



Melanocytic Pigmentation: A Single Manifestation of Myriad of Pathologies

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ARTICLE INFO ABSTRACT

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The colour of oral pigmentation can vary depending on the quantity and depth or location of the melanin pigment. Melanin is an endogenous pigment which is responsible for physiological pigmentation, produced by melanocytes. Melanin is also synthesized by nevus cells, which are derived from the neural crest and are found in the skin and mucosa. In the current article three cases have been discussed which showed different demonstrations of melanin pigmentation. First case was intra dermal nevus, a benign neoplasm of melanocytes. Histopathologically, aggregates of epitheloid cells showing peripheral cells filled with melanin pigment. Second case was malignant melanoma, a neoplastic condition of melanocytes presented on anterior palate. On histopathological examination the tissue revealed neoplastic melanocytes, deeper epitheloid cells with hyperchromatic nuclei with active mitosis. Third case was anaplastic condition of melanocytes, amelanotic melanoma, where non pigmented epitheloid cells exhibiting cellular atypia, loss of cohesiveness. Immunohistochemistry assisted in concluding final diagnosis.

Keywords:

Oral Pigmentation, Melanin Pigment, Melanocytes, Intra Dermal Nevus, Epitheloid Cells

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1. Introduction

Oral mucosa is not uniformly coloured. The colour varies in different physiological and pathological conditions^{1,2}. Pigments associated with mucosal discoloration could be classified as endogenous (e.g. melanin and blood-related pigments) and exogenous (e.g. metals and drug-related pigments)³.

Melanin is produced by melanocytes in the basal layer of the epithelium and is transferred to adjacent keratinocytes via membrane-bound organelles called melanosomes. Melanin is also synthesized by nevus cells, derived from the neural crest cells. Colour differences in different areas result from the relative activity of the melanocytes in producing melanin³. The melanocytes are present in any region of the



oral cavity and can be present in reactive, benign or malignant lesions.

Oral and perioral lesions of melanocytic origin, while uncommon can be very challenging to identify as neoplastic or non-neoplastic based on clinical appearance, making histopathological examination of all cases essential. However their variable microscopic presentation often makes even histopathological diagnosis a challenge.

Thus the current article describes such challenging three melanocytic lesions which show myriad of pathologies. They are non-neoplastic intradermal nevi, neoplastic malignant melanoma, and anaplastic amelanotic melanoma.

2. Case Presentations

1. Intradermal Nevi:

A 21 year old female patient reported with long standing, asymptomatic, solitary pigmented growth on left naso labial fold. The lesion was measuring 1cm in size, round in shape with regular borders and smooth surface [**Figure: 1**].

Complete excision was done. On histopathological examination specimen showed an encapsulated sub epithelial collection of epitheloid cells in lobular pattern. The peripheral cells of these aggregates showed melanin pigment. Cellular atypia was not observed [**Figure: 2**]. These histopathologic features decisive of benign neoplasm of melanocytes, intradermal nevus.

Intradermal nevus harbour oncogenic serine/threonine-protein kinase B-Raf (BRAF), less commonly, neuroblastoma ras viral oncogene homolog (NRAS) mutations⁵. Nevomelanocytes tend to cluster in compact so called theques⁶. Regarding morphogenesis, the melanocytic proliferation can be divided into three phases: proliferation of benign neoplastic melanocytes along the submucosal-mucosal

junction (junctional nevus); migration of these cells to the underlying mesenchymal tissue (compound nevus); and loss of the junctional component of the nevi, so that all remaining nevomelanocytes are located within the sub epithelial connective tissue stroma (intra dermal nevus)⁸.

2. Malignant Melanoma

A 65 year old male patient reported with a solitary, pigmented proliferative growth on anterior maxillary region. The growth measured 7*4 cm in dimension, oval in shape. The lesion extends from distal gingiva in relation to 16 to gingiva of 26 and also involves labial mucosa and vestibule [**Figure: 3**].

Incisional biopsy was done for histopathological examination. Swelling was soft in consistency and borders were indurated, bled on touch.

Microscopic features revealed enlarged neoplastic melanocytes laden with melanin pigment in juxta epithelial connective tissue. Deeper connective tissue exhibited epitheloid cells with vesiculated hyperchromatic nuclei. Mitotic activity was also evident [**Figure: 4**].

Oral mucosal melanoma is rare. It accounts for less than 1% of all oral malignancies. It is characterized by proliferation of malignant melanocytes along the junction between the epithelium and connective tissue or may occur deep inside the connective tissue. The palate is the most common site, which account for about 40% of cases⁹.

3. Amelanotic Melanoma

36 year old female patient presented with solitary, pedunculated growth on gingiva in relation to right maxillary premolar region. The lesion measures 2*1.5 cm in size, oval in shape with smooth surface and normal overlying mucosa.



Clinically the lesion looked like reactive, or benign growth [Figure: 5].

On microscopic examination, tissue showed proliferating epitheloid cells arranged in nests. The cells exhibit cellular and nuclear pleomorphism. Abnormal and bizarre mitotic figures, cells unveiled loss of cohesiveness and infiltrating in deeper connective tissue were suggestive of malignant non epithelial neoplasm [Figure: 6]. Further investigations were done to get final diagnosis. Immunohistochemical slides showed strong positive for S-100, partial for vimentin, and diffuse for HMB-45 [Figure: 7]. These findings indicate malignant condition of melanocytes, neural crest cell derivatives.

3. Discussion

Melanocytes are dendritic cells derived from neural crest. They have various morphologies ranging from round, oval; fusiform to dendritic. Nevus cells are non-dendritic melanocytes^{3,7}.

Moles, or melanocytic nevi, are both markers of an increased risk of cutaneous melanoma and direct precursor lesions. Intradermal nevus can be differentiated from malignant melanoma, with good degree of certainty by clinical features like symmetric appearance, uniform pigmentation and slow rate of growth⁸.

Malignant melanoma can be diagnosed with ease when they present as extensively pigmented asymmetric growth with irregular borders.

So histopathologically, while diagnosing various round, epitheloid, and spindle cell lesions, melanoma should be the differential until otherwise ruled out.

Current strategies to minimize the morbidity and mortality associated with melanoma focus on scrutiny of individuals with identifiable moles and melanocytic nevi⁸. Benign and atypical moles have been

shown to exist in histologic contiguity with cutaneous melanomas, suggesting that these melanocytic proliferations are also susceptible to malignant transformation⁹.

Thus we conclude the melanocytic lesions myriad presentation need thorough clinical evaluation, keen histopathological examination and appropriate immunostaining as the need may be.

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Figures with Legends:

Figure 1: Intradermal nevus

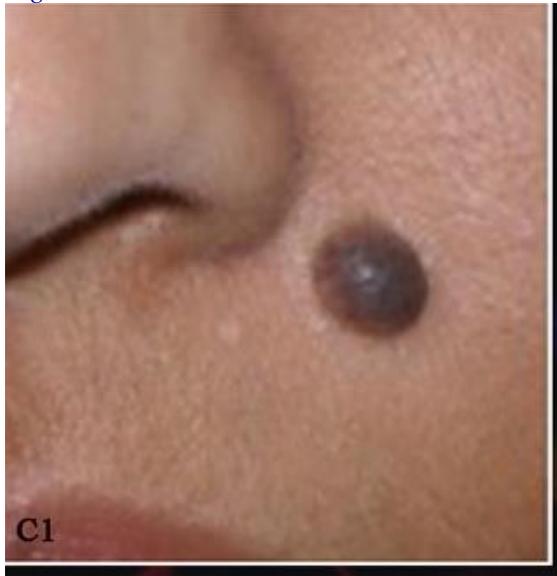


Figure 2: H & E Staining Of Intradermal Nevus

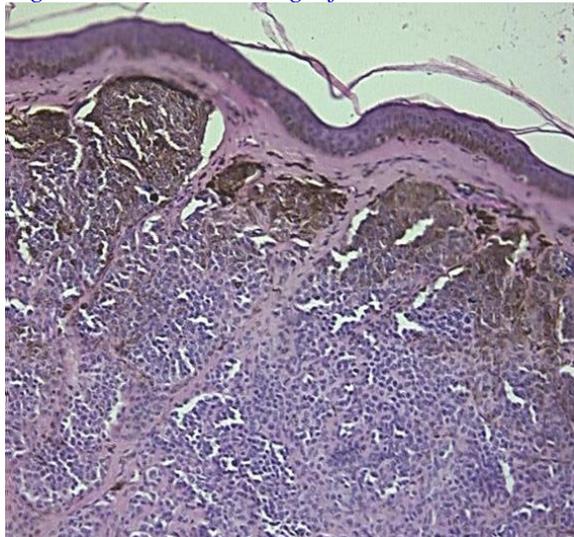


Figure 3: Malignant Melanoma



Figure 4: Malignant Melanoma under Low and High Magnification

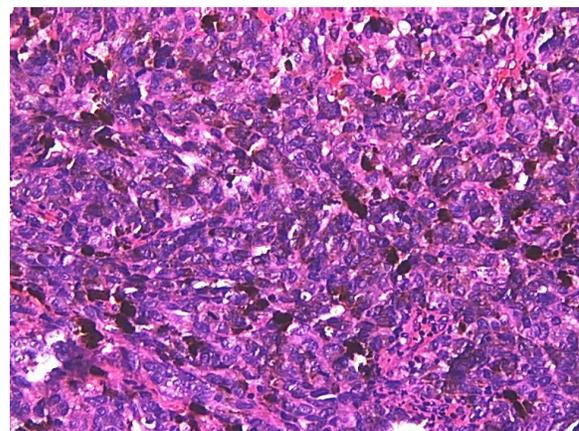
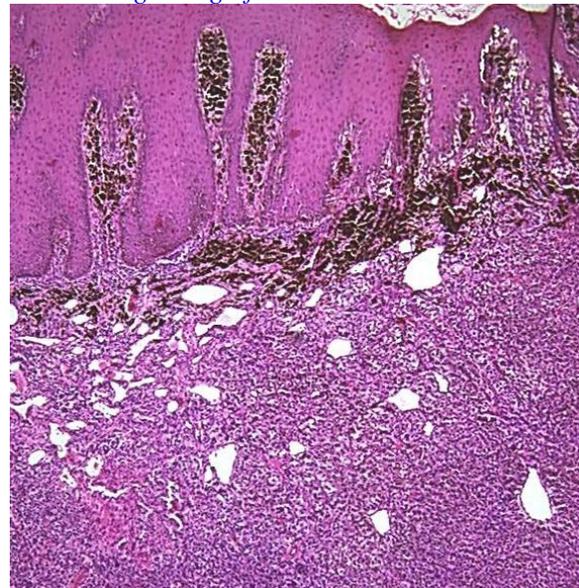


Figure 5: Amelanotic Melanoma

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Figure 6: H & E Staining of Amelanotic Melanoma

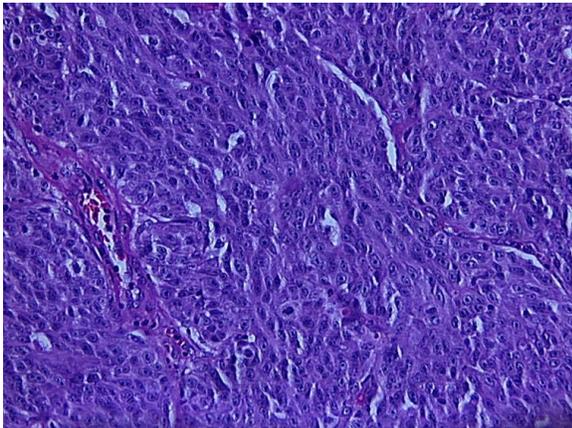


Figure 7: Vimantin and HMB 45 Immunohistochemical Staining

