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AMELANOTIC MELANOMA OF MANDIBLE A DIAGNOSTIC CHALLENGE IMMUNOHISTOCHEMISTRY PLAYS A ROLE

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Abstract : Oral amelanotic melanoma is an extremely rare neoplasm and represents less than 2 percent of all melanomas. Amelanotic melanoma (AM) with lack of melanin pigmentation often makes them difficult to diagnose. The prognosis is usually poorer than that of pigmented melanomas, because of delay in establishing the correct diagnosis, and in the initiation of treatment. Amelanotic melanoma (AM) presents a diagnostic challenge due to its wide clinical presentations, lack of pigmentation, and varied histological appearances. Immunohistochemistry plays a crucial role in the diagnosis of these lesions. We report a case of 56 years old male patient with a recurrent growth on the anterior lower alveolar ridge of mandible. Composite resection was done. Histopathologically provisional diagnosis of Spindle cell neoplasm probably Spindle cell carcinoma or Melanoma was made. A sequential series of immunohistochemical markers study showed strong positivity of Melan- A and negativity of cytokeratin (CK) and epithelial membrane antigen (EMA). A final diagnosis of Amelanotic melanoma was made.

Keyword : Amelanotic melanoma, Oral mucosa, Mandible, MELAN-A

INTRODUCTION

Malignant melanoma is a potentially aggressive tumour of melanocytic origin. About 1–8% of all melanomas arise in the oral mucosa. The most frequently affected oral sites are the palate and the maxillary gingiva. Pigmented melanomas are usually easy to diagnose clinically because of black or brown colour. But amelanotic subtype is also well documented in the literature, which is often difficult to diagnose and requires microscopic evaluation aided by immunohistochemistry for correct diagnosis.

REPORT OF A CASE

A 56 years old male patient reported with a chief complaint of growth in the anterior lower alveolar ridge of mandible since 3 months duration. On inspection, ulcero-proliferative growth is seen with size 6x3cms involving predominantly right side of anterior lower alveolar ridge of mandible and not extending into floor of mouth. Hard and soft palate, retro-molar trigone, tongue and lips were normal. On palpation,tumour do not bleed on touch and not tender but indurated. CT scan of Head and Neck revealed Malignant soft tissue lesion of inferior alveolar process of mandible with bone erosion and metastatic lymph nodes. Procedure – Segmental mandibulectomy with modified radical neck dissection was done. Tumour was excised with 2cm clearance. Partial glossectomy done with Pectoralis Major Myocutaneous flap.

GROSS : (787/14)

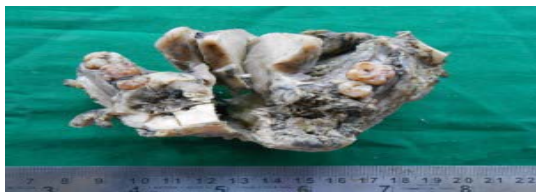

FIGURE A - GROSS SPECIMEN OF TUMOUR (787/14)

Mandibulectomy specimen with growth (Figure A) received measuring 10x6x3cms and attached anterior half of tongue measuring 5x4cms received. Cut section showed an ulcero proliferative growth of size 6x4x2cms in the anterior lower alveolar ridge, involving the underlying bone. Cut section of soft tissue showed three lymph nodes.

HISTOPATHOLOGY :

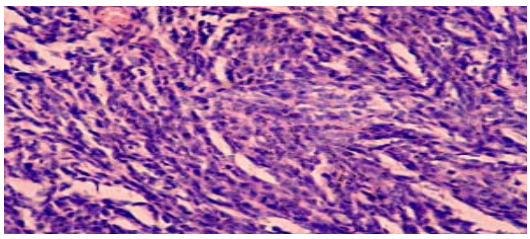

FIGURE B : HPE- The tumour cells are arranged as sheets and fascicles. The tumour cells are spindle to polygonal with ill-defined cell membranes, pale eosinophilic cytoplasm and pleomorphic nuclei with prominent nucleoli (40X)

Microscopic examination showed lining squamous epithelium with the underlying tumour tissue. The tumour cells were arranged as sheets and fascicles. The tumour cells were spindle to polygonal with ill-defined cell membranes, pale eosinophilic cytoplasm and pleomorphic nuclei with prominent nucleoli. A provisional diagnosis of **Spindle cell neoplasm**

probably Spindle cell carcinoma/Melanoma was made. Two out of three lymph nodes, nodes showed evidence of metastatic deposits.

IMMUNOHISTOCHEMISTRY :

Subsequently the tissue was subjected to a series of immunohistochemical marker study. Tumour cells were immunonegative for Cytokeratin(CK) (Figure C), and Epithelial Membrane Antigen(EMA) (Figure D) and showed strong immunopositivity for Melan-A (Figure E & F). On the basis of immunohistochemical marker study, the final diagnosis of **Amelanotic Melanoma** was made.

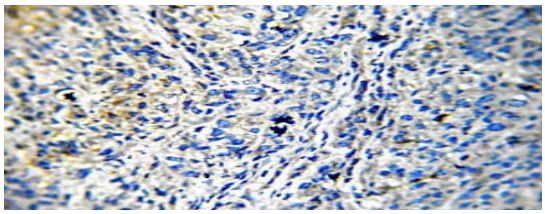

FIGURE C - IMMUNOHISTOCHEMISTRY NEGATIVE EXPRESSION FOR CYTOKERATIN (CK) , 40X

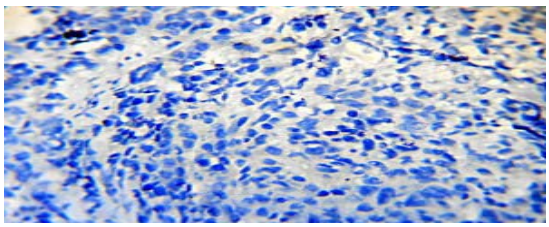

FIGURE D - IMMUNOHISTOCHEMISTRY NEGATIVE EXPRESSION FOR EPITHELIAL MEMBRANE ANTIGEN (EMA) , 40X

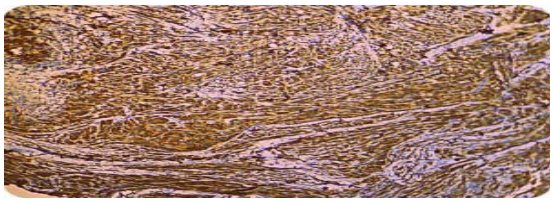

FIGURE E - IMMUNOHISTOCHEMISTRY POSITIVE EXPRESSION FOR MELAN-A,10X

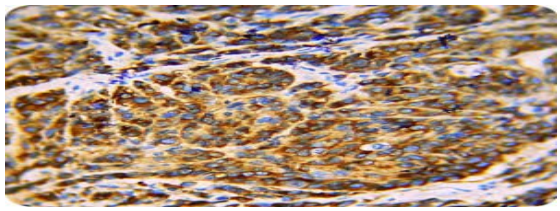

FIGURE F - IMMUNOHISTOCHEMISTRY POSITIVE EXPRESSION FOR MELAN-A, 40X

DISCUSSION

Amelanotic melanoma is an extremely rare entity, comprising 2% to 8% of all melanomas. 34 cases have been reported in the literature so far. The sites in those cases were maxillary gingiva, palatal region, mandibular gingiva and upper lip mucosa [9]. In our case, the site is anterior lower alveolar ridge of mandible. Oral mucosal melanomas have no association with sun exposure. Cigarette smoking, alcohol consumption and denture irritation are the risk factors for oral melanomas [9]. Lack of pigmentation in Amelanotic melanoma clinically and istopathologically [1] makes it a diagnostic challenge for the clinicians and pathologists. The specific cause for the lack of pigmentation is unclear. Speece et al., proposed that there is a deficiency in tyrosine and an enzyme required for melanin production.[11] As cited in Fitzpatrick, Comstock et al., postulated that this enzyme system is intact and can produce melanin but the quantity is insufficient to be seen with histological methods [12]. More recently, electron microscopic identification of premelanosomes has led several authors to favour the low melanin concentration theory for the clinical and light microscopic appearance of amelanotic melanoma [8]. In Gibson et al study.,Electron microscopy showed melanosomes in 13 cases out of 15 cases of amelanotic melanoma. This study demonstrates the difficulties associated with the histologic diagnosis of amelanotic melanoma[3]. Amelanotic Melanoma have a worse prognosis because of its delayed recognition and delayed treatment. Metastasis from Amelanotic Melanoma have similar characteristic features of primary counterpart with lack of pigmentation and rapid growth. Since oral cavity melanomas are exceedingly rare, it is difficult to determine the optimum method of staging, prognosis, and treatment[2] . Distant metastases usually occur after several years. They are often seen in the lungs, liver, and brain, and are almost always associated with recurrent disease at the primary site [10]. For histologically challenging cases, immunohistochemical techniques frequently provide correct diagnostic information[5].

The immunohistochemical panel markers of melanoma include S-100 protein (sensitive but not specific), HMB-45 (a marker of premelanosomes that stain melanoma cells) and MELAN-A/MART-1(an antigen on melanoma cells by cytotoxic T-lymphocytes)[7]. Melan- A/MART-1 is a recently identified new melanocytic differentiation marker[4]. Melan-A is an useful marker in the differential diagnosis of melanocytic tumors, since it is more sensitive and specific than other melanoma markers [7] . Based on histopathological presentation, provisional diagnosis of spindle cell neoplasm, probably Spindle cell carcinoma (SpCC)/ Melanoma was made in our case. The immunohistochemical marker study showed negativity for cytokeratin as well as epithelial membrane antigen and strong positivity for Melan-A. Hence the final diagnosis of **Amelanotic melanoma** was made in our case. The immunohistochemical markers study in such cases are very useful in arriving at an early diagnosis and treatment. Surgical excision is the primary treatment in case of oral mucosal melanotic melanoma[6]. Treatment recommendations for Amelanotic Melanoma are identical to those of pigmented melanomas, although accurately defining clinical margins of these neoplasms are often challenging [5]. The recommended treatment is wide local excision with adequate clearance of margins in combination with chemotherapy and, to a lesser extent, with irradiation therapy or immunotherapy[1].

CONCLUSION

Amelanotic Melanoma should be included in the differential diagnosis of any rapid, nonpigmented gingival enlargement. The current case posed difficulty in diagnosis of the lesion based on the uncharacteristic clinical appearance and atypical histologic features. Early diagnoses by histological examination together with immunohistochemistry are the keys to improve the survival of oral amelanotic melanoma patients with prompt and early treatment.

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