A Case of a Pleomorphic Hyalinizing Angiectatic Tumor of Soft Parts with Intracytoplasmic Hemosiderin Pigment Apparent upon Fine-Needle Aspiration Cytology

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Pleomorphic hyalinizing angiectatic tumors of soft parts are extremely rare low-grade mesenchymal lesions that frequently occur subcutaneously, especially in the lower extremity. The tumor is histologically characterized by sheets of plump, spindled or rounded cells, and clusters of ectatic blood vessels. It also has a number of previously characterized cytological features such as pleomorphic cells, intranuclear pseudoinclusion, and intracytoplasmic hemosiderin pigments. However, intracytoplasmic hemosiderin has not been carefully evaluated in cytology specimens. Here, we report the case of a 56-year-old Japanese man with an encapsulated pleomorphic hyalinizing angiectatic tumor of soft parts that included fine and coarse hemosiderin-laden tumor cells. The tumor was clinically followed up as a hematoma, but malignant tumors, including malignant melanoma, were suspected because aspiration cytology specimens contained pleomorphic cells with intracytoplasmic brown pigments. The tumor was closely associated with an intratumoral hematoma and a few microscopic satellite lesions. Pleomorphic hyalinizing angiectatic tumor of soft parts should be included in the differential cytological diagnosis of soft tissue tumors if the three cytological features described earlier are present. Enucleation therapy could facilitate local recurrence, as the tumor may have the potential to infiltrate surrounding soft tissue or form satellite lesions. Diagn. Cytopathol. 2015;43:407–411. © 2014 The Authors. Diagnostic Cytopathology Published by Wiley Periodicals, Inc.

Key Words: intracytoplasmic hemosiderin pigments; pleomorphic hyalinizing angiectatic tumor of soft parts; satellite lesions; tumor encapsulation

Introduction

Pleomorphic hyalinizing angiectatic tumor (PHAT) of soft parts is a rare mesenchymal tumor of uncertain lineage, first described in 1996 by Smith et al. Cellular features of PHAT in cytology specimens have been reported in several papers, in which pleomorphic cells and intranuclear pseudoinclusions were the characteristic findings. However, intracytoplasmic hemosiderin has not been shown conclusively, although fine granular hemosiderin pigments have been described as a conspicuous
Here, we report a case of PHAT in which intracytoplasmic hemosiderin deposits were apparent in aspiration cytology specimens and there were also previously unreported microscopic daughter lesions around the main tumor.

Case Report

A 56-year-old Japanese man had been aware of a nodule in his right thigh for eight months before its surgical resection. His primary care physician clinically followed this up as a hematoma, but the patient reported mild pain as this mass became enlarged, and he was referred for additional investigations. The mass was palpable and tender, and routine laboratory test results were normal. Pre-contrast- and contrast-enhanced computed tomography (Fig. 2A) revealed a well-demarcated oval mass, 65 × 38 × 35 mm in size, in the short head of the right biceps femoris muscle, consisting of a biphasic mass with a non-enhanced nodular area in the proximal portion, and a heterogeneous enhancement in the distal portion.

Analysis of fine-needle aspiration specimens revealed oval, rounded, spindled, or bizarre cells with pleomorphic, large vesicular nuclei and distinct nucleoli (Fig. 1A to D). Intranuclear cytoplasmic pseudoinclusions were observed in a few abnormal cells (Fig. 1B). Fine or coarse, yellow to brown intracytoplasmic granules were occasionally found in some bizarre cells (Fig. 1C and D), and the fine granules appeared to glitter or have a refractile property in some crushed cells (Fig. 1D). There were no ectatic blood vessels. Malignant melanoma, clear cell sarcoma, and melanotic schwannoma could not be excluded because of the pleomorphism and fine intracytoplasmic deposits.

Needle biopsy specimens had a fascicular arrangement of epithelioid, ovoid, or spindle cells with pleomorphic nuclei (Fig. 2E), and a few mitotic bodies were present (Fig. 2E, inset). Intracytoplasmic pigments and/or intranuclear pseudoinclusions were noted in bizarre cells (Fig. 2F and G). The tumor was associated with a collagenous stroma with hemosiderin deposits and an infiltrate of mast cells (Fig. 2E, I, and J). Iron staining of the intracytoplasmic pigments indicated that they were hemosiderin (Fig. 2J); no metachromatic properties were apparent on toluidine blue staining, and there was no HMB45 immunoreactivity. Schwannoma and melanin-producing tumors were excluded due to negativity for S-100 and HMB45, but a conclusive diagnosis could not be made. On careful retrospective examination of the biopsy specimens, a
A cluster of ectatic vessels with hyalinization or fibrinous deposition was apparent (Fig. 2D). If a malignant tumor was possible, a wide surgical resection was performed. Cut sections of the resected mass exhibited a hematoma in the upper portion (Fig. 2B), which occupied approximately 70% of the mass. Histologically, this nodule exhibited thin- to thick-fibrous encapsulation without an infiltrative border (Fig. 2C) and included a cellular area consisting of the pleomorphic cells described previously and a fibrovascular stroma, including clusters of ectatic vessels. There were scattered mitotic bodies (≤2/50 HPFs), but no osteoclast-like giant cells, and no apparent necrosis. Immunohistochemical analysis revealed positive staining for CD34, factor XIIIa, CD99, and vascular endothelial growth factor, and negative staining for muscle markers, epithelial markers, S100, HMB45, CD31, and PG-M1. The MIB-1 labeling index was 4.0%. Malignant fibrous histiocytoma was excluded because of the low mitotic activity, well-defined border, and positivity for CD34. Although solitary fibrous tumor and giant cell angiofibroma may be differential diagnoses based on this immunohistochemical result, PHAT was diagnosed based on the presence of the cellular pleomorphism and ectatic blood vessels with fibrin deposition.

In the striated muscle, and within 2 cm of the tumor capsule, there were two cellular lesions, less than 5 mm in diameter, consisting of pleomorphic cells that occasionally contained intracytoplasmic hemosiderin identified by iron staining (Fig. 2E-H). Intratumoral mast cells are indicated by arrowheads (J, toluidine blue stain). A satellite lesion under low-power (left panel, K) and high-power (right panel, L) magnification. Arrowheads in K indicate a daughter nodule in the striated muscle tissue 1.2 cm from the tumor capsule. Arrows in L indicate tumor cells with pleomorphic nuclei adjacent to a vessel. Scale bars: 4 cm in A and B, 100 μm in C–E and L, 5 mm in K, and 10 μm in F–J. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]
staining. The cellular lesions were consistent with those of the main tumor; however, these lesions appeared not to be connected to the demarcated main tumor, even in the whole mount preparation. These cellular lesions could not be considered as putative precursor lesions of PHAT, which are early PHATs or homosiderotic fibrohistiocytic lipomatous lesions, as the putative precursor lesions are defined by a proliferation of bland hemosiderin-laden spindle cells. Thus, the two microscopic cellular lesions were probably satellite or daughter nodules of the main tumor.

The resected edge was free of tumor cells, and the patient remains disease-free three years after surgery.

Discussion

PHAT is a recently recognized, slowly growing mesenchymal tumor with an intermediate malignant potential. In 41 cases of PHAT reported by Folpe and Weiss, the patients’ age ranged from 10 to 79 years, with a median age of 51 years. The initial clinical diagnosis was hematoma or a benign neoplasm in most cases. The most common site was a subcutaneous tissue, though intramuscular tumors have also been reported. There is a high rate of local recurrence (33 or 50%) and a sarcomatous component or recurrence as sarcoma has also been reported, but there have been no cases of metastases arising from PHAT.

The characteristic cellular features of PHAT in cytology specimens—pleomorphic cells, intranuclear cytoplasmic pseudoinclusions, and intracytoplasmic hemosiderin granules—need to be considered together as a possible indicator of this lesion, even in the absence of ectatic vessel clusters, which are rarely observed in these preparations. Intranuclear pseudoinclusions and cellular pleomorphism are also observed in soft tissue tumors such as schwannoma, spindle and pleomorphic lipoma, alveolar soft tissue sarcoma, clear cell sarcoma of soft tissue, and epithelioid hemangioendothelioma. In addition, cytoplasmic hemosiderin pigments are seen in soft tissue tumors, such as giant cell tumors of the tendon sheath, angiosarcoma, Kaposi sarcoma, and neoplasms with perivascular epithelioid cell differentiation. However, with the exception of PHAT, all three cytological features are rarely present in the same tissue, making their combined appearance a useful diagnostic feature. Falpe and Weiss et al described fine granular intracytoplasmic hemosiderin pigments in PHAT cells, and the lesion in the present case mainly showed a mixture of fine and coarse cytoplasmic granules. Although fine cytoplasmic granules were suggestive of melanin-producing cells in the fine-needle aspiration cytology in this case, their golden yellow and refractile appearance and the presence of coarse granules suggest that this pigment was hemosiderin rather than melanin. The pathogenesis of cytoplasmic hemosiderin deposition in PHAT cells is unknown at present, although it is thought that PHAT may be a fibrohistiocytic tumor consisting of CD34-positive dendritic cells or FXIIIa-positive dendrophages, and hence, the tumor cells may show phagocytosis of hemorrhagic materials and form intracytoplasmic hemosiderin. Indeed, hemosiderin-laden tumor cells appeared to be adjacent to the hematoma in the present case.

In comparison with the previous cases of PHAT, the present case is unique because the daughter lesions were associated with the demarcated main tumor. Smith et al reported that PHATs usually have an infiltrative margin, and Folpe and Weiss also demonstrated infiltrative growth in all cases of PHAT. However, further cases of demarcated PHAT have been reported, and among those in which the tumor’s macroscopic appearance was described, 25 had an infiltrative margin and 16 had a demarcated margin. The tumor demarcation in the present case may be related to marked intratumoral hemorrhage, which may in turn be derived from vascular permeability induced by intratumoral mast cell products. Among the previously reported macroscopically demarcated PHATs, five were described as having a microscopic infiltrative border, but no satellite lesions were found. The pathogenesis of the satellite lesions remains unclear at present. Enucleation therapy may be an appropriate treatment for demarcated PHATs, but wide resection is more likely to be curative, because satellite lesions and/or a microscopic infiltrative border may be present.

Conclusion

To the best of our knowledge, this is the first case in which a careful evaluation of intracytoplasmic hemosiderin within PHAT cells was performed using aspiration cytology. Moreover, satellite lesions have not been described in cases involving demarcated PHAT, which probably influences the choice of operative procedure. PHAT should be included in the differential cytological diagnosis of soft tissue tumors, if bizarre mesenchymal cells showing low mitotic activity, intranuclear cytoplasmic inclusion, and intracytoplasmic hemosiderin deposits are observed.

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