UC Davis
Dermatology Online Journal

Title
A misdiagnosed melanoma: a case of cutaneous epithelioid malignant peripheral nerve sheath tumor

Permalink
https://escholarship.org/uc/item/319176xb

Journal
Dermatology Online Journal, 21(4)

Authors
Linos, Konstantinos
Warren, Simon

Publication Date
2015

DOI
10.5070/D3214026270

Copyright Information
Copyright 2015 by the author(s).This work is made available under the terms of a Creative Commons Attribution-NonCommercial-NoDerivatives License, available at https://creativecommons.org/licenses/by-nc-nd/4.0/

Peer reviewed

eScholarship.org Powered by the California Digital Library
University of California

Volume 21 Number 4
April 2015

Case presentation

A misdiagnosed melanoma: a case of cutaneous epithelioid malignant peripheral nerve sheath tumor

Konstantinos Linos MD, Simon Warren MD

Dermatology Online Journal 21 (4): 4

Department of Pathology/Division of Dermatopathology, Indiana University, IN, USA

Correspondence:

Konstantinos Linos MD
350 W. 11th Street, Room 4083
Indianapolis, IN, 46202
Ph: (+1) 317-491-6350

Abstract

Malignant Peripheral Nerve Sheath Tumor (MPNST) is a rare soft tissue sarcoma that can occur in superficial locations. Histologically it is categorized into two variants: a conventional/spindled and an epithelioid variant. The latter one is very rare and can be confused histologically with malignant melanoma as it is diffusely positive for S100-protein. Herein we present a case that was initially misdiagnosed as malignant melanoma and discuss morphological and immunohistochemical clues to reach a correct diagnosis.

Keywords: Malignant Peripheral Nerve Sheath Tumor, MPNST, epithelioid, INI1

Introduction

Malignant peripheral nerve sheath tumor (MPNST) is a relatively rare soft tissue sarcoma accounting for approximately 5% of all soft tissue sarcomas and having an incidence of 0.001% in the general population [1,2]. Although it usually involves major nerves, extremely rarely it can occur in superficial locations such as the skin or subcutis, presumably arising from peripheral nerves or neurofibromas [3]. A subset of MPNSTs can have entirely or nearly entirely epithelioid features histologically and be diffusely S100-protein positive by immunohistochemistry, resembling melanoma.

Case synopsis

We present the case of a 39 year-old man with a history of histoplasmosis, who had initially a superficial small nodule about the size of a dime in the high thoracic area of his back; it was initially evaluated by his primary care physician and felt to be a sebaceous cyst. It increased in size to 5.3 x 4.0 cm and the patient subsequently underwent a resection at another local institution in August 2010.

Histologic sections showed a superficially located malignant neoplasm with a multilobulated growth pattern (Figure 1) consisting of cytologically uniform but atypical epithelioid cells with copious pale amphophilic cytoplasm and vesicular nuclei (Figure 2). Numerous mitoses were identified. The tumor was diffusely positive for S100-protein by immunohistochemistry (Figure 3A) and

negative for other melanocytic markers (HMB45, Melan A, MITF) as well as epithelial markers (High Molecular weight Cytokeratin-HMWCK and Pancytokeratin-AE1/AE3). The diagnosis of malignant melanoma was rendered. The slides were sent from the local pathologist to a major academic institution for consultation where they concurred with the diagnosis of malignant melanoma, favor metastasis (MITF was interpreted as focally positive). Subsequent wide excision in October 2010 showed no residual tumor.

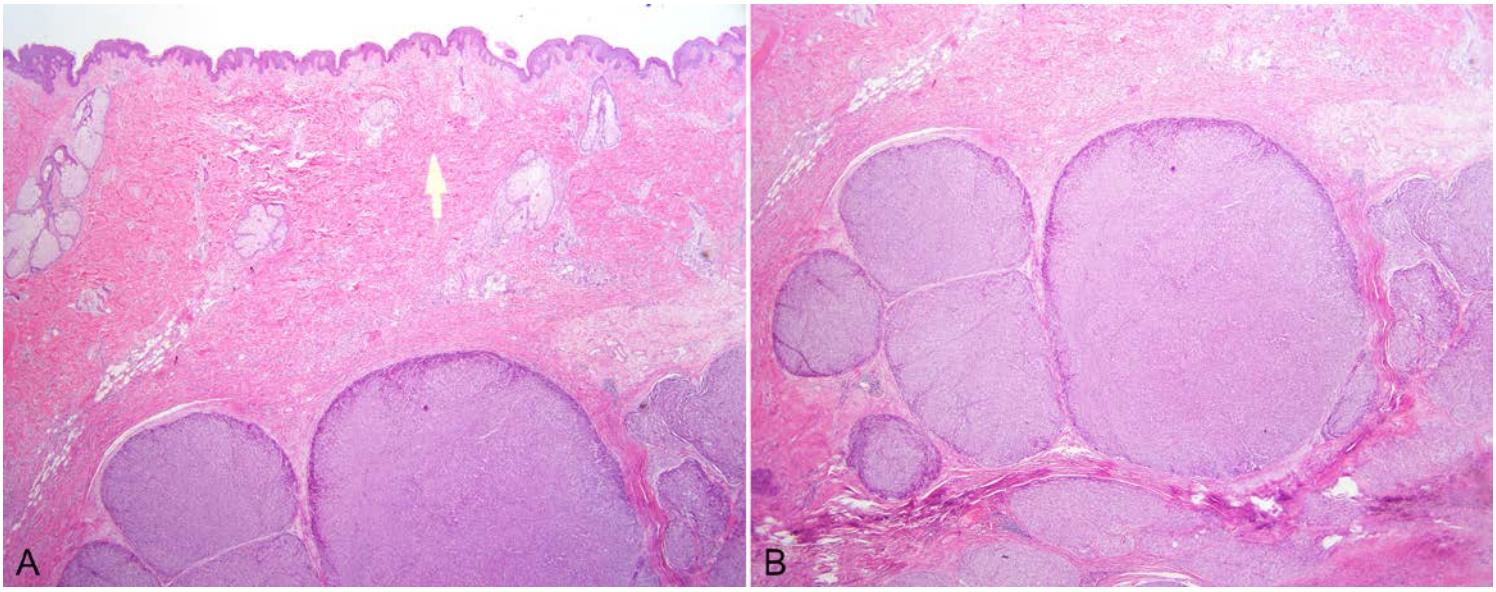

Figure 1 A-B. Low Power magnification showing the superficial location of the tumor with the characteristic multilobulated growth pattern (H&E 20X)

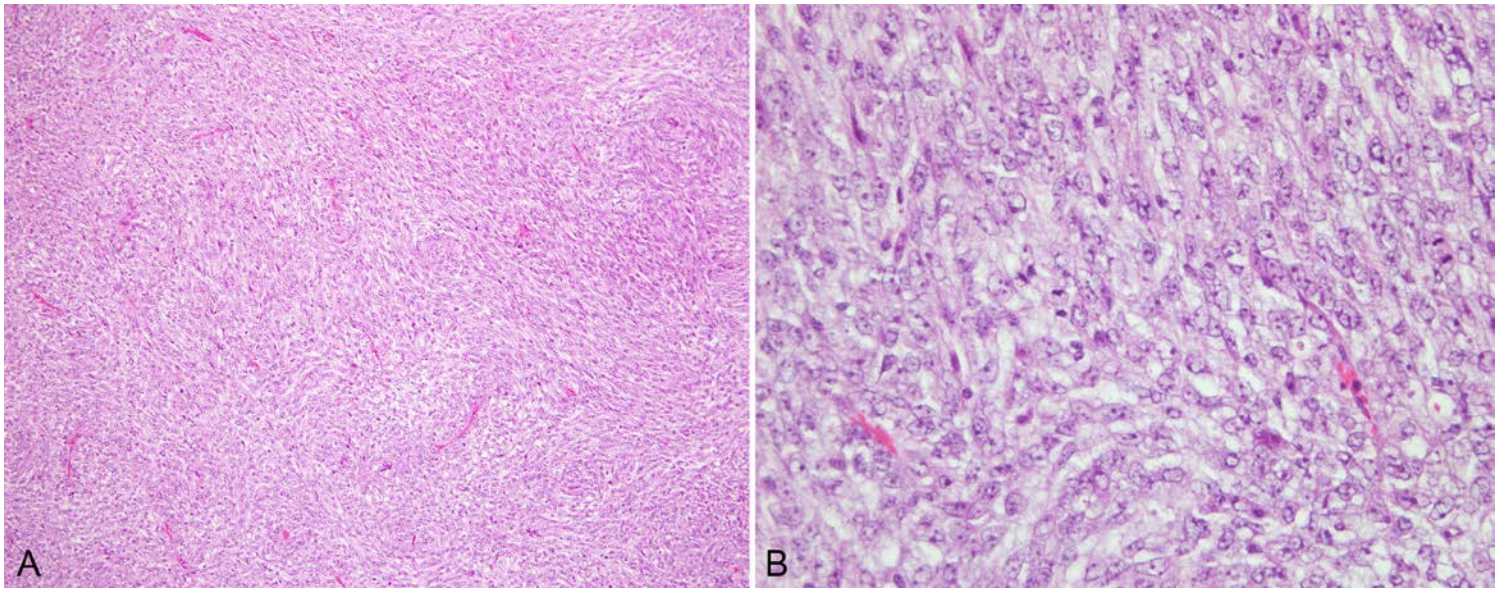

Figure 2A-B. Medium and high magnification showing uniform atypical epithelioid cells with copious palely amphophilic cytoplasm and vesicular nuclei with a fascicular growth pattern and some perivascular accentuation. Numerous mitotic figures are evident. (H&E 200x and 400x)

The patient was referred to an oncologist in our institution in November 2010 for further management of a presumptive malignant melanoma Stage III or IV. As part of Indiana University policy the slides were requested for confirmation of the diagnosis and were reviewed in January 2011. We rendered the diagnosis of S100 positive neoplasm compatible with metastatic malignant melanoma in the appropriate clinical setting. However, further history revealed no evidence of a primary site; subsequent additional immunostains were performed and electron microscopy revealed no evidence of pre-melanosomes or melanosomes. We raised the possibility of Malignant Peripheral Nerve Sheath Tumor and the case was sent for consultation to Dr Christopher Fletcher at Brigham and Women's Hospital, Harvard Medical School. INI1 immunohistochemistry was performed showing loss of nuclear staining and the final diagnosis of Epithelioid MPNST was issued in May 2011.

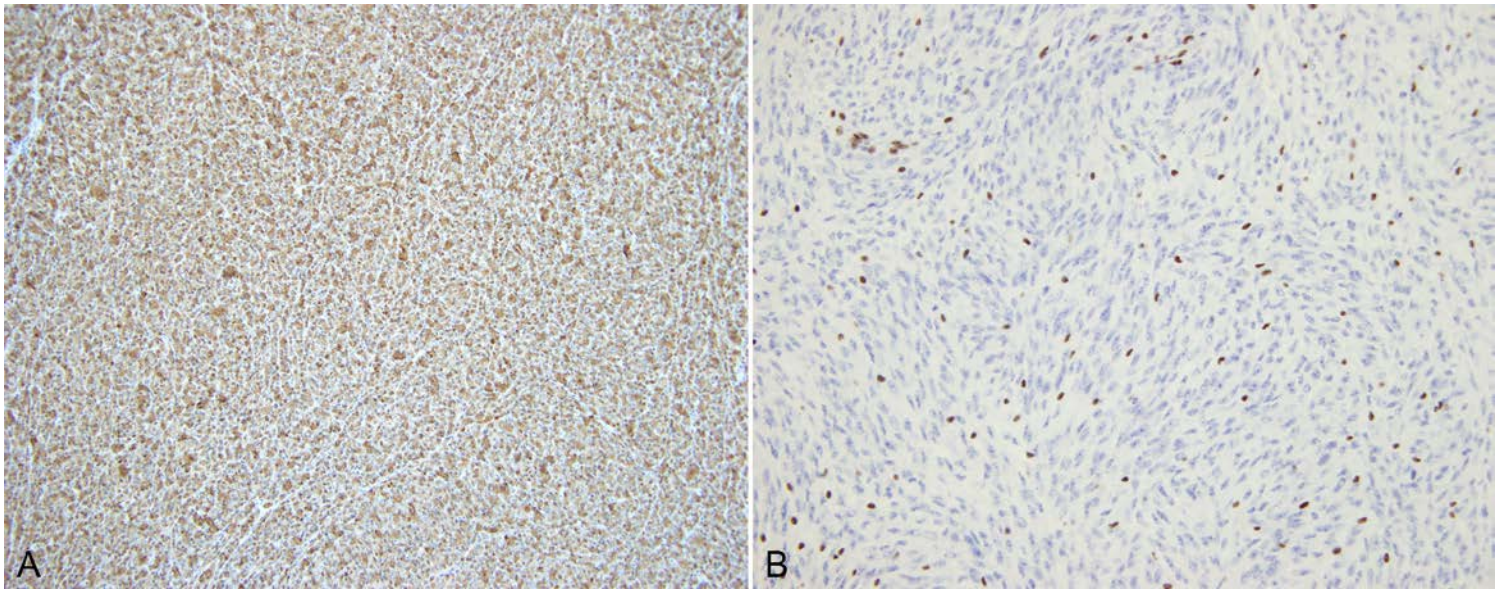

Figure 3 A-B. A) Diffuse S100-protein positivity by immunohistochemistry B) INI1 immunohistochemistry showing loss of nuclear reactivity indicating that the product of this gene on the long arm of chromosome 22 is lost/deleted. Note the positive internal control in intratumoral lymphocytes.

The patient received no adjuvant therapy. There is no evidence of recurrence or metastasis after 45 months of follow-up (last follow-up appointment May 2014).

Discussion

Superficial MPNSTs are extremely rare. Wick et al reported that they account for approximately 2% of all cutaneous malignant spindle cell tumors[4]. They are often associated with neurofibromas and a subset of them is associated with Neurofibromatosis Type 1 (NF-1), although this association is much stronger for deep-seated tumors [3]. The latter, as expected, occur in younger patients, whereas in the sporadic ones there is no age predilection [5]. Superficial MPNSTs often have a history of slow growth followed by a period of rapid growth [3]. They are associated with a better clinical outcome presumably because they come to clinical attention earlier owing to their superficial location, although there is a risk for recurrence and metastasis [6-7]. Head and neck is the most common location, albeit they have been reported in a variety of sites [1].

Histologically, there are two variants: a conventional/spindled and an epithelioid variant. Interestingly the latter is more common in the cutaneous tumors, affects adults most frequently on the lower extremities, has a weak association with NF1, and occasionally originates from a schwannoma [7-11] . It is the one that poses the most difficulties and pitfalls in the differential diagnosis with melanoma [12]. The conventional variant is composed of hyperchromatic spindled cells arranged in sweeping fascicles, creating a marble-like effect owing to alternation of dense cellular fascicles and hypocellular myxoid zones [13]. The epithelioid variant, as the name implies, is composed, predominantly or exclusively, of monomorphous cells with polygonal epithelioid appearance arranged in a multinodular pattern. The cells have primitive round nuclei with large eosinophilic nucleoli in a collagenous to myxoid stroma [13].

The main entity in the differential diagnosis histologically is between carcinoma and melanoma. If the origin from a nerve or a neurofibroma can be established then the diagnosis is straightforward. In the absence of this feature, ancillary studies are imperative to reach a definite diagnosis in conjunction with some morphologic clues. Epithelioid MPNST lacks melanin pigment and immunohistochemically shows diffuse, strong positivity for S100-protein (in contrast to the conventional variant which shows focal patchy positivity), lacks melanoma-associated markers (Melan-A, MITF, HMB45, tyrosinase), and is rarely positive for keratin (focally). The latter is very helpful in excluding carcinoma, which is expected to be negative for S100-protein and diffusely positive for keratin. Distinguishing the tumor from melanoma is more challenging, as it is well known that the latter can show only S100-protein positivity and lose its melanocytic markers; in addition an intraepidermal component or melanin pigment is not always apparent. One morphologic clue, although not by any means conclusive, is the multinodular growth pattern and the monomorphous cytology in contrast to the pleomorphism exhibited by melanomas. An extremely helpful and essentially conclusive study is INI1 immunohistochemistry; epithelioid MPNST shows loss of nuclear staining in contrast to melanoma, which consistently retains expression. Unfortunately, this is observed in approximately 50% to 67% of the cases [14]. It is important to emphasize that occasionally a clear-cut distinction from melanoma is virtually impossible as the two tumors can be indistinguishable.

In summary we present a very rare case of cutaneous epithelioid malignant peripheral nerve sheath tumor (MPSNST) that was misdiagnosed as malignant melanoma. We show the difficulty and pitfalls in distinguishing between these two tumors. The multinodular growth pattern and the monomorphism are morphological clues; the loss of INI1 nuclear retention by immunohistochemistry is essentially diagnostic in this setting.

References

1. Thomas C, et al. Cutaneous malignant peripheral nerve sheath tumors. Journal of cutaneous pathology 2009;36;896-900.[PMID:19586501]
2. Folpe AL. Selected topics in the pathology of epithelioid soft tissue tumors. Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc 2014;27 Suppl 1;S64-79.[PMID:24384854]
3. Allison KH, et al. Superficial malignant peripheral nerve sheath tumor: A rare and challenging diagnosis. American journal of clinical pathology 2005;124;685-692.[PMID:16203275]
4. Wick MR. Malignant peripheral nerve sheath tumors of the skin. Mayo Clinic proceedings 1990;65;279-282.[PMID:2304365]
5. Ducatman, et al. Malignant peripheral nerve sheath tumors. A clinicopathologic study of 120 cases. Cancer 1986;57;2006-2021.[PMID:3082508]
6. Dabski C, et al. Neurofibrosarcoma of skin and subcutaneous tissues. Mayo Clinic proceedings 1990;65;164-172. [PMID:1689440]
7. VY Jo, et al. Epithelioid malignant peripheral nerve sheath tumor:Clinicopathologic features of 48 cases. Abstract, USCAP, San Diego 2014.
8. Laskin WB, et al. Epithelioid variant of malignant peripheral nerve sheath tumor (malignant epithelioid schwannoma). The American journal of surgical pathology 1991;15;1136-1145. [PMID: 1746681]
9. Lodding P, et al. Epithelioid malignant schwannoma. A study of 14 cases. Virchows Archiv. A, Pathological anatomy and histopathology 1986;409;433-451.[PMID:3090772]
10. Carter JM, et al. Epithelioid malignant peripheral nerve sheath tumor arising in a schwannoma, in a patient with "neuroblastoma-like" schwannomatosis and a novel germline smarcb1 mutation. The American journal of surgical pathology 2012;36;154-160.[PMID:22082606]
11. McMenamin ME, et al. Expanding the spectrum of malignant change in schwannomas: Epithelioid malignant change, epithelioid malignant peripheral nerve sheath tumor, and epithelioid angiosarcoma: A study of 17 cases. The American journal of surgical pathology 2001;25;13-25.[PMID:11145248]
12. Morgan MB, et al. Cutaneous epithelioid malignant nerve sheath tumor with rhabdoid features: A histologic, immunohistochemical, and ultrastructural study of three cases. Journal of cutaneous pathology 2000;27;529-534.[PMID:11100813]
13. John R. Goldblum, A L. Folpe, Sharon W. Weiss. Enzinger & weiss's soft tissue tumors: Elsevier, 2014.
14. Hollmann TJ, et al. Ini1-deficient tumors: Diagnostic features and molecular genetics. The American journal of surgical pathology 2011;35;e47-63.[PMID:21934399]