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CASE REPORT

Hepatic spleen nodules (HSN)

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Abstract

Hepatic splenosis is a nodular implant of normal spleen tissue in the liver. This innocent liver nodule is frequently misinterpreted as a malignancy. Almost all hepatic splenoses have been associated with a clinical history of splenic trauma or prior surgery. This report describes two cases of hepatic splenosis. In both patients, the nodular lesions were initially thought to be liver malignancies and they were ultimately assessed by histology. The clinico-pathological findings of all published cases of liver splenosis underwent critical review. Although they are rare, hepatic spleen nodules should always be included in the diagnostic spectrum of nodular liver lesions because of their impact on treatment decisions.

Key Words: *Granulomatous hepatitis, hepatic splenosis, splenic angioma*

Introduction

In 1939, Buchbinder and Lipkoff [1] defined as *hepatic splenosis* the occurrence of a nodular island of splenic tissue within the liver. Liver splenosis is rare and generally results from liver seeding of splenic tissue following either splenic trauma or elective splenectomy. Since they lack characteristic signs on diagnostic imaging, intra-hepatic splenic seeds are difficult to distinguish from other liver nodules and can ultimately only be confirmed by histology. Twenty-six cases of hepatic splenosis have been reported to date [2–26]. Liver splenosis is not simply an anatomical curiosity; its misinterpretation can have a potentially significant impact on a patient's clinical management.

This report describes two cases of hepatic splenosis, one in a patient who had previously undergone splenectomy. In both cases, the nodular liver lesions had been clinically misinterpreted as malignancies, and in both cases this would have had severe clinical consequences, significantly altering the clinical management of one, a cirrhotic patient, and preventing the other from being treated surgically for his primary esophageal cancer.

Case reports

Case 1

In February 2007, a 68-year-old female with no clinical history of surgery or abdominal trauma was referred to the Department of Surgical and Gastroenterological Sciences of the University of Padova because of recurrent abdominal pain. Computed tomography and MR confirmed a nodular liver lesion, previously documented in 2001; a needle liver biopsy (18 gauge needle; biopsy 1.8 cm long) was originally reported as 'granulomatous hepatitis'. A year later, a

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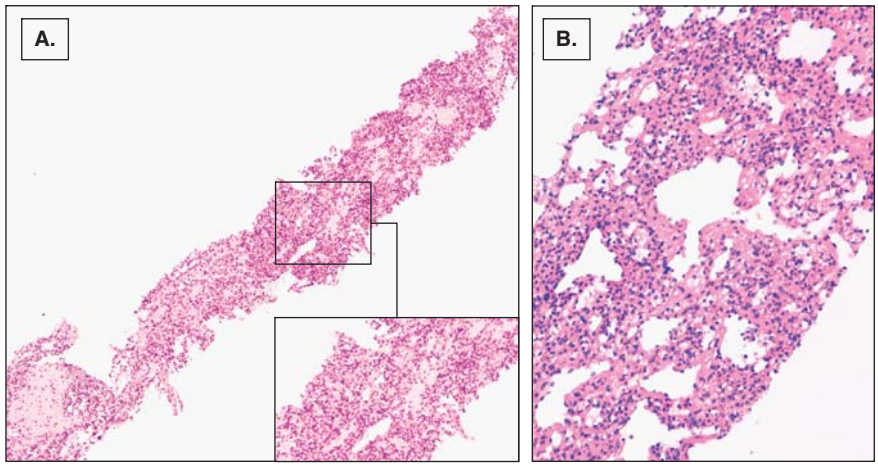

Figure 1. Fine needle biopsy of the the largest liver nodule of case 1 (A – H&E; original magnification ×10: loose connective tissue delimits lacunar spaces lined by reticular cells. A higher magnification (B – case 2, H&E; original magnification ×40) shows the same histology pattern closely resembling spleen parenchyma.

diagnosis of cirrhosis was clinically established and three nodular lesions (two in the left lobe, 6.2 and 2.3 cm in size; a pedunculated mass in the right lobe, 11 cm in size) were identified at US. All the lesions were iso-echogenic, with a necrotic core. The spleen measured 13 cm in its widest diameter. The presence of ascites was consistently confirmed both clinically and by US. The patient refused exploratory laparoscopy. In May 2008, a liver biopsy targeted on the largest nodular lesion produced a sample of connective tissue including vascular spaces (consistent with angioma). A repeat CT (February 2009) showed three nodular lesions (in segments III, V, and VII) hyper-enhanced in both the arterial and the portal phases. The largest nodule (15 cm in size) featured an evident hypo-dense central (necrotic) area. The CT scan (which ruled out the hypothesis of liver angioma) suggested a focal nodular hyperplasia. The spleen revealed four lesions 'compatible with angiomas'. A biopsy sample obtained from the lesion in segment VII contained loose connective tissue including sinusoidal lacunar spaces lined with reticular and endothelial cells. The histological findings were considered consistent with hepatic splenosis (Figure 1A).

Case 2

In November 2008, a 54-year-old man with a clinical history of splenectomy in 1996, for peritonitis caused by a perforation after Heller-Dor anti-reflux surgery, was referred to the Department of General Surgery and Organ Transplantation at the Padova University because of a recently-established histological diagnosis of esophageal primary squamous cell cancer (ESCC). CT showed no focal hepatic lesions. After neo-adjuvant chemotherapy, contrast-enhanced CT scan documented a hypervascular nodule 3 cm in size in the left liver lobe, consistent with metastasis. Based on this finding, the patient should have been rejected for any surgical treatment, but it was clinically unlikely that down-staging of the ESCC could coincide with a new-onset liver metastasis. PET-CT was performed and the results were negative. Given the uncertain nature of the liver nodule, the patient underwent surgery. Intra-operative histology (on frozen sections) revealed sinusoidal, spleen-like, vascular structures included in lymphoid-reticular tissue; the lesion was sharply distinguishable from the surrounding liver, with no capsular structure. Having ruled out any metastatic liver disease, the patient underwent radical esophagectomy. Routine liver histology was consistent with liver splenosis (Figure 1B). Eight months after surgery, the patient is alive with locally recurrent ESCC.

Discussion

Ectopic splenic tissue includes both congenital (accessory spleen) and acquired (splenosis) variants. Accessory (congenital) spleen usually results from a defective embryogenesis; it may be solitary or multiple and is most frequently located close to the primary spleen. The 'spleen in miniature' is supplied by a branch of the splenic artery and features both vascular hilum and a recognizable capsule.

Acquired splenosis consists of un-encapsulated splenic tissue located outside the spleen. It is reported in up to 67% of patients with traumatic splenic rupture [27] and more than 100 cases have been

Table I. Hepatic spleen nodules as reported in the literature.

Reference	M/F	Age	Splenectomy or splenic trauma	Risk factors	Time interval (months)	Size (cm)	No. of nodules	Site	Subcapsular location	Capsule	Diagnostic hypothesis	Diagnostic procedure
Yoshimitsu 1993	F	51	Splenectomy	Cirrhosis Banti's syndrome	23	2,5	1	L	Yes	Yes	HCC	Surgical excision
Lacerda 1993	F	64	Splenectomy	PSC; Hypersplenism	24	6,2	1	L	Yes	Yes	?	OLT
Davidson 1997	M	54	Abdominal surgery	None	20	2	1	L	Yes	No	/	Autopsy
Gruen 1997	F	38	Trauma	Oral contraceptive	20	3,9	1	L	Yes	?	Adenoma FNH	Surgical excision
D'Angelica 1998	F	38	Trauma	Oral contraceptive	20	3,6	1	L	Yes	?	Adenoma	Surgical excision
Foroudi 1999	F	59	?	Breast cancer	47	?	Multiple	R/L	Yes	?	Metastasis	FNAB + CT
De Vuysere 2000	M	50	Trauma	None	34	6	3	R/L	Yes	Yes	HS	Biopsy
Hierholzer 2001	?	?	?	?	?	?	?	?	?	?	?	?
Pekkafali 2002	M	21	Trauma	None	15	3,4	1	L	Yes	Yes	HS	US-CT-MRI
Lee 2002	M	43	Trauma	B hepatitis	20	3,5	1	R	Yes	Yes	HCC	Surgical excision
Nakata 2003	M	55	?	?	?	?	1	R	?	?	HS	CT, MRI, angiography
Kim 2003	M	43	Trauma	B hepatitis	21	3	1	R	Yes		HCC	Surgical excision
Di Costanzo 2004	M	58	Trauma	Cirrhosis B	46	4,8	1	L	Yes	Yes	HCC	Biopsy
	F	48	Trauma	B hepatitis	41	3,1	1	L	Yes	Yes	HCC	Biopsy
Izzo 2004	M	60	Trauma	C hepatitis	43	6	1	Hilo	Yes	Yes	HCC	Biopsy
Zhao 2004	?	?	?	?	?	?	?	?	?	?	?	?
Kondo 2004	M	55	Trauma	C hepatitis	31	3,5	1	R	Yes	?	Haemangioma HCC	SPIO-MRI
Brancatelli 2005*	F	38	Trauma	Oral contraceptive	32	5	1	L	Yes	?	Adenoma or FNH	Biopsy
Tieska 2005	M	?	Trauma	None	42	?	1	?	?	?	HCC HS	Surgical excision
Chun 2007	F	59	None	None	/	?	1	?	?	No	HCC	Surgical excision
Ishikawa 2007*	M	32	Trauma	C hepatitis	14	4	1	R	Yes	?	HCC	Biopsy
Choi 2008	M	32	Trauma	B-hepatitis	16	1-2-3	3	R	Yes	Yes	HCC	Surgical excision
Nakajima 2008	M	41	Trauma	None	21	?	1	R	Yes	?	HS	BIOPSY
Labat-Debelleix 2008	M	55	Trauma	C hepatitis Lung cancer	22	?	1	?	?	?	Malignancy	?
Grande 2008*	M	41	Trauma	None	35	4,5	1	R	Yes	Yes	HS	US, CT, Scintigraphy
Abu Hilal 2009*	M	60	Trauma	C hepatitis	46	2,7	1	R	Yes	Yes	HCC	Laparoscopy excision

*Case in which HSNs coexisted with peritoneal splenosis; risk factors: concomitant liver disease or risk factors for liver diseases; time interval: time elapsing between splenectomy or liver trauma and HSN detection; liver location: R = right lobe, L = left lobe.

described [14]. The incidence of this lesion is unknown because it is usually asymptomatic and is found incidentally during surgery for unrelated diseases or at autopsy.

Splenosis is interpreted as a splenic auto-graft following splenic trauma or elective splenectomy. After capsular/parenchymal disruption, spilt splenic pulp becomes implanted in the peritoneal cavity, growing in the form of multiple 'splenunculi' supplied by neoarteries and having neither hilum nor capsular structure. Abdominal splenosis is frequently multiple and randomly located on the serosal surfaces [28,29]. Depending on its different location, peritoneal splenosis has been misinterpreted as renal tumor [30,31], abdominal lymphoma [27], endometriosis [27], mural gastric mass [32], angioma, and metastatic cancer [33]. Extraperitoneal sites (after penetrating abdominal trauma) have also been reported, including subcutaneous tissue, pleural cavity and pericardium [33-35].

Twenty-six cases of hepatic splenosis have been described to date (Table I). Most patients had a clinical history of splenectomy. It has been suggested that hepatic splenosis results from the invagination in the liver of spleen tissue implants resulting from splenic traumas, and their sub-capsular liver location would be consistent with such a hypothesis. Alternatively, deep-seated hepatic splenic islands would result from the dissemination of spleen emboli (via the splenic vein) [33].

At the time of diagnosis, the 26 reported patients' mean age was 48 years (range 21–64); the male to female ratio was 2:1 (Table I). In patients who had undergone splenectomy, the mean interval between splenectomy and the liver nodule's detection was 29 years (range 14–47). In all cases, the lesion was nodular (ranging from 2 to 6.2 cm in size), and it was usually solitary; no site prevalence was documented. In all reported cases, these hepatic spleen nodules were not suspected clinically and the differential diagnosis included hemangioma [33], endometriosis [33], hepatic adenoma [5], focal nodular hyperplasia, hepatocellular carcinoma [14,22,26], lymphoma [36] and liver metastasis [7] (Table I). Because they lack any particular features on imaging, most hepatic spleen nodules (HSNs) were assessed by histology. It is important to emphasize that HSNs are innocuous and their non-surgical identification should rule out any subsequent surgical resection.

Radionuclide scintigraphy with sensitive heat-denatured technetium-99 m-labeled red blood cells is the most specific imaging technique. Superparamagnetic iron oxide (SPIO)-enhanced MRI is useful in distinguishing HSN from hepatic malignancies. The population of reticular cells (wherever they are located in the liver and spleen) phagocytose SPIO particles, showing loss of signal intensity on T2-weighted MRI (which does not occur in epithelial malignancies).

Hematological evaluation can be helpful in assessing any persistence of functioning splenic tissue by identifying damaged erythrocytes (Howell-Jolly bodies, Heinz bodies, and pitted cells), which are not seen, or are fewer than normally expected, after splenectomy.

Only one of the two cases described in the present report was associated with prior splenic trauma/surgery. Case 1 (who had not undergone splenectomy) had the largest lesion to have been reported in the literature so far (15 cm) coexisting with multiple splenic angiomas. It may be that the splenic angiomas were responsible for repeated splenic embolization, resulting in intrahepatic implants of splenic islands (in segments III, V and VII). None of the diagnostic procedures used were able to confirm the nature of the lesions, until histology was performed.

In conclusion, based on the available literature and the two cases described here, we recommend that HSN be defined as nodular implants of splenic tissue inside the liver; such a definition means that HSNs must be considered in the diagnostic spectrum of nodular liver lesions.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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