Case report

Atypical spindle cell lipomatous tumour presenting as a large retroperitoneal mass – a case report and review of the literature

Martyna Aleksandra Krupinska[1], Carmen Nieves Hernandez León[1], Rocío López Henríquez[1], Beatriz Esquivel Vázquez[1], Rosa Nieves Rodríguez Rodríguez[1], Patricia Marrero Marrero[2], Luciano Delgado Plasencia[2], Eduardo Salido[1]

[1]Department of Pathology, University Hospital of the Canary Islands, University of La Laguna, San Cristóbal de La Laguna, Santa Cruz de Tenerife, Spain
[2]Department of General and Digestive Surgery, University Hospital of the Canary Islands, San Cristóbal de La Laguna, Santa Cruz de Tenerife, Spain

Atypical spindle cell lipomatous tumour (ASCLT) is a benign neoplasm that presents a variable proportion of atypical spindle and adipocytic cells, frequently expressing CD34, and embedded in myxoid or collagenous matrix. An important feature is a constant lack of either *MDM2* or *CDK4* amplification. It typically arises in the extremities. The retroperitoneum is a rare site of involvement. We report a case of a retroperitoneal ASCLT in a 62-year-old male. A differential diagnosis of ASCLT from the other mesenchymal, spindle-cell, and lipomatous tumours is crucial for optimal treatment and significantly influences the prognosis. A diagnosis should be warranted by the immunohistochemistry and molecular findings.

Key words: lipomatous, spindle cell, neoplasm, retroperitoneal, *RB1* deletion.

Introduction

Atypical spindle cell lipomatous tumour (ASCLT) is a benign adipocytic neoplasm with low potential for local recurrence (10–15% for incompletely resected lesions) and no risk of dedifferentiation or metastases [1, 2]. The neoplastic proliferation shows a variable proportion of mild-to-moderately atypical spindle cells, adipocytes, and lipoblasts set in a myxoid or collagenized stroma [1]. The tumour cells express CD34 (60%), S100 (40%), and desmin (20%) [3]. The loss of nuclear pRb expression is observed in 50–70% of cases and correlates with *RB1* deletion [1–3]. An important characteristic is a constant absence of either *MDM2* or *CDK4* amplification [1]. Chromosome 7 monosomy is encountered in some cases [1]. Atypical spindle cell lipomatous tumour affects mainly middle-aged adults, with a slight predominance in males [1, 2]. It is most commonly seen in the subcutis and soft tissues of the limbs and limb girdles, but it can occur in a variety of locations such as head and neck, genital area, trunk, and back, among others [1]. The retroperitoneal space is an exceptional location for ASCLT. We report a case of an ASCLT arising in the retroperitoneal region of a 62-year-old male. The purpose of this article is to present a case of ASCLT with an unusual location and review the literature to improve its diagnostics.

Case report

A 62-year-old male presented with a 3-month history of fever and dry cough persistent despite antibiotic and corticosteroid treatment. He also complained of asthenia, hyporexia, and progressive weight loss of 9 kg with a growing abdominal perim-

eter. Physical examination revealed a large palpable abdominal mass with no signs of peritonitis. Anaemia and hyperfibrinogenaemia were the main laboratory findings. A chest-abdominal-pelvic computed tomography with intravenous contrast revealed a fatty mass of 52 × 17 cm displacing loops of the small and large intestine. The lesion was extending from the retroperitoneum towards the pelvis, presenting 2 areas of heterogeneous soft tissue density, and encompassing the right iliac vessels and left ureter. The findings were suggestive of liposarcoma. A specimen obtained during the ultrasound-guided core needle biopsy revealed a mesenchymal spindle cell proliferation with low histological aggressiveness. As the result was not conclusive, and so a surgical excision was performed. The mass was successfully resected. Postoperative recovery was satisfactory. The patient was alive and well, with no evidence of recurrence or metastases at 5 months after the surgery.

Material and methods

Formalin-fixed, paraffin-embedded tumour samples were handled according to standard procedures, and 3-μm-thick tissue sections were obtained to perform further techniques.

All immunohistochemistry was carried out using a Ventana Benchmark Ultra autostainer. Immunostaining was performed for CD34 (QBend10, Ventana), MUC4 (8G7, Cell Marque), S100 (4C4.9, Ventana), Melan-A (A103, Ventana), Melanosome (HMB45, Ventana), Desmin (DE-R-11, Ventana), Smooth Muscle Actine (1A4, Cell Marque), Specific Muscle Actine (HHF35, Cell Marque), Caldesmon (E89, Cell Marque), MITF (C5/D5, Ventana), STAT6 (S-20, Santa Cruz Biotechnology), CDK4 (ab226474, Abcam), p16 (CINtec® p16 Histology, Ventana), Calponin (EP798Y, Cell Marque), TFE3 (MRQ-37, Cell Marque), β-Catenin (14, Cell Marque), oestrogen receptor (SP1, Ventana), and progesterone receptor (1E2, Ventana).

Fluorescent in situ hybridization (FISH) was conducted using XL RB1/DLEU/LAMP (Metasystems), LSI 7q31/CEP7 (Vysis), XL MDM2 (Metasystems), LSI reord. CHOP (12q13) Break Apart (Vysis), LSI reord. EWSR1 (22q12) Break Apart (Vysis), and LSI reord. SS18 (SYT, 18q11) Break Apart (Vysis) probes. Hybridization was carried out according to the manufacturer's protocol. Slides counterstained with DAPI (Vysis) were observed under a fluorescent microscope (Nikon Eclipse 50i). Pictures were analysed by Metasystems Isis software.

Results

The surgical specimen weighed 7984 g and was 45 × 30 × 11 cm in size. The cut surface showed an ill-defined lesion of approximately 30 × 23 × 10 cm. Grossly, the tumour presented mostly fatty appearance with 2 heterogenous and firm zones of multinodular growth pattern (Fig. 1A). The nodules demonstrated a fleshy or gelatinous aspect with apparent necrotic areas and had quite well-circumscribed borders, reminiscent of pseudo-capsule in some points.

Microscopically, the neoplastic proliferation was composed of variably prominent adipocytic and spindle cell components, immersed in a collagenous or myxoid matrix, and showing only subtle atypia. A distinct regional morphologic variation was observed within the lesion. Areas consisting mainly of mature-appearing adipocytes were transitioning to solid sheets of spindle cells with a few scattered adipocytic elements (Fig. 1B). Purely spindle cell areas with increased cellularity were locally forming fascicles arranged in herring-bone pattern (Fig. 1C). The elongated spindle-shaped cells presented ovoid nuclei and pale eosinophilic cytoplasm with indistinct borders. The adipocytes were predominantly mature looking but demonstrated a broad variation of size. A small number of univacuolated or bivacuolated lipoblasts were identified (Fig. 1D). Extracellular matrix was abundant and varied from myxoid to densely collagenous, occasionally forming bundles of ropey collagen (Fig. 1G). Mitoses were scarce, averaging one figure per 10 high-power fields. The tumour background showed thin-walled dilated or staghorn-shaped blood vessels, imparting a hemangiopericytoma-like growth pattern (Fig. 1E), or a prominent branching capillary network with a vague tendency for perivascular cell disposition (Fig. 1H). There were also myxoid liposarcoma-like areas observed, presenting plexiform capillary vasculature (chicken wire-like) in abundant myxoid stroma (Fig. 1F). Densely cellular areas harboured zones of ischaemic necrosis.

Immunohistochemically, the tumour cells were strongly and diffusely positive for CD34 (Fig. 2A). A weak and/or focal expression of Calponin, HMB45, STAT6, and TFE3 was encountered. There was no reliable reaction against p16 (Fig. 2B), CDK4 (Fig. 2C), MUC4, β-Catenin, Desmin, Smooth Muscle Actine, Specific Muscle Actine, Caldesmon, S100, Melan-A, MITF, and oestrogen and progesterone receptors in the spindle cell component.

FISH analysis demonstrated the absence of *MDM2* amplification (Fig. 2D). *RB1* deletion was identified (Fig. 2E), and monosomy 7 was also detected (Fig. 2F). No rearrangement of *CHOP*, *EWRS1*, or *SS18(SYT)* was observed.

Discussion

A differential diagnosis of tumours involving the retroperitoneal space spans a wide spectrum of neoplasms. Unlike other sites of the body, malignant lesions of the retroperitoneum are roughly

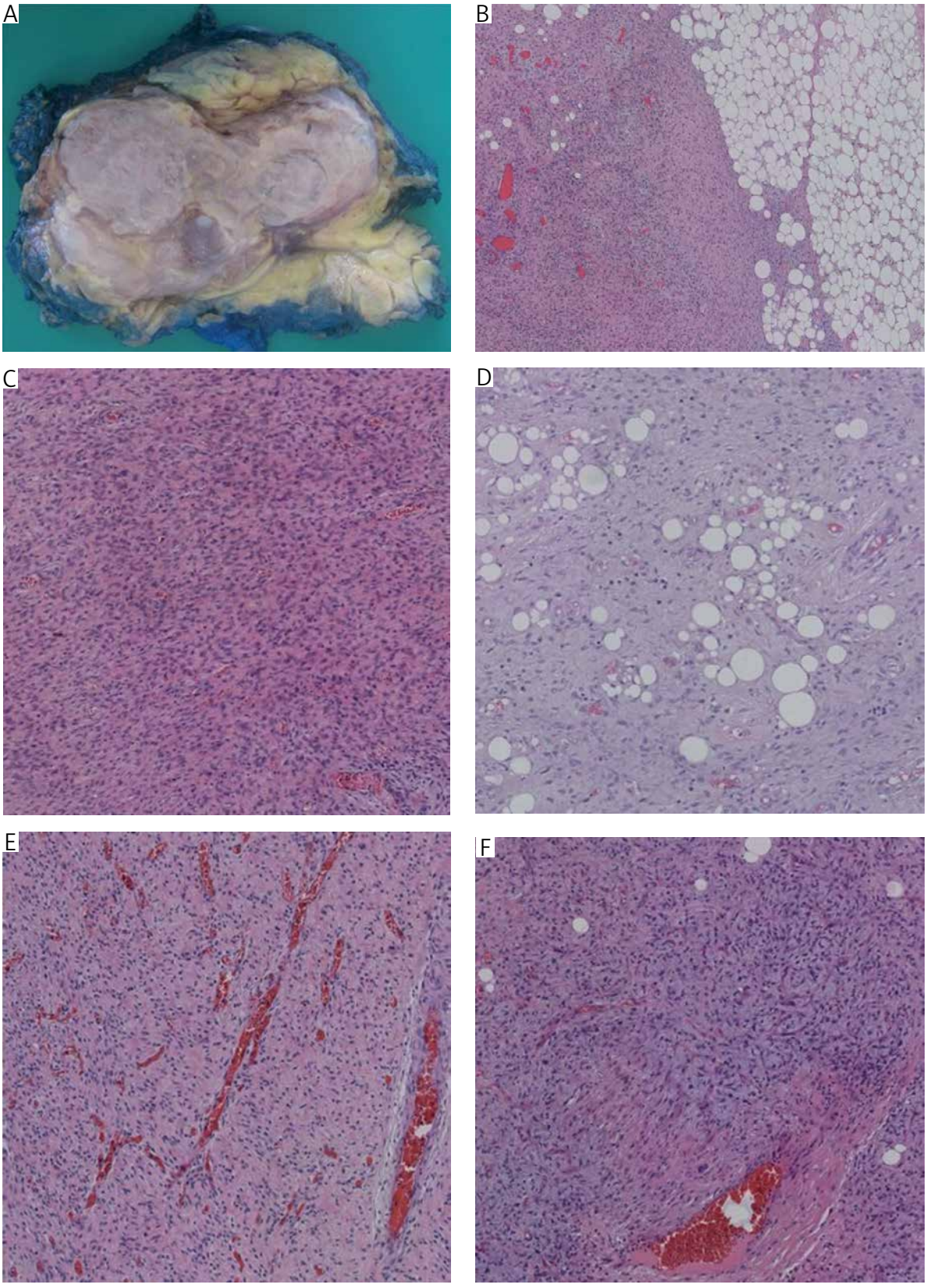

Fig. 1. Gross and histopathological findings. A) Cut surface of a fatty tumour with fleshy or gelatinous nodules rimmed by pseudo-capsule; B) Abrupt transition between adipocytic and spindle cell components (HE, 4×); C) Solid sheets of spindle cells forming fascicles arranged in herring-bone pattern (HE, 100×); D) Univacuolated or bivacuolated lipoblasts presenting scant atypia (HE, 100×); E) Staghorn-like vessels in a collagenous-rich background resembling solitary fibrous tumour (HE, 100×); F) Myxoid liposarcoma-like areas with abundant myxoid matrix and plexiform capillary (chicken wire-like) vasculature (HE, 100×)

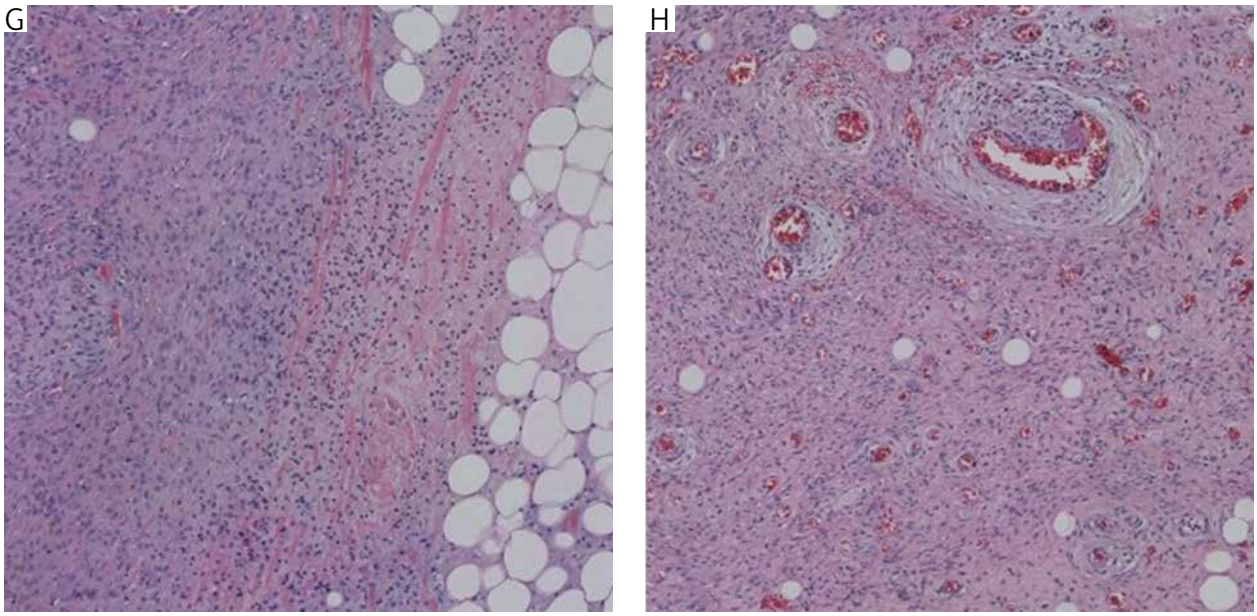

Fig. 1. Cont. G) Spindle cells showing a subtle nuclear atypia and extracellular matrix with focal formation of ropey collagen bundles (HE, 100×); H) Prominent branching capillary network (soft tissue angiofibroma-like) with perivascular distribution of spindle cells (pericytic mimicry) (HE, 100×)

4 times more frequent than benign ones [4]. The most common primary retroperitoneal soft tissue tumours are liposarcoma (well-differentiated and dedifferentiated subtypes) and leiomyosarcoma [4]. Nevertheless, mesenchymal malignancies, such as solitary fibrous tumour (SFT), inflammatory myofibroblastic tumour, malignant peripheral nerve sheath tumour (MPNST), monophasic synovial sarcoma, and myxofibrosarcoma, among others, rarely arise in this localization [4]. Furthermore, melanoma, metastatic carcinoma, and sarcoma-mimicking benign lesions should be excluded [4].

Atypical spindle cell/pleomorphic lipomatous tumour (ASPLT) is a new terminology included in the latest 5th edition (2020) of the World Health Organization (WHO) classification. The categorization of a subset of "atypical adipocytic neoplasms with spindle cell features" has been a subject of scientific debate for the last few decades [2]. In 1994 Dei Tos *et al*. introduced for the first time the term "spindle cell liposarcoma" (SSLs) as a variant of well-differentiated liposarcoma, with potentially aggressive clinical behaviour [5]. The 4th edition (2013) of the WHO classification considers SSLs to be a subtype of atypical lipomatous tumour/well-differentiated liposarcoma (ALT/WDLs), with local recurrence capacity but no potential for metastasis, unless it suffers dedifferentiation [6]. In 2017, researchers investigated the molecular characteristics of atypical pleomorphic lipomatous tumour (APLT) and demonstrated a significant overlapping of morphologic and genetic features between APLT and ASCLT, suggesting that these tumours belong to the same entity and should be classified as a separate category, distinct from the liposarcoma group, and for which the term ASPLT has been proposed [2, 7, 8]. Currently ASPLT is regarded as a benign neoplasm, although with a low recurrence rate of 10–15%, if incompletely excised, but with no risk for dedifferentiation [1]. This emphasizes the importance of distinguishing ASPLT from ALT/WDLs and dedifferentiated liposarcoma (DDLs), in order to avoid aggressive treatment [3, 7–9].

Histologically ASCLT presents a broad morphological spectrum. At one extreme, it may be composed predominantly of abundant extracellular matrix with a few, cytologically bland spindle cells and scattered adipocytes, involving the differential diagnosis with diffuse neurofibroma, mammary-type myofibroblastoma, dermatofibrosarcoma protuberans, fat-forming SFT, or low-grade MPNST [2, 3, 8]. At the other extreme, highly cellular variants are characterized by numerous spindle cells and easily identified lipoblasts set in less prominent stroma and showing mild-to-moderate nuclear atypia [2, 8]. Other peculiar growth patterns that have been described in ASPLT are as follows: spindle cell-rich variant forming compact fascicles (fibrosarcoma-like pattern), a striking perivascular location of the atypical cells (so-called pericytic mimicry), the presence of staghorn-like vessels in a collagenous-rich background (reminiscent of SFT), the presence of a prominent branching capillary network (similar to soft tissue angiofibroma), and myxoid liposarcoma-like areas with abundant myxoid matrix and prominent capillary chicken wire-like vascular network [2, 7]. Cellular cases may be morphologically indistinguishable from low-grade DDLs – a critical distinction, given its metastatic potential; therefore, these fatty lesions should be extensively sampled [2, 3, 8].

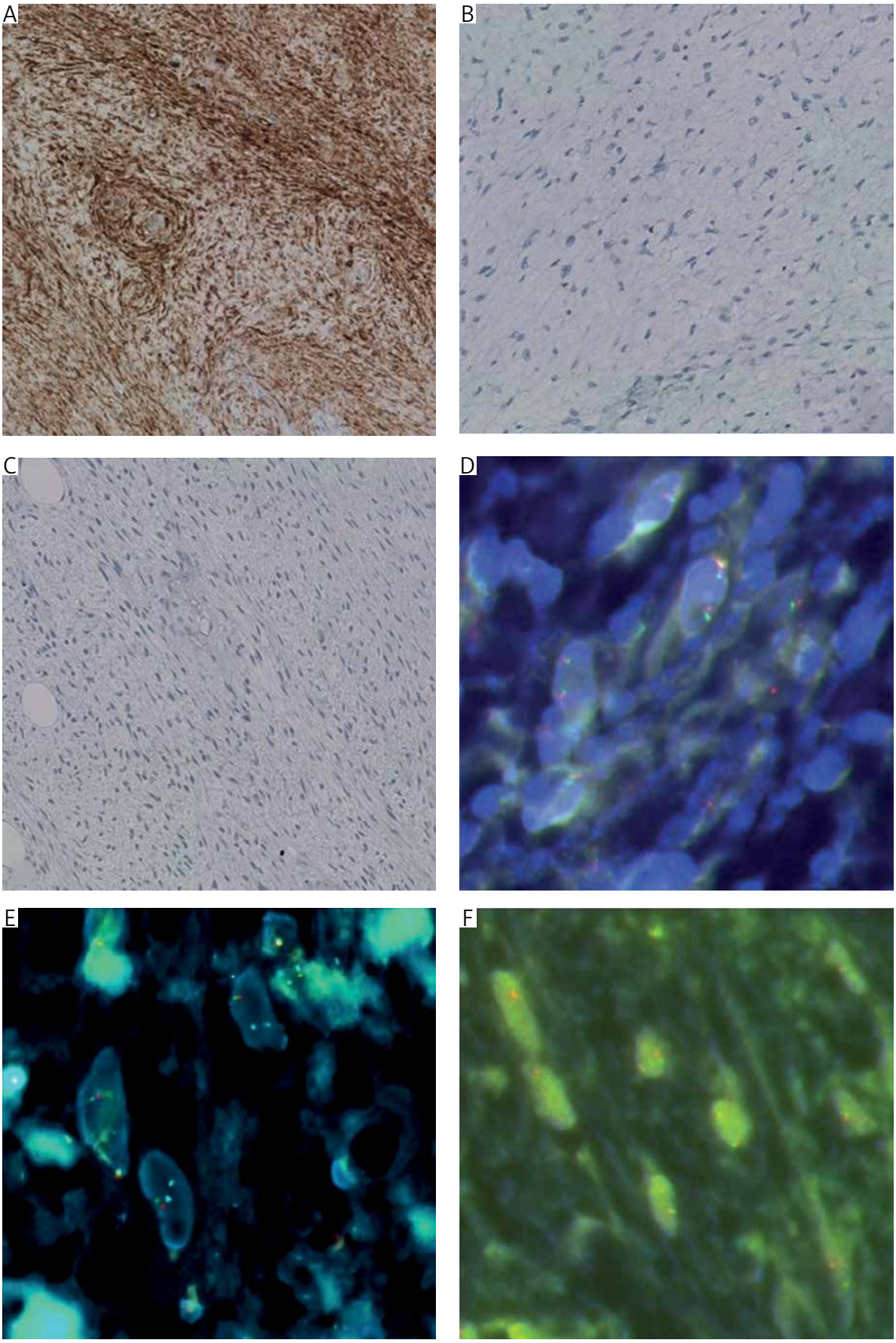

Fig. 2. Immunohistochemical and molecular findings. A) Strong and diffuse, cytoplasmatic CD34 expression (IHC, 100×); B) No reactivity for p16 (IHC, 200×); C) Lack of CDK4 expression (IHC, 200×); D) Absence of *MDM2* amplification (FISH, 1000×); E) *Rb1* deletion (FISH, 1000×); F) Monosomy 7 (FISH, 1000×)

Table I. Clinicopathological summary of retroperitoneal atypical spindle cell lipomatous tumour cases

Author, year	Age, gender	Tumour size [cm]	Relevant IHC and molecular findings	Follow-up (months), outcome
Shioi [13]	60, male	9.8 × 9.5	Positive IHC: CD34, S100, Vimentin Negative IHC: *MDM2*, CDK4 FISH: absence of MDM2 amplification	13, AND
Kirisawa [14]	74, male	4.6 × 4.2	Positive IHC: CD34, S100, Rb (retained), p16, Vimentin Negative IHC: CDK4, *MDM2*, Desmin FISH: absence of *MDM2* amplification	12, AND
Bae [15]	18, female	38 × 24 × 11.5	Positive IHC: CD34, Desmin, S100 (focal), Rb (retained) Negative IHC: MDM2 FISH: absence of *MDM2* amplification	12, AND
Our case	62, male	30 × 23 × 10	Positive IHC: CD34 Negative IHC: p16, CDK4, S100, Desmin FISH: absence of *MDM2* amplification; presence of RB1 deletion and monosomy 7	5, AND

AND – alive with no evidence of disease, ASCLT – atypical spindle cell lipomatous tumour, FISH – fluorescent in situ hybridization, IHC – immunohistochemistry, SCLs – spindle cell liposarcoma

The morphological differentiation of ASPLT from other lipomatous neoplasms can be challenging, or even impossible [9]. Specific, recurrent genetic abnormalities are well-established for most types of liposarcoma, and cytogenetic analysis seems essential to conclude a diagnosis [9–11]. Atypical lipomatous tumour/well-differentiated liposarcoma and DDLs are characterized by the consistent presence of supernumerary ring or giant chromosomes containing amplified material from chromosome 12q14-15, including multiple copies of the *MDM2* and *CDK4* oncogenes, whereas myxoid cell liposarcoma harbours a specific translocation t(12;16)(q13.3;p11.2) with *CHOP* and *FUS* gene fusion [8, 10, 11]. These aberrations are not seen in ASPLT [9].

Retinoblastoma 1 (*RB1*) is a tumour suppressor gene located at chromosome 13q14.2, and its product (RBp) is a chromatin-associated protein involved in the cell cycle control [9, 12]. *RB1* inactivation has been implicated in the pathogenesis of different tumours, such as myofibroblastoma, cellular angiofibroma, and spindle cell/pleomorphic lipoma (SPL), and was also detected in a significant subset of the ASPLT cases [9, 11, 12]. The deletions of 13q14 found in ASPLT are more complex than in SPL, including *Rb1* and its flanking genes (*RCBTB2, DLEU1*, *ITM2B)* [2, 7, 8, 11]. These additional genetic alterations might explain the local recurrence potential of ASPLT, especially when further gains and losses are observed in the malignant pleomorphic liposarcoma (*RB1* loss occurs in up to 50% of cases) [2, 7–9, 11]. Moreover, monosomy 7 has been reported in some cases of ASPLT [3, 8 ,9].

Immunohistochemically ASPLT shows a variable, often diffuse expression of CD34 in most cases (60%) and less frequently expresses S100 (40%) and desmin (20%) [3, 8, 9]. p16 expression tends to be strong and diffuse to patchy in APLT, and negative in ASCLT [3, 7, 9]. The loss of nuclear pRb expression is encountered in 50–70% of cases and correlates with *RB1* heterozygous deletion [1–3, 8, 12]. A weak or focal expression of MDM2 or CDK4 can be occasionally observed, but always in the absence of corresponding gene amplification [3, 8].

In the series reviewed, ASCLT has been described as a mass located mainly in the upper and lower limbs [8, 10, 11]. Of a total of 232 patients in the review by Mariño-Enriquez, only 2 cases had retroperitoneal lesions [8]. To the best of our knowledge, there are only 3 (two cases from the Mariño-Enriquez review lack individual description and were not included) previous reports of retroperitoneal ASCLT in the literature (Table I) [13–15].

Conclusions

We report a case of ASCLT presented as a huge mass arising in the retroperitoneal space. Facing a retroperitoneal tumour that radiologically, macroscopically, and microscopically suggests a well-differentiated or DDLs, an ASCLT should be considered as a diagnostic alternative. Benign behaviour of ASCLT assures an excellent prognosis in patients with completely resected lesions. This fact highlights the importance of distinguishing it from more aggressive neoplasms. A meticulous histologic examination together with the evaluation of *MDM2* or *CDK4* amplification and *Rb1* deletion, preferentially by FISH technique, seems to be the most useful tool to establish an accurate diagnosis in such cases.

The authors declare no conflict of interest.

References

1. WHO classification of tumours editorial board. Soft tissue and bone tumours. International Agency for Research on Cancer, Lyon (France) 2020. (WHO Classification of tumours series, 5th ed., vol. 3).
2. Creytens D. What's new in adipocytic neoplasia? Virchows Arch 2020; 476: 29-39.
3. McCarthy AJ, Chetty R. Tumours composed of fat are no longer a simple diagnosis: an overview of fatty tumours with a spindle cell component. J Clin Pathol 2018; 71: 483-492.
4. Choi JH, Ro JY. Retroperitoneal sarcomas: an update on the diagnostic pathology approach. Diagnostics (Basel) 2020; 10: 642.
5. Dei Tos AP, Mentzel T, Newman PL, et al. Spindle cell liposarcoma, a hitherto unrecognized variant of liposarcoma. Analysis of six cases. Am J Surg Pathol 1994; 18: 913-921.
6. Fletcher CDM, Bridge JA, Hogendoorn PCW, Mertens F. WHO classification of tumours of soft tissue and bone. International Agency for Research on Cancer, Lyon 2013
7. Creytens D, Mentzel T, Ferdinande L, et al. "Atypical" pleomorphic lipomatous tumor: a clinicopathologic, immunohistochemical and molecular study of 21 cases, emphasizing its relationship to atypical spindle cell lipomatous tumor and suggesting a morphologic spectrum (atypical spindle cell/pleomorphic lipomatous tumor). Am J Surg Pathol 2017; 41: 1443-1455.
8. Mariño-Enriquez A, Nascimento AF, Ligon AH, et al. Atypical spindle cell lipomatous tumor: clinicopathologic characterization of 232 cases demonstrating a morphologic spectrum. Am J Surg Pathol 2017; 41: 234-244.
9. Libbrecht S, Van Dorpe J, Creytens D. The rapidly expanding group of RB1-deleted soft tissue tumors: an updated review. Diagnostics (Basel) 2021; 11: 430.
10. Mentzel T, Palmedo G, Kuhnen C. Well-differentiated spindle cell liposarcoma ('atypical spindle cell lipomatous tumor') does not belong to the spectrum of atypical lipomatous tumor but has a close relationship to spindle cell lipoma: clinicopathologic, immunohistochemical, and molecular analysis of six cases. Mod Pathol 2010; 23: 729-736.
11. Creytens D, van Gorp J, Savola S, et al. Atypical spindle cell lipoma: a clinicopathologic, immunohistochemical, and molecular study emphasizing its relationship to classical spindle cell lipoma. Virchows Arch 2014; 465: 97-108.
12. Chen BJ, Mariño-Enríquez A, Fletcher CD, Hornick JL. Loss of retinoblastoma protein expression in spindle cell/pleomorphic lipomas and cytogenetically related tumors: an immunohistochemical study with diagnostic implications. Am J Surg Pathol 2012; 36: 1119-1128.
13. Shioi Y, Hasegawa T, Otsuka K, et al. Primary retroperitoneal spindle cell liposarcoma: pathological and immunohistochemical findings. Pathol Int 2010; 60: 472-476.
14. Kirisawa T, Kobayashi K, Nofuji S, et al. [A case of retroperitoneal atypical spindle cell lipomatous tumor]. Hinyokika Kiyo 2018; 64: 431-433.
15. Bae JM, Jung CY, Yun WS, Choi JH. Large retroperitoneal atypical spindle cell lipomatous tumor, an extremely rare neoplasm: a case report. World J Clin Cases 2022; 10: 2584-2590.

Address for correspondence

Martyna Aleksandra Krupinska, MD
Department of Pathology
University Hospital of the Canary Islands
Ofra, s/n. La Cuesta
38320 San Cristóbal de La Laguna
Santa Cruz de Tenerife, Spain
e-mail: martynakrup@gmail.com