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Review

Superficial CD34 positive fibroblastic tumor: report of three cases and review of the literature

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Abstract

Superficial CD34 positive fibroblastic tumor (SCPFT) is a recently recognized, unique neoplasm with distinctive histomorphological features such as high pleomorphism, low mitotic rate, and diffuse CD34 reactivity. Hereby we present three cases of our experience with clinicopathological, morphological, and immunohistochemical characteristics. The patients were a 31-year-old female, 53-year-old female, and 33-year-old male. The tumors were all superficially located; left forearm, medial aspect of the left ankle, and left thigh, respectively. Histomorphologically they had expansile and focal infiltrative growth pattern consisting of highly pleomorphic spindle cells with intranuclear inclusions, yet low mitotic rate. Tumoral cells showed strong and diffuse reactivity for CD34. One of our cases showed focal and weak reactivity for pancytokeratin. Unlike the other two tumors, one case was positive for desmin. During the clinical follow-up, one case showed local recurrence four times. SCPFT is a newly recognized, borderline mesenchymal neoplasm of soft tissues that can show local recurrence or even rarely metastasize. To the best of our knowledge, this three case series is the first to be reported from Turkey. Our aim to report these three cases was to make contribution to the literature about this rare entity and increase awareness.

Introduction

Superficial CD34 positive fibroblastic tumor (SCPFT) is a rare, recently described, borderline malignancy of soft tissues. Carter *et al.* re-evaluated mesenchymal tumors of superficial location, showing abundant pleomorphism, strong CD34 reactivity, and low mitotic rate and concluded that these tumors are morphologically, biologically, and immunohistochemically different from the previously defined cases.[1] Morphologically, SCPFT resembles fibrohistiocytic tumors. After the description of this entity by Carter *et al.*, 34 similar cases have been reported to date.[2–7] Our three cases hereby show the characteristic morphological and immunohistochemical features described in the literature, with a few additional unique features.

Materials and methods

The three consultation cases that had come to the Istanbul University Cerrahpasa-Cerrahpasa Faculty of Medicine Pathology Department were reviewed. Clinical data was obtained from the patients. The information about the macroscopic features were taken from the original pathology reports. The routine Hematoxylin–Eosin (H–E) and immunohistochemical workup was performed on four micron sections made from paraffin blocks. The Ventana Benchmark autostainer was used for immunohistochemistry (Ventana Medical Systems, Tuscon, AZ, USA). A wide immunohistochemical panel including CD34, CD68, p53, p16, EMA, PanCK, HMB45, MelanA, S100, SMA, Calponin, STAT6, Desmin, INI1, and Ki67 was applied (Table 1).

Results

Macroscopic, microscopic, and immunohistochemical features of all three cases are summarized in Tables 1 and 2. The first patient (referred to hereafter as case 1), a 31-year-old female, had a 5 cm tumoral mass localized superficially in the left forearm. A 53-year-old female (referred to hereafter as case 2) had a 4 cm tumoral mass in the medial aspect of the left ankle, which extended to deep dermis. The last patient (referred to hereafter as case 3) was a 33-year-old male. He had a 5.5 cm tumoral mass localized in the left thigh superficially. None of the patients had a history of any cutaneous neoplasms. All three cases had extension to subcutaneous adipose tissue.

Histomorphological assessment of these cases revealed tumors growing in an expansive fashion with only focal infiltrative areas. Tumors were located superficially in cases 1 and 3, however case 2 was located in deep subcutaneous tissue

Table 1 Immunohistochemical staining patterns of cases

			Immunohistochemical findings		
Antibody	**Clone**	**Dilution**	**Case 1**	**Case 2**	**Case 3**
CD34	QBEND	1 : 350	Diffuse strong +	Diffuse strong +	Diffuse strong +
Pancytokeratin	AE1/AE3	1 : 500	Negative	Negative	Focal +
SMA	1A4Biocore	1 : 300	Negative	Negative	Negative
p16	G175-405	1 : 50	Negative	Negative	Negative
EMA	G1.4 Thermo	1 : 1,000	Negative	Focal +	Focal +
HMB45	Ventana	Ready to use	Negative	Negative	Negative
CD68	KP1 Thermo	1 : 2,500	Patchy +	Patchy +	Patchy +
S100	Ab-1	1 : 400	Negative	Negative	Nodule +
MelanA	Ventana	Ready to use	Negative	Negative	Negative
Calponin	Calp-biocare	1 : 200	N/A	Negative	Negative
INI1	MRQ-27	1 : 250	Retained expression	Retained expression	Retained expression
p53	Ventana	Ready to use	20%	5–6%	10%
STAT6	Santa Cruz	1 : 100	N/A	Negative	Negative
Desmin	Ventana	Ready to use	Negative	Negative	Focal +
Ki67	SP6	1 : 200	2–3%	1–2%	5%

Table 2 Histopathological characteristics of cases

	Case 1	**Case 2**	**Case 3**
Tumor margins	Well defined – expansive, focal infiltrative	Ill defined – infiltrative	Expansive and infiltrative
Depth	Superficial – subcutaneous	Superficial – deep subcutaneous	Superficial – subcutaneous
Cellularity	++	++	++
Atypia	+++	++	++
Pleomorphic cells	+++	++	++
Spindle cells	+	+	+
Epitheloid cells	+	+	+
Xanthomatous cells	+	+	+
Intranuclear pseudoinclusions	+	+	+
Inflammatory cells	Moderate: plasma cells, lymphocytes, PNL, few mast cells	Mild: plasma cells, lymphocytes; rare eosinophils	Mild: plasma cells, PNL, lymphocytes, eosinophils
Hyalinizing vessels	–	+	–
Hemosiderin pigment	+	+/–	++
Mitosis (50 HPF)	0	1	1
Atypical mitosis	–	–	–

–, none; +, mild; ++, moderate; +++, intense.

showing focal infiltration to adjacent structures (Fig. 1). Spindled and epithelioid tumor cells, mostly arranged in fascicles and solid sheets, some of which showed xanthomatous changes, were observed. Highly pleomorphic cells were the first to draw attention for all cases (Figs. 2–5). Most tumor cells were pleomorphic with lobulated, bizarre, hyperchromatic nuclei, and conspicuous nucleoli. Not rarely, intranuclear pseudoinclusions were noted (Fig. 6). In case 2, hyalinizing vessels were observed in focal areas. Inflammatory response, composed of lymphocytes, plasmocytes, and rare eosinophils, accompanying the tumor cells were evaluated as mild for cases 2 and 3. For case 1, the moderate amount of inflammatory cells consisting of lymphocytes, plasmocytes, and neutrophils intermingled with the tumor was noted, as well as a few mast cells scattered in between. Moderate and mild amounts of intracytoplasmic hemosiderin pigment were noted for cases 3 and 1, respectively, whereas this accumulation was only subtle for case 2 (Figs. 7 and 8). As a unique feature, in case 3, nodular areas composed of rhabdoid-like cells within the tumor were remarkable (Fig. 9). Mitotic figures were extremely rare (0-1/50HPF).

A wide immunohistochemical panel was applied (summarized in Table 1). The workup showed diffuse and strong reactivity for CD34 (Fig. 10a,b), patchy reactivity for CD68. The INI1 expression was retained in all cases. HMB45, MelanA, calponin, SMA, and STAT6 were all negative. Focal reactivity for EMA and pancytokeratin was noted for cases 2 and 3, respectively (Fig. 11).

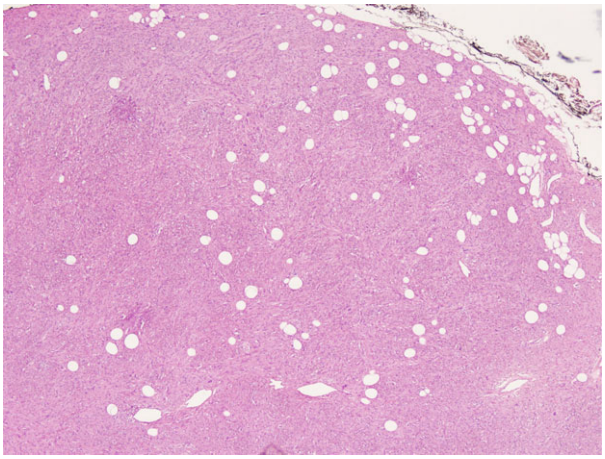

Figure 1 Well-circumscribed tumor located in deep subcutaneous tissue; infiltrating the adipose tissue (hematoxylin and eosin, ×40)

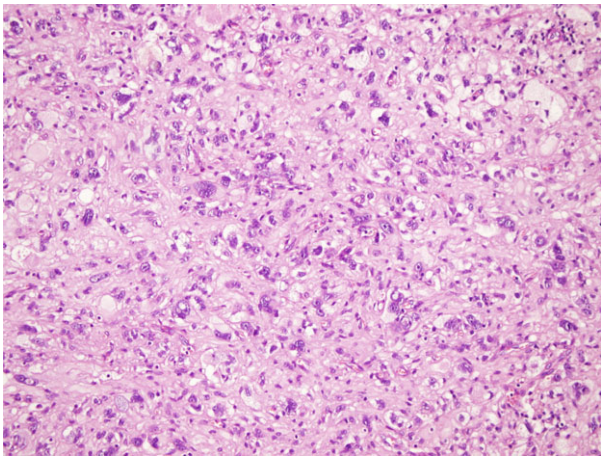

Figure 3 Spindled, highly pleomorphic epithelioid tumor cells, some showing xanthomatous changes (hematoxylin and eosin, ×400)

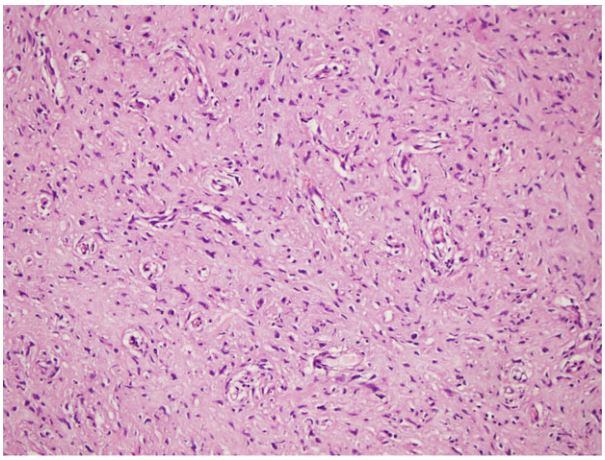

Figure 2 Spindle cells arranged in fascicles (hematoxylin and eosin, ×200)

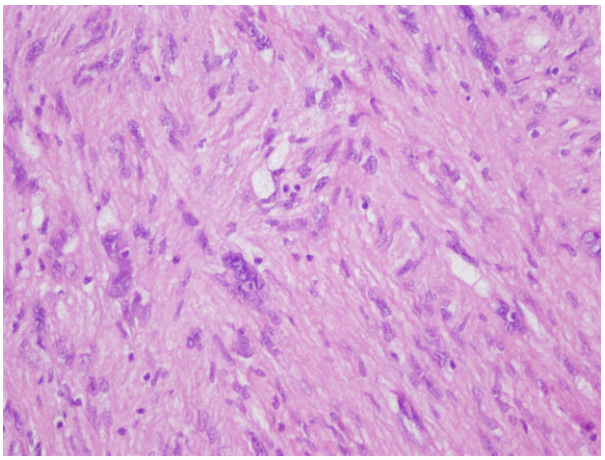

Figure 4 Pleomorphic, spindled, epithelioid tumor cells, some showing xanthomatous changes (hematoxylin and eosin, ×400)

The nodular area formed by rhabdoid-like cells in case 2 was focally positive for desmin (Fig. 12). The P53 reactivity was 20%, 5–6%, and 10%, respectively (Fig. 13). The Ki67 proliferative index varied between 1 and 5% (Fig. 14).

Cases 2 and 3 showed no recurrence or metastasis in 22 months and 13 months during the clinical follow-up, respectively. In spite of showing no mitotic activity, case 1 recurred four times in the follow-up period of 24 months.

Discussion

Carter *et al.* first described SCPFT as a new and unique entity, in a series of 18 cases.[1] Thirty-four cases were reported to date to the best of our knowledge.[1–7] These tumors, although composed of highly pleomorphic cells, have low mitotic rate and are classified under borderline mesenchymal tumors of soft tissues. In a series of 18 cases documented by Carter *et al.*, median age was 38 (20–76). The tumor masses tended to grow slowly and were mostly located in the lower extremities superficially. No muscle involvement was observed in any of the cases. Lao *et al.* documented the second largest series of 11 cases in 2017.[5] In Lao *et al.*'s series, median age was 33 (18–46). The sites of involvement were shoulder, arm, and waist. Most of the patients presented with painless subcutaneous nodular masses. Median size was 2.7 cm (1.6–5). A few more reported cases had similar clinical presentations with neck or Achilles tendon involvement.[2,4,6] Our cases were consistent with the literature.

SCPFTs were described as well circumscribed but at least focal infiltrative when examined carefully in Carter *et al.*'s series. Likewise Lao *et al.* also reported that these tumors had well-defined borders, still they can show focal infiltration to adjacent structures and the adipose tissue. Morphological features

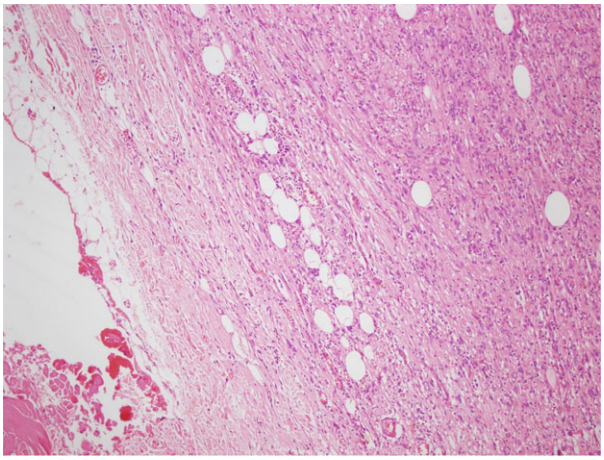

Figure 5 Pleomorphic, spindled and epithelioid tumoral cells showing focal infiltrative pattern (hematoxylin and eosin, ×100)

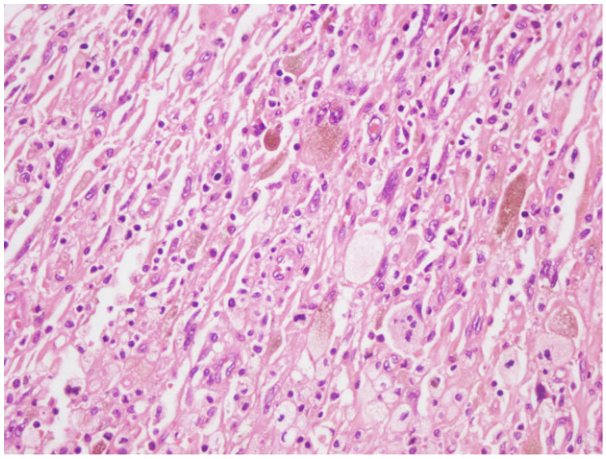

Figure 7 Moderate amount of intracytoplasmic hemosiderin pigment in tumor (hematoxylin and eosin, ×400)

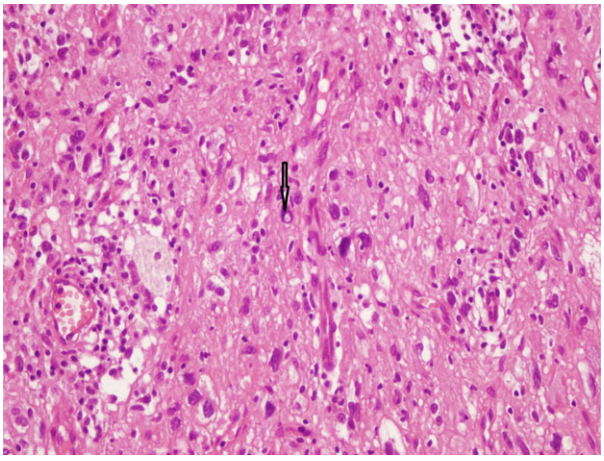

Figure 6 Intranuclear pseudoinclusions in some tumor cells (hematoxylin and eosin, ×200)

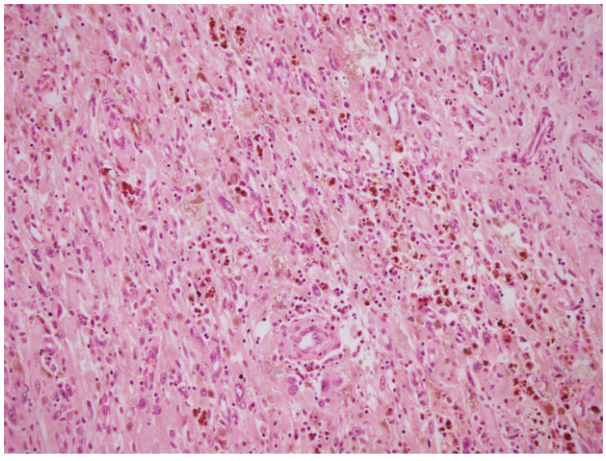

Figure 8 Mild amount of intracytoplasmic hemosiderin pigment in the tumor (hematoxylin and eosin, ×200)

included epithelioid tumor cells with fibrillary, glassy, and granular cytoplasm, arranged in fascicular and sheet-like architecture accompanied by capillary-sized branching vessels. The tumor cells had large, lobulated, hyperchromatic nuclei and conspicuous nucleoli, showing striking nuclear pleomorphism. Mitosis per 50 HPF was generally 0–1, and no atypical mitoses was seen. Only one case showed higher mitotic rate, which was a re-excision material. Intranuclear inclusions and mixed chronic inflammatory response were also observed. Only one case was found to have necrosis. Additional histologic characteristics were focal xanthomatous changes, focal hemosiderin accumulation, and elongated, dilated, and thin-walled vessels. Other case reports showed no significant differences except lymphovascular invasion in Hendry's one case.[2] Different from the published cases up-to-date histomorphologically, hyalinizing vessels were present in case 2. Aside from the distinct hemosiderin accumulation, another feature making case 3 unique was the presence of desmin reactive intratumoral nodule, which showed no reactivity for CD34 immunohistochemically.

Immunohistochemically, all reported cases were diffusely and strongly reactive for CD34. In Carter *et al.*'s series, 11 of the cases showed limited positivity for cytokeratins, whereas all 18 cases were negative for ERG, S100, desmin, and SMA. Retained INI1 expression, unlike the great majority of epithelioid sarcomas, was also noted. Reported cases to date showed similar immunohistochemical characteristics. In our cases, one case showed focal reactivity for pancytokeratin and another for EMA. Immunhistochemical p53 reactivity was noted in all our three cases. Case 1 reactivity for p53 was evaluated as 20%, higher than reported cases up to date.

SCPFT can be misdiagnosed as undifferentiated pleomorphic sarcoma, myxofibrosarcoma, atypical fibroxanthoma (AFX),

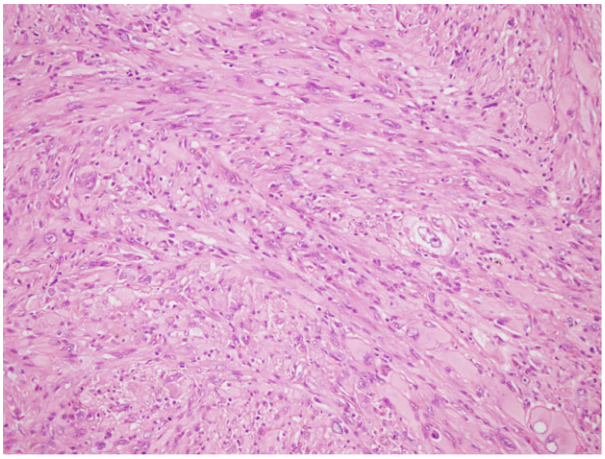

Figure 9 Nodular area consisting of rhabdoid-like cells in the tumor (hematoxylin and eosin, ×200)

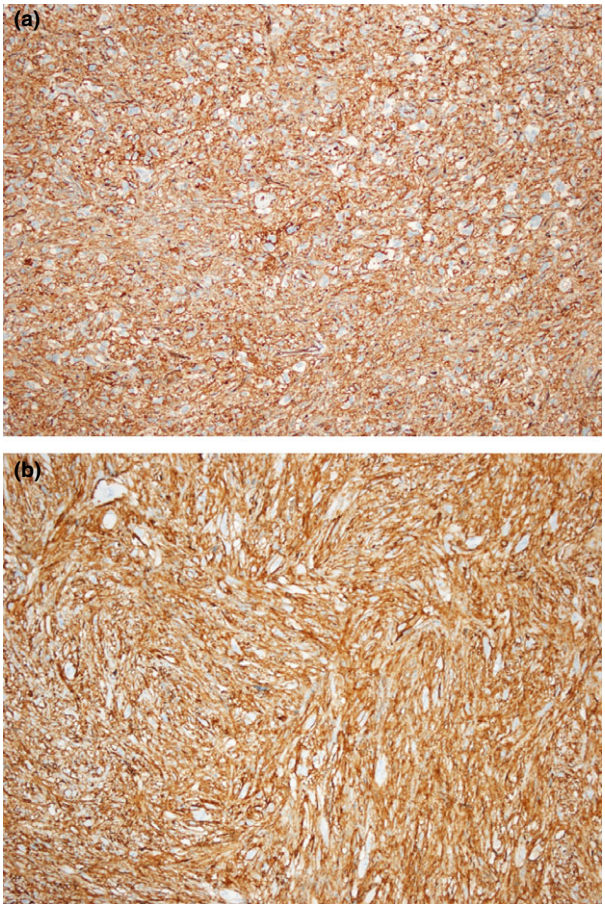

Figure 10 (a) Diffuse and strong CD34 reactivity (×100). (b) Strong and diffuse CD34 reactivity (×200)

atypical fibrous histiocytoma (AFH), epithelioid sarcoma, dermatofibrosarcoma protuberans (DFSP), inflammatory myofibroblastic tumor (IMFT), and malignant solitary fibrous tumor.

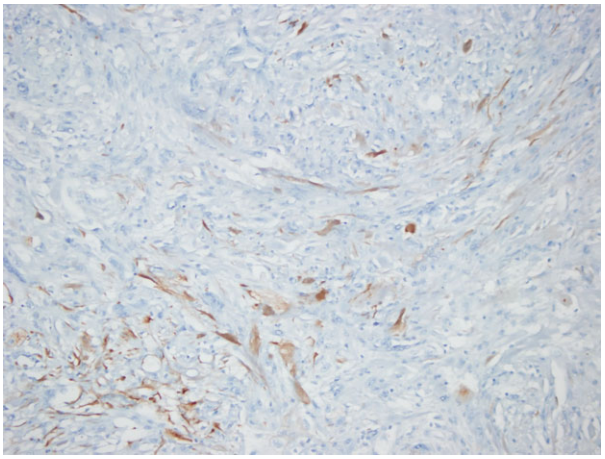

Figure 11 Focal reactivity with pancytokeratin (×200)

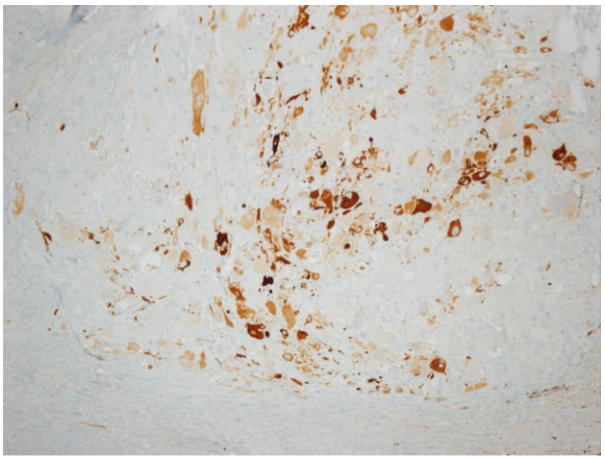

Figure 12 Desmin reactivity within the tumor; particularly in the nodular area formed by rhabdoid-like cells (×200)

Because of some similarities such as immunohistochemical features, low mitotic rate, and accompanying inflammatory response, pleomorphic hyalinizing angiectatic tumor (PHAT) should also be included in the differential diagnosis. Myxoinflammatory fibroblastic sarcoma (MIFS), sharing some histomorphological features with SCPFT, should also be taken into consideration.

SCPFT cells showing striking pleomorphism can lead to a misdiagnosis of AFX or undifferentiated pleomorphic sarcoma. AFX is a tumor localized in the dermis of sun-damaged skin especially in the head and neck region of the elderly. Characteristically involvement of subcutaneous tissue is not seen. Conspicuous nuclear atypia and high mitotic rate are present, and CD34 is negative.[8] Undifferentiated pleomorphic sarcoma resembles the AFX morphologically but is larger and invades deeper tissues. It is composed of pleomorphic, epithelioid, and spindle cells showing high mitotic rate and atypical mitosis.[9]

Myxoinflammatory fibroblastic sarcoma is a neoplasm localized in the distal extremities of adults. Morphologically large,

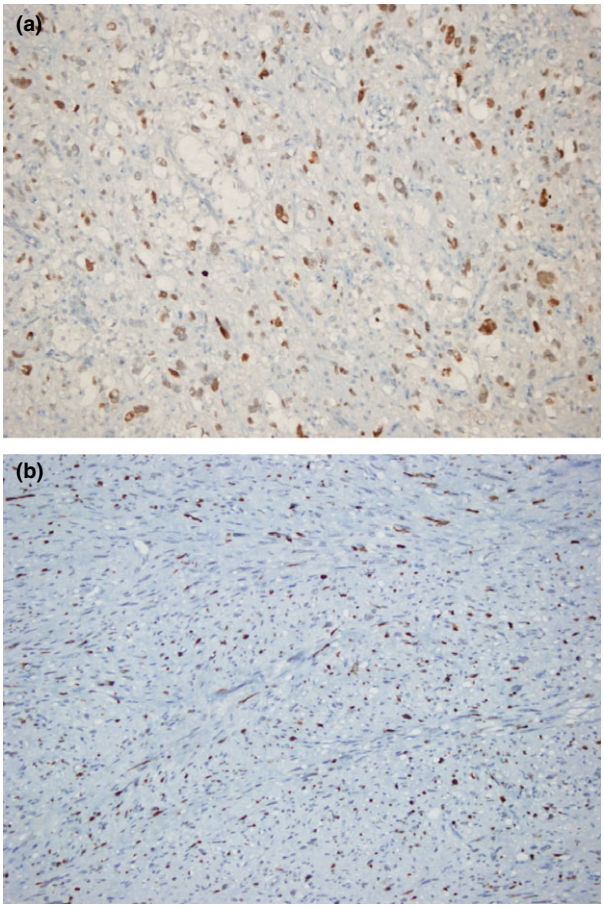

Figure 13 (a) p53 reactivity in about 20% of tumor cells (×200) in case 1. (b) p53 reactivity in about 5–6% of tumor cells in case 2 (×200)

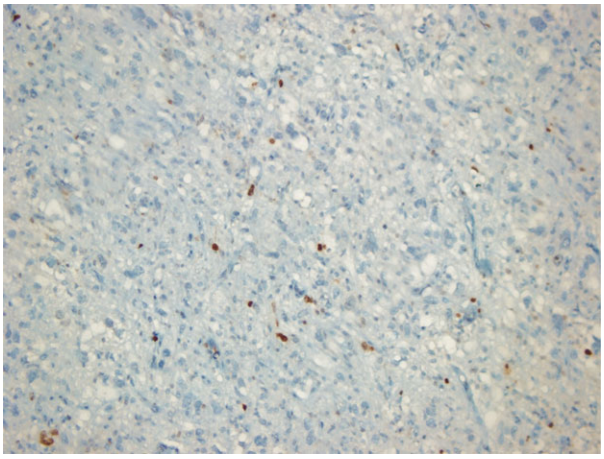

Figure 14 Low Ki67 proliferative index (2–3%) (×200)

atypical cells are seen in multinodular, myxoid, fibrohyalinized, and inflammatory background. MIFS' atypical cells resemble ganglion or even Reed-Sternberg cells. They show focal positivity for CD34, rarely for cytokeratins. SCPFT, sharing some morphological and immunohistochemical features with these tumors, is thought to be a different entity.

Sharing some morphological features, Carter *et al.* stated that PHAT should also be taken into consideration. However, SCPFT lacks ectatic vessels and hemosiderin accumulation unlike PHAT.[10–12] In our reported case 2, focal hyalinized vessels were seen. In cases 1 and 3, hemosiderin accumulation was noted, like Lao *et al.*'s reported series though more intense.

Dermatofibrosarcoma protuberans is known to be a tumor located in the dermis, infiltrating the subcutaneous adipose tissue. SCPFT can be mistaken for a DFSP that has undergone sarcomatous differentiation. DFSP is characterized by *COL1A1/PDGFB* fusion.[13,14] Lao *et al.* tested for this fusion by FISH, yet the results were negative.

Myxofibrosarcoma is a tumor of the elderly characterized by the superficial location, multinodular growth pattern, conspicuous myxoid matrix, presence of pseudolipoblasts, and curvilinear vessels.[15,16]

Of 34 cases reported till now to our knowledge, only one showed regional lymph node metastasis after incomplete excision.[1] SCPFT is a mesenchymal tumor of intermediate/borderline malignancy known to metastasize very rarely. The clinical follow-up data is not sufficient, so we need further information.

In summary, SCPFT is a recently recognized new entity with unique histomorphological and immunohistochemical features such as high pleomorphism, low mitotic rate, and diffuse CD34 reactivity. In our cases, different than the literature, case 1 showed higher p53 expression than reported cases up to date and also recurred four times, which brings local reccurence-p53 expression association to mind, yet it needs to be deeply investigated in a larger series. SCPFT may represent a variant of a known tumor although it is thought to be a new entity now. Further molecular investigations would help discriminate these tumors under a certain category.

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