CASE STUDY

Recurrent and metastatic cellular cutaneous fibrous histiocytoma: A case report and literature review

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Abstract

Cutaneous fibrous histiocytoma (FH) is considered a benign dermal tumor. The cellular variant is rare and poorly documented. Besides presenting a high risk of local recurrence, it has a low but serious metastatic potential. We present a case of metastatic cellular FH and also review the literature on this tumor, given its unusual metastatic development. A 47-year-old male patient presented with a lesion in the anterior surface of the right thigh, which has been present since adolescence but had grown during last year. Anatomopathological evaluation revealed a cellular FH, and the lesion was completely removed. Six months later, tumor recurrence with multiple compartment muscle involvement and pulmonary metastasis were detected. Both lesions were completely resected and after 3 years of follow-up, the patient is asymptomatic and free of the disease. We conclude that FH should be carefully sampled to detect variants with high local recurrence rates or with some metastatic risk such as the cellular one. We recommend wide surgical resection and a close follow-up including chest x-rays or thorax computed tomography (CT) in all cellular FH cases with local recurrence.

KEYWORDS
cellular, dermatofibrosarcoma protuberans, fibrous histiocytoma, Tumors Committee

1 | INTRODUCTION

Cutaneous fibrous histiocytoma (FH; or dermatofibroma) is one of the most common cutaneous soft-tissue tumors.[1] It is considered a benign tumor but there exist some variants, such as the cellular one, that can present high local recurrence rates but low metastatic potential.[2–5] Only a few cases that progressed to metastasis have been reported in the medical literature.[4,6–11]

We present the clinical, radiological, histopathological features, and management of this rare variant of FH, given its unusual metastatic development.

2 | CASE REPORT

A 47-year-old male was referred to our center for evaluation of a lesion in the anterior region of the right thigh. The patient related that its size was about 2×1 cm and that he had it from adolescence. One year ago, he noticed changes in the lesion and surrounding skin with a rough appearance and bleeding. He was evaluated by the dermatology department in his original center, where a punch biopsy was performed.

A densely cellular proliferation distributed in randomly organized fascicles, occupying the dermis and subcutis, was observed in the biopsy specimen (Figure 1A). Epidermal changes such as hyperkeratosis and acanthosis were seen (Figure 1A,B). No Grenz zone was detected (Figure 1B). Entrapment of peripheral collagen bundles was seen (Figure 1C). Cells were monotonous with large cytoplasm and ovoid nuclei without nucleoli (Figure 1D). Scanty mitotic figures were present. No significant atypia or necrosis was observed (Figure 1D). Tumor cells were diffusely positive against CD10 (Clone 56C6, Ready to use [RTU], Agilent-Dako) (Figure 1E) and CD44 (Clone DF11485, RTU, Agilent-Dako), and focally positive against
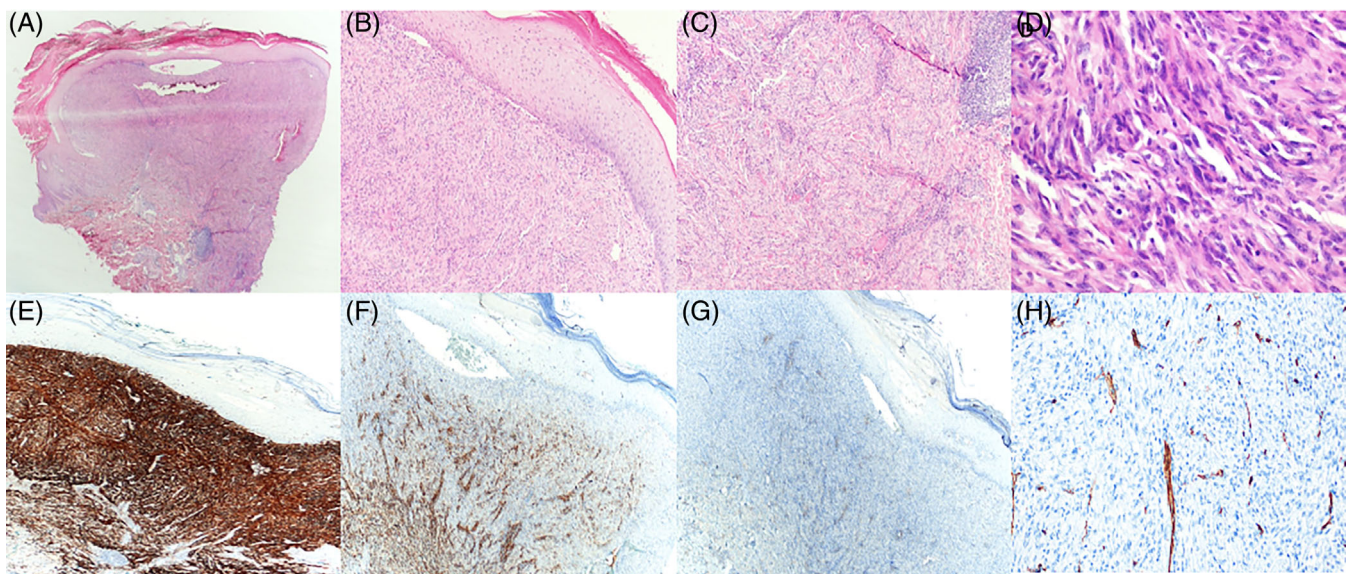
FIGURE 1 Punch biopsy. (A) Dermal and subcutaneous densely cellular proliferation (H&E, ×40). (B) Respected hyperkeratotic and acanthotic epidermis with no Grenz zone (H&E, ×100). (C) Peripheral collagen bundles entrapped by tumoral cells (H&E, ×200). (D) Ovoid nuclei and wide eosinophilic cytoplasm. Scanty mitotic figures (H&E, ×400). (E) CD10 (CD10, ×40). (F) Factor XIIIa (factor XIIIa, ×100). (G) CD68 (CD68, ×100). (H) CD34 (CD34, ×200).

factor XIIIa (AC-1A1, RTU, Gennova) (Figure 1F) and vimentin (clone V9, RTU, Agilent-Dako). CD68 (Clone, PG-M1 RTU, Agilent-Dako) (Figure 1G), CD34 (Clone QBEnd-10, RTU, Agilent-Dako) (Figure 1H), S100 (polyclonal, RTU, Agilent-Dako), smooth muscle actin (Clone 1A4, RTU, Agilent-Dako), MelanA (Clone A103, RTU, Agilent-Dako), STAT6 (Clone EP325, RTU, Gennova), herpes virus 8 (HHV8) (Clone 13B10, RTU, Agilent-Dako), CD31 (Clone JC70A, RTU, Agilent-Dako), podoplanin (Clone D2-40, RTU, Agilent-Dako), cytokeratins (Clone AE1/AE3, RTU, Agilent-Dako), caldesmon (Clone h-CD, RTU, Agilent-Dako), desmin (Clone D33, RTU, Agilent-Dako), EMA (Clone E29, RTU, Agilent-Dako), and calponin (Clone CALP, RTU, Agilent-Dako) were negative. Cell proliferation index (Ki67 [clone MIB-1, RTU, Agilent-Dako]) was approximately 5%.

Based on the histopathological findings, the diagnosis of cellular FH was made. Four months later, magnetic resonance imaging (MRI) showed that the mass had grown to 2 × 2 cm. It was widely resected, revealing the same histopathological findings as in the original biopsy and free margins.

During follow-up, 6 months after the intervention, he presented signs suggestive of local recurrence in the surgical area, assessed by ultrasound and a new MRI (Figure 2A,B). In the extension study with a thorax radiography and PET-CT, a single pulmonary nodule suspicious for malignancy was identified (Figure 2C,D). After these findings, he was referred to our center for evaluation.

The patient reported symptoms of asthenia and hyporexia with 4 kg weight loss in the last month, accompanied by a dry cough. In the anterolateral region of the proximal third of the right thigh, a graft in good condition with several painful nodules was observed (Figure 3A). Ultrasound and contrast-enhanced MRI were requested,

which were compared with those of earlier studies (Figure 3B). Tumor recurrence and multiple compartment muscle involvement were detected.

After evaluation by the Bone and Soft Tissue Tumors Committee (BSTTC), the local recurrence was widely resected (Figure 4A–D), together with the single lung lesion suspicious for metastasis.

The surgical specimen comprised skin, subcutis, and muscle (Figure 4E–G) and exhibited four well-defined, rubbery, whitish subcutaneous nodules (Figure 5A) composed of a densely cellular, mesenchymal, spindle-cell, fibrohistiocitic proliferation intermixed with chronic inflammatory infiltrate and isolated multinucleated giant cells (Figure 5B). The main cell component was bland cells with wide eosinophilic cytoplasm and ovoid nuclei (Figure 5C). However, some areas were composed of more pleomorphic cells with more epithelioid aspect, less eosinophilic cytoplasm, and round nuclei with prominent nucleoli (Figure 5D). Up to 12 mitotic figures were counted in 10 high-power fields. The tumor cells showed diffuse immunopositivity for CD10, CD44, and focal staining for factor XIIIa (Figure 5E). CD68 was positive mainly in the accompanying macrophagic cells and in scanty tumoral cells (Figure 5F). No necrosis was seen. Surgical margins were free. Negative stains were the same as those mentioned in the punch biopsy. Molecular biology study for the COL1A1–PDGFB gene fusion using the fluorescence in situ hybridization (FISH) technique on interphase nuclei (COL1A1-PDGFB Dual-Color Dual-Fusion Custom Probe, Agilent-Dako) was negative. The directed sequencing of fusions performed through TruSight RNA Pan-Cancer Panel in the Ilumina Mise Dx platform did not detect gene fusions. Based on these findings, the diagnosis of cellular and atypical FH was made.
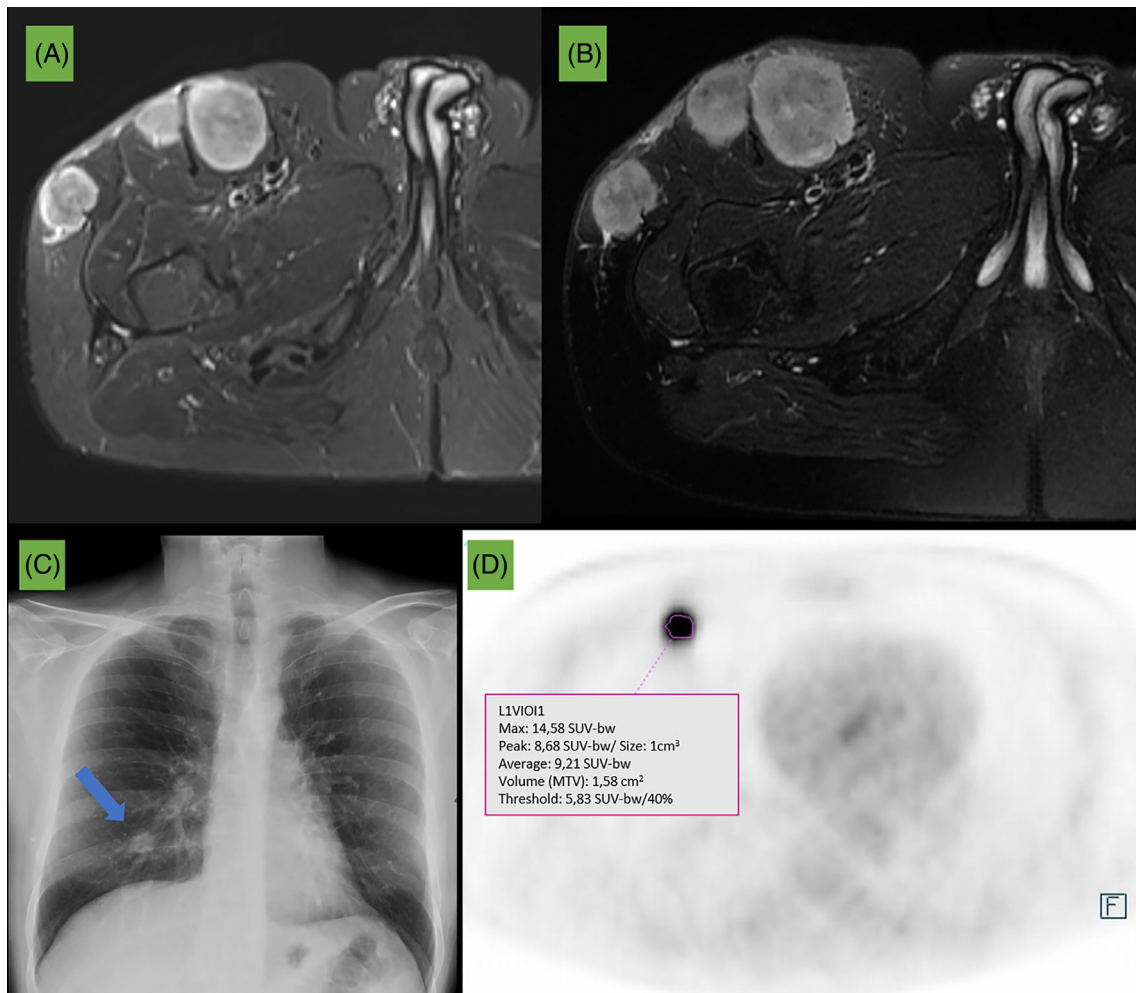
FIGURE 2 (A) Initial MRI: STIR sequence in axial view. In the anterolateral aspect of the right thigh, there is thickening and increased signal of the dermis in an approximate segment of 8 cm. Underlying this dermal alteration are three nodular lesions with well-defined borders of heterogeneous and hyperintense signal where the largest of them has a diameter of 4.5 cm. The two most anterior lesions imprint and bulge the superficial margin of the rectus muscle and the most lateral one the tensor fasciae latae. There is also thickening and increased signal of the muscular fascia between the anterior rectus and tensor fasciae latae suggestive of infiltration. (B) STIR sequence in axial view 3 months later. The aggressive behavior of the tumor was observed with an increase in the size of the lesions and new lesions in the dermis that communicate with multiple intramuscular nodules with involvement of the sartorius, rectus femoris, and tensor fasciae latae. (C) Chest x-ray in PA view: 2 cm nodular lesion in the right lower lobe (blue arrow). (D) PET-CT: 19-mm single lesion in the middle lobe with malignant characteristics.

FIGURE 3 (A) Clinical picture: green arrow: nodule 6 × 6 cm; blue arrow: nodule 3.5 × 3 cm; yellow arrow: nodule 1 × 1 cm. (B) STIR sequence in sagittal view: a hyperintense tail (arrow) extending along the fascia of the anterior rectus is observed at the superior border of the lesion.
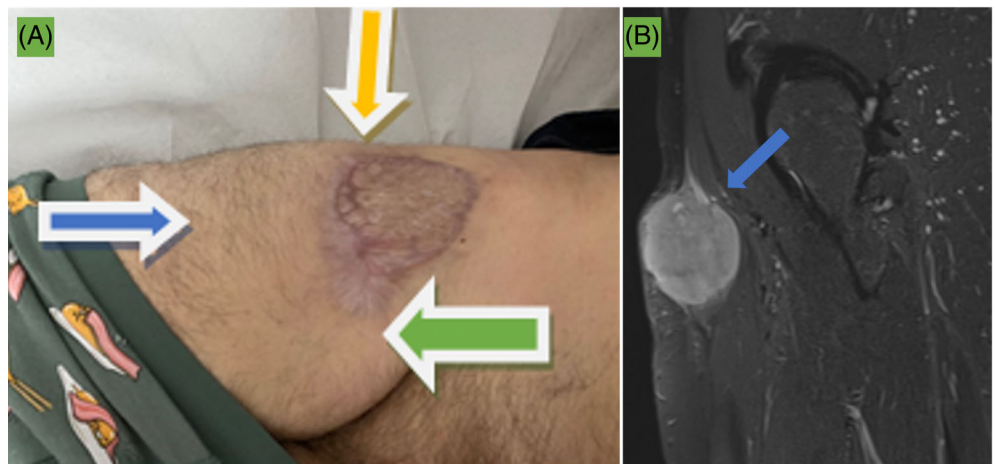
FIGURE 4 (A) Sartorius muscle resection. (B) Result after multiple affected muscle resection with a 4-cm margin of the tumor. (C) External aspect and marking of the approach to the lesion on the anterior face of the right thigh. (D) Cosmetic result after wide resection with reconstruction and coverage with a pedicled rectus abdominis muscle cutaneous flap (6 months post surgery). (E) Resected sample showing involvement of the sartorius muscle by a whitish nodule. (F) Resected sample showing involvement of the tensor fasciae latae by a subcutaneous whitish nodule. (G) Resected sample showing involvement of the rectus femoris.

A gross whitish nodule that measured 2.2 cm was detected in the medial lobe segmentectomy. The same cells that were described in the original tumor confirmed the nodule (Figure 5) and showed patchy immunoreactivity against CD10 (Figure 5H), CD44, and factor XIIIa (Figure 5I). Surgical margins were free. It was diagnosed as the metastasis of cellular FH.

After reevaluation in the BSTTC, 30 sessions of adjuvant radiotherapy were administered. After 2 years of oncological follow-up, the patient has not reported any new local recurrences or metastases. He leads a daily life of unrestricted and unaided mobility with full range of motion.

3 | DISCUSSION

FH are benign dermal lesions with fibroblastic and histiocytic differentiation.[1] Some variants may coexist in the same tumor.[12] Cellular variant represents <5% of FH.[12,13] It may occur at any site and age, although they are typically located in the lower limbs of middle-aged White patients.[3,4] Their most characteristic presentation is as a solitary skin nodule, either firm or cystic, skin-colored or brown, followed by a polypoid nodule or slightly elevated plaque.[3,4] The initial clinical suspected diagnosis is broad, mainly with dermatofibrosarcoma protuberans (DFSP), other fibrohistiocytic skin tumors, or even melanocytic tumors.
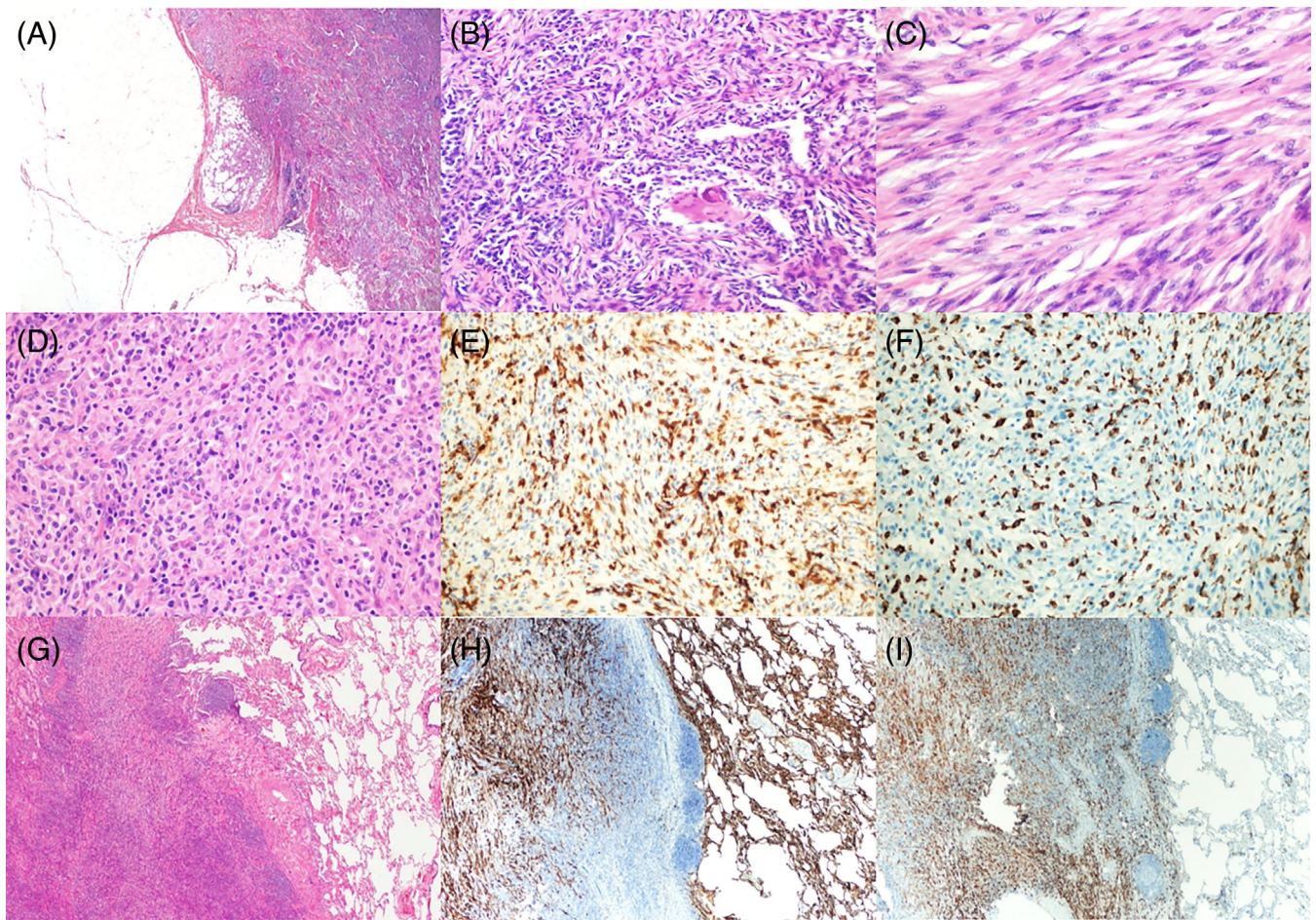
FIGURE 5   (A) Tumor nodule in the subcutaneous tissue (H&E, ×40). (B) Tumor cells and intermixed chronic inflammatory cells with isolated multinucleated giant cells (H&E, ×100). (C) Bland cells with ovoid nuclei (H&E, ×400). (D) Cells with epithelioid appearance, round nuclei, and prominent nucleoli (H&E, ×400). (E) Factor XIIIa (factor XIIIa, ×200). (F) CD68 (CD68, ×200). (G) Metastatic lung nodule (H&E, ×40). (H) CD10 (CD10, ×40). (I) Factor XIIIa (factor XIIIa, ×40).

On imaging, FH are described as well-demarcated oval tumors with well-defined borders and a fatty plane of separation with the muscle fascia if they are not large. On ultrasound, they are hypoechoic and moderately vascularized on color Doppler study. In MRI, they are mostly homogeneous, hypointense in T1, and hyperintense in T2 and STIR. They may show central vascularization, hemorrhage, or necrosis. After administration of paramagnetic contrast, they show intense peripheral enhancement.[14,15] Differential diagnosis includes metastasis (mainly melanoma), lymphoma, DFSP, and other sarcomas such as myxofibrosarcoma.[14,15] However, the patient's clinical history and the previous anatomopathological diagnosis with the subsequent study made us rule out these entities.

There are several variants of this entity that can coexist, and an adequate sampling of the superficial, central, and peripheral zones is needed to not misdiagnose any component. The main histopathologic differential diagnosis of cellular FH is DFSP.[3] DFSP may also infiltrate subcutaneous adipose tissue but present a storiform growth pattern and pigmented dendritic cells.[4,6] DFSP are negative for CD44 and factor XIIIa and show diffuse positivity for CD34.[5] FH may be CD34+ in deep and peripheral borders.[16] DFSP harbor COL1A1–PDGFB fusion,

although up to 5% of the cases do not present it.[17] Morphologically, the differential diagnosis also includes leiomyosarcomas and melanomas. Leiomyosarcomas show spindle cells with cigar-shaped nuclei and diffuse SMA, calponin, and caldesmon stains.[12] Non-pigmented spindle or epithelioid cell melanomas may also present marked nucleoli but show diffuse positivity for S100, HMB45, and MelanA.[18] Hyperkeratosis, hyperpigmentation, and acanthosis are observed in 75% of the cellular FH cases,[12] as in our case, which could also help in the diagnosis.

Local recurrence rates of up to 26% in the cellular variant[12] have been documented, in contrast to rates <2% in common FH, regardless of margin status.[4,5] In our case, there was not only a local recurrence at the subcutaneous level but also multifocal, deep involvement of the surrounding muscles. The literature describes metastases as single cases reported with lymph nodes and lungs as the main sites affected, and only in four cases soft tissues were affected.[3–6] Complete resection of metastatic disease appears to be associated with a higher success rate.[4] No histopathologic features have been detected that predict recurrence or metastasis development.[3,4] The literature review is summarized in Table 1.

TABLE 1 Metastasizing histiocytoma: Review of the literature with clinicopathologic data.

Histologic type	Author	Age	Sex	Primary site	Metastatic sites	Time to metastasis (m)	Treatment	Disease status	Follow-up (m)
Cellular	Colome-Grimmer (7)	18	M	Thigh	Lung	48	Segmentectomy	NED	96
		33	M	Neck	Lung	84	CT + surgery	AWD	96
	Lodewick (6)	67	M	Thigh	Lung	9	Unknown	Died	11
	Charli-Joseph (8)	41	M	Shoulder	Lung	95	Resection	NED	182
		62	F	Back	Lung	17	RT + CT	Died	182
		38	M	Neck	Lung	3	CT	AWD	182
		56	M	Finger	Soft tissue	3.5	Resection	Died	17
		68	M	Leg	Lung + pleural + chest wall	9	Unknown	Died	17
	Guillou (9)	28	M	Neck	Lung + liver + bone + skin	167	Unknown	Died	167
	Doyle (4)	63	F	Leg	Lung	132	CT	Died	168
		62	F	Back	Lung + liver	17	CT	Died	23
		38	M	Neck	Lung	3	Resection	AWD	68
		56	M	Finger	Skin (hand)	3.5	Unknown	Died	17
		23	F	Shoulder	Lung	11	CT	AWD	12
		25	F	Buttock	Chest wall + skin + intraabdominal	84	Unknown	Died	96
		31	F	Back	Soft tissue	12	Resection + RT	NED	186
	Mentzel (10)	F	65	Shoulder	Lung + brain	6	Unknown	Died	14
		M	M	Neck	Liver + bone + skin	35	Unknown	Died	167
	De Hertogh (11)	M	33	Back	Both lungs	24	CT	Unknown	24
Atypical	Guillou (9)	M	27	Thigh	Soft tissue (inguinal region)	72	Resection	Unknown	228
	Doyle (4)	F	62	Toe	Lung	60	Resection + CT	AWD	132
Atypical and cellular	Doyle (4)	M	42	Back	Lung	24	CT	Died	32
		F	31	Back	Soft tissue (shoulder)	12	Resection + RT	NED	63
	Current study	M	47	Thigh	Lung + soft tissue	18	Resection + RT	NED	36

Abbreviations: AWD, alive with disease; CT, chemotherapy; F, female; M, male; m, months; NED, no evidence of disease; RT, radiotherapy.

Surgery is the treatment of choice for this aggressive tumor type. A wide resection in specialized centers reduces the recurrence rate. There is no defined adjuvant protocol, whereas in certain cases radiotherapy is used.[19–22] In our case, because of deep muscle recurrence and metastasis, treatment was completed with radiotherapy after resection of the pulmonary nodule. A close oncological follow-up is therefore essential.[3–6,13,22]

4 | CONCLUSION

Given the worse prognosis than conventional FH, the diagnosis of the cellular variant is crucial. It is necessary to carry out an adequate sampling because different variants can coexist in the same tumor. In case of local recurrence, regular follow-up including thorough clinical examination and chest x-rays or thorax CT is recommended.

CONFLICT OF INTEREST STATEMENT

The authors declare no competing interests.

ETHICS STATEMENT

The patient consented that the data concerning his case could be submitted for publication. Informed consent was obtained according to national and institutional guidelines.

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