DOI: 10.7860/JCDR/2022/57823.17023

Case Report

Dentistry Section

Amelanotic Malignant Melanoma of Buccal Mucosa: A Case Report

VIDYALAKSHMI SANTHANAM[1], VEZHAVENDHAN NAGARAJA[2], SANTHADEVY AROUMUGAM[3], R SUGANYA[4], SHIVARAMAKRISHNAN MUTHANANDHAM[5]

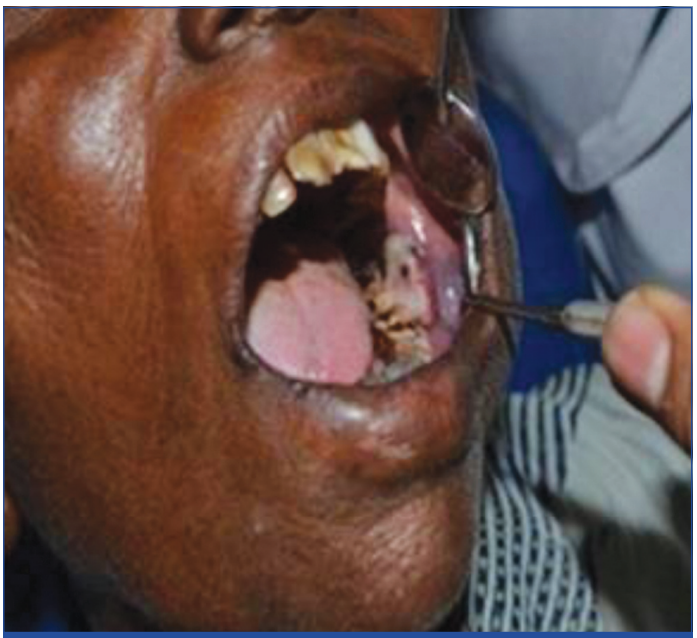
ABSTRACT

Amelanotic melanoma is an atypical variation from pigmented malignant melanoma. The clinical lack of pigment compromises the physician's clinical diagnosis of the lesion. Presence of certain features like red hair, freckles, photosensitivity, previous history or family history predispose the possibility of occurrence of amelanotic melanoma. As the name suggests, the lesions lack pigmentations clinically and mimic many benign and malignant lesions which can be life threatening and thus, cause a diagnostic challenge. Hence, clinicians are expected to have a high suspicion on such lesions, and also judiciously employ biopsy, thus eluding the possibility of emerging of lethal lesions. About 50% of head and melanomas occur in the oral cavity. Of all the melanomas, 2% are amelanotic and majority of them occur in oral cavity. These lesions pose a greater degree of threat, because of the possibility of delayed diagnosis. The timely clinical and laboratory diagnosis favours the patient prognosis. No specific aetiologic factors or risk factors have been recognised for oral melanomas. Hereby, the authors present a case of 60-year-old female patients with ulceroproliferative growth in the left cheek region, which was provisionally diagnosed as malignant ulcer, immunohistochemical investigation of the biopsied sections revealed the diagnosis of amelanotic melanoma. The present case report illustrates the need of addition of a panel of Immunohistochemistry (IHC) markers in the routine diagnosis. The application of such panels avoid the delay in diagnosis and scale-up the prognosis.

Keywords: Neoplasm, Neuroendocrine tumours, Neuroectodermal tumours

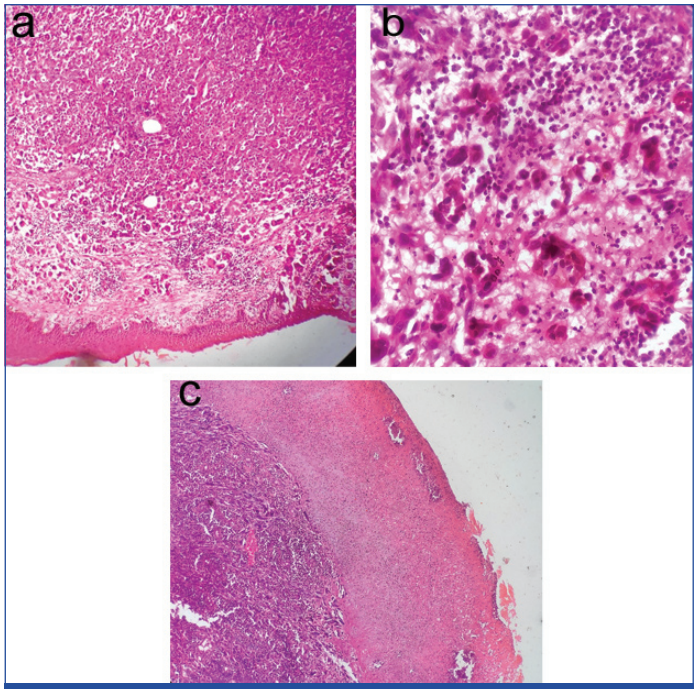
CASE REPORT

A 60-year-old female patient, presented with chief complaint of growth in left cheek region for a period of one month. Patient gave a history of betel nut chewing for 15 years, without any relevant medical history. On extraoral examination, gross facial asymmetry was noticed. Swelling was noticed in the lower third of the face of size 2×2 cm, extending to the inferior border of the mandible. On examination, the left submandibular lymph node (3×4 cm) and left cervical lymph node (2×2 cm) were palpable, hard, non tender and fixed. On intraoral examination, ulceroproliferative growth in the left cheek region of size 2.5×2.5 cm was noticed. The growth was in relation to 38 region, with its anterior and posterior extension to the buccal vestibule of 37 and pterygomandibular raphe, respectively. Medially, the lesion involved the lingual aspect of 38 impinging on the occlusal plane. The margins were irregular with everted edges. The surface was corrugated and bleeding upon probing was noticed [Table/Fig-1]. The swelling was non tender on palpation. Provisional diagnosis of malignant ulcer was attained. Squamous cell carcinoma, melanoma and mucoepidermoid carcinoma were considered in the clinical differential diagnosis.

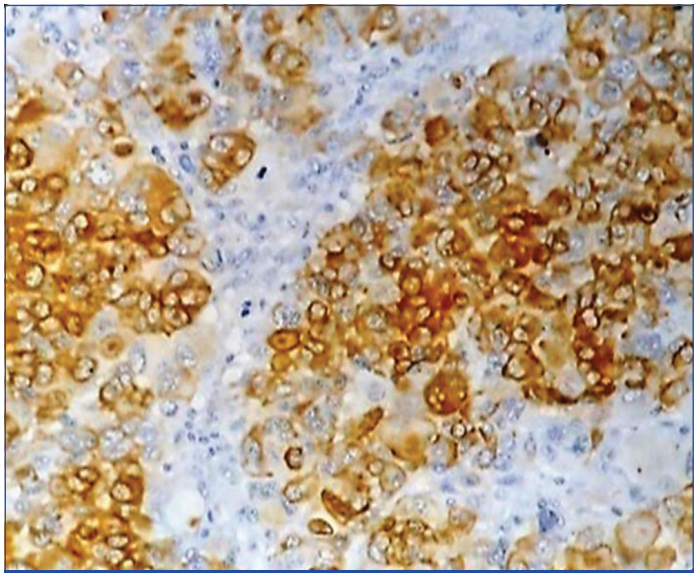


[Table/Fig-1]: Ulceroproliferative lesion in the left buccal mucosa in relation to 37, 38.

The patient was then, subjected to incisional biopsy. Upon microscopic examination, the sections revealed a highly cellular connective tissue with a superficial stratified squamous parakeratinised epithelium of varied thickness. The epithelium showed moderate amount of cellular atypia. The underlying connective tissue was dominated by a high degree of cellularity. Numerous epithelioid cells were found in islands and sheets. Sheets of hyperchromatic cells with abundant eosinophilic cytoplasm and large peripherally placed nucleus with bizarre shapes were noticed. Subepithelially, hyperchromatic cells with dense eosinophilic cytoplasm exhibiting cellular and nuclear pleomorphism arranged in numerous small islands resembling theques, were also noticed. Numerous mitotic figures were noticed. The neoplastic cells also, found to exhibit spindle transformation in the periphery of the lesion. [Table/Fig-2a,b,c]. Diagnosis of undifferentiated carcinoma was given. Poorly differentiated squamous cell carcinoma, high-grade mucoepidermoid carcinoma, malignant melanoma and metastatic tumour should be ruled out, since they poise a histopathological similarity. The tissue was then immunohistochemically analysed for the panel of markers: Pan cytokeratin, Vimentin, S-100 protein, Human Melanoma Black (HMB)-45, Desmin, Muscle Specific Actin (MSA), CD34, LCA. Strong Positive immunoreactivity was noticed for vimentin, S-100, and HMB-45. S-100 and HMB-45 positivity revealed the cells, which were of neuroectodermal origin, more precisely melanocytes [Table/Fig-3]. The final diagnosis of primary amelanotic melanoma plasmacytoid variant was made. The lesional tissue was surgically resected with wide margins. Patient had a symptom free, follow-up period for one and a half year.



[Table/Fig-2]: a) Superficial epithelium and underlying proliferating epithelioid cells showing pleomorphism admixed with chronic inflammatory cell infiltrate (H&E,10x); b) Atypical epithelioid cells with extensive pleomorphism admixed with lymphoplasmacytic infilterate in a fibromyxomatous background. Brown pigmentation is noticed in the cytoplasm of the neoplastic cells and also extracellularly in focal areas (H&E,40x); c) Spindle transformation of neoplastic cells under a thick fibrinopurulent membrane admixed with chronic inflammatory infiltrate (H&E,10x).



[Table/Fig-3]: Tumour islands showing strong immunoreactivity for Human Melanoma Black (HMB)-45 protein (IHC,10x).

DISCUSSION

Melanoma is less commonly occurring deadly mucocutaneous malignancy. About 90% of melanoma arises from skin surface and around 1-2% occur in oral mucous membrane [1]. There is a strong coincidence between the mutation status and the clinicopathological subtypes of melanoma which supports the existence of biologically distinct types of melanoma, thereby, presenting a diagnostic challenge. More than half of the lesions arise de novo. Age and susceptibility to chronic accumulated sun exposure, familial history and presence of a potential precursor are the major risk factors of melanoma [2]. About 50% of the head and neck melanomas occur in the oral cavity. Less than 2% of all melanomas are amelanotic, and majority of them occur in the oral cavity perplexing the clinical diagnosis [1,3].

The primary mucosal melanomas of the oral cavity are relatively rare compared to the head and neck melanomas and from time to time, they tend to manifest without melanin pigmentation [4]. Oral melanomas clinically manifest as nodular, macular and ulcerative lesions with or without pigmentations [5,6]. Oral malignant melanomas can also present as multiple nodular lesions in the palate [7]. The diagnosis of amelanotic melanoma is quiet challenging and portray a clinical resemblance to quite a few benign malignant mucosal lesions. The specific cause for lack of pigmentation is unclear. Speece proposed in his work that, the deficiency of tyrosine is associated with the lack of pigmentation [8].

Some authors believe that, melanin quantity is insufficient to be seen histopathologically, which is further substantiated by electron microscopical demonstration of melanosomes in amelanotic melanoma. Oral melanoma is usually asymptomatic, and aetiology is associated with smoking tobacco, pre-existing nevi, ill-fitting dentures and amalgam tattoo [9]. The prognosis of amelanotic melanoma is poorer than its pigmented counterpart, attributed to the absence of pigment, not favouring an early diagnosis. The prognosis is about 20% and 58% for amelanotic and melanotic melanoma, respectively for a survival rate of three years [10]. Amelanotic melanoma presents as a metastatic tumour in the lung from the primary melanoma in oral cavity [11]. The present case presented an ulceroproliferative growth in the posterior buccal mucosa with no evidence of pigmentation. Patient gave a clinical history of tobacco and betel nut chewing for 15 years, favouring the clinical diagnosis of squamous cell carcinoma.

Microscopically, melanoma presents itself in three patterns. In-situ intraepithelial radial growth pattern, invasive vertical growth pattern (30%) involving epithelium and connective tissue, combination of first and second pattern. Presence of melanin pigment, dysplastic melanocytes facilitate the diagnosis of melanoma. However, when the lesion lacks pigmentation clinically, malignancy of oral epithelium, keratoacanthoma, and granulomatous lesions should be considered in the differential diagnosis. Melanoma microscopically is confused with a wide spectrum of tumours of epithelial, haematological, neurological and mesenchymal origin [12]. The histopathological differential diagnosis is considered based on the morphological appearance of the cell. Spindle cell malignant tumour (leiomyosarcoma, angiosarcoma, spindle cell carcinoma) round cell tumour (lymphoma and neuroendocrine tumour) clear cell tumour (renal cell carcinoma) and epithelioid malignant tumour (squamous cell carcinoma) should be considered for microscopic differential diagnosis. In the present case, the authors noticed atypical epithelioid cells and bizarre appearing hyperchromatic cells arranged in the form of islands, sheets and theques. The diagnosis of undifferentiated carcinoma was arrived. However, to rule out the origin of the tumour, immunohistochemistry was opted.

Pan melanoma cocktail comprise HMB-45 (Human Melanoma Black), MART-1 (Melanoma-associated antigen recognised by T-cells), tyrosinase, S-100 are effective in diagnosis of amelanotic melanoma [13,14]. S-100 is highly sensitive but not a specific marker, HMB-45, which is a marker of premelanosome proved to be good enough in detecting hypopigmented melanocytes. MART -1/Melan-A (Antigen of Melanocytes of Cytotoxic T-cells), sensitivity of this antigen is greater than HMB-45 but its specificity is almost same and less sensitive in spindle cell melanomas [14]. MAGE-1 (Melanoma Associated Antigen) Tyrosinase may be very useful in diagnosis when HMB-45 is negative. Pan melanoma cocktail is 98% sensitive with all melanomas with 60% sensitivity in desmoplastic melanomas [15]. Vimentin, S-100 and HMB-45 positivity was observed in the present case. In the present case, the melanocytes predominantly presented itself in bizarre shapes and arranged in the form of theques and islands. The atypical cells nowhere in the sections expressed pigmentation. The lesional cells had large eosinophillic cytoplasm with peripherally placed nucleus resembling plasma cells. Hence, the final diagnosis of primary amelanotic melanoma-plasmacytoid variant was given after

thorough examination of the patient, for similar lesions, elsewhere in the body.

CONCLUSION(S)

Hypopigmented lesions are clinically deceptive, thereby, hindering the pace of diagnosis and further favouring the disease progress. Melanoma cells in tissue sections takes up various shapes ranging from round, polyhedral, spindle, fusiform, epitheliod masquerading other malignancies. The melanin pigment may not be traced frequently in cases of amelanotic melanoma, like its counterpart. Very few traces of melanin pigment can be either found in the cytoplasm of tumour cells and phagocytes and extracellular areas. Pan melanoma cocktail comprising HMB-45, MART-1, tyrosinase, S-100 are greatly helpful in the diagnosis of melanomas, that lack pigmentation both in clinical and tissue sections. The authors, would like to emphasise the significance of reach and the availability of the IHC panel of markers in the histopathological laboratory, as one among the routine primary diagnostic markers.

REFERENCES

[1] Shetty A, Kumar SA, Geethamani V, Rehan M. Amelanotic melanoma masquerading as a superficial small round cell tumor: A diagnostic challenge. Indian J Dermatol. 2014;59(6):631.
[2] Elenitsas R, Johnson BL, Xu X, Murphy GF. Lever's histopathology of the skin. Wolters Kluwer; 2009.
[3] Adisa AO, Olawole WO, Sigbeku OF. Oral amelanotic melanoma. Ann Ib Postgrad Med. 2012;10(1):06-08.
[4] Feller L, Khammissa RAG, Lemmer J. A Review of the aetiopathogenesis and clinical and histo-pathological features of oral mucosal melanoma. Scientific World Journal. 2017;2017:9189812.
[5] Esmaeili M, Hosseini A. Amelanotic primary malignant melanoma of the maxilla: A case report. J Arch Mil Med. 2017; 5(1):e13225.
[6] Gong HZ, Zheng HY, Li J. Amelanotic melanoma. Melanoma Res. 2019;29(3):221-30.
[7] Limongelli L, Cascardi E, Capodiferro S, Favia G, Corsalini M, Tempesta A, et al. Multifocal amelanotic melanoma of the hard palate: A challenging case. Diagnostics (Basel). 2020;10(6):424.
[8] Rimal J, Kasturi DP, Sumanth KN, Ongole R, Shrestha A. Intra-oral amelanotic malignant melanoma: Report of a case and review of literature. Journal of Nepal Dental Association. 2009;10(1):49-52.
[9] Saghravanian N, Pazouki M, Zamanzadeh M. Oral amelanotic melanoma of the maxilla. J Dent (Tehran). 2014;11(6):721-25.
[10] Aziz Z, Aboulouidad S, Bouihi ME, Hattab NM, Chehbouni M, Raji A, et al. Oral amelanotic malignant melanoma: A case report. Pan Afr Med J. 2020;37:350.
[11] Matsuoka K. Oral malignant melanoma detected after resection of amelanotic pulmonary metastasis. Int J Surg Case Rep. 2013;4(12):1169-72.
[12] Panda S, Dash S, Besra K, Samantaray S, Pathy PC, Rout N, et al. Clinicopathological study of malignant melanoma in a regional cancer center. Indian J Cancer. 2018;55(3):292-96.
[13] Kawasaki G, Yanamoto S, Yoshitomi I, Mizuno A, Fujita S, Umeda M, et al. Amelanotic melanoma of the mandible: A case report. Oral Science International. 2011;8(2):60-63.
[14] Cheung WL, Patel RR, Leonard A, Firoz B, Meehan SA. Amelanotic melanoma: A detailed morphologic analysis with clinicopathologic correlation of 75 cases. J Cutan Pathol. 2012;39(1):33-39.
[15] Xu X, Chu AY, Pasha TL, Elder DE, Zhang PJ. Immunoprofile of MITF, tyrosinase, melan-A, and MAGE-1 in HMB45-negative melanomas. Am J Surg Pathol. 2002;26(1):82-87.

PARTICULARS OF CONTRIBUTORS:

1. Professor, Department of Oral and Maxillofacial Pathology and Oral Microbiology, Indira Gandhi Institute of Dental Sciences, Sri Balaji Vidyapeeth University, Puducherry, India.
2. Professor, Department of Oral and Maxillofacial Pathology and Oral Microbiology, Indira Gandhi Institute of Dental Sciences, Sri Balaji Vidyapeeth University, Puducherry, India.
3. Professor, Department of Oral and Maxillofacial Pathology and Oral Microbiology, Indira Gandhi Institute of Dental Sciences, Sri Balaji Vidyapeeth University, Puducherry, India.
4. Reader, Department of Oral and Maxillofacial Pathology and Oral Microbiology, Indira Gandhi Institute of Dental Sciences, Sri Balaji Vidyapeeth University, Puducherry, India.
5. Reader, Department of Oral and Maxillofacial Pathology and Oral Microbiology, Indira Gandhi Institute of Dental Sciences, Sri Balaji Vidyapeeth University, Puducherry, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Vidyalakshmi Santhanam,
Professor, Department of Oral and Maxillofacial Pathology and Oral Microbiology,
Indira Gandhi Institute of Dental Sciences, Sri Balaji Vidyapeeth University,
Puducherry, India.
E-mail: vidyan@igids.ac.in

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: May 19, 2022
- Manual Googling: Jul 21, 2022
- iThenticate Software: Oct 05, 2022 (4%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **May 18, 2022**
Date of Peer Review: **Jun 29, 2022**
Date of Acceptance: **Oct 08, 2022**
Date of Publishing: **Nov 01, 2022**