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Primary Small Cell Carcinoma Of Base Of Tongue

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Abstract:
Neuroendocrine small cell carcinomas are most commonly seen in the lung and they rarely aries in the extrapulmonary sites. Small cell carcinoma of tongue is an extremely rare entity with only eight cases reported till date.A50 years old male presented with left side neck swelling proliferative growth at the base of tongue Histopathologically and immunohistochemistry confirmed as a small cell carcinoma of base of tongue. We discuss clinical, pathological, radiological finding and management of small cell carcinoma of base of tongue. These are all important for the correct diagnosis of small cell carcinoma. As no standard therapeutic regimen exists for extrapulmonary SCC .The patient was treated with combination of chemotherapy and radiotherapy.
Keyword: *Extrapulmonary SCC, Base of Tongue.*

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I. Introduction

Oral cavity cancer is the second most common cancer in India according to globocan 2020. Almost 10.3% new cases diagnosed in 2020 in both sexes of all age group. Orophyreangeal cancer are in eighteen number with 1.6% of new cases diagnosed in 2020, in both sexes of all age group [1].

As per our hospital based cancer registry oral cavity cancer is the most common cancer in last five years. Almost 22% new oral cancer cases registered every year in our hospital.

Histopathologically squamous cell carcinoma contributes remarkably i.e.84-97% of oral cancer. Tobacco consumption including smokeless tobacco, betel-chewing, excessive alcohol consumption, poor oral hygiene, nutrient-deficient diet, and sustained viral infections, i.e. human papillomavirus (HPV) are some of the risk associated with occurrence of oral cancers [2].

The vast majority of small cell carcinoma develops from the lung and only about 2.5% of small cell cancer arises in extra pulmonary sites [3]. Extra pulmonary small cell carcinoma was first described by Duguid and Kennedy in 1930, as a different entity from the small cell carcinoma lung [4] .The extra pulmonary small cell carcinoma is recognized as a clinicopathological entity distinct from small cell carcinoma of lung; however it is still often confused with metastatic small cell lung cancer [5]. The most commonly reported extra pulmonary sites with small cell carcinoma are aero-digestive tract including nasal cavity, para nasal sinuses, salivary glands, larynx, trachea and thyroid gland [4]. It has also been rarely found in breast, urinary bladder, prostate gland, ovaries and cervix [6]. The extra pulmonary small cell lung cancer shares the same histopathological features as small cell lung cancer and is also chemotherapy sensitive [6]. The Extra pulmonary small cell lung cancers more aggressive and typically demonstrates a poorer prognosis [7].

II. Case Report:

A 50 years old male with a history of cigarette smoking, chewing tobacco for thirty years and social drinker presented to our department with chief complaints of dysphagia for solid food for the past 2-3 months, left side neck swelling which was progressively increasing in size, bilateral lower limb paraplegia, severe backache and abdominal pain. There was no associated weight loss, his appetite was good. There were no other risk factors such as any history of Human Papilloma Virus or betel nuts. The patient's family history was not significant.

On examination of oral cavity revealed a large growth at the base of tongue mainly left side crossing midline and also left sides neck level II,2x2 cm conglomerated firm mass was palpable. Diffuse abdominal tenderness present in whole quaderents of abdomen no spinal tenderness. The fibre optic endoscopy by the ENT specialist showed a large proliferative growth arising from left side base of tongue involving the vallecula, while both of the vocal cords were normal and mobile.

The fine needle aspiration of the neck node revealed ATYPICAL Polygonal to round cells having scanty cytoplasm & large hyperchromatic nucleoli suggestive of HIGH GRADE MALIGNANT NEOPLASM.

Biopsy from a lesion in base of tongue suggestive of small cell carcinoma. The immunohistochemical staining was positive for pancytokeratin (PCK AEI/E3), synaptophysin, cd56, and thyroid transcription factor 1 (TTF1), with 70-75% Ki67, suggestive of small cell carcinoma.

The pretreatment CECT scan face & neck revealed well defined hetrogenously enhancing mass lesion noted in base of tongue predominant of left side with extension into the vallcula measures 3x2.8x4.4 cm with multiple enhancing enlarge lymphnodes in bilateral upper middle & lower juglar, largest 4x4x3.5 cm. in left middle juglarregion,cect whole abdomen suggestive of multiple liver metastasis with in the both lobes of liver . The x-ray of lumbo sacral spine AP/PA lumber spondylosis.

The tumor was staged CT3N2CM1 stage IVA and the patients was given chemotherapy docetaxel, and Cisplatin 3 weekly along with granulocyte colony stimulating factor support followed by planned for external beam radiotherapy to gross tumor and draining lymph nodes to total dose of 7000cGy,in 35 fractions 200 cGy per fraction five days in a week for seven weeks along with concurrent 3 weekly cisplatin, the biologically effective dose (BED) is 8400 cGy but patient was not willing for concurrent chemotherapy and after receiving 6000cGy of radiation dose due to developed back pain patient was not able to take further radiation .

After six weeks of complete of radiation on follow up in PET/CT scan revealed no abnormal FDG uptake /lesion involving base of tongue. Metabolically active extensively skeletal lesion involving bilateral scapula, ribs, multiple thoracolumbar vertebrae with D4 and D12 compression vertebrae. No FDG uptake in primary site i.e, base of tongue and no liver metastasis.

Later patient radiate to D4 to D6 vertebrae in palliative setting where maximum spinal tenderness present with total dose 2000cGy, 400cGy per fractions total five fractions in a week with 3DCRT technique along with steroid and zolendronic 4mg monthly followed by palliative chemotherapy Etoposide 100 mg/m2 day 1 to day3 and Carboplatin AUC 5 three weekly for six cycles with granulocyte-colony stimulating factor support. After first cycle of chemotherapy patient went to septic shock, despite of all cardio-pulmonary resuccitation and supportive care patient certified dead.

III. Discussion

Small cell carcinoma is seen in the lungs and gastrointestinal tract .20% of lung carcinomas are small cell carcinoma[16].Small cell lung carcinoma is usually located centrally, adjacent to major airways [19].They uncommonly arise in extrapulmonary sites [16].

Pathology-

The histopathologic features of small cell carcinoma include dense sheets of small cells with scant cytoplasm, finely granular nuclear chromatin, inconspicuous or absent nucleoli, and frequent mitoses. Necrosis is universally present and frequently extensive. The tumor cells typically measure less than three small resting lymphocytes in diameter. They are round to fusiform in shape and have scant cytoplasm. Nuclear molding is characteristic. Proliferation rate is typically among the highest of all tumor types: mitotic counts average 60 to 80 per^2 mm^2, and Ki67 proliferation rate is consistently >50%, and typically 80% to 100%. Crush artifact is a frequent finding in small biopsy specimens and can make pathologic interpretation difficult [19].

Although the diagnosis of small cell lung carcinoma can be made based on histopathologic features using the haematoxylin and eosin-stained sections, immunohistochemistry (IHC) is increasingly utilized in pathology practice to support the small cell lung carcinoma diagnosis and to exclude alternative diagnoses. In recent studies, IHC was shown to increase

The accuracy of small cell lung carcinoma diagnosis [20]. The IHC markers commonly used to support the diagnosis of small cell lung carcinoma include a panel of three neuroendocrine markers—chromogranin A, synaptophysin, and CD56 (NCAM). Of these, CD56 is most sensitive but is least specific,given that it is expressed in a variety of non-neuroendocrine neoplasms, including various hematolymphoid malignancies. However, 20% of SCLC may be negative for the more specific neuroendocrine markers, synaptophysin and chromogranin A, and up to 10% may be negative for all three markers. The more recent neuroendocrine marker insulinoma-associated 1 (INSM1) has similar sensitivity to CD56 but is more specific, and it is becoming commonly utilized for the diagnosis of small cell lung carcinoma [21]. Thyroid transcription factor 1 (TTF1) is positive in ~80% of SCLC. Notably, TTF1 can be positive in extrapulmonary small-cell carcinomas, so it is not useful in determining the primary site of small-cell carcinomas [22].

Presentation-

Presenting symptoms in patients with small cell lung carcinoma can be constitutional, pulmonary, the result of extrathoracic spread, or due to paraneoplastic disorders [23]. In one series, fatigue was the most common symptom, with decreased physical activity, cough, dyspnea, decreased appetite, weight loss, and pain all occurring sometime in the course of the illness in the majority of patients [24]. As the primary tumor often

presents as a large central mass invading or compressing the mediastinum superior vena cava obstruction has been reported at diagnosis in 10% of patients with small cell lung carcinoma [25].

Most patients with small cell carcinoma have metastases at diagnosis [19].Hepatic and adrenal lesions are typically asymptomatic. Brain metastases are reported in up to 18% of patients at diagnosis and are often asymptomatic [26]. Bone involvement is usually characterized by asymptomatic osteolytic lesions, often without elevation of serum alkaline phosphatase [27].

Paraneoplastic syndromes (PNS) are common in small cell lung carcinoma [21]. Small cell lung carcinoma accounts for approximately 75% of the tumors associated with the syndrome of inappropriate antidiuretic hormone (SIADH) [21]. Increased serum levels of adrenocorticotropic hormone (ACTH) can be detected in up to 50% of patients with small cell lung carcinoma [21]. Neurologic PNS seen in patients with small cell lung carcinoma include sensory, sensorimotor, and autoimmune neuropathies and encephalomyelitis and can be clinically disabling [28]. The extra pulmonary small cell carcinoma is now recognized as a separate clinicopathological entity but behaves similar to small cell carcinoma with more aggressive course and carries a poorer prognosis. It has more male predominance and more common in smokers.[3,4].

Cancer of base of tongue relatively uncommon and typically occur in fifth through seventh decade of life, men are afflicted three to five times more often than women[9;10].Like other head and neck cancers ,tobacco, alcohol, and more recently human papillomavirus(HPV)infection represent most significant risk factors for development of carcinoma of base of tongue [9]. Histopathologicaly almost all orophyryngeal cancers are squamous cell carcinoma and very rarely any other histology is seen [10].

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Small cell carcinoma is a systemic disease and localized treatment alone is not sufficient; there for, even at an early stage, multimodality therapy including systemic therapy is preferred [6].

Prophylactic cranial irradiation is not recommended routinely in extrapulmonary small cell carcinoma. The incidence of brain metastasis is low, and there are differences in disease biology and metastasis spread between extrapulmonary small cell carcinoma and small cell lung cancer [16].

Our patient have history of difficulty in swallowing ,neck mass, back pain, and did not have respiratory problem .At the time of diagnosis disease already spread to neck nodes and liver. On CECT thorax there was no parenchymal lung lesion .On CECT face and neck there is a lesion presented on left side of base of tongue with pathological specimen from base of tongue showed small cell carcinoma, immunohistochemistry showed pancytokeratin (PCKAE1/AE3) positive along with synaptophysin, CD56 and thyroid transcription factor1 suggestive of extra pulmonary small cell carcinoma origin.

There are no standard guidelines to treat patients with extra pulmonary small cell cancer however; because of its relative chemo sensitive nature, the majority of extra pulmonary small cell cancer patients are treated with Platinum based chemotherapy regimens similar to small cell lung cancer [4,7].

Naeem Ltif et al.[6] treated T2N2M0 small cell carcinoma 0f tongue with full dose of cisplatin and etoposide every three weekly concomitant radiation therapy with total dose of 74Gy,but due to pancytopenia and severe mucositis patient could not continue further treatment.

Shah ,Isha et al. [16] treated stage III small cell carcinoma of base of tongue with concurrent chemo radiation with cisplatin 50 mg/m2 weekly with radiation total dose of 66 Gy with three year follow up without evidence of recurrence.

Soni et al.[17] treated T4aN2aM0 stage disease with cisplatin and etoposide in neoadjuvent setting three weekly interval with radiatiation total dose of 64Gy with 6 months disease free interval.

Khurana et al.[18] treated with three weekly chemotherapy vincristine, doxorubicin and cyclophosphamide for 3 cycles with grade II neutropenia followed by radiation total dose of 66Gy . Patient have four months of disease free interval on follow up but subsequently he developed recurrence over base of tongue.

The median survival for extra pulmonary small cell cancer irrespective of site of origin is almost 14 months [4]. The initial stage at time of diagnosis and location of the disease are independent prognostic factors for survival, and it is unfavourable when patient presents with extensive disease [4]. Small cell cancer of the gastro intestinal tract or oral cavity is rare and most commonly found in patients with advanced age and caries a dismal prognosis [19].

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