AN UNCOMMON ENTITY; PRIMARY SMALL CELL NEUROENDOCRINE CARCINOMA OF MANDIBLE: A CASE REPORT

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INTRODUCTION

The mandible is a physiologically complex bone and is analogous to long bone. More than 30 lesions, including benign and malignant tumours, frequently occur in the mandible. In the spectrum of pathologies that present in the posterior mandible, ameloblastoma shows a marked prevalence. A variety of non-odontogenic solid malignancies can also occur in the mandible, but the mandible is not usually the primary site of diagnosis, rather it is known for metastatic involvement[1].

Small cell neuroendocrine carcinomas (SNECs) are poorly differentiated high-grade neuroendocrine tumours that usually present as primary lung tumours near the bronchial region. Head and neck events are infrequent, with the larynx being the most prevalent site. SNEC is diagnosed based on histology and confirmation of origin by immune histochemistry[2]. Primary SNECs in the head and neck region are sporadic tumours, with only a few cases reported in the English literature.

This case report describes a primary SNEC diagnosed in the mandibular ramus of an elderly female patient who presented to the department with a swelling over the posterior mandible. The clinical presentation, and imaging findings initially were consistent with that of the benign odontogenic tumour, Ameloblastoma, until the immunohistochemistry reports were received.

CASE DESCRIPTION

An 80-year-old female patient presented to our department with a chief complaint of swelling over the right side of the face in the past 1 year. The swelling gradually increased in size within 10 months. The patient noticed a rapid increase in swelling over the last two months which was associated with intermittent pricking pain. The patient also reported having difficulty in opening her mouth and a lack of sensation in the lower lip on the right side. She gave a history of exfoliation of all her teeth by the age of 60, and there was no history of discomfort or swelling, which made her visit a health practitioner.

On extra oral examination, a solitary oval-shaped swelling was noted along the right posterior body and ramus of the mandible measuring approximately 5 cm X 3 cm in the greatest dimensions, roughly oval in shape with a smooth surface. The skin overlying the swelling appeared to be smooth and tense. On palpation, the swelling was warm, tender, firm to hard in consistency, and had a smooth surface and well-defined margin. Lymph nodes were not palpable [Figure 1].

Intra orally, a solitary irregularly shaped swelling measuring approximately 4 cm X 2 cm in its largest dimensions was noted along the posterior third of the lower right edentulous alveolar ridge causing expansion of the alveolus bucco - lingually. The swelling was pale pink in color and had a lobulated surface. Obliteration

of buccal vestibule and tense buccal mucosa were also noted [Figure 2]. On palpation, the swelling was afebrile, firm with areas of tenderness over the superior aspect of the swelling.

A provisional diagnosis of ameloblastoma was made considering the history, age, aggressive nature of the tumour, and location. Differential diagnoses of malignant non-odontogenic tumours, and metastatic tumours to the jaw were also considered. Basic investigations were undertaken, including hematological parameters, renal function tests and liver function tests, an orthopantomogram (OPG), and CT scan.

Panoramic radiography revealed a large radiolucent lesion, located over the right side of the mandible involving the entire ramus and body up to the right para-symphysis region. It measured approximately 4 cm X 7 cm roughly oval in shape with an epicenter at the ramus of the mandible and had a partially corticated border. The internal structure appeared to be completely radiolucent. Expansion and thinning of the anterior border, and thinning of the posterior and inferior border of the mandible were evident with few areas of perforations at the anterior border along the ascending ramus of the right side of the mandible [Figure 3].

A computed Tomography scan demonstrated a uniformly expansile, oval-shaped osteolytic lesion around the right side of the mandible, involving the ramus, coronoid, and body, measuring approximately 4 cm X 4.84 cm X 7.5 cm in its largest dimension. The internal structure appeared to be hypodense, with radiodensity equivalent to soft tissue. The lesion had caused expansion, thinning, and loss of cortex in bucco-lingual, antero-posterior, and superior-inferior directions. Irregular bone destruction with bony spicule was noted over the body of the mandible in relation to the para symphysis region. The inferior alveolar canal could not be visualized due to lesion invasion [Figure 4].

Screening CT of the thorax and USG abdomen revealed no evidence of any lesion. Liver function tests and renal function tests showed normal values.

On histopathological evaluation, Hematoxylin and eosin-stained section showed a nonencapsulated tissue stroma with proliferating tumour cells arranged in solid sheets and cords. The tumour cells were uniformly arranged round cells with round oval-shaped nuclei, scanty pale cytoplasm, and showing abundant mitotic figures. Spindle-shaped cells arranged in pagetoid fashion were also noted with few areas showing blood vessels along with extravasated RBCs, and focal areas of bony trabeculae infiltrated by tumour cells [Figure 5].

The immunohistochemical staining was performed. The percentage of the tumour marker Ki-67 was positive and the proportion was assessed to be 90%. Additionally, the markers cytokeratin (AE1/AE3), synaptophysin, and chromogranin A were found to be positive. Hence, a diagnosis of small cell neuroendocrine carcinoma was made.

Resection and chemo and radiotherapy were planned for the patient. But patient passed away due to post covid complications within one month of diagnosis; hence definitive treatment could not be given.

DISCUSSION

Neuroendocrine cells are specialized cells that exhibit characteristics of both endocrine cells and neurons. Neuroendocrine carcinomas originate from these cells [2]. NETs have a reported incidence of 2.5–5 cases/100 000 people. Common primary sites are lungs and associated structures. Extrapulmonary SNECs account for only 2.5-5% of all SNECs, while head and neck events account for 10-16%.[2] Reported cases of NETs in the oral cavity are scarce[3].

Ki-67 is a cellular proliferation marker crucial for detecting tumour growth. The proposed WHO 2010 grading system divides NETs into three classes on the basis of mitotic count and Ki-67 index. They include Grades 1, 2, and 3. Grade 1 exhibit a low proliferative index with Ki-67 3% or 2 mitoses per 10 high power fields, Grade 2 exhibit moderate proliferative with Ki-67 3%-20% or 2-20 mitoses per 10 high power fields, and Grade 3 exhibit a high proliferative index with Ki-67 >20% or >20 mitoses per 10 high power fields. Another way of evaluating a tumour proliferation rate is to count the number of mitoses per unit tumour

area. However, in tissue with limited volume, Ki-67 is more convenient to measure than mitotic count. The survival rate of patients who had G3 tumours compared to other classes was significantly lower. In the present case, it was a mandibular lesion with extensive distribution. Ki-67 values were 90%, consistent with clinical findings [4,5].

Histopathology and immunohistochemistry play a crucial role in the diagnosis of SNEC. It has typical histologic features of small cell carcinoma such as densely packed cells with sparse cytoplasm and hyperchromatic nuclei with finely divided chromatin and discrete nucleoli. It is often associated with extensive necrosis as well as high mitotic figures. The immunohistochemistry evaluation of these tumours indicates the presence of neuroendocrine markers, particularly synaptophysin and chromogranin A, and low-molecular-weight cytokeratins[6,7]. The present case showed a small cell carcinoma with the presence of synaptophysin and chromogranin A which is typical for small cell neuroendocrine tumours.

Diagnostic Imaging is an essential component, in staging and assessing treatment outcomes for NET patients. For the evaluation of NETs, CT scans are often the primary imaging modality. MRI is a supplementary modality. It is necessary to perform a systemic whole-body assessment utilizing PET/CT and scintigraphy after NETs are suspected or diagnosed to establish whether the tumour is primary or metastatic[5].

A multimodal approach is needed to treat SNEC due to its aggressive nature and high rates of recurrence and metastatic spread. Surgery is not feasible for most patients due to disseminated disease at diagnosis. Therapeutic radiotherapy and chemotherapy are recommended in these cases. For extrapulmonary lesions, cisplatin and etoposide are typically used as chemotherapy, the same regimen used to treat pulmonary lesions[7,8].

CONCLUSION This case report describes a case of a small cell neuroendocrine tumour extensively involving the right side of the mandible, diagnosed in an elderly woman. Although NETs are rare, it is important to differentiate NETs from other tumours in the region because of their therapeutic importance. Since there is a paucity of reported cases in literature, a detailed description of such unique cases is needed as it would aid in developing an overall diagnostic protocol.

AUTHOR CONTRIBUTIONS

Deepthi M: analyzed and interpreted the patient data and was a major contributor in writing the manuscript. Manisha M Khorate: analyzed and interpreted the patient data. Nigel Figueiredo: analyzed and interpreted the patient data and contributed in writing the manuscript. Deepthi Priya M: analyzed and interpreted the patient data All the authors have read and approved the final version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

None

CONSENT

A written consent form has been signed by patient's son and collected in accordance with the journal's patient consent policy. Consent for the publication of the patient photographs and medical information was obtained by the authors stating that patient's son gave consent for photographs and medical information to be published in print and online and with the understanding that this information may be publicly available. We will retain the original written consent form and provide it to the Publisher if requested.

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FIGURES

Figure 1: Image showing an oval swelling along the right side of the face with tense overlying skin.

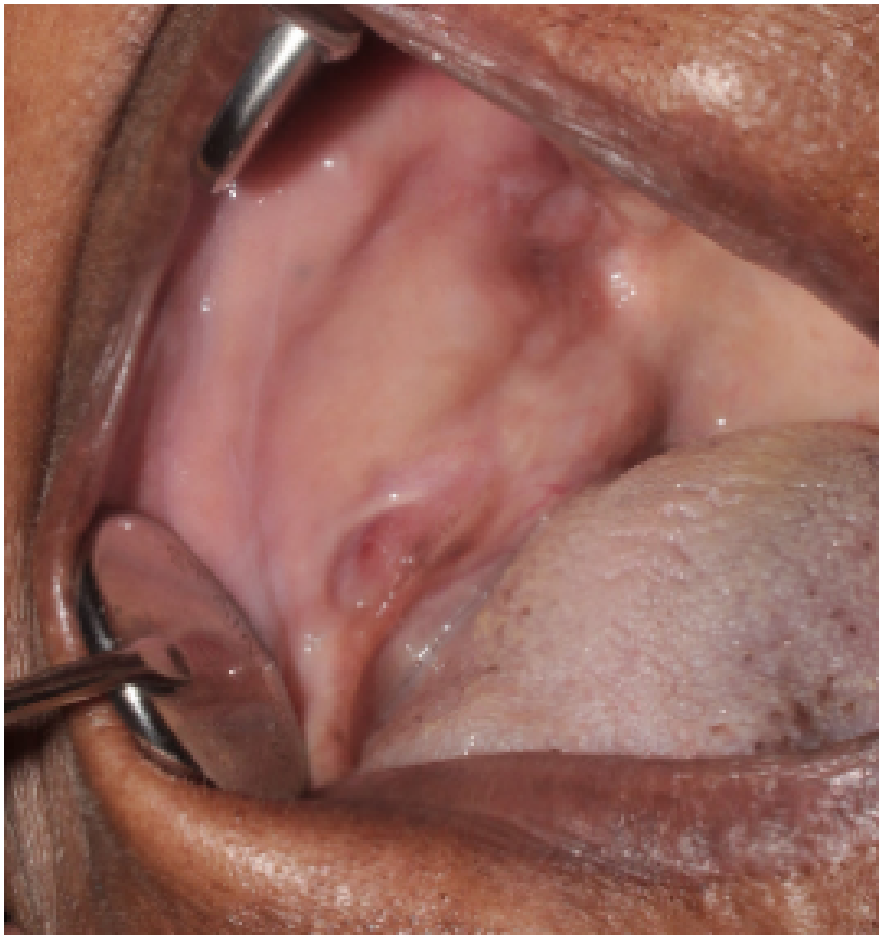

Figure 2: Image showing irregularly shaped swelling along the posterior third of the lower right edentulous alveolar ridge causing expansion of the alveolus bucco - lingually.

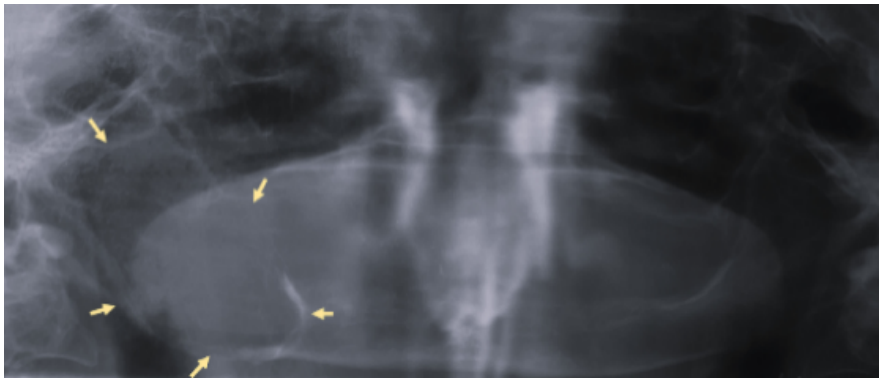

Figure 3: Panoramic radiograph showing an oval-shaped radiolucency in relation to the right side of the mandible involving the entire ramus and body up to the right para-symphysis region with few areas of perforations at the anterior border along the ascending ramus of the right side of the mandible**.**

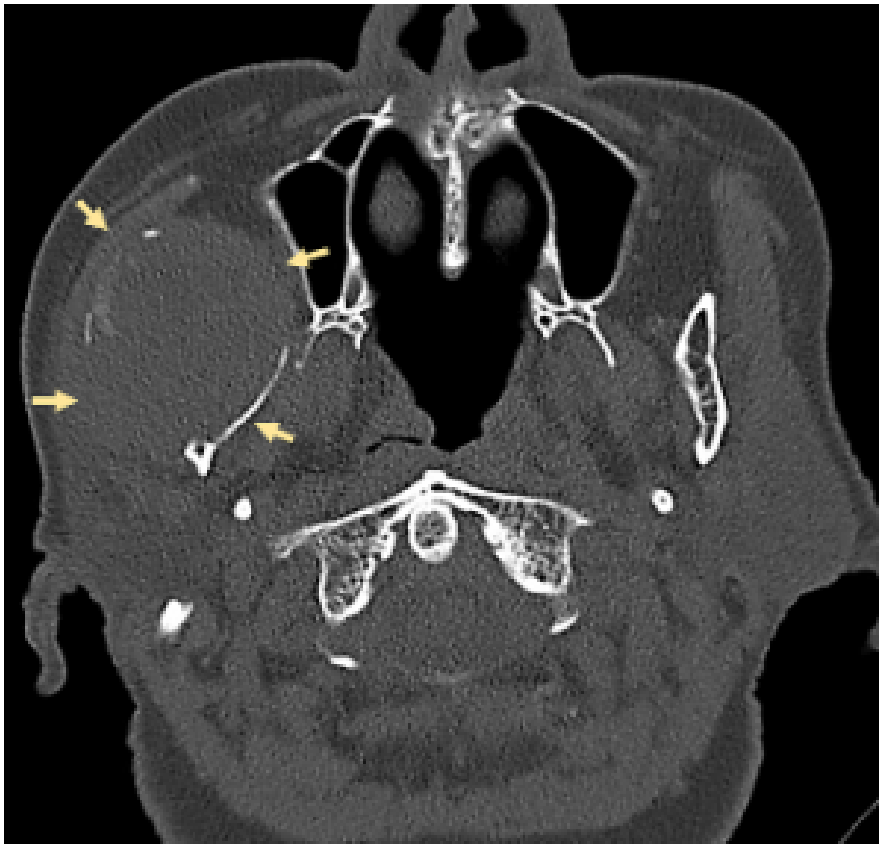

Figure 4: Axial section CT Image showing an oval shaped hypodense lesion, located over the right side of the mandible causing expansion, thinning, and loss of cortex bucco-lingually.

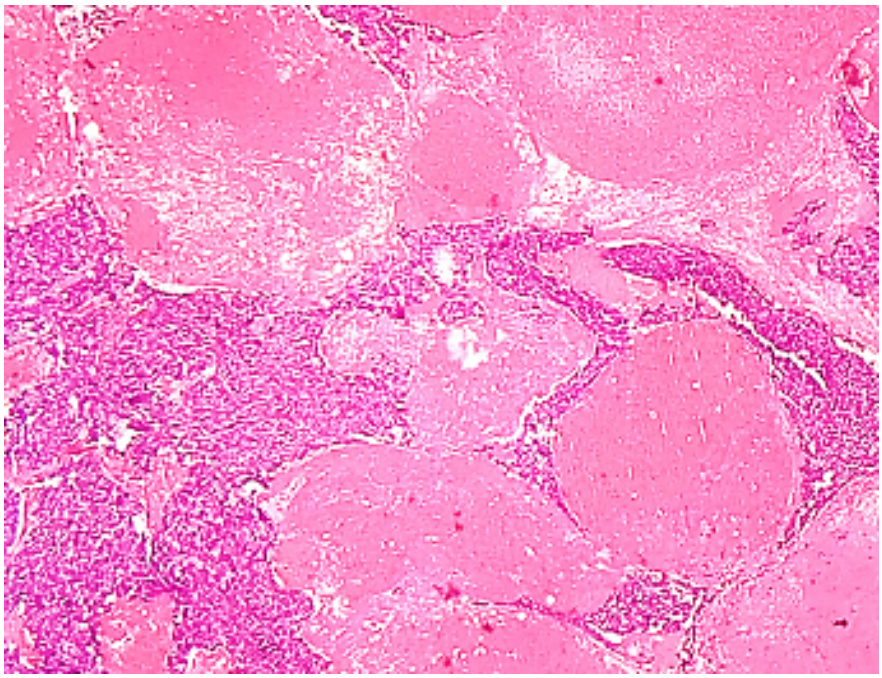

Figure 5: H&E section showing nonencapsulated tissue stroma with proliferating tumour cells arranged in solid sheets and cords.