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REVIEW ARTICLE

Solitary Fibrous Tumor of the Liver: a Review of the Current Knowledge and Report of a New Case

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Abstract
Introduction Solitary fibrous tumors of the liver (SFTL) are uncommon tumors; to the present day, less than 50 cases has been reported in the English scientific literature, most of which behaved as benign tumors. The present article reports a new case of SFTL and has the main purpose of updating the current knowledge of SFTL because due to its rarity, its clinical presentation, study, treatment, and prognosis are not well known. The clinical presentation, radiologic study, surgical treatment, immunohistochemical study, and prognosis are updated and comprehensively discussed.
Methods Using the common search engines, a search of the English literature was conducted for "Solitary Fibrous Tumor of The Liver," and the relevant articles were retrieved, reviewed, and analyzed.
Results All published articles reported anecdotal SFTLs, or SFTLs were included in large series analyzing solitary fibrous tumors on different sites.
Conclusion The SFTL is an uncommon neoplasm. The clinical presentation is habitually indolent and its behavior is uncertain. In some cases, the SFTL acts as an aggressive sarcoma with poor prognosis. Currently, only surgery offers a therapeutic opportunity for these patients. Due to the lack of current knowledge of long-term behavior of supposedly benign SFTLs and to the lack of specific therapies, methodical long-term follow-up is essential to ensure the survival of patients treated for SFTL.

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Keywords Solitary fibrous tumor of the liver · Mesenchymal neoplasms · Hepatic tumors · Hemangioperycitoma · Hepatectomy

Introduction

Solitary fibrous tumors (SFT) are rare neoplasms composed of fusiform cells, originating in the mesenchyme, and presenting frequently in thoracic structures, most commonly in the pleura [1–3]. They occur as well in other localizations involving serous cavities such as the pericardium and peritoneum [3]. These tumors have also been described in cavities not covered by serosa and in other solid organs such as the upper respiratory tract, mediastinum, lung, meningeal membranes, oral cavity, orbitary cavity, thyroid gland, liver, pancreas, greater omentum, retroperitoneal surface, prostatic gland, spermatic cord, and other soft tissues such as the diaphragm and smooth muscle [4, 5]. Solitary fibrous tumors of the liver (SFTL) are some of the most uncommon SFTs and count for only few cases described in the English scientific literature. The present article reports a new case or SFTL recently treated at our Institution and has the main purpose to update and provide a detailed complete summary of the current knowledge of SFTL; because due to its rarity, its clinical presentation, study, treatment, and prognosis are not well known.

Case Report

A 58-year-old man presented at our Institution complaining of abdominal epigastric distention and dull pain that evolved for 5 months. He was studied with a computed tomography abdominal scan that revealed a solid lobulated hepatic tumor measuring 102 × 70 mm

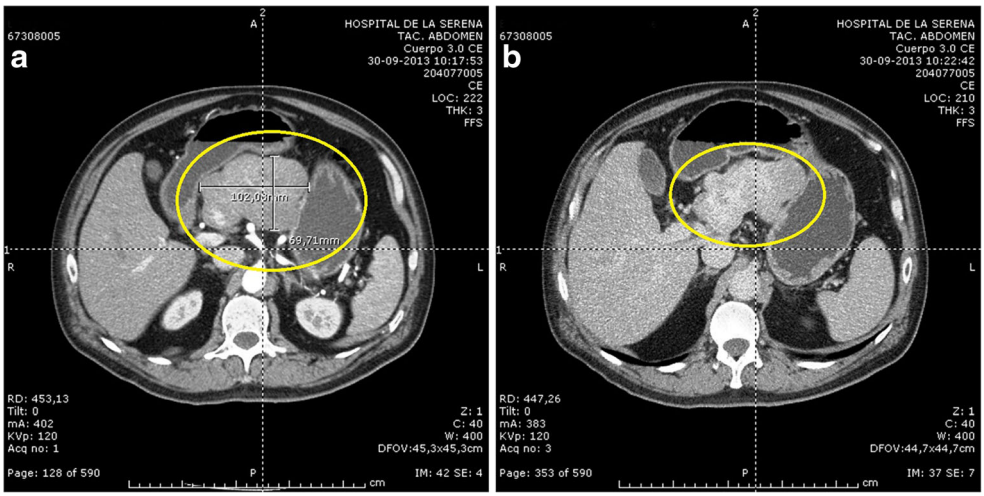

Fig. 1 **a** Early arterial phase of abdominal computed tomography depicting a hypodense, heterogeneous, hypervascularized, well-defined, and delimited by a thick capsule, hepatic mass presenting in a 58-year-old patient with a confirmed solitary fibrous tumor of the liver. **b** Portal phase where it is possible to identify multiple hypodense areas with different degrees of enhancement in the tumor

originating from the caudate lobe (Fig. 1). At surgery, a multilobed, multinodular tumor, well circumscribed, and delimited by a soft, thick, firm, and elastic fibrous whitish capsule was found hanging from the caudate lobe (Fig. 2). The tumor was attached to the hepatic lobe by a 3-cm pedicle and was excised by sectioning the pedicle with at least 2 cm of hepatic parenchyma. The tumor measured 15 × 9 × 6 cm weighting 794 g. It was surrounded by a thick, smooth, elastic whitish capsule. The contour was lobulated and well delimited (Fig. 3). At optic microscopy with hematoxylin-eosin staining, the tumoral cells were fusiform with oval nucleus arranged in short bundles and fascicles crossed by abundant thick collagen bands and focal areas with scarce plasmocyte infiltrate. There was no mitosis, atypia, or necrosis. The immunohistochemical reaction was positive to CD34 and vimentin, and negative to CD117, S100, and smooth muscle α-actin. At follow-up, 3 years after the surgical intervention, the patient is asymptomatic with no signs of recurrence.

Epidemiology

Most cases of SFTs have a benign behavior. When they originate in the pleura, SFTs have a higher frequency of malignity varying between 13 and 23 % of all cases [2, 6]. This fact is in contrast with SFTs localized in other sites where the development of malignant tumors is almost anecdotic [1, 2, 4, 7, 8]. Solitary fibrous tumor of the liver was scientifically reported for the first time in an article published in 1959 by Donald B. Nevius and Nathan B. Friedman. They described three SFTs in different localizations, one of them was a liver SFT and presented clinically with hypoglycemia [9]. Hypoglycemia has been shown to be part of the clinical presentation of SFTL [7]. Hepatic SFTs are uncommon. To present day, 44 cases have been reported in the English scientific literature [10–30], most of which behaved as benign tumors.

Methods

The present article has been written using information from the English scientific literature available in common search engines such as PubMed and Google Academics. A search was conducted for "Solitary Fibrous Tumor of The Liver," and the relevant articles were retrieved, reviewed, and analyzed. The references list of each article was manually inspected searching for other articles reporting SFTL and all the pertinent articles were retrieved, analyzed, and included in this report.

Results

At present, 45 cases, including the patient described in this article, have been reported in the available English literature. Most of them (30 cases, 67 %) are single case reports. There were two case series; one included three patients and the other nine cases. Three patients were included in two-case series reporting multiple SFTs in different sites. SFTLs are more common in women than in men, 26 cases (58 %) versus 17 cases (42 %) and presents in adult patients from 24 to 83 years of age (median 60 years). They localize commonly in the right hepatic lobe (24 cases, 53 % versus 19 cases, 47 %). A concise summary of all reported cases is depicted in Table 1 along with the main author, reference number, and year of publication.

Pathology, Histopathology, and Molecular Background

Solitary fibrous tumors are uncommon spindle cell neoplasms that occur in multiple and different sites within the human body. They are found most often in the pleura, its development in the liver is relatively rare. Solitary fibrous tumors arise from mesenchymal cells and represent a diverse group of benign

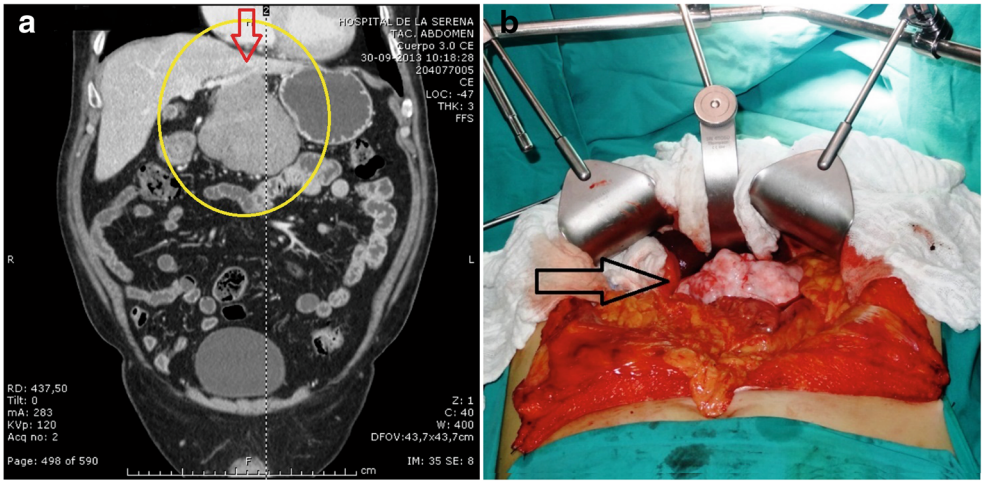

Fig. 2 **a** Solitary fibrous tumor of the liver *hanging* from the caudate lobe. **b** The same tumor *in situ* before surgical resection

and malignant tumors [39]. Definitive diagnosis depends on certain histologic and morphologic features supported by immunohistochemical staining and molecular analysis [2].

Macroscopic Appearance

Solitary fibrous tumors of the liver are multilobed or multinodular tumors, well circumscribed and delimited by a soft, thick, fibrous whitish or grey-white capsule. They may present with cystic degeneration and necrosis. The tumor consistency is firm and elastic [7, 8, 20, 30, 34, 37] (Fig. 3). When cut, fasciculate, irregular, yellowish and whitish areas interspersed with soft areas and focal myxoid degeneration may be observed. It is also possible to observe areas of cystic degeneration, necrosis, or bleeding [23, 27, 30, 33, 36]. The size of the tumor is variable but usually greater than 10 cm in diameter, reaching in some cases up to 30 cm or more in diameter [7, 21–30, 32–34, 36, 37, 40, 41]. The weight depends on the size reached, tumors weighting between 2.8 and 4.7 k have been reported [21, 23, 30, 33, 34, 36, 37].

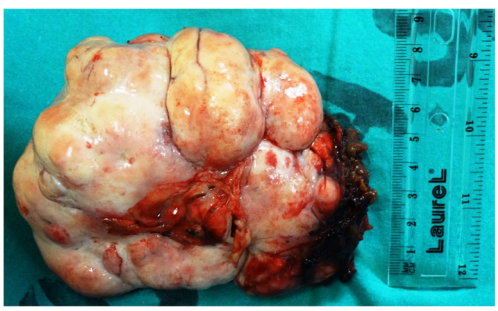

Fig. 3 Excised solitary fibrous tumor of the liver, this specimen shows all the characteristics habitually described: A multilobed, multinodular tumor, well circumscribed and delimited by a soft and thick, firm, elastic fibrous white pearlescent capsule. Some hepatic tissue where the tumor was attached to the liver can be seen

Microscopic Appearance

Microscopically, at hematoxylin-eosin staining, SFTs are characterized by a wide range of morphological features that vary from those tumors predominantly fibrous that contain large areas of collagen fibers and blood vessels with thick hyaline walls, to more cellular tumors with less fibrous content [20, 42]. The usual histological description is characterized by the presence of hyaline radiated acellular or hypocellular areas rich in collagen alternating with more cellular disorderly distributed areas populated by spindle-like, fusiform and elongated cells with ovoid nuclei [2, 7, 8, 10–21, 27, 30–32, 36]. The presence of necrosis is frequently observed in benign and malignant cases [8, 23, 30, 31, 37, 39]. In malignant tumors, it is possible to appreciate the presence of nuclear atypia and mitotic figures that are not observed in benign cases [7, 8, 31, 32, 37, 39]. Benign SFTL have little atypia or cellular pleomorphism; the absence of mitosis or inflammatory cell infiltration is notable [20, 24, 27, 30, 36]. Malignant tumors have nuclear pleomorphism and prominent nucleoli [7, 32, 39]. Another feature of SFTL is the presence of a *matted* vascular pattern with numerous thick-walled vessels constituting the reason why solitary fibrous tumors were previously classified as hemangiopericytomas [8, 21, 31, 39, 42]. Gengler and Guillou in an elegant article describe two types of basic histological features of solitary fibrous tumors, a fibrous shape and a cellular shape [42] (Table 2).

Immunohistochemistry

The basic features of SFTL immunohistochemistry is the expression of CD34, CD99, vimentin, and bcl-2 [7, 8, 10–28, 30–32, 37]. The CD34 is an antigen found in progenitor myeloid cells that are also expressed in endothelial cells and mesenchymal cells including some subtypes of fibroblasts [2]. In Table 3, immunohistochemical markers used in the study of SFTL with their respective positive and negative

Table 1 Summarized data on published reports concerning solitary fibrous tumors of the liver

Author	Gender	Age (years)	Liver lobe	Therapy	Type of report	Publication year	Search engine
Nevius and Friedman [9]	M	56	R	Radiation	One case included in a series of other cases	1959	PubMed
Kim and Damjanov [11]	F	27	L	Surgery	Case report	1983	PubMed/ Google
Kottke-Marchant et al. [12]	F	83	L	Surgery	Case report	1989	PubMed/ Google
Kasano et al. [13]	F	39	L	Surgery	Case report	1991	PubMed
Bost et al. [14]	F	50	R	Surgery	Case report	1995	PubMed
Barnoud et al. [18]	M	50	R	Surgery	Case report	1996	PubMed
Levine and Rose [15]	M	57	L	Surgery	Case report	1997	PubMed/ Google
Guglielmi et al. [30]	F	61	R	Surgery	Case report	1998	PubMed
Moran et al. [16]	M(2)/F(7)	32 to 83	R(5)/L(4)	Surgery	Case series	1998	PubMed/ Google
Fuksbrumer et al. [31]	M (1)/F(2)	40 to 80	R(1)/L(2)	Surgery	Case series	2000	PubMed
Yilmaz et al. [32]	F	25	R	Surgery	Case report	2000	PubMed
Gold et al. [4][a]	–	–	–	–	Two cases included in a series of other cases	2002	PubMed
Saint-Marc et al. [19]	F	69	R	Surgery	Case report	2002	PubMed
Neeff et al. [122	F	63	R	Surgery	Case report	2004	PubMed
Chithriki et al. [29]	F	75	R	Surgery	Case report	2004	PubMed
Vennarecci et al. [23]	M	65	R	Surgery	Case report	2005	PubMed
Moser et al. [33]	F	73	R	Surgery	Case report	2005	PubMed
Ji et al. [20]	F	42	R	Surgery	Case report	2006	PubMed
Terkivatan et al. [21]	M	74	L	Surgery	Case report	2006	PubMed
Nath et al. [34]	F	61	R	Surgery	Case report	2006	PubMed
Chan et al. [7]	M	70	R	Surgery	Case report	2007	PubMed
Obuz et al. [17]	M	52	L	Surgery	Case report	2007	PubMed/ Google
Fama et al. [28]	M	68	R	Surgery	Case report	2007	PubMed
Perini et al. [24]	F	40	L	Surgery	Case report	2008	PubMed
Korkolis et al. [27]	F	82	L	Surgery	Case report	2008	PubMed/ Google
Taboada-Rodríguez et al. [35]	M	71	R	Surgery	Case report	2010	PubMed/ Google
Novais et al. [36]	F	34	R	Surgery	Case report	2010	PubMed/ Google
Sun et al. [25]	M	59	L	Surgery	Case report	2011	PubMed
Peng et al [37]	F	24	R	Surgery	Case report	2011	PubMed/ Google
Jakob et al. [8]	F	62	L	Surgery	Case report	2013	PubMed
Soussan et al [38]	M	64	L	Surgery	Case report	2013	PubMed
Liu et al. [26]	M	42	L	Surgery	Case report	2013	PubMed
Makino et al. [10]	M	55	R	Surgery	Case report	2015	Google
Present case	M	50	L	Surgery	Case report	2015	–
Total	M(17)/ F(26)	24 to 83	R(24)/ L(19)		45 cases reported		

[a] Includes two cases without any detail

reactions are depicted. These immunohistochemical markers characterize these tumors; some are positive in some cases while others are negative in other cases [7, 8, 20–28, 30–33, 37, 38, 43]. Fibrous SFTLs besides being positive for CD34

Table 2 Histological classification of solitary fibrous tumors according to Gengler and Guillou[38]

Fibrous tumors	*Cellular* tumors
– More frequently found	– Less frequently found
– Present alternating fibrous hipocellular and hipercellular areas	– Present mostly hipercellular areas
– Presence of fusiform or round cells arranged in fascicles	– Present few fibrous areas
– The cellular nucleus have a vesicular appearance and present pseudoinclusions	– The cell nucleus has a round or oval shape
– Blood vessels are numerous with multiple branches and thick hyaline walls	– Blood vessels have numerous branches and thin walls
– Immunohistochemistry positive to CD34 (90 %), CD99 (70 %), bcl-2 (30 %), epithelial membrane antigen (30 %), and smooth muscle actin (20 %)	– The tumor size is habitually larger than benign tumors
– Frequently behave as benign tumors	– Immunohistochemistry positive to CD34 (80 %)
	– Frequently behave as malignant tumors

are also positive to CD99, bcl-2, epithelial membrane antigen, and smooth muscle α-actin. Cellular SFTLs are positive only for CD34 and negative to any other markers [44] (Table 3). Benign SFTLs have a ki-67 positivity in 5 % or less of their cells [10, 23, 33]. Some researchers have suggested a ki-67 higher than 5 % as a marker of malignancy [7, 8, 35, 37].

Molecular Analysis, Cell Ultrastructure, and Genetics

Solitary fibrous tumors are very heterogeneous tumors in their cellular ultrastructure, showing a wide differentiation, in variable proportions, of different cell types such as fibroblasts, myofibroblasts, endothelial cells, pericytes, and undifferentiated perivascular cells [35]. Genetically, SFTLs show predominantly structural abnormalities in chromosomes X, 2, 9, 15, and 18; however, there is no current definitive consensus on the genetic abnormalities that can be found in these tumors [45].

Table 3 Immunohistochemical markers studied in SFTL

Positive reaction	Negative reaction
– CD34	– CD31
– CD99	– CD117
– bcl-2	– CAM-5.2
– My-10	– VIII Factor
– Vimentin	– XIIIa Factor
– Desmin	– S-100
– Smooth muscle actin	– HHF-35
– Epithelial membrane antigen	– HMB-45
– Epithelial growth factor	– AE-1
– Progesterone receptors	– Fli-1
	– KL-1
	– Cytokeratin
	– Desmin
	– Smooth muscle actin
	– Epithelial membrane antigen
	– Her-2-neu
	– Progesterone receptors

Clinical Presentation

Clinical symptoms for SFTL are unspecific [4, 10, 23, 25–35, 37, 38, 40, 41, 46]. Approximately, 80 % are asymptomatic at the time of diagnosis [10]. Symptoms related to SFTL depend on the size of the tumor, they present when the SFTL reaches certain volume or compresses adjacent organs [20–35, 37, 38, 40, 41, 46]. Symptoms include sensation of gastric plenitude associated to nausea and postprandial vomit when the SFTL presses the gastric wall [11–16, 21–23, 30, 31, 34], dull pain located over the right hypochondria [26, 27, 30, 40], weight loss [12–17, 21, 30], shortness of breath [41], fatigue [25, 28], as well as other symptoms related to hypoglycemia [9, 20, 23, 28–30]. Advanced cases presents with liver insufficiency or failure [9]. The physical examination is frequently unspecific [10–21, 24, 26–35, 37, 40, 41, 46]. Occasionally, it is possible to palpate a solid mass localized over the right superior hemiabdomen and epigastrium [20, 21, 23, 25, 27–35, 37, 38, 41, 46]. In other cases, the abdominal circumference increases [22], and peripheral edema develops [20, 22, 28] (Table 4).

Table 4 Clinical presentation of solitary fibrous tumor of the liver

Symptoms	Signs
– Asymptomatic (80 %) [10]	– Palpable solid mass localized over the right superior hemiabdomen and epigastrium [20, 21, 23, 25, 27–35, 37, 38, 41, 46]
– Gastric plenitude [20]	– Increased abdominal circumference [22]
– Nausea/vomit [11–16, 21–23, 30, 31, 34]	– Peripheral edema [20, 22, 28]
– Right hypochondria dull pain [26, 27, 30, 40]	
– Fatigue [25, 28]	
– Weight loss [12–17, 21, 30]	
– Shortness of breath [41]	
– Symptoms of hypoglycemia [9, 20, 23, 28–30]	

SFTL Associated Hypoglycemia

Since the first description of SFTL, hypoglycemia associated to these tumors has been reported in 4 cases [7, 9, 28–30]. Hypoglycemia associated to mesenchymal tumors originating in diverse abdominal and thoracic localizations is an uncommon phenomenon, although well-known and documented [30, 32]. The clinical syndrome has been described as the presence of an abdominal mass associated to recurrent hypoglycemia, sometimes intractable [30], that has been attributed to ectopic production within the tumor of insulin or other similar hormone [32]. In SFTL, hypoglycemia has been related to many different factors. Initially, it was thought that these tumors secreted a substance similar to insulin to which the hypoglycemia was attributed [9], it was postulated that this substance was a high molecular weight protein fraction with Insulin-like activity and was named Non-Suppressible Insulin-Like Activity, NSILA [30]. Currently, it has been proved that the cause of hypoglycemia is the tumor production and secretion of insulin-like growth factor 2, IGF2 [7, 28]. IGF2 expression is high during fetal life and is relatively independent from growth hormone [34]. That is the reason why its expression is coherent with the development of this primitive mesenchymal tumor. High-serum circulating levels of IGF2 associated to hypoglycemia in patients with SFTL have been demonstrated [7, 28]. And also, it has been observed that in cases of malignant transformation, the hypoglycemia is intractable, suggesting that this phenomena is due to increased biologic activity in malignant SFTL cells [7]. Complete resection of SFTLs has been proved to be enough to achieve complete resolution of hypoglycemia in these patients [7, 28].

Malignant SFTL

Most SFTLs are benign tumors; however, some SFTLs have been reported to behave as highly malignant and aggressive tumors [7, 8, 32, 37]. The clinical presentation of malignant SFTL did not differ notably from the clinical presentation of benign SFTL. One patient with malignant SFTL presented with intractable hypoglycemia [7]; in another patient, the symptoms were unspecific including abdominal pain and weight loss [8]. Another two patients presented with muscular and neurological symptoms due to metastatic disease [32, 37]. In all of these cases, the diagnosis was made after radiologic studies. Surgical treatment has not been definitively shown to be curative for patients with malignant SFTL. In one patient with intractable hypoglycemia, surgical therapy normalized the glycemia; however, after 9 months from the surgery, pulmonary and hepatic metastasis developed causing recurrence of the episodes of intractable hypoglycemia [7]. One patient with malignant non-metastatic SFTL underwent successful and curative surgery [8]. Other two patients with metastatic disease died at 3 and 16 months after surgical resection of the primary hepatic tumor [32, 37]. Anatomical and pathological characteristics of malignant SFTLs include a tumor size over 10 cm, intratumoral necrosis, and presence of metastasis [7, 8, 32, 37]. At microscopy, it is possible to observe the presence of abundant pleomorphic spindle cells scattered in disarray between areas of high collagen content [7, 8, 32], tumor margins infiltrated by malignant cells [7, 8, 37], abundant cellular atypia [7, 8], and a mitotic index higher than 4 mitosis per 10 high-power fields [2, 7, 8, 32, 37]. During the year 2002, the World Health Organization included SFT in the chapter concerning fibroblastic and myofibroblastic tumors under the heading of "Solitary fibrous tumors and hemangioperycitoma," and included a description of the criteria reported by Douglas M. England et al. in 1989 to define malignant tumors (Table 5) [46]. All malignant SFTL tumors reported to date had a positive immunohistochemical reaction to CD34, bcl-2, and vimentin [7, 8, 32, 37]. Nonetheless, all of these pathological and histological characteristic are similar to the characteristics present in benign SFTLs, and that is because the definition of benign or malignant disease is based on the tumor pathological and biological behavior including the development of distant metastasis or recurrent disease. Consequently, SFTLs although habitually benign, must be considered potentially malignant in all cases.

Diagnosis

Diagnostic studies to identify and characterize SFTL are mainly radiological. Laboratory tests such as blood count or C reactive protein do not show any abnormalities [23, 24]. Occasionally, liver function tests such as alkaline phosphatase and gamma glutamic transpeptidase may show mild increases over their normal levels [20, 22, 30, 31]. Serum tumor markers such as carcinoembryonic antigen (CEA), alpha-fetal-protein (AFP), and carbohydrate antigen 19-9 (CA19-9) are normal [20–22, 27, 30]. In some cases, the presence of an abdominal mass palpable over the hepatic area associated to intractable hypoglycemia may lead to suspect the presence of a SFTL [20, 28–30, 33]. The clinical suspicion of an abdominal tumor, probably localized in the liver, leads to radiological studies, starting with an abdominal ultrasound and followed by an

Table 5 England et al. criteria for the definition of malignant solitary fibrous tumors adapted to liver tumors[27]

Major criteria
– Mitotic index higher than 4 mitosis per 10 high-power fields
– Tumor necrosis and hemorrhage
– Nuclear pleomorphism
– Metastasis
Minor criteria
– Tumor size higher than 10 cm
– Cellular atypia

abdominal computed tomography (CT). In other cases, the study is completed with an abdominal magnetic resonance (MR) and positron emission tomography (PET; Table 6) [10, 31, 33, 35, 38]. Radiological studies are, however, unspecific and even though they may suggest a SFTL, they cannot definitively distinguish between malignant or benign hepatic tumors [25, 27, 31, 34, 35].

Ultrasound

Habitually, ultrasound identifies the presence of a solid well-defined ovoid heterogeneous mass, in some cases homogenous and hyperechoic compared with the normal hepatic parenchyma. Sometimes, it is possible to identify cystic images included in the tumor [20, 21, 24, 30, 31, 35, 38].

Abdominal Computed Tomography

Computed tomography with intravenous contrast demonstrate an hypodense, heterogeneous, hypervascularized, well-defined, and delimited by a thick capsule hepatic mass that enhances during the early arterial phase (30 s; Fig. 1a) [20, 24, 25, 27, 31–35, 37, 38, 40, 41, 46, 47]. During the portal phase (1 min), it is possible to identify multiple hypodense areas with different degrees of enhancement (Fig. 1b) [22, 24, 26, 31, 34, 37]. Finally, during the latest venous phase (5 min), the tumor enhancement reaches their maximal expression [31]. Often it is possible to observe necrosis within the tumor and calcifications in the capsule [21, 28, 30, 38]; these characteristics may lead to confuse the tumor with a hepatic multilobed cyst [22]. However, these cystic images do not modify during all the study phases [33]. Frequently, the tumoral mass displaces the neighboring organs (Fig. 4a) and compresses nearby arterial and venous vessels (Fig. 4b) [22, 28, 31]. Occasionally, the biliary tract might be obstructed by the mass and the patient presents a dilated bile duct and jaundice [31]. Computed angiography and tridimensional reconstruction might be useful to identify the tumor vascularization and their origin from the hepatic artery (Fig. 5) [22, 30].

Table 6 Radiological studies and characteristics of solitary fibrous tumors of the liver

Radiological study	Characteristics
Ultrasound [10–18, 20, 21, 24, 30, 31, 35, 38]	– Solid well-defined ovoid heterogeneous mass – In some cases, homogenous and hyperechoic – Presence of cystic images
Abdominal computed tomography scan [20–22, 24, 25, 27, 28, 30–35, 37, 38, 40, 41, 46, 47]	– Hypodense, heterogeneous, hypervascularized, well-defined, and delimited hepatic mass – Presence of necrosis within the tumor and calcifications in the capsule – Displacement of neighboring organs and compression of nearby arterial and venous vessels – Obstruction and dilation of the common bile duct
Abdominal magnetic resonance [10, 31, 35, 38]	– T1-weighted images: heterogeneous hypodense mass – T2-weighted images: hypodense, hyperdense, and isodense areas – Presence of necrosis or cystic degeneration
Positron emission tomography [38]	– Not well-defined role – Increase of tumoral density compared with normal hepatic parenchyma – Probably useful to identify distant metastasis

Abdominal Magnetic Resonance

Radiological findings on abdominal MR are similar to the ones described for abdominal CT [27, 35, 47]. Tumoral enhancement increases progressively in MR; this suggests the presence of a fibrous stroma composed of collagen [38]. In T1-weighted images, SFTL is observed as a heterogeneous hypodense mass compared with normal hepatic parenchyma [10, 35, 38], while T2-weighted images show hypodense, hyperdense, and isodense areas compared with cerebrospinal fluid [10, 31]. These hypodense and hyperdense areas suggest the presence of necrosis or cystic degeneration [35]. The injection of a gadolinium contrast bolus causes marked and progressive increase of SFTL density starting at the center of the tumor and spreading towards the periphery, and concurrent increase in heterogeneity [31, 33, 38].

Positron Emission Tomography

The clinical utility of PET in SFTL has not been established. An increase of SFTL density compared with normal hepatic parenchyma has been described [38]. Possibly, in cases suspected of malignity or during the staging study of malignant SFTLs, PET would be useful to identify distant metastasis.

Fine-Needle Biopsy

Few reports describe the use of fine-needle biopsy during the diagnostic study of SFTL [10]. The histological findings described diffuse proliferation of spindle-like cells randomly arranged within collagen bundles with immunohistochemistry staining positive for CD34, bcl-2, and CD 99 and negative for S100, desmin, and CD117. In this case, the procedure was useful to confirm the diagnosis of SFTL.

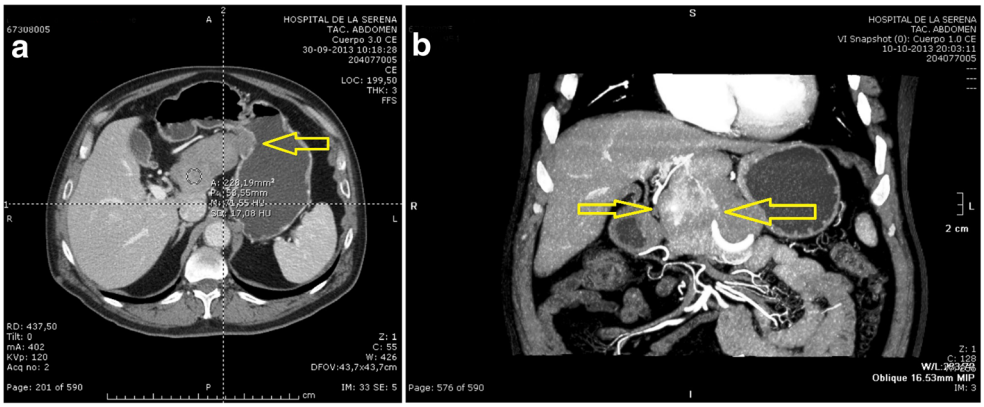

Fig. 4 **a** A large solitary fibrous tumor of the liver compressing and displacing the stomach wall. **b** Blood vessels compressed by an adjacent tumor

Treatment

Most SFTLs are considered benign tumors with malignant potential. Due to its rarity, large series with long-term follow-up have not been published neither clinical trials have been undertaken. For these reasons, the diagnosis, study, treatment, and prognosis are not clearly established. Surgical indications in benign hepatic tumors, such as adenoma, hemangioma, and focal nodular hyperplasia, are given by the inability to rule out malignancy or when symptoms associated with to the tumor affects the patient' quality of life or constitute a threat to his or her life [48–50]. It has been shown that surgical removal of benign liver tumors is safe and advisable [43, 50, 51]. However, surgical indication should be carefully evaluated in each case [51]. In SFTL, surgical resection is the only therapeutic option available. For this reason, resective surgical therapy has been used in all reported cases. However, surgery is not free of potentially severe complications [36]. A variety of surgical procedures for removal of SFTL have been described, in all cases an R0 resection must be achieved, which improves the prognosis and increases the 5-year survival [52]. In patients where the tumor involved a portion of the right or left hepatic lobe, the solution was a left or right hepatectomy or any combination of segmentectomies, according to the degree of hepatic involvement by the tumor [7, 8, 10–29, 31–35, 37, 41, 43, 46]. In one case treated at our Institution, the SFTL hung from the caudate lobe, so pedicle resection of the tumor was considered sufficient (Figs. 2 and 3).

Prognosis

Solitary fibrous tumors have an uncertain prognosis due to their unpredictable behavior [20, 25, 30, 43, 53]. The malignant potential of SFTL is unknown [8, 21, 25, 43, 53]. Approximately 10 to 15 % of all malignant SFT present initially with malignant behavior that manifest as recurrence, metastasis, or intractable hypoglycemia [7, 8, 42]. Metastases occur most frequently in the lungs, bone, skull, and liver [32, 37]. Usually, cellular type SFTs are more aggressive and are habitually located in the mediastinum, peritoneum, retropritoneum, and pelvis [42]. Only in exceptional cases that malignant progression from initially benign tumors has been demonstrated and was manifested by loss of CD34 positivity due to overexpression of p53 and p16 genes [53]. Surgical resection is the mainstay of treatment and recurrence-free survival exceeds 90 % with complete resection [54]. For that reason, the single most important prognostic factor in SFTLs is the complete tumor resection with free of disease margins; consequently, a

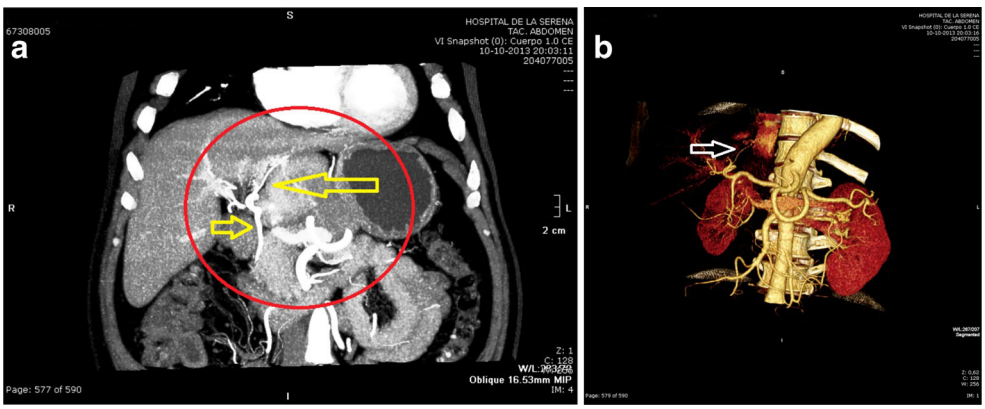

Fig. 5 **a** Arterial supply of a solitary fibrous tumor of the liver originating from the hepatic artery. **b** Tridimensional reconstruction showing the arterial vessel irrigating the tumor

R0 resection is fundamental because the malignant transformation into a high-grade sarcoma carries a poor prognosis [7, 8, 21, 23, 24, 27, 33, 42, 52]. Besides positive resection margins, other risk factors known to increase the risk of local recurrence and metastases are tumors higher than 10 cm and tumors with a high mitotic rate [55]. England's criteria constitute the available criteria to predict the prognosis of SFT [46]. Positive England's criteria associated to *borderline* histology have been related to high risk of recurrence [54]. Nonetheless, about 10 % of SFTs will recur locally or distally, often more than 10 years after surgery [54]. Malignant primary SFTL is a rare occurrence with only 4 cases reported and documented in the scientific English literature [7, 8, 32, 37]. Malignant SFTLs have a very aggressive presentation with poor prognosis in the short-term. For all of these reasons, the methodical long-term follow-up of surgically treated SFTLs is strongly recommended [23, 24, 27, 35, 36, 38].

Recent Evolutions and Future Challenges

There is no evidence of any benefit from chemotherapy for SFTL [8, 23, 27, 34]. Solitary fibrous tumors have a very low sensitivity to conventional chemotherapy [56]. Nonetheless, there have been experimental studies with sunitinib malate in SFT in locations other than the liver with promising results [57]. Sunitinib malate is an inhibitor of the tyrosine kinase with activity against the platelet-derived growth factor receptor alpha and beta (PDGFRA and PDGFRB), and has been used successfully as a second-line treatment in gastrointestinal stromal tumors. Studies performed by Silvia Stacchiotti in 35 patients have demonstrated that this chemotherapeutic agent has an excellent activity against SFTs with adequate long-term response at 4 years [57, 58]. Although none of the studied patients had a hepatic solitary fibrous tumor, data derived from these studies may be taken into account when treating patients with SFTL.

Conclusions

The SFTL is an uncommon neoplasm. The clinical presentation is habitually indolent and its behavior is uncertain. In some cases, the SFTL acts as an aggressive sarcoma with poor prognosis. Currently, only surgery offers a therapeutic opportunity for these patients. Due to the lack of current knowledge of long-term behavior of supposedly benign SFTLs and to the lack of specific therapies, methodical long-term follow-up is essential to ensure the survival of patients treated for SFTL.

Compliance with Ethical Standards

Conflict of Interest None

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