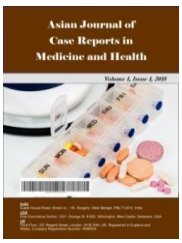

Asian Journal of Case Reports in Medicine and Health

2(1): 14-20, 2019; Article no.AJCRMH.47283

Primary Cutaneous Malignant Melanoma with Papillary Features: A Case Report Signifying Morphologic Diversity in Malignant Melanoma

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Author's contribution

The sole author designed, analyzed, interpreted and prepared the manuscript.

Article Information

Editor(s):
(1) Ayhan Goktepe, Professor, Department of Geodesy and Photogrammetry, Selcuk Universitesi, Teknik Bilimler MYO, Kampus, Turkey.
Reviewers:
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(3) María Julia Cura, Hospital Italiano de Buenos Aires, Argentina.
Complete Peer review History: http://www.sdiarticle3.com/review-history/47283

Case Study

Received 30 November 2018
Accepted 23 February 2019
Published 03 April 2019

ABSTRACT

Aim: The purpose of this work was to describe the way how primary cutaneous malignant melanoma can present with papillary features and hence mimicking malignant tumours which are commonly accompanied with papillary features such as papillary thyroid carcinoma.
Presentation of Case: The case reported in this article was of an African female aged 61 years who presented with a darkish small swelling on the dorsum of the right hand, slightly painful and tender for 3 months since its onset.
Discussion: Malignant melanoma as it is encountered in daily clinical practice ought to be deemed as being a malignant tumour that can sometimes show diverse histomorphological presentation including papillary features as it was in the case herein reported. This kind of presentation can lead to wrong diagnosis, thus, contributing to delaying of proper diagnosis and even jeopardizing the prognosis of the patient.
Conclusion: Malignant melanoma should be included in the differentials of malignant tumours presenting histologically with papillary features.

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Keywords: Cutaneous melanoma; papillary features; mimicking.

1. INTRODUCTION

Primary cutaneous malignant melanoma is a malignant tumour arising from melanocytes of the skin; these are cells located at the basement membrane in the epithelium [1]. Melanocytes are cells of neural crest origin which function in the body by producing and distributing melanin. Malignant melanoma is one of the commonest skin cancers with high incidence in people with fair skin. Reports indicate that the highest incidence rates of malignant melanoma are found in Australia (39 new cases per 100,000 people per year), New Zealand (34 new cases per 100, 000 persons) and USA (17 new cases per 100,000 persons) followed by the Scandinavian countries such as Germany [2]. Geographic location and genetics are the known factors for the cause of variation in occurrence of malignant melanoma across regions in the world. Malignant melanoma has been reported to have morphologic diversity posing diagnostic challenges especially when is both amelanotic and is presenting with significant papillary features histologically [3]. Here a 61-year old female with primary cutaneous malignant melanoma consisting of papillary features is presented.

2. CASE PRESENTATION

A 61-year old African female presented at the surgical department with a darkish and roundish swelling involving the posterior aspect of the right fore hand below the wrist joint which was associated with pain and tenderness. The patient reported duration of 3 months since onset. She explained that initially it was a small blackish dot-like which some years back it started itching and widening. She denied a history of trauma or history of malignant melanoma in her family.

On physical examination, the swelling was blackish with ill- raised margins measuring 3 x 2 cm. Regional lymph nodes were palpable. Other systems were unremarkable. Clinical differentials such including melanotic naevus, pigmented actinic keratosis and keratoacanthoma and malignant melanoma were provided as it was in other case studies reported [4,5]. Then an incisional biopsy was done followed by submission to the histopatological laboratory for histological evaluation. Five fragments of soft tissue, some with epidermis without ulceration, measuring 4 x 3 cm in aggregates were grossed. Microscopically, the tissue sections were infiltrated by a nodular solid tumour composed of malignant highly pleomorphic large epithelioid cells with brownish intracytoplasmic pigments (Fig. 1). The mitotic count was 3 mitoses per high power field (HPF). Perineural and lymphovascular invasion were seen. There were areas with prominent tumour cells and fibrovascular cores forming papillary patterns (Fig. 2A and 2B). Using Clark level system for assessing level of depth of tumour invasion, it

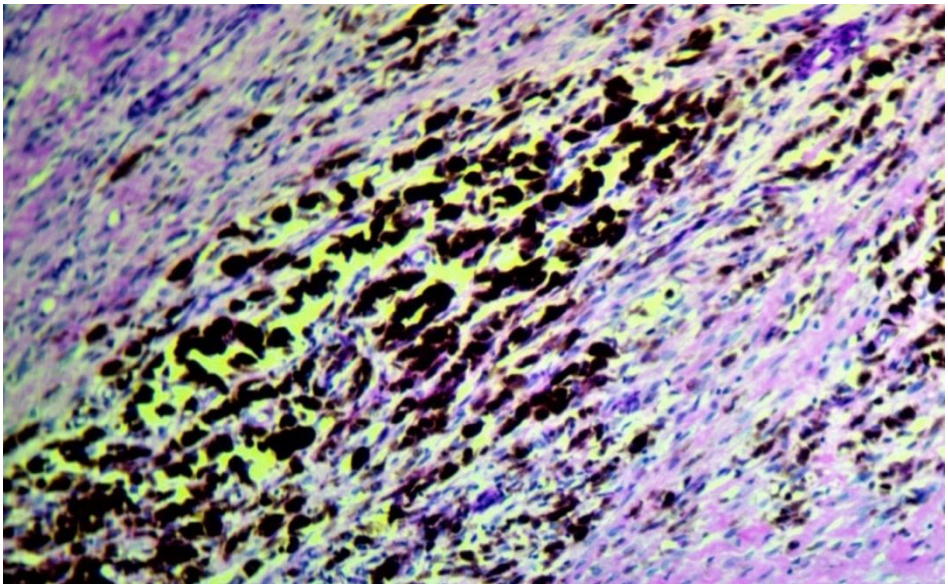

Fig. 1. Photomicrograph of H & E stain showing infiltrating tumour cells intracytoplasmic brown pigments (X200 Original magnification)

was found that the level of invasion was level V. The tumour cells were strongly positive for HMB-45 antigen (Fig. 3) and S-100 protein (Fig. 4). Because this tumour was presenting with papillary features; which is a feature of many carcinomas, therefore, AE1/AE3 cytokeratin staining was done to exclude the possibility of diagnosis of carcinoma and the result was negative.

3. DISCUSSION

Papillary and pseudopapillary features are commonly histopathologic findings typically associated with carcinomas arising from thyroid, pancreas, breast, prostate, bladder, kidney, ovary or mesothelioma [6]. Observation of such features in malignant melanoma may become a challenge at some point because of being

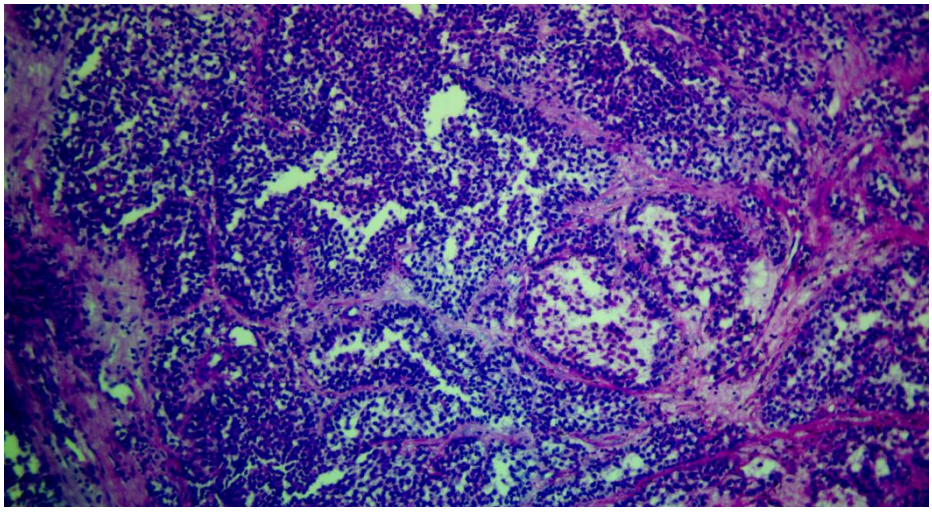

Fig. 2A. Photomicrograph of H & E showing fibrovascular cores indicating the papillary features where the tumour cells are amelanotic (X200 Original magnification)

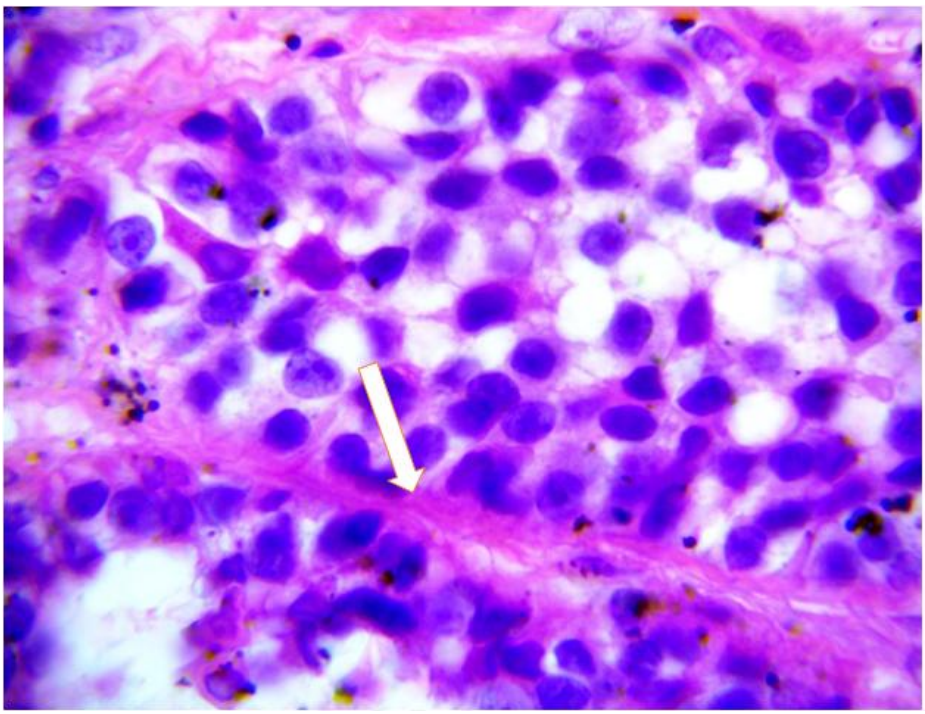

Fig. 2B. Photomicrograph of H & E showing fibrovascular cores indicating the papillary features (arrow) where the tumour cells are amelanotic (X400 Original magnification)

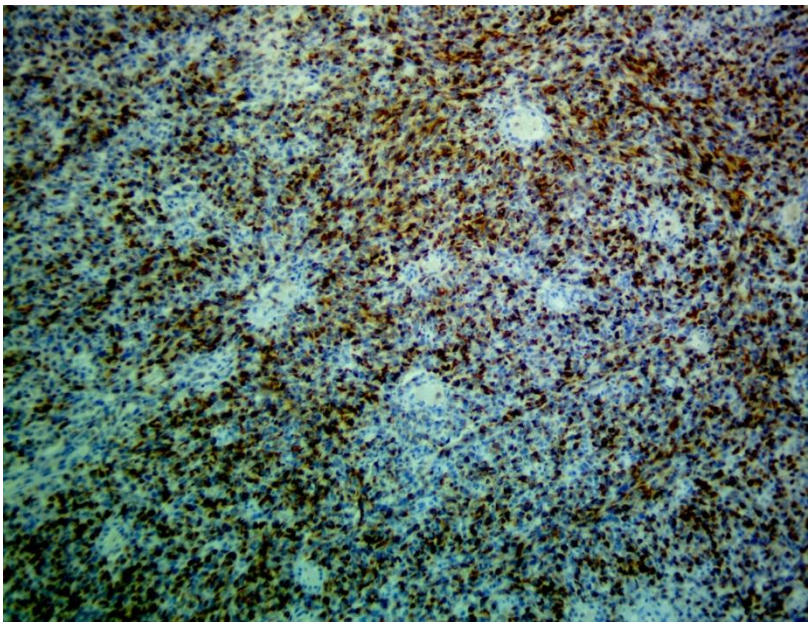

Fig. 3. Photomicrograph showing immunohistochemistry strong positivity of HMB-45 antigen (X200 Original magnification)

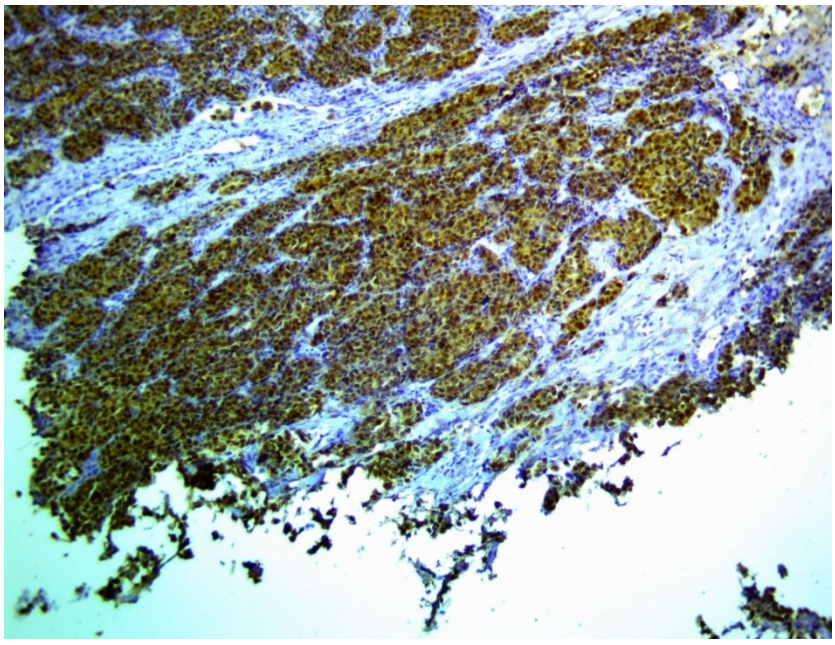

Fig. 4. Photomicrograph showing immunohistochemistry strong and diffuse staining positivity of S-100 protein (X200 Original magnification)

uncommon. One of the possible challenges is thinking of the presence of metastatic carcinoma from one of the organs in which carcinomas with papillary features are very common. In a brief report of Balocch et al. [7] on papillary formations in metastatic malignant melanoma, the authors argued that, the prominent papillary groups in Fine Needle Aspiration (FNA) smears from various body sites may be mistaken for metastases from other malignant tumours with similar features such as ovary, thyroid, pancreas, and kidney. This can lead to inappropriate management. Therefore, the key issue in understanding this subject of malignant melanoma having papillary or pseudopapillary features is centered on avoiding the possibility

for the one encountering such case to think that malignant melanoma never presents with papillary features morphologically and for that reason, it should be included in the differentials of carcinomas with papillary or pseudopapillary features.

Findings of papillary features in malignant melanoma, in fact, are well-known in the discipline of histopathology. Several authors name this pattern as ‘‘pseudopapillary’’ due to discohesion for some of the tumor cells, leading to the formation cuffs of tumor cells around stromal vessels, giving a picture of fibrovascular core appearance [6,7]. Most of studies in this subject involve case reports and case series and very few studies reported involve a large sample size. Nakhleh et al. [8], conducted a large study which included 335 patients with malignant melanoma. In their study, the authors wanted to evaluate the different variants of morphological patterns of malignant melanoma for 27 cases which showed diverse morphology histologically. It was found that 33.3% of the 27 cases had pseudopapillary features and the rest had other unusual histological features such as myxomatous changes. They insisted that, where the malignant melanoma lesion is not pigmented (amelanotic) and at the same time it presents with unusual histological features including possession of papillary features, use of confirming tests becomes unavoidable such as HMB-45 antigen, S-100 protein, Fontana-Masson, vimentin and melan-A. In another study which was done by Bacchi et al. [9] which involved 20 cases of metastatic malignant melanoma presenting as isolated breast tumour. Of all the 20 cases, 7 cases had unusual histological morphology and 14.3% showed papillary feature. Niederberger et al. [10] reported a case of an adolescent girl with central nervous system (CNS) malignant melanoma which had papillary histological features. Valero-Torre et al. [6] reported a 23-year old man with a diagnosis of cutaneous malignant melanoma with significant papillary features.

Melanocytic tumour cells in malignant melanoma in general do not stain for cytokeratins. Reports indicate that 4-10% of malignant melanoma may show aberrant immunophenotype and may stain cytokeratins especially CAM 5.2 when it is metastatic [3,10]. In the study of Nakhleh et al. [8], it was reported that none of 9 cases of malignant melanoma with papillary features was positive for AE1/AE3 cytokeratin stain. Niederberger et al. [10] reported a case of malignant melanoma with papillary features which was also negative for cytokeratin similar to the present case. Therefore, it can be understood that malignant melanoma with papillary features don’t stain positive with cytokeratins.

There are very few studies or case study reports in the English literature of malignant melanoma presenting with papillary features microscopically. Table 1 represents some of the cases of malignant melanoma which were found with papillary features histologically.

Because of malignant melanoma presenting histologically with papillary features or pseudopapillary pattern, which poses diagnostic challenges and even leading to wrong diagnosis; histopathological differential diagnoses which are more likely to be mimicked by malignant melanoma with papillary features have been

Table 1. Cases reported in the literature with malignant melanoma consisting either papillary or pseudopapillary features

Authors	Age (Years)	Sex	Size	Site	Primary/ Metastatic	IHC panel
Baloch et al. [7]	47	M	3 x 2.3 cm	Right ankle	Primary	S-100, HMB-45, Factor VIII
Mondal et al. [11]	11	F	5 x 3 cm	Posterior fossa	Primary	Synaptophysin
Niederberger et al. [10]	53	F	4.4x2 cm	Urinary bladder	Primary	CK, SMA, S-100, HMB-45
Hong et al. [12]	65	F	4.0 x 1.0 cm	Thyroid	Metastatic	S-100, TTF-1, HMB-45
Valero-Torre [6]	23	M	5 x 2.8 cm	Left heel	Primary	S-100, HMB-45

highlighted in the literature. At different time, Barnajee et al and Nakhleh et al. reported that malignant melanoma with papillary features is more likely to mimic other tumours presenting histologically with papillary features such as renal cell carcinoma-papillary type, low grade papillary adenocarcinoma of the pancreas, clear cell sarcoma-melanocytic type and poorly differentiated carcinoma (sarcomatoid carcinoma) [3,8]. Other histopathological differentials are lymphoma, neuroendocrine tumours and germ cell tumours [12].

The biological behaviour of malignant melanoma with papillary features is not known. In addition, the role of cytological features in determining the prognosis of malignant melanoma has not been studied extensively and the few studies which highlighted briefly for example on the role of papillary or pseudopapillary features in determining the prognosis of malignant melanoma seem to be contradicting. Levene pointed out that in malignant melanoma, the cytology features or type do not carry any prognostic value [13]. Rutkowski et al. [5] reported that cytological features have a prognostic role which must be included in the histological report in addition to the well-known prognostic factors such as Breslow thickness, histological type, status of the surgical margin and many others. However, in their work, it was not stated clearly the role of each cell type example epithelioid, spindle and small tumour cells.

4. CONCLUSIONS

Malignant melanoma is supposed to be included in the differential of malignant tumours with papillary features. For amelanotic malignant melanoma (AMM) presenting with papillary morphological features, the use of immunohistochemical and/or histochemical test is mandatory. There is a need of conducting a study in patients with malignant melanoma presenting histologically with either papillary or pseudopaillary features.

CONSENT

As per international standard or university standard, patient's written consent was obtained and has been kept by the author.

ETHICAL APPROVAL

It is not applicable.

ACKNOWLEDGEMENTS

I thank the surgeons and the laboratory technicians for working with me when I was developing this article.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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The peer review history for this paper can be accessed here:
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