Case Report

An enigmatic combined tumour of oral malignant melanoma and oral squamous cell carcinoma – A rare case report

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Abstract

Combined tumours are those composed of two benign tumours or a benign and malignant tumour or two malignant tumours occurring within the same tumour population. The incidence of combined tumours is very rare. Due to the rarity of these tumours, their biological behaviour remains unlashed. Incisional biopsy of a 48 years old female patient with single, diffuse tumour mass in the oral cavity showed combined tumour or collision tumour of malignant melanoma and squamous cell carcinoma. This was confirmed with immunohistochemistry study. The incidence of combined tumour of malignant melanoma and squamous cell carcinoma in oral cavity is extremely rare. To the best of our knowledge based on the previous literature records, this is the first case report of its kind where there is incidence in the human oral cavity.

Keywords: Malignant melanoma, oral cancer, oral squamous cell carcinoma

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BACKGROUND

Combined tumours of malignant melanoma and squamous cell carcinoma are very rare with unknown biological potential. Their incidence in the oral cavity is extremely rare. Various theories for development of combined tumours have been proposed, such as collision theory, dual differentiation theory, and divergent differentiation theory.[1]

Hybrid tumours and collision tumours represent the incidence of two or more distinct, synchronous primary tumours that may be benign or malignant and appearing in the same anatomic site.[1] Hybrid tumours are composed of two or more divergent tumoural entities within a single neoplasm and arise within a definite topographical region.[2] Collision tumours originate in different regions and coalesce in a particular area.[3]

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CASE REPORT

A 48-year-old female patient presented with a growth on the upper front teeth region since 5 months. It was slow-growing and intermittent in nature. Initially, it was asymptomatic and the patient started to experience pain gradually.

The patient was seropositive for human immunodeficiency virus (HIV) since 1 year, and she was under antiretroviral therapy. Her CD4 + count was 357.

On extra-oral examination, a diffuse swelling was noted on the right middle third of the face, sized approximately 5 × 4 cm. It extended anteroposteriorly from the ala of

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nose till 4 cm posterior to it and superoinferiorly from the ala of nose to commissure of lips. It was firm in consistency and tender on palpation.

On intra-oral examination, a tender, non-mobile, oval, blackish nodular mass was noted on the labial mucosa with relation to 11, 12, 13, 14, and 15. It extends superiorly to the labial vestibule, inferiorly covering the crown of 11 to 15, anteriorly from the distal aspect of 11 and posteriorly to the medial aspect of 16 [Figure 1]. The lesion was about 5 × 7 cm in size, attached, and firm to hard in consistency. The lesion was readily bleeding on palpation.

The ipsilateral submandibular lymph nodes were palpable, mobile, tender, and soft in consistency. Family history and personal history were not contributory.

A provisional diagnosis of kaposis sarcoma was given. Incisional biopsy has been done.

Grossing details: One soft tissue bit of size 1.7 × 0.9 × 0.5 cm was received. It was black in colour with an irregular shape and a rough surface and firm in consistency.

HISTOPATHOLOGICAL EXAMINATION

The normal haematoxylin (H) and eosin (E)-stained section showed numerous dark-stained melanocytes, and they were challenging for examination too. So, the bleaching procedure was done and following that, normal H and E staining was performed. Both normal H and E-stained and bleeched H and E-stained sections were examined. They showed a stratified squamous epithelium and underlying connective tissue. The epithelium had dysplastic features such as loss of polarity of basal cells, irregular stratification, an increased nuclear cytoplasmic ratio, cellular and nuclear pleomorphism, and an increased number of nucleoli. The basement membrane showed breach, and epithelial cells were invading deep into the connective tissue [Figure 2]. Epithelial cell islands and keratin pearls were admixed in the atypical melanocyte population [Figure 3]. The connective tissue shows clusters of atypical melanocytes of variable size and shape [Figure 4b] and scattered in a cord-like fashion throughout the connective tissue [Figure 4a] with numerous keratin pearls admixed.

For confirmation, the immunohistochemical study was performed.

S 100, HMB45 was done for melanocytes [Figures 5, 6a and 6b], whereas AE1/3 (pancytokeratin) was performed for keratinocytes [Figure 7].

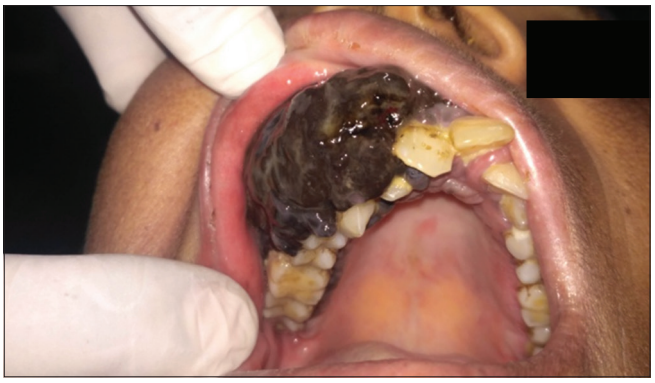

Figure 1: A diffuse blackish mass in the oral cavity of the patient

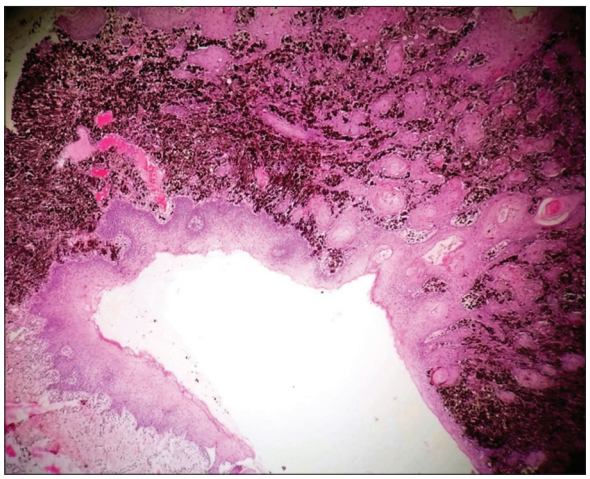

Figure 2: Connective tissue infiltrated with squamous cells and numerous melanocytes (H and E-stained section. Magnification: 10x)

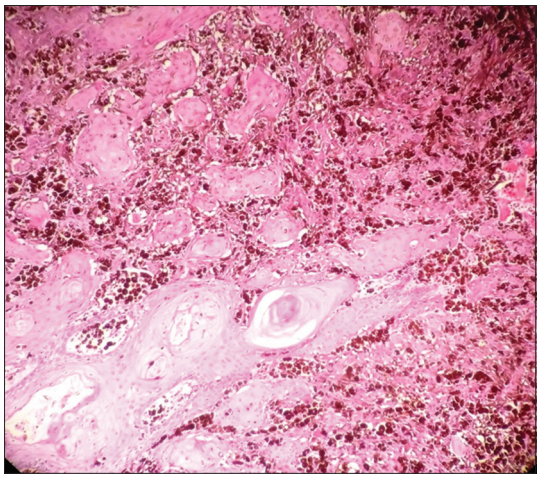

Figure 3: Keratin pearls and squamous island admixed with atypical melanocytes. (H and E-stained section. Magnification: 20x)

This was suggestive of combined tumour of malignant melanoma and squamous cell carcinoma.

DISCUSSION

The present case had shown the features of both malignant melanoma and squamous cell carcinoma within the single

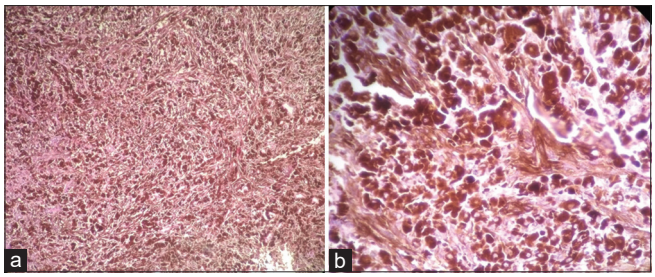

Figure 4: (a) Numerous atypical melanocytes scattered in the connective tissue in a cord-like fashion. (H and E-stained section. Magnification: 20x). (b) Atypical melanocytes of variable shape and size (H and E-stained section. Magnification: 40x)

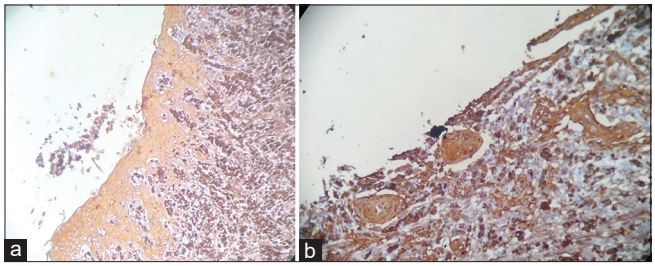

Figure 6: (a) IHC staining with AE1/3 (pancytokeratin) marker showing positivity for epithelial lining and infiltrating squamous cells (Magnification: 20x). (b) IHC staining with AE1/3 (pancytokeratin) marker showing positivity for keratin pearls and squamous islands. (Magnification: 40x)

tumour mass. In such a case, it is necessary to consider pigmented squamous cell carcinoma. In pigmented squamous cell carcinoma, the neoplastic cells will show positive staining for pan cytokeratin A1-A3 and negative staining for S-1OO, HMB-45, and Melan-A proteins that will help to rule out the diagnostic perplexity.[4] In our case, neoplastic kertinocytes showed positive staining for AE1/3 and the neoplastic melanocytes showed positive staining for S-1OO, HMB-45.

Though a variety of combined tumours involving keratinocytes and melanocytes have been described in dermatopathology,[2] their incidence in the oral cavity is very rare. These tumours have been described using the terms "squamomelanocytic" and "basomelanocytic" tumours based on their composition. These tumours have also been mentioned as "melanocarcinoma". But criticism arose as this particular term was originally used as a term for melanoma.

Based on the development of these tumours, several theories have been proposed. They may be categoised into three distinct categories:

1. **Collision between two adjacent neoplastic processes:**

According to this theory, colonisation of a squamous cell carcinoma and malignant melanoma adjacent to each other and gradual collision between them will result in combined

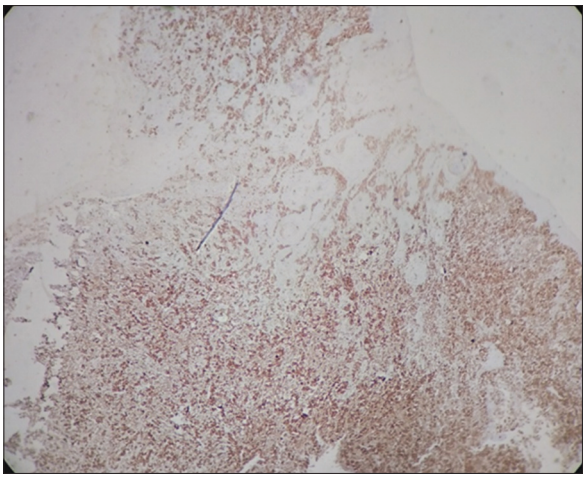

Figure 5: IHC staining with S100 marker showing diffuse positivity for melanocytes. (Magnification: 10x)

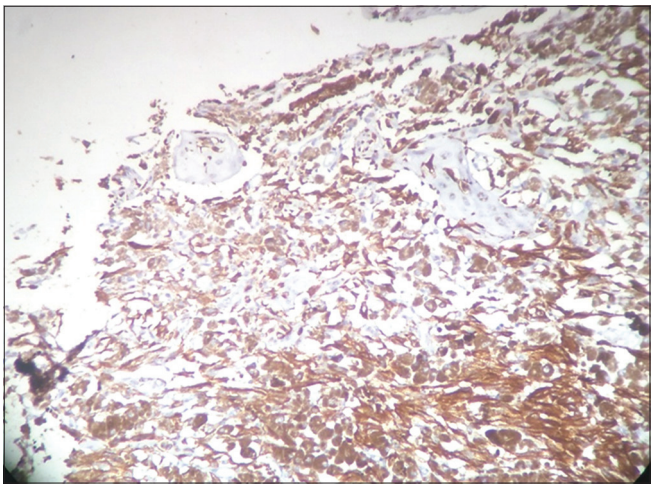

Figure 7: IHC staining with HMB45 marker showing diffuse positivity for atypical melanocytes (Magnification: 40x)

tumour. Miteva et al.[3] suggest that paracrine stimulation of a cell through a tumour cytokine milieu might "induce" a secondary tumour within the confines of primary tumour.

2. **Dual differentiation of a single neoplastic cell line:**

Dual differentiation in a single neoplastic cell line could be responsible for the formation of a monoclonal cell population. This monoclonal cell population might express both keratinocytic and melanocytic cell markers.[5] Rosen reported a case of squamomelanocytic tumour where the cells had expressed both S100 and keratin.[6] For that same case, he had done an ultra-structural analysis, which confirmed the presence of both melanosomes and tonofilaments within the same tumour cells.

We have not performed dual staining for our case as interpretation may be challenging due to overlapping nuclear and cytoplasmic staining patterns.

3. **Divergent differentiation of pluripotent stem cells:** The resultant tumour from divergent differentiation of pluripotent stem cells might represent a variant of a single tumour.

Pool *et al*. were the first to describe a series of four squamomelanocytic tumours where the melanocytes and keratinocytes are intermingled together.[7] In the tumour cells of Pool *et al*.'s case series, the divergent differentiation was demonstrated with immunostains. Similar findings were reported by Satter *et al*.[2] Several authors have also described the presence of ductal structures within squamomelanocytic tumour.[8,9] Amerio *et al*. described a case of squamomelanocytic tumour that was treated as malignant melanoma with a depth of 4.3 mm, followed by the excision and sentinel lymph node biopsy.[10,11] though some authors had suggested that this tumour follows an indolent course; a few cases with metastasis of malignant melanoma in the lymph node were also been reported.[12]

Because of the extreme rarity of squamomelanocytic tumour, the knowledge on the incidence and prognosis remains unlashed. It was mentioned as "tumor with uncertain biological potential".[13] Some authors who observed their patients for a period of 9 years post diagnosis had suggested this tumour to possess a more indolent course,[7] but in our case, the patient passed away within 1 week of postdiagnosis. Even though the patient's seropositivity for HIV may be a contributory factor for the death, her CD4+ count was 357 (i.e., >200), which is considered quite normal.

More studies are needed to confirm the origin of squamomelanocytic tumours and to elucidate the origin as well as the clinical behaviour. Due to the uncertainity of the prognosis, these tumours should be treated and measured as malignant melanomas. Multiple step sections and meticulous examination of the re-excised specimens should be performed in order to ensure the complete elimination of the tumour. Even though a few cases of combined tumours of malignant melanoma and squamous cell carcinoma have been described by some authors, all these cases occurred as cutaneous tumour and one case was reported in the oral cavity of a dog.[14] To the best of our knowledge based on previous literature records, this is the first case of its kind to occur in the oral cavity of a human to be reported. Many case reports, research, and review on combined tumours of the oral cavity should be encouraged, which will give insight into their unlashed clinical behaviour.

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Conflicts of interest

There are no conflicts of interest.

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