Hemosiderotic dermatofibroma mimicking melanoma: A case report and review of the literature

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INTRODUCTION

Dermatofibroma (DF) is a common benign skin tumor. Hemosiderotic dermatofibroma (HDF) is a rare variant of DF. It often mimics other skin lesions including melanocytic lesions and vascular tumors. In this report, we described the clinical features and histopathological findings of a rare HDF case that mimics melanoma.

Dermatofibroma (DF) is a common benign cutaneous lesion generally reported in the trunk or extremities of young or middle-aged adults with a slight predominance in females. Based on specific histopathological features, DF has multiple variants which may include but not limited to aneurysmal/hemosiderotic, cellular, epithelioid cell histiocytoma, atypical (pseudosarcomatous), atrophic, and lipidized. It usually presents as a solitary well-circumscribed nodule with reddish/brown color on gross examination and central white patch and peripheral pigment network on dermatoscopy. However, this disease has a wide range of presentations. About 29% DF cases harbor atypical macroscopic features resembling other skin malignancies including melanoma (16% of all cases), vascular tumor, and basal cell carcinoma. Hemosiderotic DF (HDF) is a rare variant of DF which is known to have melanoma-like pattern. Skin examination by dermatoscopy is not able to reliably distinguish HDF from melanoma.

In this scenario, a definite diagnosis could only be made by histopathological examination. There are three cases of HDF reported in the literature from the United States. Here, we report another case of HDF which was clinically suspicious for melanoma.

CASE REPORT

Patient is an 85-year-old woman presenting to clinic for a full-body skin check. Skin examination revealed an isolated, black-colored skin nodule on left thigh measuring 1.0 cm in greatest dimension with an asymmetric and irregular border (Figure 1). Patient denies any associated symptoms and has had no trauma or previous treatment to the area. Based on the history and clinical presentation, the initial differential diagnosis was dermatofibroma versus melanoma. H&E-stained sections of skin biopsy show dermis-based proliferation of histiocytic and fibroblastic cells with deposition of abundant yellow-brown–colored granules. These granules are stained blue via Prussian blue staining.
consistent with accumulation of hemosiderin (Figure 2A-2C). Papillary dermis is not involved (Grenz zone). The overlying epidermis shows mild basal layer proliferation with basal hyperpigmentation (Figure 2A). Entrapment of thick hyalinized collagen bundles by the fibrohistiocytic cells is noted at the peripheral of the lesion (Figure 2D). The lesion is largely confined in the dermis and does not involve the subcutaneous fat.

High-power examination of the lesion shows fibrohistiocytic cells mixed with foamy histiocytes. Occasionally, cells with large cytoplasmic vacuoles are identified (Figure 2B). Majority of these foamy histiocytes loaded with hemosiderin are adjacent to slit-like vascular spaces (Figure 2B). Red blood cells leaked into the interstitial spaces are engulfed and digested by the histiocytes giving rise to hemosiderin (Figure 2B, 2E). In focal areas, foamy histiocytes and lipoblast-like cells with pyknotic nuclei are enriched which mimics lipidized DF (LDF) (Figure 2F).

Ancillary studies were employed to exclude dermatofibrosarcoma protuberans (DFSP) and melanoma. Immunostaining with antibodies against CD34, CD10, CD68, factor XIIIa (FXIIIa), SOX-10, and HMB-45 was performed. The tumor cells show strong membranocyttoplasmic staining for CD10, positive for FXIIIa, weak positive for CD68, but negative for SOX-10, HMB-45 (Figure 3A-3E), and CD34 (data not shown). Based on the clinical presentation, characteristic histopathological findings, and immunohistochemistry pattern, this lesion was finally diagnosed as HDF.

**FIGURE 1** Picture showing a black skin lesion with an ill-defined border on the left thigh

**FIGURE 2** Representative picture shows A, fibrohistiocytic proliferation in the dermis with Grenz zone, acanthosis, and focal epidermal basal layer hyperpigmentation, original magnification 40x; B, diffuse intracellular hemosiderin deposition in histiocytes, original magnification 400x; C, Prussian blue stain, original magnification 400X; (D) peripheral collagen entrapment by fibrohistiocytes, original magnification 400x; E, extravasation of RBCs into the interstitial spaces, engulfment of RBCs by macrophages, and production of intracellular hemosiderin; and F, area with abundant foamy histiocytes and lipoblasts, original magnification, 400x
3 | DISCUSSION

HDF is considered to be a rare variant of DF, constituting 5.7% of all DF cases.1 It is reportedly associated with melanoma-like pattern or vascular tumor-like pattern on dermatoscopy.10,13 In this case, the black-colored lesion with asymmetric border combined with peripheral blackish hue in an 85-year-old woman poses a diagnostic challenge for the dermatologist. Because wide local excision with negative margins is performed for melanoma, a definitive diagnosis of DF is crucial to avoid unnecessary surgical treatment. Histopathologically, this lesion demonstrates extensive intracellular and extracellular accumulation of hemosiderin by iron stain, which correlates with the dark-color appearance of the lesion. Therefore, the differential diagnosis of a pigmented skin papule, plaque, or nodule on the extremities could always include HDF.

Review of the literature revealed 16 case reports of HDFs from 21 patients (table 1), 3 of which are from the United States. Consistent with classic DF, HDF also demonstrates a slight female predominance (11 versus 9) and most commonly occurs on the extremities in young to middle-aged adults. Only one case was reported to occur in a patient over 80s. To the best of our knowledge, this is the fourth case of HDF from the United States and the second case of HDF in a patient over 80s. Majority of these cases raise concern for melanoma following initial dermatoscopic examination and excision was performed for a definite diagnosis.11,13-27

The area rich in poorly formed vessel-like structures can make the lesion look like a vascular tumor such as Kaposi's sarcoma both microscopically and clinically.28 Given the patient having no clinical history of immunosuppressive diseases/conditions, the chance of Kaposi's sarcoma is likely to be very low. When in doubt, immunohistochemical staining for HHV-8 and vascular markers including CD31 and ERG can pinch the diagnosis. Some studies suggest that HDF is a precursor of aneurysmal DF (ADF)3,20,21 which is characterized by cavernous-like blood-filled large space in the dermis. The hypothesis favors a slow process of blood leaking and building up, thus forming the final large blood-filled space. Trauma could also be a contributing factor as some reports show cases arising from the prior injury site. Extravascular red blood cells are phagocytized by macrophages which leads to the production of hemosiderin. Rapid expansion of the lesion caused by dermal hemorrhage can also raise the concern for the progression of a malignant disease.21

Other fibrohistiocytic lesions that can clinically mimic melanoma or melanocytic lesions include atypical...
Fibroxanthoma (AFX), pigmented dermatofibrosarcoma protuberans (DFSP), clear cell DF, and epithelioid cell histiocytoma (ECH). In our case, the fibrohistiocytic cells do not show significant cytological atypia, nuclear polymorphism, high index of mitosis, or necrosis. The lesional cells are negative for melanoma marker including SOX-10 and HMB-45, negative for CD34, and positive for CD10, CD68 (focal weak positive), and FXIIIa. Therefore, these microscopic and immunohistochemical findings help to rule out melanoma, AFX, and DFSP. The distinction between different variants of DF relies on microscopic features. Clear cell DF consists predominantly of sheets of clear cells with PAS positivity.\(^{29}\) ECH presents as nodular to sheet-like well-circumscribed proliferation in papillary dermis which is clinical and histologic mimic of intradermal Spitz nevus.\(^{30}\) It is associated with rearrangement and overexpression of anaplastic lymphoma receptor tyrosine kinase (ALK).\(^{30-32}\) An immunostaining for ALK can be helpful to confirm the diagnosis of ECH. It is also interesting to note that lesional cells in a focal area show features of LDF. However, the tumor cells in this case do not have stromal hyalinization, a defining feature for LDF.\(^{8}\)

DF is generally a benign lesion with very low recurrence rate even when margins are positive (< 2%).\(^{4,8}\) There are no data available in the literature describing the recurrence rate of HDF. However, ADF is associated with relatively more aggressive clinical course.\(^{4,33}\) A study showed that ADF carries a recurrence rate of up to 19% which is significantly higher than other subtypes of DFs.\(^{34}\) In addition, HDF seems to have the potential to grow into a large lesion. Two reports illustrated giant HDFs which clinically resemble soft tissue sarcomas.\(^{14,17}\) In addition, one report from Japan has shown the evidence of ADF metastasis to local regional lymph nodes.\(^{35}\) The mechanism underlying the pathogenesis of HDF remains elusive. However, cytogenetic studies have identified recurrent rearrangement of \(PRKC\) gene in ADFs and other subtypes.\(^{36,37}\) Recent studies showed that dysfunction of FXIIIa protein may be also involved in the pathogenesis of DF.\(^{38}\)

| Case No. | Age | Gender | Location of lesion | Size of lesion (cm) | Country | Citation |
|----------|-----|--------|--------------------|---------------------|---------|----------|
| 1        | 25  | Male   | Left calf          | 1.0                 | United States | 13       |
| 2        | 47  | Female | Left leg           | 17.0                | United States | 14       |
| 3        | 65  | Male   | Right Achilles tendon | 1.0                 | United States | 15       |
| 4        | 74  | Female | Left arm           | 0.6                 | Spain     | 16       |
| 5        | 28  | Female | Back               | 0.3                 | Spain     | 16       |
| 6        | 25  | Male   | Left thigh         | 0.9                 | Spain     | 16       |
| 7        | 59  | Male   | Right temple       | 0.5                 | Spain     | 16       |
| 8        | 54  | NR     | Left foot          | 5.0                 | Switzerland | 17       |
| 9        | 85  | Female | Right leg          | 0.8                 | Portugal  | 18       |
| 10       | 36  | Female | Right breast       | NR                  | Brazil    | 19       |
| 11       | 38  | Male   | Abdomen            | 1.0                 | Italy     | 20       |
| 12       | 12  | Male   | Right knee         | 1.0                 | Turkey    | 21       |
| 13       | 50  | Female | Left leg           | 0.9                 | Portugal  | 22       |
| 14       | 43  | Female | Right forearm      | NR                  | Spain     | 23       |
| 15       | 47  | Female | Left leg           | NR                  | Spain     | 23       |
| 16       | 27  | Male   | Right shoulder     | 0.9                 | Germany   | 24       |
| 17       | 21  | Male   | Right knee         | 3.0                 | Spain     | 25       |
| 18       | 38  | Male   | Left hand          | 1.6                 | South Korea | 26       |
| 19       | 25  | Female | Right knee         | 1.5                 | Guatemala | 27       |
| 20       | 30  | Female | Left forearm       | 1.0                 | Guatemala | 27       |
| 21       | 52  | Female | Left leg           | 2.5                 | Portugal  | 28       |

Abbreviation: NR, not reported.

**TABLE 1** Summary of HDF cases reported in the literature
In summary, we reported a rare case of HDF which simulates melanoma in clinical setting. Thus, when evaluating a pigmented lesion on the extremities, HDF could be always a potential differential diagnosis. Histological evaluation and immunohistochemistry are critical to rule out melanoma and other mimickers. Given relatively higher recurrence rate and aggressive behavior associated with ADF, close watch and/or complete excision of HDF is recommended.

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CONFLICT OF INTEREST
The authors declare no conflict of interests.

AUTHOR CONTRIBUTIONS
CL: collected the data and wrote the report. HA, ML, and PS: analyzed the data and revised the manuscript. All authors: approved the final version of the manuscript.

ETHICAL APPROVAL
Need for ethical approval waived.

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