had undergone surgery out of which two have received adjuvant radiotherapy whereas other two patients were inoperable during presentation and have received induction chemotherapy followed by definitive radiotherapy.

- *Oral Cavity, Oropharynx and Salivary Glands:-*

Squamous cell carcinomas (SCC) constitute approximately 90% of all oral and oropharyngeal cancers[9]. Other malignant tumours can arise from the epithelium, connective tissue, minor salivary glands, lymphoid tissue, and melanocytes or metastasis from a distant tumor[10]. Salivary gland neoplasms represent <5% of head and neck tumors[11]. Oral cancers are more common in males beyond 5th decade of life. However, there is a rising trend in the younger age group who has been influenced by a smokeless tobacco brand called Gutkha[12]. Adenoid cystic carcinoma is a rare tumor accounting for <1 % of all head and neck malignancies and 10 % of all salivary gland neoplasms[13].We have encountered five cases of atypical malignancies in oral cavity, oropharynx and salivary gland out of which two are adenoid cystic carcinoma, one sarcomatoid carcinoma, one marginal zone lymphoma of parotid and one follicular dendritic cell sarcoma hard palate. Three patients were male while two were female and the mean age of presentation was 50.6yrs. According to the recent American Cancer Society statistics, the average age of most people diagnosed with these cancers is 62 years[14]. Surgery is the prime modality of treatment in oral cavity and salivary gland malignancies whereas oropharyngeal carcinomas are mostly treated by definitive chemoradiotherapy. Three of our patients in this subset underwent surgery followed by adjuvant radiotherapy. One patient with marginal zone lymphoma of parotid gland received targeted therapy in form of Rituximab followed by involved field radiotherapy(IFRT).

- *Neck:-*

Cervical lymphadenopathy, laryngeal and hypopharyngeal carcinoma are the common neoplastic lesions found in neck region. We have encountered three atypical malignancies in neck region which include sarcomatoid carcinoma, dendritic cell sarcoma and a case of large cell carcinoma with neuroendocrine differentiation.Sarcomatoid / Spindle cell carcinomas (SpCC) of the head and neck are a rare variant of the squamous cell carcinoma (SCC), representing less than 3% of all head and neck malignancies of epithelial origin[15]. Surgery is considered to be the mainstay in the

management of SpCC. The effectiveness of radiotherapy was suggested by Ballo *et al* in 1998, however, more recent studies did not confirm the impact of radiotherapy on survival. We have dealt with two cases of sarcomatoid carcinoma (1 in buccal mucosa and 1 in neck region). In both the cases patients have undergone surgery .The case in buccal mucosa had microscopic margin positivity and has received adjuvant radiotherapy. However the disease recurred locoregionally with skin ulceration after about one year of radiotherapy, for which he received chemotherapy in palliative intent.

V. CONCLUSION

Atypical malignancies though uncommon; are not rare in head and neck region. Hence their diagnosis should always be done by biopsy and IHC should be performed whereever necessary. The management of such patients should be customised according to histopathological variant, site and the stage of presentation. As much of literature is not available regarding this subgroup of malignancy, extensive research needs to be done and subjecting patients to clinical trials should be encouraged.

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Serial no	Sex	Age(yrs)	Histopathology	Site	Treatment	Status	Followup period
1	M	53	Adenoid cystic ca	Hard palate	CCRT	On f/u	70 mnths
2	F	40	Pseudotumor orbit	Rt lacrimal gland	Steroid	On f/u	65 mnths
3	F	40	Adenoid cystic ca	Lt maxilla	Surgery	On f/u	42 mnths
4	M	16	Ewings sarcoma	Rt maxilla	NACT--CCRT--CT	On f/u	30 mnths
5	M	62	Undifferentiated ca	Rt maxilla	ESS-recurrence (metronomic therapy)	Recurrence -on f/u	30 mnths
6	M	45	Pleomorphic sarcoma	sinonasal	NACT—RT	On f/u	31 mnths
7	M	70	Large cell ca with neuroend diff	Lt neck	CT--RT—CT	dead	1 mnth
8	M	59	Sarcomatoid ca.	Rt neck	NACT—surg	On f/u	13 mnths
9	F	26	Rhabdomyosarcoma	Lt nasal cavity	Surg—CT	on f/u	22 mnths
10	M	47	Sarcomatoid ca	Rt buccal mucosa	Surg—RT-recurrence-salvage surg-pall CT	Recurrence -on f/u	18 mnths
11	M	42	Malignant sweat gland tumor	scalp	Surg--RT—recurrence-salvage surg-pall CT	Recurrence -on f/u	30 mnths
12	M	28	Sebaceous ca	Lt upper eyelid	Surgery	On f/u	10 mnths
13	M	44	lipofibromatosis	Lt orbit	Rituximab+pred--RT	On f/u	5 mnths
14	F	63	Marginal zone lymphoma	Lt parotid	Rituximab--RT	On f/u	33 mnths
15	M	15	Eosinophilic granuloma	scalp	Surg--CT	On f/u	31 mnths
16	M	56	Follicular dendritic cell sarcoma	oropharynx	Surg--RT	On f/u	24 mnths
17	F	60	Dendritic cell sarcoma	Lt neck	Surg--RT	On f/u	32 mnths
18	F	34	Adenoid cystic ca	Rt parotid	Surg--CCRT	On f/u	40 mnths

Table 1:- Table Showing Demographic and Treatment Details of Patients

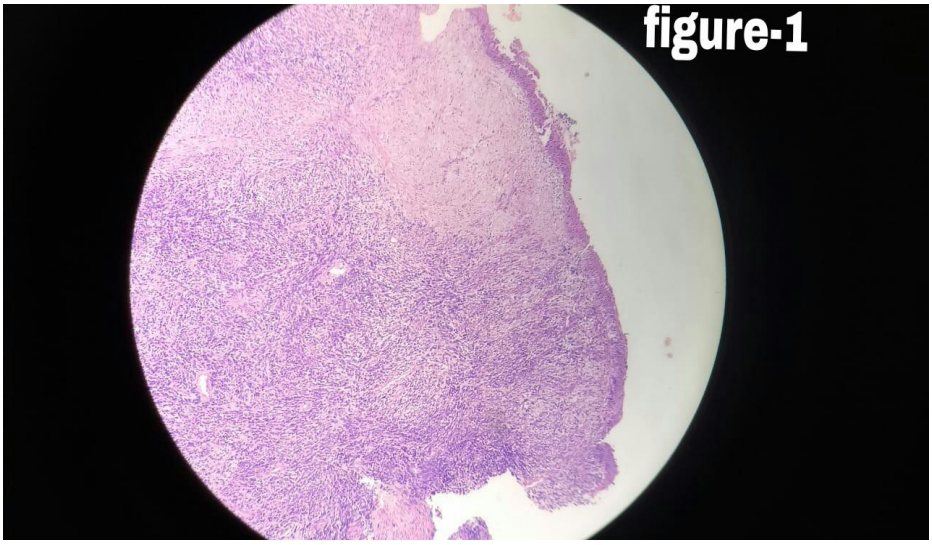

Fig 1:- 100X Image -Showing Diffuse Infiltration of Subepithelial Stroma by Tumor,which is Composed of Short Fascicles and Bundles of Tumor Cellswith Plump to Elongated Hyperchromatic Nuclei with Rhabdomyoblastic Differentiation.

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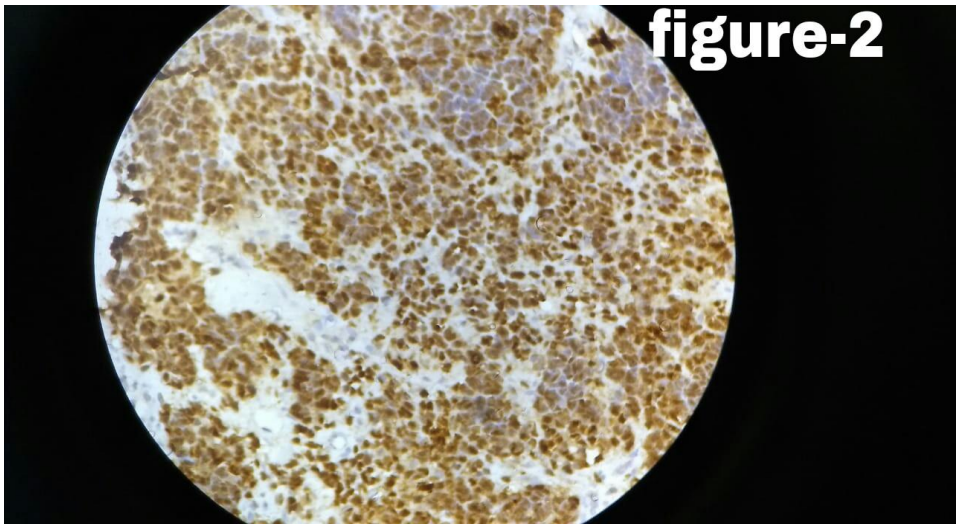

Fig 2:- MyoD1 Positivity in 400X

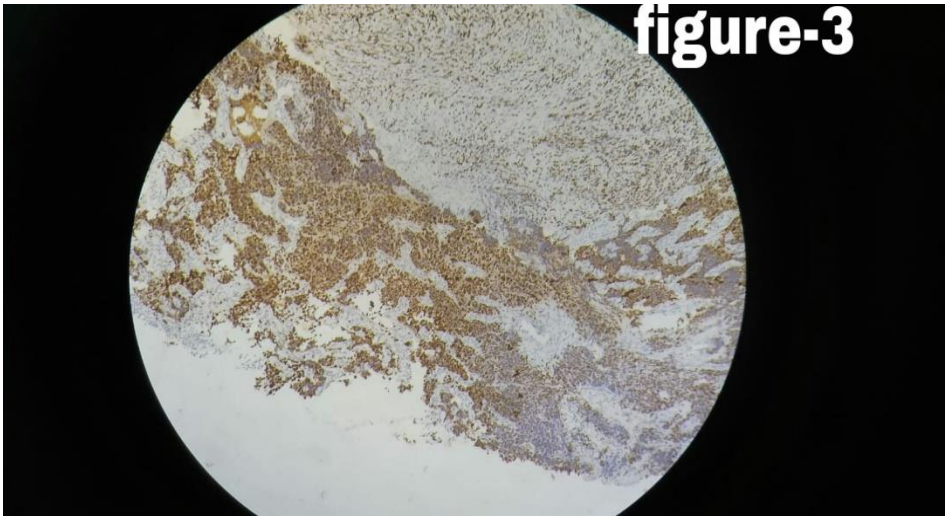

Fig 3:- Myogenin Positivity in 100X