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Hemosiderotic Fibrolipomatous Tumor or Pleomorphic Hyalinizing Angiectatic Tumor of Soft Parts?: Cytology and Histology of an Unusual Tumor

Nigar Fathima M, Meenakshi Swain*, Tejal Modi, SVN Anuradha
Department of Histopathology, Apollo Hospitals, Jubilee Hills, Hyderabad, India

Case Report

***Corresponding author**
Meenakshi Swain

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Abstract: Hemosiderotic Fibrolipomatous Tumor (HFLT) and pleomorphic hyalinizing angiectatic tumor of soft parts (PHAT) are rare, locally aggressive neoplasms with overlapping morphological and immunohistochemical features. HFLT is a recently described neoplasm whose cytological features have not been widely described in the literature. We present the cytological and histopathological features of this case because of its rarity and the intermediate features exhibited in this tumor, suggesting a continuous spectrum of tumors of uncertain differentiation, which includes both HFLT and PHAT. A 29 year old female presented with a painful swelling over the dorsum of foot for 1½ months. FNA of the swelling showed features of a spindle cell neoplasm with marked pleomorphism, cytoplasmic pigment, intranuclear and intracytoplasmic inclusions. A possibility of a sarcoma was given. Histopathological examination of the excised specimen showed features in favor of a soft tissue tumor of intermediate malignancy of uncertain type. Immunohistochemistry showed immunoreactivity for CD34 and negativity for CD31, S-100, HMB-45, Melan-A and pancytokeratin. These findings favoured the possibility of a HFLT. An early PHAT was also considered owing to considerable overlap seen in these two tumors.

Keywords: CD34, cytoplasmic pigment, hemosiderotic fibrolipomatous tumor(HFLT), intranuclear inclusions, pleomorphic hyalinizing angiectatic tumor of soft parts(PHAT), spindle cell tumor

INTRODUCTION

Hemosiderotic Fibrolipomatous Tumor (HFLT) is a recently described, locally aggressive neoplasm included in the latest WHO classification (2013). It was first described by Marshall-Taylor and Fanburg-Smith in the year 2000, following which approximately 35 cases have been reported in the literature till date [1]. However, the cytological features of this entity have not been widely described in the literature. Hence, we report this case because of its rarity and to fill the lacuna regarding the cytology of this entity in the current literature.

CASE REPORT

A 29 year old female presented with a painful swelling over the dorsum of left foot between the first and second toes since 2 years. There was no prior history of trauma. Smears from the FNA of the lesion showed a population of markedly pleomorphic spindle cells seen singly and in loose clusters with coarse chromatin, irregular nuclear contours and abundant cytoplasm with many of the cells showing intracytoplasmic pigment. Occasional intranuclear inclusions, multinucleate and uninucleate giant cells were also identified. Few cells had cytoplasmic inclusions (Figure 1). Melanoma and sarcoma were the possibilities suggested. In view of the large atypical cells with some containing cytoplasmic pigment, an excision was advised.

The specimen was received in multiple pieces which measures 3.5x3 cm. The consistency was soft to firm and cut surfaces of these bits were solid yellow, with few brownish areas and ill-defined grey white foci. Histopathological examination revealed an ill-circumscribed tumor composed of spindled to polygonal cells intimately admixed with mature adipose tissue. The cells were spindle to epithelioid with some of them showing cytoplasmic hemosiderin pigment. The nuclei were hyperchromatic and some of the them showed large intranuclear inclusions similar to those seen in cytology. Bizarre cells with large atypical nuclei were seen. Few mitoses averaging 2-3/10HPF were noted. Foci of necrosis and a mild inflammatory infiltrate was seen within the tumor (Figure 2). Immunohistochemical studies done for further typing showed immunoreactivity for CD34. The tumor cells were negative for CD31, S-100, HMB-45, Melan-A and pancytokeratin (Figure 3). These findings favored the possibility of a HFLT. An early PHAT was also considered owing to considerable morphological overlap seen in these two tumors.

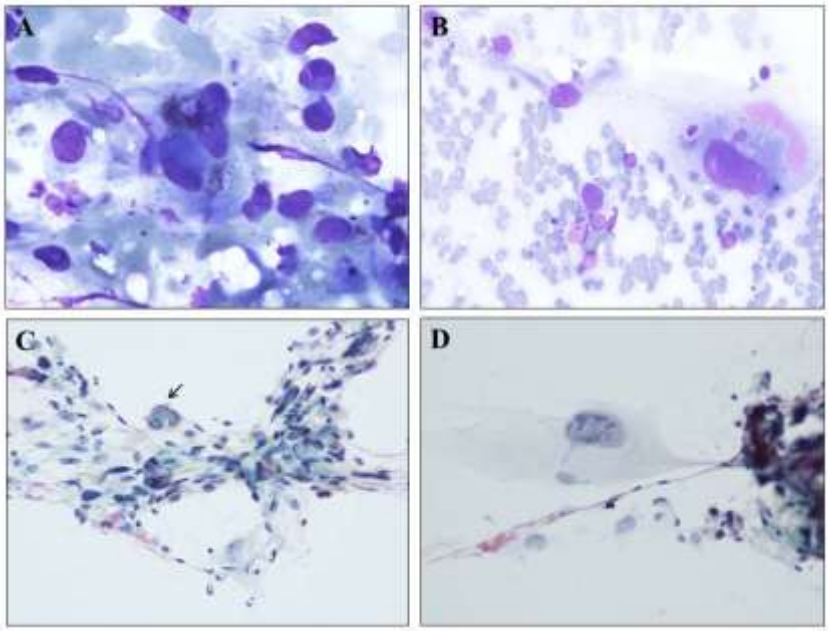

Fig-1: Cytology. (A) Smears show clusters of cells with marked nuclear atypia. Few cells show cytoplasmic pigment (Giemsa, 40x); (B) Multinucleated cell (Giemsa, 40x); (C) Intranuclear inclusion marked by arrow (Papanicolaou, 10x); (D) Multinucleated cell with inclusions (Papanicolaou, 40x)

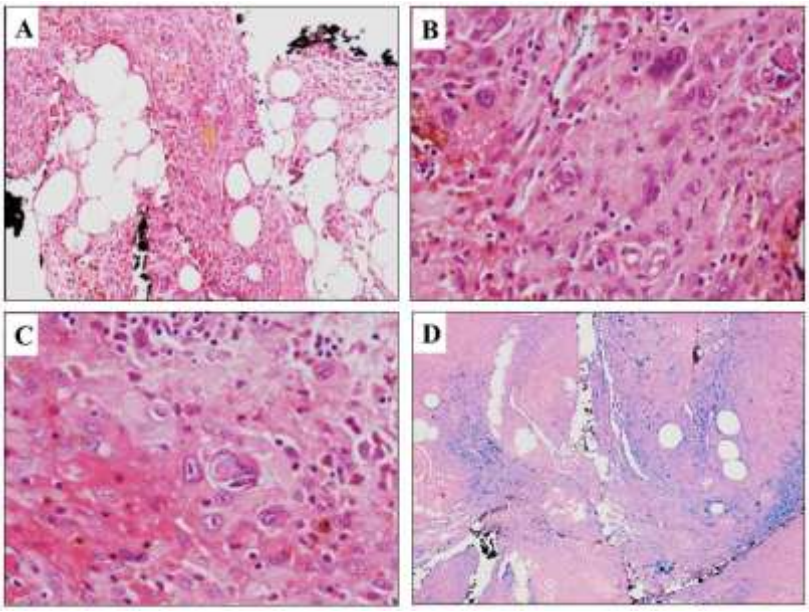

Fig-2: (A) Lesion shows admixture of spindle cells and adipocytes (HE, 4x); (B) Cells show nuclear pleomorphism with many of them showing cytoplasmic pigment (HE, 20x); (C) Intranuclear inclusions (HE, 20x); (D) Cytoplasmic iron pigment (Perl stain, 4x)

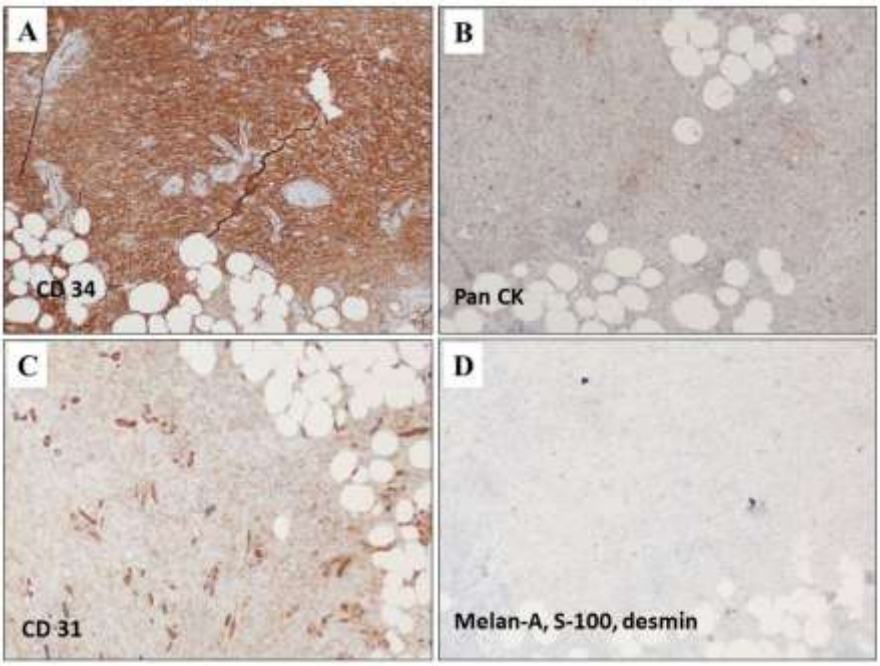

Fig-3: (A) Cells showing positivity for CD34; (B) Tumor cells are negative for pancytokeratin; (C) Blood vessels highlighted by CD31; (D) Tumor cells are negative for Melan-A, S-100 and desmin

DISCUSSION

HFLT is a rare, recently described neoplasm, categorised under tumors of uncertain differentiation in the WHO 2013 classification of soft tissue tumors. Approximately 35 cases have been published in the literature since its first description in the year 2000 by Marshall-Taylor and Fanburg-Smith, who reviewed cases with features of lipoma with fibrohistiocytic proliferation showing heavily pigmented spindle cells. These lesions were then termed as 'Hemosiderotic fibrohistiocytic lipomatous lesion' [1].

These lesions were considered to result from an inflammatory reaction to previous trauma or prolonged vascular stasis. However, cytogenetic analyses identifying translocation between chromosome 1 and 10, resulting in a fusion gene, TGFBR3-MGEA5, now suggest that HFLT has a neoplastic origin [2].

Moretti *et al.*, in 2010, reviewed all the 31 cases then published in the literature and reported that these painful, slow-growing tumors occur predominantly in the sub-cutaneous tissue of foot and ankle, while other less common sites include hand, calf, thigh and cheek [3]. There was a strong female predilection occurring mainly in the fifth and sixth decades of life. The skin overlying the lesion shows green to black discoloration. Macroscopic examination of these tumors show yellow to brown discoloration of the sub-cutaneous adipose tissue leading to skin discoloration.

FNA smears show pleomorphic spindle cells in a fibromyxoid matrix and mature adipocytes. The cells have pleomorphic nuclei, coarse chromatin, abundant cytoplasm showing intracytoplasmic hemosiderin granules [4]. Rare intranuclear cytoplasmic pseudoinclusions and osteoclast-type giant cells are also seen. The marked nuclear pleomorphism and atypia seen on cytology could be mistaken for a malignancy. Hence, awareness and correct recognition of this entity is of prime importance to prevent a misdiagnosis. The histological features parallel those of the cytological preparation showing fascicles of spindle cells with cytoplasmic hemosiderin demonstrable by Prussian Blue reaction. These spindle cells are admixed with adipocytes along with few scattered osteoclast-type giant cells. Inclusions, however, as seen in our case, were not mentioned.

These tumors lack a definite capsule or anatomic boundaries. The high rate of recurrence is attributed to the difficulty in assessing the adequacy of surgical margins intra-operatively. During the course of recurrences, few cases have progressed to low grade sarcoma. However, none of the cases showed metastasis. Moretti *et al.* reported that of the 27 cases in literature with follow-up details, 10 cases (37%) showed local recurrence, approximately 28 months following treatment on an average [3].

In 2017, Etchebehere *et al.* reported a case with two recurrences which later transformed to a low-grade unclassifiable pleomorphic sarcoma with myofibroblastic differentiation. This malignant form showed increased cellularity, marked nuclear pleomorphism, mitoses and immunoreactivity for smooth muscle actin and desmin suggesting myofibroblastic differentiation. Hence, a rigorous and regular follow-up of cases is advised [5].

HFLT can be misdiagnosed as well-differentiated liposarcoma or other lipomatous tumors and in the paucity of adipocytes, they can mimic fibroblastic and fibrohistiocytic lesions [3]. There is a significant morphologic overlap between HFLT and early PHAT. PHAT is another locally aggressive tumor of the soft tissue with a similar high recurrence rate as that of HFLT ranging from 30-50%.

PHAT was first described by Smith *et al.* in 1996 after analyses of 14 cases which resembled neurilemmoma with their hyalinised vessels and those which resembled malignant fibrous histiocytoma due to presence of pleomorphic cells [6]. This lesion is commonly described in distal extremities and rarely in shoulder, axilla, buttock, renal hilum etc. Cytology samples from these lesions show pleomorphic spindle cells with few intranuclear cytoplasmic pseudoinclusions and intracytoplasmic hemosiderin granules. Histologic examination shows numerous hyalinised angiectatic blood vessels surrounded by pleomorphic spindle cells and prominent intranuclear inclusions [7]. Early PHAT shows short fascicles of hemosiderin laden spindle cells infiltrating fat along with a few blood vessels. These areas are seen co-existing with areas of classic PHAT in the centre and early PHAT areas in the periphery suggesting that early PHAT is a precursor to classic PHAT [8]. Table 1 shows the comparison of features of both entities and that of the presented case. It is also worth noting that early PHAT is morphologically identical to HFLT and both lesions show similar molecular alterations resulting in TGFBR3 and MGEA5 rearrangements.

Table 1: Comparison of features of HFLT and PHAT with the reported case

	HFLT	PHAT	Case
Clinical features	• 5^{th} -6^{th} decade • Dorsum of foot, ankle, hand, calf, cheek • Sub-cutis	• Adult men and women • Sub-cutis of ankle and foot, deep soft-tissue	• 32 year female • Dorsum of foot
Morphology	• Fascicles of spindle cells with hemosiderin • Admixed with adipocytes • Hemosiderin laden macrophages • Osteoclast-like giant cells	• Thin-walled ectatic vessels • Perivascular hyalinisation • Spindle to pleomorphic cells • Intranuclear inclusions • Hemosiderin granules	• Fascicles of spindle cells with hemosiderin • Admixed with adipocytes • Hemosiderin laden macrophages • Osteoclast-like giant cells • Intranuclear inclusions • No ectatic vessels
IHC	• Positive: CD34, calponin • Negative: S-100, caldesmon, desmin, keratins	• Positive: CD34 • Negative: S-100	• Positive: CD34 • Negative: S-100, desmin, CK, CD31, Melan-A
Prognosis	30-50% local recurrence	30-50% local recurrence	

CONCLUSION

We present this case because of its rarity, and since cytology of this entity has not been widely described in English literature. The features exhibited in this tumor, suggest a continuum in the spectrum of tumors of uncertain differentiation, which includes both HFLT and PHAT.

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