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Case Report

Amelanotic melanoma masquerading as a plantar wart: A case report and review

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ABSTRACT

A 69-year-old male presented with asymptomatic skin coloured, exophytic, verrucous plaque on right sole of three months duration. He had been diagnosed as a plantar wart and treated with chemical destructive methods. Biopsy from the lesion showed infiltrate of nests of atypical melanocytes extending upto reticular dermis. The malignant cells were positive for S100 and human melanin black 45(HMB 45) with a high MiB-1 proliferative index thus confirming diagnosis of amelanotic melanoma (AM). We report this case to highlight the atypical presentation of amelanotic melanoma, the possibility of misdiagnosis and the importance of immunohistochemistry in diagnosing the same.

1. Introduction

Amelanotic melanoma can have varied and atypical clinical presentations, often mimicking conditions such as pyogenic granuloma, verruca vulgaris, Bowen's disease and basal cell /squamous cell carcinoma due to lack of pigment. This often makes diagnosis difficult and delays correct treatment.

2. Case Report

A 69 years old male presented with an asymptomatic verrucous growth of three months duration on right sole. He had been earlier treated with topical antibacterial, keratolytics and later as plantar wart with chemical destructive methods without any improvement. His concurrent medical history included diabetes mellitus, hypertension and ischemic heart disease. Cutaneous examination revealed a skin coloured, exophytic, verrucous plaque on right sole of size 6cm*5cm with sharply demarcated margins and few haemorrhagic spots (Figure 1). There was no popliteal and inguinal lymphadenopathy. Differential diagnosis of plantar wart, tuberculosis verrucosa cutis, chromoblastomycosis and verrucous carcinoma were considered. Dermoscopy showed a papilliform surface with hemorrhagic spots and a few linear brown streaks at the periphery of the lesion.(Figure 2) A biopsy from the plaque showed marked hyperkeratosis, atypical melanocytes as nests at the dermoepidermal junction and as single units in epidermis as well as papillary dermis and reticular dermis (Figure 3 A,B,C). Melanin pigment was not evident on H&E stain. Fontana-Masson stain showed minimal melanin pigment in the stratum corneum but tumor cells were mostly negative (Figure 3D). Immunohistochemical staining revealed that the cells were positive for S-100, HMB-45 and high MiB-1 proliferative index (Figure 4A,B,C). The pathological and immunohistochemical findings were consistent with nodular amelanotic malignant melanoma (AMM).Whole body PET scan did not reveal any evidence of metastases. Patient was referred to oncosurgery department for further management. However he refused further treatment.

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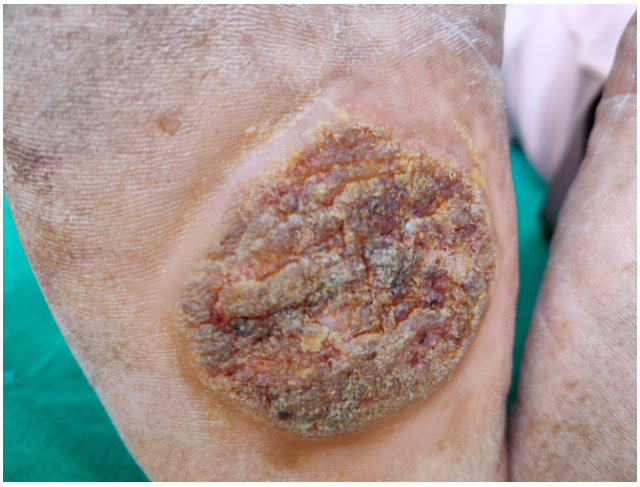

Figure 1: Well defined verrucous plaque on right sole of size 6cmX5cm with sharply demarcated margins and few haemorrhagic spots

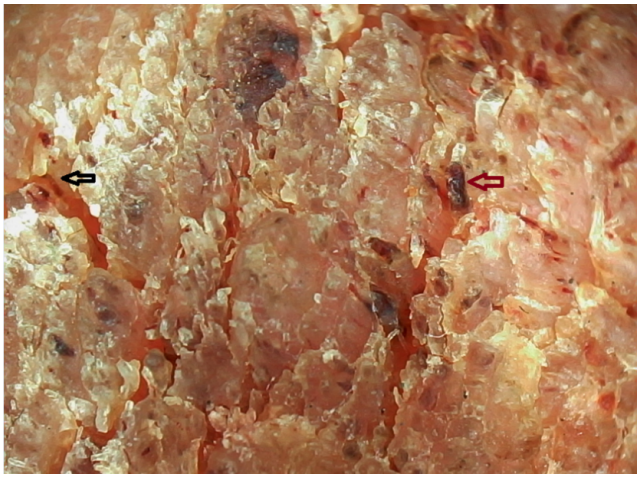

Figure 2: Dermoscopic image showing papilliform surface with hemorrhagic spots (Red arrows) and a few linear brown streaks (Black arrow) at the periphery of the lesion

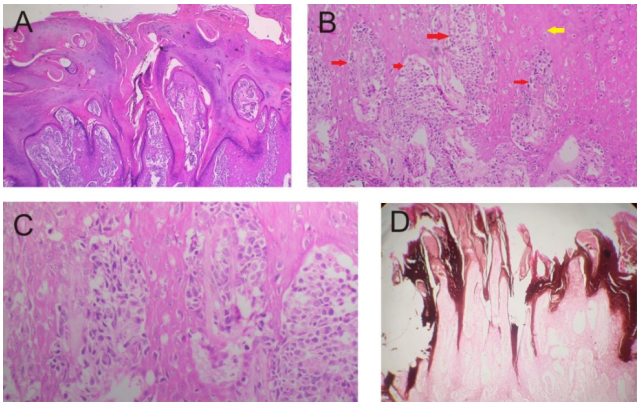

Figure 3: Histopathology from the plaque; **A:** Showing marked hyperkeratosis, nests of atypical melanocytes at the dermoepidermal junction, papillary dermis and reticular dermis. (4X) (H&E); **B:** Nests of atypical melanocytes at the dermo epidermal junction, papillary dermis(Red arrow) Few melanocytes are seen as single units in epidermis. (Yellow arrow) (10X) (H&E); **C:** The melanocytes show large, pleomorphic, hyperchromatic nuclei and abundant eosinophilic to amphophilic cytoplasm. (40X) (H&E); **D:** Fontana- Masson stain showed melanin pigment in the stratum corneum but tumor cells were mostly negative (4X).

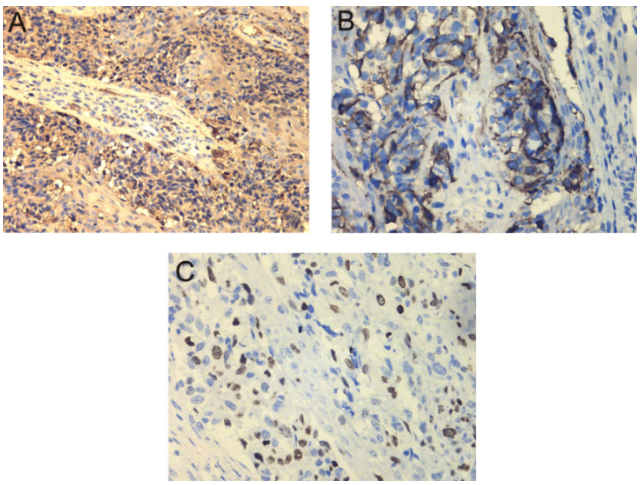

Figure 4: Immunohistochemistry study; Tumor cells were positive for S-100(**A**) HMB-45(**B**) With a high Mi-B-1 proliferative index (**C**) (40X)

3. Discussion

AMM is a subtype of malignant melanoma with absence of melanin pigment clinically and histologically (H&E). Its incidence varies between 1.8 and 8.1% of all melanomas with equal predilection in men and women.[1] It is more common on chronically sunexposed areas. It is a clinical masquerader of several malignant as well non malignant dermatological conditions due to lack of visible pigment. AMM can present as erythematous scaly plaques, non pigmented nodules, ulcers on the skin, mucosa, plantar region or even in subungual area.[2] There are several case reports in the literature mistaking AMM for eczema, inflammatory plaques, pyogenic granuloma, verruca vulgaris, bowen's disease and basal cell or squamous cell carcinoma.[2–4] Other differential diagnoses include seborrheic keratosis, clavus, intraepidermal merkel cell carcinoma, foreign body granuloma and deep mycoses. Due to variety of clinical presentations, AMM often presents as an advanced lesion that has been wrongly treated by topical agents or local destructive procedures. Although lesions of AMM clinically appear without pigment, some amount of pigment may be present especially at the periphery of the lesion and may be seen on dermascopy.[5] In such instances, hypomelanotic melanoma may be a more appropriate terminology. An umbrella

term of amelanotic/hypomelanotic melanoma (AHM) has also been used to describe these tumors. Loss of pigment gene expression leading to decrease in the expression of tyrosinase is possibly responsible for the amelanosis. A polymorphous vascular pattern with milky red areas, irregular linear and dotted vessels has been described on dermoscopy and can help to distinguish from other benign amelanotic lesions.[5,6]

Histopathological patterns are similar to typical melanoma with nodular pattern being the most common type. Absence of pigment however can make histological diagnosis difficult.The histopathologic differential diagnosis of AMM includes irritated benign melanocytic nevus, Spitz nevus, Paget's disease, atypical fibroxanthoma, malignant fibrous histiocytoma, malignant schwannoma or spindle cell squamous cell carcinoma. Other tumors presenting as collections of small cells such as adenocarcinoma, merkel cell carcinoma, lymphomas, eccrine carcinoma, peripheral neuroepithelioma, and metastastic neuroendocrine carcinoma can resemble AMM on histopathology.Hence immunohistochemical markers like S-100 protein and HMB-45 are essential to distinguish AMM from other clinical and histologic mimicking entities.

The most definitive treatment for localised cutaneous amelanotic melanoma remains surgical excision, which can also be useful in more advanced disease with isolated metastatic foci.[7,8] Radiotherapy may be considered as second-line therapy for cutaneous melanoma, when surgery is not an option. FDA-approved BRAFIs (vemurafenib and dabrafenib), MEKIs (trametinib and cobimetinib), immune checkpoint inhibitors - anti-CTLA4 (ipilimumab), antiePD-1 (pembrolizumab and nivolumab) and anti- PDL-1 (atezolizumab) have been used for advanced disease (stage III and IV).[7,8]

Amelanotic melanoma is more aggressive in behaviour in comparison to pigmented melanoma and is more likely to metastasize. Melanin in melanoma cells modifies the nanomechanical properties of melanoma cells by limiting their ability to undergo extensive deformation when passing through a mechanical barrier such as the endothelial wall or the basement membrane thereby limiting their potential to metastasize.[9] Frequently a late diagnosis due to atypical features is also responsible for poor prognosis.

4. Conclusion

In conclusion, this case is being reported for the unusual clinical manifestation of amelanotic melanoma closely resembling a mosaic plantar wart thus emphasising the need for high degree of clinical suspicion in diagnosis of amelanotic melanoma. It also highlights the importance of immunohistochemistry in confirming diagnosis of amelanotic melanoma

5. Source of Funding

None.

6. Conflict of Interest

None.

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