Management of intrahepatic splenosis: a case report and review of the literature

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Abstract

Background: Splenosis is the heterotopic autotransplantation and implantation of splenic tissue after splenic trauma or splenectomy. Considering that splenosis often occurs in the mesentery, omentum, and peritoneum, intrahepatic splenosis has seldom been reported. We report a rare case of isolated intrahepatic splenosis in a 54-year-old man who presented with a liver mass thought to be hepatocellular carcinoma.

Case presentation: A 54-year-old man was referred to our hospital for further evaluation of a liver lesion. The patient was asymptomatic and had a history of emergent splenectomy after a high-altitude falling accident. Abdominal contrast-enhanced computed tomography revealed a 4.5 × 3.3 cm lesion that was located in segment IV of the left liver lobe. The lesion had an inhomogeneous enhancement during the arterial phase and diminished enhancement during the portal and equilibrium phases. Similar radiological features were also observed on a contrast magnetic resonance imaging scan. Partial hepatectomy was performed with the suspicion of hepatocellular carcinoma. Pathological examination of the liver specimen revealed intrahepatic splenosis.

Conclusion: Splenosis should be considered in differential diagnosis of a liver mass discovered years after splenic trauma or surgery. A proposed scoring system may be helpful in evaluating the suspicious degree of intrahepatic mass to be splenosis. Invasive treatments are not recommended for asymptomatic patients, since the splenosis can provide beneficial immunologic function.

Keywords: Liver neoplasm, Intrahepatic splenosis, Splenectomy, Trauma

Background

Splenosis is the heterotopic autotransplantation of splenic tissue throughout the peritoneal and pelvic cavities, even the thoracic cavity, following splenic trauma or elective splenectomy [1]. The splenic fragments usually seed onto exposed vascularized peritoneal surface, receiving blood supply from the surrounding tissue. Intrahepatic splenosis is quite rare, as the majority of splenosis reported in the English literature was found to be located in the mesentery, omentum, and peritoneum [2]. The lack of typical radiological features makes it difficult to distinguish splenosis from liver tumors and reach a correct diagnosis. Herein, we present a case of isolated intrahepatic splenosis and summarize the relevant radiological and pathological characteristics. On the basis of literature review, imaging techniques that may contribute to the diagnosis and appropriate treatment measures are also discussed.

Case presentation

A 54-year-old Chinese male was referred to our hospital for further evaluation of a liver mass, which was discovered incidentally during routine physical examination in a local hospital. The patient had a 10-year history of hypertension and was diagnosed with diabetes mellitus approximately 5 years before. He denied history of liver cirrhosis and hepatitis B virus (HBV) or hepatitis C virus (HCV) infection. The patient underwent splenectomy 5 years earlier owing to a high-altitude falling accident. No mass was identifiable on abdominal palpation exam. Serum tumor markers (alpha-fetoprotein, CA199, and CA125) were within the normal range. Abdominal ultrasonography (US) revealed a 5 cm iso-echoic lesion that located in the left hepatic lobe near the capsule. A
1.2 cm gallstone was also observed. An abdominal plane-computed tomography (CT) scan revealed an oval, slightly hypodense mass located in segment IV of the left liver lobe measuring 4.5 × 3.3 cm. The lesion had an inhomogeneous enhancement during the arterial phase and diminished enhancement during the portal and equilibrium phases on a contrast-enhanced CT scan (Fig. 1). Abdominal magnetic resonance imaging (MRI) showed a slightly hypointense mass on both T1- and T2-weighted images, which appeared slightly hyperintense on diffusion-weighted images. After the injection of gadoxetic acid, the lesion appeared strongly heterogeneous and hyperintense during the arterial phase and relatively hypointense during the portal and equilibrium phases (Fig. 2). An indication of a pseudo-capsule was also observed. Partial hepatectomy and cholecystectomy were performed with the suspicion of hepatocellular carcinoma (HCC).

During the operation, the intrahepatic mass was found to be located in segment IV of the liver, measuring 4.0 cm in diameter. It was completely embedded in the liver tissue, and no other mass was found. Postoperative hematoxylin and eosin staining revealed sinusoidal structures and lymphoid tissue hyperplasia. A capsule separating the spleen tissue from liver tissue could be clearly detected (Fig. 3), which confirmed intrahepatic splenosis. Detailed immunohistochemical staining showed positivity for CD3 and CD20, specific markers for lymphocyte T cells and B cells, respectively. Meanwhile, the expression of the Ki-67 antigen was quite limited. The polyclonal nature of the lymphocytes and the low proliferation activity further confirmed the benign characteristic of the mass, as malignant tumors are always monoclonal with active proliferation. The patient discharged uneventfully after the operation, and no symptoms of recurrence have been observed during 2 years of follow-up.

**Literature review**

We searched the PubMed and Scopus databases for relevant English literature from the year 2000 through March 2018 using the Medical Subject Headings (MeSH) “Hepatocellular Carcinoma,” “Liver Neoplasm,” and “Splenosis.” In total, 37 cases of intrahepatic splenosis were identified and reviewed [3–37]. Characteristics of the cases such as age and sex of patients, clinical symptoms, diagnostic modality, and location of the masses were reviewed and analyzed (Table 1). There were 31 (83.8%) male and 6 (16.2%) female patients, and the mean age of the patients was 49.2 years (ranging from 21 to 73 years).

In the 37 documented cases, 35 (94.6%) patients had histories of trauma or/and splenectomy, and the mean time elapsing between trauma/splenectomy and diagnosis of intrahepatic splenosis was 24.9 years (ranging from 5 to 46 years). A total of 20 (54.1%) patients had related liver diseases, among which 8 (40%) had HBV infection, 11 (55%) had HCV infection, and 11 (55%) had cirrhosis. Most of the patients were asymptomatic upon admission, except for 6 (16.2%) who had abdominal pain. US, CT, and MRI were common imaging techniques, but they did not clearly differentiate intrahepatic splenosis from other liver lesions, such as HCC, liver metastases, or liver adenoma. Scintigraphy was used in 7 (18.9%) patients, and in 3 (42.9%) of them, the imaging led to the correct diagnosis without further invasive measures. The majority of intrahepatic splenosis were located in the subcapsular region of the liver, surrounded by capsules. A total of 34 (91.9%) patients had undergone invasive procedures. Surgery in 21 (61.8%) patients, including laparoscopic resection and laparotomy, was the most common invasive procedure followed by biopsy in 13 (38.2%).

**Discussion**

Splenosis represents the heterotopic autotransplantation and implantation of splenic tissue after elective splenectomy or traumatic spleen rupture. Once considered to be a rare condition, a recent estimated incidence is up to 67% of patients who have a history of splenic rupture or surgery [38]. Intrahepatic splenosis is still rare, as most of the splenoses were located in the mesentery, omentum, or peritoneum. Except for some extraordinary cases, almost all of the cases with intrahepatic splenosis have a history of splenic trauma or splenectomy [11, 19]. Hence, intrahepatic splenosis should be taken into
consideration in patients with a relevant history, especially if the mass is found to be located close to the liver capsule.

The absence of typical radiological features makes it difficult to reach a correct diagnosis with common imaging techniques, such as US, CT, and MRI. As a result, intrahepatic splenosis can be confused with HCC, adenoma, or other liver diseases, leading to unnecessary surgery or other invasive treatments. Therefore, more sensitive novel methods to diagnose intrahepatic splenosis are needed. Scintigraphy with sensitive technetium-99 m-labeled heat-denatured red blood cells (Tc-99 m-DRBC) is reported to be the most specific and efficient diagnostic method [20]. As approximately 90% of damaged erythrocytes will be trapped by splenic tissue, remarkable differences in uptake of the radioactive isotope can be observed between intrahepatic splenic tissue and normal liver tissue. Krawczyk et al. [14], Grande et al. [27], and Pekka-fali et al. [35] reported three cases that successfully avoided invasive treatments by using Tc-99 m-DRBC scintigraphy. Scintigraphy with sulfur colloid is considered to be another useful diagnostic method, but has a lower sensitivity in identification of splenosis [39]. Superparamagnetic

![Fig. 2 Magnetic resonance imaging scan of intrahepatic splenosis. Note a slightly hypointense mass on both T1-weighted (a) and T2-weighted (b) images. After the injection of gadoxetic acid, the mass became strongly heterogeneous and hyperintense during the arterial phase (c) and relatively hypointense during the portal phase (d).](image)

![Fig. 3 Histopathological features of intrahepatic splenosis. Hematoxylin and eosin staining. a A capsule clearly separated the liver (white arrow) and spleen (black arrow) parenchyma, x 100. b Intrahepatic splenosis with lymphoid tissue hyperplasia and sinusoidal structures, x 400.](image)
| Author, year | Age (years), gender | Trauma, splenectomy | Liver diseases | Time interval (years) | Symptoms | Diagnostic modality | Number | Subcapsular location | Capsule Diagnostic hypothesis | Segment, size (mm) | Invasive measure | Follow-up |
|--------------|---------------------|---------------------|---------------|----------------------|----------|---------------------|--------|---------------------|-----------------------------|---------------------|----------------|-----------|
| Teles 2018 [1] | 73, M | Splenectomy | No | N/D | Lower back pain | US, CT, MRI, scintigraphy | 2 | Yes | Yes | hepatic neoplasia | II, III | Surgery | No symptoms for 2 years |
| Wang 2017 [4] | 54, M | Both | HBV | 23 | Abdominal pain | US, CT, MRI | 1 | Yes | Yes | HCC | Right posterior lobe 31 × 27 | Surgery | No symptoms for 18 months |
| Wang 2017 [5] | 42, M | Both | HBV/BCV | 16 | Lower back pain | CT, MRI | 1 | Yes | Yes | HCC | IV | Surgery | N/D |
| Keck 2017 [6] | 66, M | Both | HCV | N/D | No | MRI | 2 | Yes | N/D | HCC | VII, VIII | Biopsy | N/D |
| Jereb 2016 [7] | 22, M | Both | No | 18 | No | US, CT, MRI | 5 | Yes | N/D | Liver metastases | II, VI, VII | Surgery | N/D |
| He 2016 [8] | 51, M | Both | No | 20 | No | US, CT, MRI | 2 | N/D | N/D | HCC | Left lobe, right lobe 33 × 26 | Biopsy | N/D |
| Liu 2015 [9] | 33, M | Both | No | 30 | No | US, CT, MRI | 3 | Yes | N/D | HCC/Liver metastases | III, Right lobe 42 × 30 | Biopsy | No symptoms for 2 years |
| Li 2015 [10] | 67, F | Both | HCV, cirrhosis | 5 | No | CT, MRI angiography | 1 | N/D | Yes | HCC | Left lobe | Surgery | No symptoms for 3 years |
| Sato 2014 [11] | 58, M | Neither | HCV, cirrhosis | No | No | US, CT, MRI | 1 | Yes | Yes | HCC | Right lateral lobe 39 × 30 | Surgery | No symptoms for 1 year |
| Levi Sandri 2014 [12] | 54, M | Both | HBV, cirrhosis | 25 | N/D | CT | 1 | N/D | Yes | HCC | III | 45 × 35 × 15 | Surgery | N/D |
| Leong 2013 [13] | 56, M | Both | No | 25 | Abdominal pain | US, CT, MRI, PET | 1 | N/D | N/D | Neuroendocrine tumor | III | 46 × 37 × 31 | Surgery | No symptoms for 6 months |
| Krawczyk 2013 [14] | 39, F | Both | No | N/D | Abdominal pain | CT, MRI, scintigraphy | 1 | Yes | N/D | Hepatocellular adenoma | II | 32 × 20 | No | No symptoms for 3 months |
| Inchingoilo 2013 [15] | 53, M | Both | Non alcoholic steatohepatitis | 33 | No | US, CT, MRI | 1 | Yes | N/D | HCC/hepatic adenoma | III, IV | 35 | Surgery | N/D |
| Liu 2012 [16] | 49, F | Both | No | 20 | Subxiphoid pain | US, CT | 3 | Yes | N/D | Liver tumor | Left lateral lobe 50 × 50 | Surgery | No symptoms for 4 months |
| Liu 2012 [17] | 38, M | Both | HBV | 14 | No | US, CT | 1 | Yes | Yes | Liver tumor | Left lateral lobe 33 × 27 | Surgery | N/D |
| Kang 2011 [18] | 54, M | Both | No | 15 | No | US, CT, MRI, PET-CT | 2 | Yes | Yes | Liver metastatic nodules | II | 23 × 19 | Surgery | N/D |
| Mescoli 2010 [19] | 68, F | Neither | Hepatitis, cirrhosis | No | Abdominal pain | US, CT, MRI | 3 | N/D | N/D | Liver tumor | III, V, VII | 150 | Biopsy | N/D |
| Mescoli 2010 [19] | 54, M | Splenectomy | No | 12 | No | CT, PET-CT | 1 | N/D | No | Liver metastatic nodule | Left lobe 30 | Surgery | No symptoms for 8 months |
| Author, year | Age (years), gender | Trauma, splenectomy | Liver diseases | Time interval (years) | Symptoms | Diagnostic modality | Number | Subcapsular location | Capsule | Diagnostic hypothesis | Segment, size (mm) | Invasive measure | Follow-up |
|-------------|---------------------|---------------------|---------------|----------------------|----------|---------------------|--------|---------------------|---------|-----------------------|------------------|-----------------|-----------|
| Yu 2009 [20] | 54, M               | Both                | No            | 20                   | No       | US, CT, MRI         | 1      | Yes                 | Yes     | N/D                   | Left lobe 40     | Surgery         | No symptoms for 6 months |
| Merth 2009 [21] | 43, M             | Both                | HCV, cirrhosis | 30                   | Fatigue  | US, CT, MRI angiography, scintigraphy | Multiple | Yes                 | N/D     | HCC                   | II 36            | Biopsy          | No symptoms for 9 months |
| Kashgari 2009 [22] | 52, M           | Both                | HCV, cirrhosis | 30                   | No       | US, MRI             | 1      | Yes                 | N/D     | HCC                   | VII 21 \times 15 | Biopsy          | No symptoms for 4 months |
| Abu Hial 2009 [23] | 60, M          | Both                | HCV, cirrhosis | 46                   | Flu-like symptoms | US, CT, MRI | 1      | Yes                 | Yes     | HCC                  | VII 30          | Surgery        | No symptoms for 2 years |
| Yeh 2008 [24] | 64, M              | Both                | HCV            | 8                    | No       | US, CT, MRIangiography | 1      | Yes                 | Yes     | HCC                 | VI 25           | Surgery        | N/D       |
| Nakajima 2008 [25] | 41, M            | Both                | N/D            | 21                   | Abdominal pain and diarrhea | US, CT, MRI | 1      | Yes                 | N/D     | N/D                  | VI N/D           | Biopsy          | N/D       |
| Imbricco 2008 [26] | 39, M            | Both                | No             | 24                   | Abdominal pain | US, CT, MRI | Multiple | Yes                 | N/D     | Liver metastatic nodules | Left lobe, right lobe 30 | Surgery | N/D       |
| Grande 2008 [27] | 41, M             | Both                | No             | 35                   | No       | US, CT, scintigraphy | Multiple | Yes                 | N/D     | N/D                  | VII 45          | No             | N/D       |
| Choi 2008 [28] | 32, M             | Both                | HBV            | 26                   | No       | CT, MRIangiography | 3      | Yes                 | Yes     | HCC                  | IVa, IVb, VI 30 | Surgery | N/D       |
| Brancatelli 2005 [29] | 38, F         | Both                | No             | 32                   | No       | CT, MRI angiography | 1      | Yes                 | N/D     | Liver adenoma | Left lobe 50 | Biopsy          | N/D       |
| Zhao 2004 [30] | 49, M             | Both                | No             | 17                   | No       | US, CT             | 1      | Yes                 | Yes     | Liver adenoma/HCC | VII 50 \times 30 \times 30 | Surgery | No symptoms for 1 year |
| Kondo 2004 [31] | 55, M             | Both                | HCV            | 31                   | No       | US, CT, MRI(SPIO) angiography | 2      | N/D                 | N/D     | HCC                  | VII 35 \times 35 | Biopsy          | N/D       |
| Izzo 2004 [32] | 60, M             | Both                | HCV            | 43                   | Jaundice | US, CT, MRI         | 1      | N/D                 | N/D     | HCC                  | Near the hilum 60 | Biopsy          | N/D       |
| Di Costanzo 2004 [33] | 58, M           | Both                | HBV, cirrhosis | 46                   | No       | US, CT, scintigraphy | 1      | Yes                 | N/D     | HCC                  | III 48             | Biopsy          | N/D       |
| Di Costanzo 2004 [33] | 48, F           | Both                | HCV, cirrhosis | 41                   | No       | US, CT             | 1      | Yes                 | Yes     | HCC                  | III 31             | Biopsy          | N/D       |
| Kim 2003 [34] | 43, M             | Both                | HBV, cirrhosis | 21                   | No       | US, CT, angiography | 1      | Yes                 | Yes     | HCC                  | Right lobe 30 | Surgery | N/D       |
| Pekkafali 2002 [35] | 21, M            | Both                | No             | 15                   | Epigastric pain | US, CT, MRI, scintigraphy | 1      | Yes                 | Yes     | No                 | Left lobe 34 \times 23 | No              | N/D       |
Table 1 Clinical data of 37 cases of intrahepatic splenosis (Continued)

| Author, year | Age (years), gender | Trauma, splenectomy | Liver diseases | Time interval (years) | Symptoms | Diagnostic modality | Number | Subcapsular location | Capsule | Diagnostic hypothesis | Segment, size (mm) | Invasive measure | Follow-up |
|--------------|--------------------|---------------------|------------------|--------------------|----------|---------------------|--------|---------------------|---------|----------------------|------------------|----------------|----------|
| Lee 2002 [36] | 43, M | Both | HBV, cirrhosis | 20 | Fatigue | US, CT, angiography | 1 | Yes | Yes | HCC | VI 33 × 20 | Surgery | N/D |
| De Vuyser 2000 [37] | 50, M | Both | No | 34 | No | US, CT, MRI(SPIO) | 3 | N/D | Yes | Left lobe, right lobe | Biopsy | N/D |

HBV hepatitis B virus, HCV hepatitis C virus, HCC hepatocellular carcinoma, US ultrasonography, CT computed tomography, MRI magnetic resonance imaging, PET positron emission tomography, M male, F female, N/D not disclosed

aTime interval: time elapsing between trauma/splenectomy and diagnosis of intrahepatic splenosis
bWhen multiple lesions, only the size of the largest one was presented
cSurgery: included laparoscopic resection and laparotomy
iron oxide (SPIO) contrast magnetic resonance imaging may be helpful for the diagnosis of splenosis. As reported, intrahepatic splenosis will remain hyperintense relative to the liver parenchyma, while HCC will become hypointense after the SPIO administration [37]. In fact, most of the cases with intrahepatic splenosis that had been reported were treated with invasive procedures, including biopsy and surgical resection. However, intrahepatic splenosis may be beneficial in the patients who have undergone splenectomy, since it can replace part of the immunologic function of the removed spleen [40]. Hence, conservative treatment is strongly recommended for asymptomatic intrahepatic splenosis, except for some special situations, such as idiopathic thrombocytopenic purpura and Felty syndrome.

In order to avoid unnecessary invasive treatment, accurate diagnosis is essential. Although some novel imaging methods, such as scintigraphy, have shown promising application prospects in diagnosis of intrahepatic splenosis, they will not likely be used worldwide for quite some time. Instead, we think it may be helpful to use a scoring system to evaluate the suspicious degree of intrahepatic mass to be splenosis (Table 2). Compared with the CT/MRI Li-Rads v2017 [41], our scoring system seems to be more effective in diagnosing intrahepatic splenosis. The major imaging features (washout, enhancing “capsule” and threshold growth) of Li-Rads were not enough to distinguish intrahepatic splenosis from liver neoplasm. According to the table, the higher the total score is, the stronger is the possibility that the mass will be splenosis. When the total score is greater than 3, it is better to use biopsy to clarify the diagnosis, instead of taking more aggressive measures directly.

**Table 2** Suspicious degree of intrahepatic mass to be splenosis

| Parameters                                | Score | Methods       |
|-------------------------------------------|-------|---------------|
| Alpha-fetoprotein                         |       |               |
| > 400 μg/L for 4 weeks                    | No    | ELISA         |
| > 200 μg/L for 8 weeks                    | Yes   | US, CT, MRI  |
| Cirrhosis                                 | Yes   | ELISA, PCR    |
| Hepatitis                                 | No    | History taking/US, CT, MRI |
| Splenic trauma                            | Yes   | History taking/US, CT, MRI |
| Splenectomy                               | Yes   | History taking/US, CT, MRI |
| Mass location                             |       |               |
| Non-subcapsular                           | No    | US, CT, MRI  |
| Subcapsular                               | Yes   | US, CT, MRI  |
| Mass capsule                              | Yes   | US, CT, MRI  |
| Howell-Jolly and Heinz bodies after splenectomy | Yes   | Hematological examination |

For alpha-fetoprotein, exclude pregnancy, acute severe hepatitis, embryonic gonad tumors, and other digestive system tumor

**Conclusion**

Although isolated intrahepatic splenosis is rarely encountered, it should be taken into account in the differential diagnosis of a liver lesion, especially if the patient has a history of splenic trauma or splenectomy. The proposed scoring system may be useful in diagnosing intrahepatic splenosis when effective diagnostic methods, like scintigraphy and SPIO MRI, are lacking. If intrahepatic splenosis has been confirmed, conservative treatment is strongly recommended for the patient without any symptoms.

**Abbreviations**

CT: Computed tomography; ELISA: Enzyme-linked immunosorbent assay; PCR: Polymerase chain reaction; F: Female; HBV: Hepatitis B virus; HCC: Hepatocellular carcinoma; HCV: Hepatitis C virus; M: Male; MeSH: Medical Subject Headings; MRI: Magnetic resonance imaging; N/D: Not disclosed; PET: Positron emission tomography; SPIO: Superparamagnetic iron oxide; Tc-99 m-DRBC: Technetium-99 m-labeled heat-denatured red blood cells; US: Ultrasonography

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**Authors’ contributions**

SSZ performed the partial hepatectomy and cholecystectomy, and designed the analysis. ZFX and JC drafted the manuscript. DWL reviewed the literature. PHS and YHD supervised the draft and managed the patient’s follow-ups. LW participated in the interpretation of pathological data. All authors read and approved the final manuscript.

**Ethics approval and consent to participate**

The ethics committee of First Affiliated Hospital, School of Medicine, Zhejiang University approved the study.

**Consent for publication**

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

**Competing interests**

The authors declare that they have no competing interests.

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