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Hepatic schwannoma: A case report and an updated 40-year review of the literature yielding 30 cases

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Abstract. Hepatic schwannoma is a rare benign disease with a good prognosis. Early diagnosis is difficult due to the absence of specific clinical presentations and its rarity. The present study briefly described a 64-year-old female patient with hepatic schwannoma mimicking intrahepatic cholangiocarcinoma. Furthermore, the clinical data of 30 patients with hepatic schwannoma were also reviewed and analyzed. The mean age of the 30 patients was 51.7 years (range, 21-83 years) and ~2/3 were female. All patients in the benign group underwent surgical treatment and survived until the last follow-up, of whom 19 received complete resection and the remaining 1 underwent liver transplantation. However, in the malignant group, only three cases who underwent the surgical resection remained alive at last follow-up. Another seven cases were succumbed to mortality, 4 cases of whom had deteriorated to have no operation opportunity by the time they saw a doctor, and among the remaining three cases with hepatectomy, 1 died of liver dysfunction at 21 days postoperatively, 2 succumbed to recurrences at 18 and 23 months postoperatively. In conclusion, hepatic schwannoma is a rare benign disease with a good prognosis. However, once the malignant transformation occurs, the prognosis is not satisfied. Complete resection is the mainstay for cure and liver transplantation is often necessary.

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Key words: hepatic schwannoma, liver tumor, malignant transformation, liver transplantation

Introduction

Schwannomas are benign, encapsulated and slowly growing neoplasms which are composed exclusively of Schwann cells. Schwannomas usually occur in the upper extremities, trunk, head and neck, retroperitoneum, mediastinum, and pelvis (1). It has been reported to occasionally occur in the rectum, pancreas, bile duct and stomach; however, schwannomas arising from the liver parenchyma are extremely uncommon. Hepatic schwannoma may cause non-specific clinical symptoms. Since hepatic schwannoma is such a rare finding, a definitive diagnosis by radiological methods is difficult and they are sometimes misinterpreted as liver metastases or primary liver cancer. Surgery is typically required in order to establish the diagnosis and treatment (2).

The present study found only 30 cases reported in the literature to date after carefully excluding those papers which are duplicated and with insufficient clinical data. The present study described a case of hepatic schwannoma and provide a pertinent review of the literature.

Case report

On March 12th 2015, a 64-year-old Chinese male was referred to The First Affiliated Hospital of Zhejiang University (Hangzhou, China), with complaints of upper abdominal pain for a month. A month ago, the patient suffered from upper abdominal pain without obvious reasons and no chills, no fever, no vomiting, no cough or other symptoms. No family history or obvious evidence of neurofibromatosis was present. The abdominal physical examination revealed no marked findings and all laboratory data were normal, including tumor markers and liver function. The computed tomography (CT) scan (Fig. 1A-C) revealed an 11.5x9.5 cm mass in the left liver, slightly enhanced in the arterial phase, progressive enhanced in the portal and equilibrium phase, and the left branch of the portal was not visible. The hilar and retroperitoneal area revealed a shadow of multiple lymph nodes. So cholangiocarcinoma was considered initially with the left portal vein branch violation. Magnetic resonance imaging (MRI) (Fig. 1D-F) also revealed an 11.5x9.5 cm mass, with a low signal on T1-weighted images and higher signal on T2-weighted images. The left

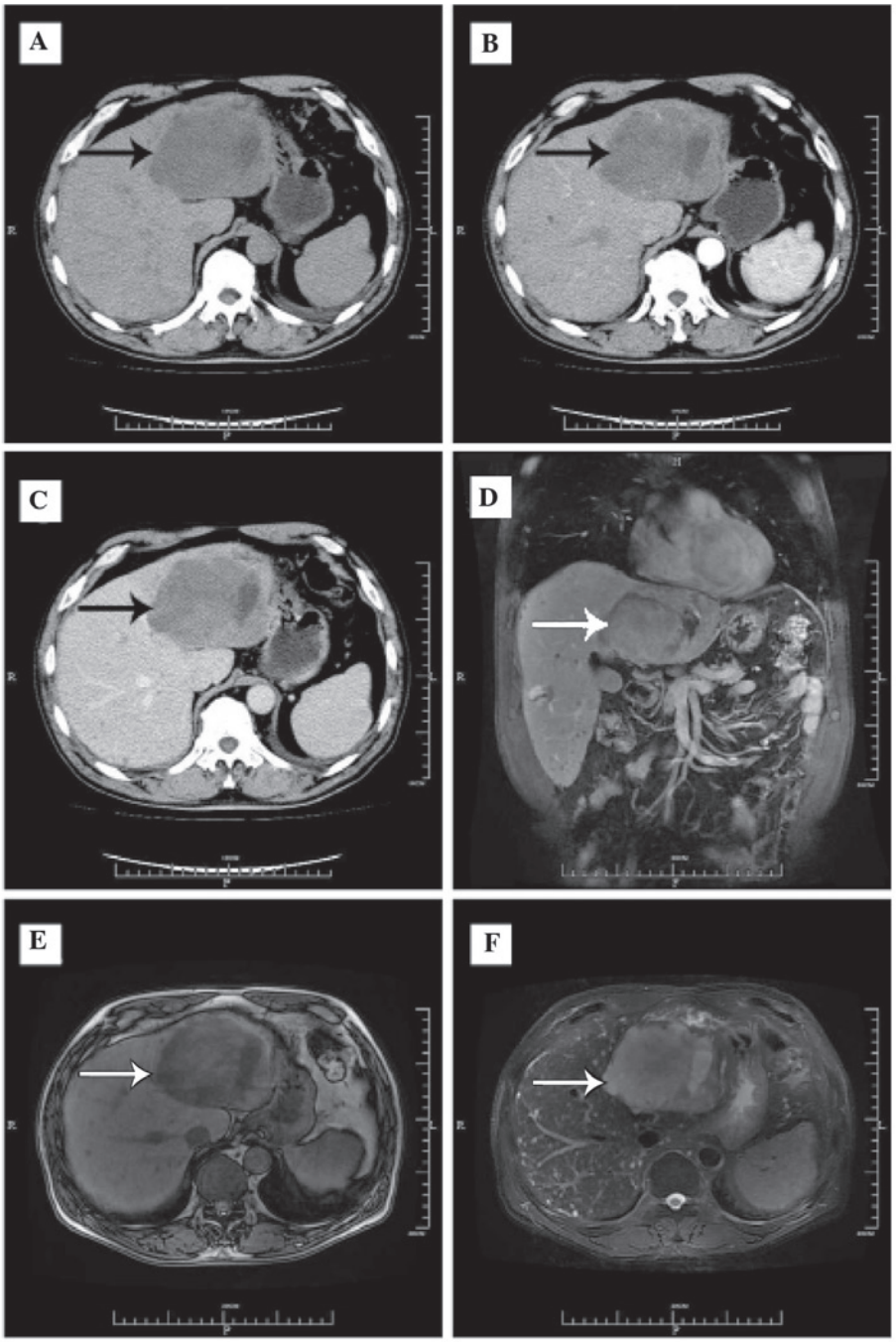

Figure 1. Abdominal CT and MRI findings of the patient. (A) An abdominal CT scan revealed an 11.5x9.5 cm mass in the left liver (arrow). (B) An enhanced abdominal CT scan revealed a mild heterogeneous enhancement signal (arrow) and a (C) wash-out pattern in the portal phase (arrow). (D) MRI revealed an 11.5x9.5 cm mass in the sagittal section (arrow), (E) low-signal intensity in T1-weighted axial imaging (arrow) and (F) high signal intensity in T2-weighted imaging (arrow). CT, computed tomography; MRI, magnetic resonance imaging.

portal vein branch was not observed. According to the history and radiographic examination of the patient, surgical resection was selected for diagnosis and cure together by the patient and the treatment team in various departments, including those of Hepatobiliary Surgery, Radiology and Chemotherapy. During the laparotomy, a hard protruding mass with a size of ~11.5x9 cm was observed on the II, III and IV segment of the liver. Therefore, a left hepatectomy and post-operative detailed histopathological examination was performed, and revealed hepatic benign schwannoma (Fig. 2): cytokeratin (pan)(-), Vimentin(+), CD117(-), S-100(+), Desmin(-), CD34(-) and smooth muscle actin [(SMA)-]. The patient was discharged on postoperative day 14. Until now, no symptoms of recurrence were observed in the patient.

Literature review

PubMed (https://www.ncbi.nlm.nih.gov/pubmed), MEDLINE (http://webofknowledge.com/MEDLINE), EMBASE (https://www.embase.com), The Cochrane center (https://china.cochrane.org), The Chinese Biology and Medicine Database (http://sinomed.imicams.ac.cn/zh/), The Chinese Wanfang

Table I. Summary of cases with hepatic schwannoma.

Author	Country	Sex/age	Presenting symptoms	Examination	Primary diagnosis	Size (cm)	Location	Treatment	Histology	Outcome	Ref
Current case	China	M/64	RUG pain	US/CT/MRI	ICC	11.5	Left	Surgery	Benign	Survival	-
Hytiroglou *et al*, 1993	USA	F/57	Right flank and back pain	US/CT	Liver tumor	13.0	Right	Surgery	Benign	Survival	(1)
Ozkan *et al*, 2010	Turkey	M/56	Epigastric pain	US/CT	Liver hydatid cyst	15.0	Left	Surgery	Benign	Survival	(2)
Ota *et al*, 2012	Japan	F/72	Incidental finding	US/CT/MRI/PET/CEUS	BCAC or ICC	4.5	Left	Surgery	Benign	Survival	(5)
Heffron *et al*, 1993	USA	F/38	RUG pain	CT/Biopsy	Schwannoma	5.0	Left	Surgery	Benign	Survival	(7)
Iddings *et al*, 2008	USA	M/83	Incidental finding	CT/Biopsy	Myxoid liposarcoma	7.0	Right	Surgery	Malignant	Survival	(8)
Kobori *et al*, 2008	Hungary	F/22	RUG pain/ Edema	CT/Biopsy	Atypical malignant tumor	2.6	Both	Surgery	Malignant	Survival	(9)
Morikawa *et al*, 1995	Japan	M/63	Abdominal pain	CT	ICC	20.0	Right	Autopsy	Malignant	Death	(10)
Zhang *et al*, 2008	China	F/59	Incidental finding	US/CT	ICC	8.0	Left	Surgery	Benign	Survival	(11)
Wada *et al*, 1998	Japan	F/64	Asymptomatic	US/CT/MRI	Liver tumor	4.0	Left	Surgery	Benign	Survival	(12)
Wada *et al*, 1998	Japan	F/69	Asymptomatic	US/CT	Liver tumor	15.0	Left	Surgery	Benign	Survival	(12)
Akin *et al*, 2009	Turkey	F/66	Incident finding	US/CT	Breast cancer metastasis	4.4	Left	Surgery	Benign	Survival	(13)
Kim *et al*, 2010	South Korea	M/52	Incident finding	US/CT	Malignant or inflammatory tumor (liver)	3.0	Left	Surgery	Benign	Survival	(14)
Xu *et al*, 2007	China	F/43	RUG pain	CT	GIST metastasis	5.0	Left	Surgery	Benign	Survival	(15)
Piao *et al*, 2009	China	F/43	RUG pain	US/CT	Liver tumor	4.2	Left	Surgery	Benign	Survival	(16)
Hayashi *et al*, 2012	Japan	M/64	Incident finding	US/CT/MRI/PET	GIST metastasis	2.3	Left	Surgery	Benign	Survival	(17)
Kapoor *et al*, 2005	India	F/mid-aged	Epigastric lump and dull pain	US/CT	Liver adenoma	23.0	Left	Surgery	Benign	Survival	(18)
Yoshida *et al*, 1994	Japan	F/56	Epigastrium and chest discomfort	US/CT	Liver tumor	16.0	Right	Surgery	Benign	Survival	(19)
Flemming *et al*, 1998	Germany	F/57	Upper abdominal pain	US/CT	Hydatid disease	Huge	Right	Surgery	Benign	Survival	(20)
Jin *et al*, 2001	China	M/42	RUG pain and fever	CT/MRI/Biopsy	Hepatapostema	6.7	Right	Surgery	Benign	Survival	(21)
Momtahen *et al*, 2008	USA	F/52	Back pain	CT/MRI/Biopsy	Schwannoma	4.4	Right	Surgery	Benign	Survival	(22)
Liu *et al*, 2005	China	F/27	RUG lump and dull pain	US/CT/Biopsy	Spindle tumor	30.0	Right	LT	Benign	Survival	(23)
Lee *et al*, 2008	South Korea	F/38	Vague epigastric pain	US/CT/Biopsy	Mesenchymal tumor	5.0	Right	Surgery	Benign	Survival	(24)
Young *et al*, 1975	England	M/23	RUG/Jaundice	Biopsy	Liver tumor	20.0	Both	Autopsy	Malignant	Death	(25)
Lederman *et al*, 1987	USA	M/21	RUG pain/Shaking chills	US/HA	NF	30.0	Both	HAE/ Autopsy	Malignant	Death	(26)
Yu *et al*, 1999	China	F/55	RUG pain	US/CT	Huge liver cyst	26.0	Right	Surgery	Malignant	Death	(27)
Fiel *et al*, 1996	USA	F/49	Obstructive jaundice	CT/Biopsy	Spindle tumor	14.0	Right	Surgery	Malignant	Survival	(28)
Fang *et al*, 1999	China	M/42	Abdominal pain after trauma	CT	Intrahepatic hematoma	14.0	Right	Surgery	Malignant	Death	(29)
Li *et al*, 2009	China	F/40	RUG pain	CT	Schwannoma	Huge	Right	TACE	Malignant	Death	(30)

M, male; F, female; HA, Hepatic angiography; RUG, Right upper quadrant pain; HAE, Hepatic artery embolization; TACE, Transcatheter arterial chemoembolization; ICC, Intrahepatic cholangiocarcinoma; BCAC, Biliary Cystadenocarcinoma; GIST, Gastrointestinal stromal tumors; NF, Neurofibrosarcoma; CEUS, Contrast-enhanced ultrasound; LT, liver transplantation; CT, computed tomography; MRI, magnetic resonance imaging; US, ultrasound; PET, positron emission tomography.

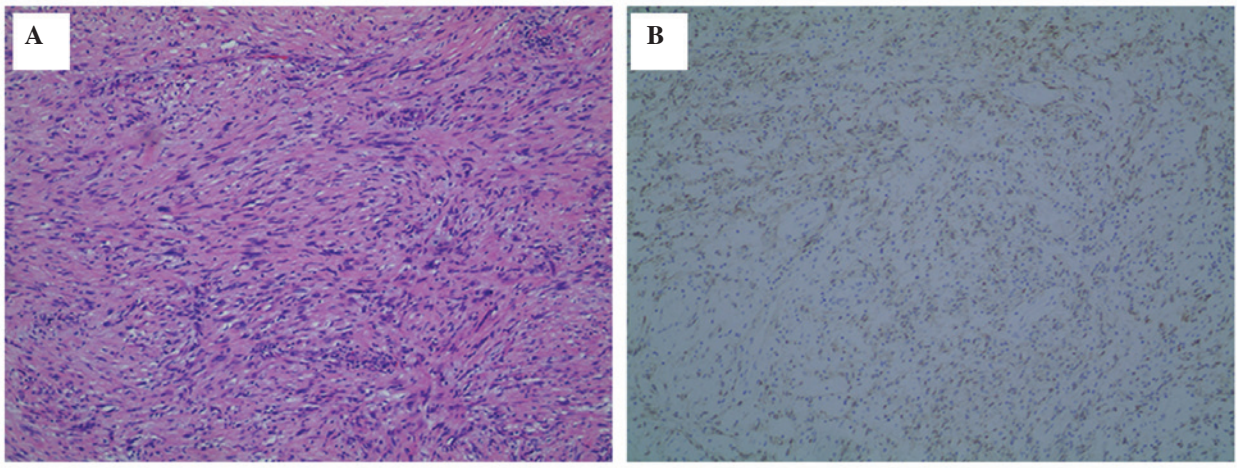

Figure 2. Histological examination of the tumor. (A) Hematoxylin and eosin staining revealed bundles of uniform spindle cells whose elongated nuclei were arranged in a palisading pattern (magnification, x100). (B) Immunohistochemistry revealed that tumor cells were positive for S100 protein (magnification, x100).

Database (http://g.wanfangdata.com.cn) and The China Hospital knowledge Database (http://www.chkd.cnki.net) were searched for cases of primary hepatic parenchyma schwannoma between January 1974 and December 2014. Reports which are duplicated or lacked clinical data were carefully excluded and 30 cases, along with the current case report, were identified (Table I).

Discussion

Verocay (3) first reported schwannoma as a true neoplasm in 1990. The name schwannoma is often termed differently in primary research, including neurilemmoma, neuroma, neurinoma and nerve sheath tumor. The latest 4th edition of the World Health Organization pathology classification put the peripheral nerve tumors, which included schwannomas, into the soft tissue tumor types, which further demonstrated the understanding of schwannomas (4).

Generally speaking, schwannomas are benign, encapsulated and slowly growing neoplasms, which are composed exclusively of Schwann cells. Schwannomas usually occur in the upper extremities, trunk, head and neck, retroperitoneum, mediastinum and pelvis. It has been reported that occasionally, schwannomas occur in the rectum, pancreas, bile duct and stomach; however, schwannomas arising from the liver parenchyma are extremely uncommon (1). Only 30 cases were found to be reported in the literature to date, following the careful exclusion of those papers which are duplicated and with insufficient clinical data.

Schwannomas occur at all ages, but are most common in individuals aged between 30 and 60-years-old, and the ratio between genders is ~1:1 (2). In the present study, the mean age of the 30 patients was 51.7 (range, 21-83 years), which was consistent with the previous report and ~2/3 was female. A total of 18 patients were from Asia, 6 from Europe and 6 from North-America, which may represent that hepatic schwannoma was more common in Asian; however, more evidence is required.

As described previously, the majority of patients were admitted with the complaint of pain or discomfort in the upper abdomen or epigastrium (5). In the present study, 8 patients were asymptomatic, whose liver tumors were found during routine examination or the follow-up when combined with other diseases. A total of 22 patients were symptomatic and symptoms included abdominal pain (91%), back pain (9%), chill and fever (9%), abdominal mass (9%), jaundice (9%), edema (5%), and weight loss (5%).

To differentiate from other primary liver tumors, including hepatocellular carcinoma and intrahepatic cholangiocarcinoma, liver metastases when the patient suffered certain types of malignant tumor, and hydatid disease of the liver when cystic transformation were present, auxiliary examinations including ultrasonography (US), CT, MRI and even positron emission tomography (PET)-CT are required. These techniques can determine tumor position, size, and an appropriate staging of the tumor extension and involved structures, which is of great assistance to diagnose and design an operation scheme. However, since hepatic schwannoma is such a rare finding, a definitive diagnosis by radiological methods is difficult. Liver biopsy may be useful for accurate preoperative diagnosis (5,6).

In the present study, 28 patients received CT for diagnosis in 30 cases with auxiliary examinations. US, MRI or PET-CT was also selected in certain cases. A total of 9 cases selected preoperative biopsy for diagnosis. Even though the imaging examination is more precise, only 2 patients had the exact diagnosis and other 28 patients were misdiagnosed with other diseases or no confirmed diagnosis.

The final diagnosis of depends on the pathology and immunohistochemistry. Microscopically, a typical schwannoma is composed of Antoni A and Antoni B areas. The Antoni A area is a hypercellular area, which contains a large number of closely packed spindle cells. By contrast, the Antoni B area is a loose myxoid structure with a few sparse cells. The proportion of the two components can shift gradually or change suddenly (7). Cystic degeneration, including calcification or hemorrhage, is often recognized in the Antoni B area, which may result from vascular thrombosis and subsequent necrosis. Immunohistochemical analysis is necessary to distinguish hepatic schwannoma from metastatic gastrointestinal stromal

tumor types and other soft tissue tumor types. A schwannoma is usually positive for S-100, negative for both CD34 and CD117. However, metastatic gastrointestinal stromal tumors are positive for S-100, and positive for either CD34 or CD117. A leiomyoma would be negative for S-100 and positive for desmin or SMA (8). When the hepatic schwannoma presented with numerous sub-foci around or grown rapidly or associated with a highly-aggressive course of recurrence during follow-up, it almost certainly was the malignant type (9).

In the present statistics, of the 9 malignant schwannoma cases, 1 was semi-malignant and 20 were benign. Although the tumor in certain cases was reported to be S-100 negative, other characteristics of it proved the malignant nature (9). When the patient wants to take a conservative treatment, the pathology and immunohistochemistry of the liver tumor tissue must be performed to exclude the malignant transformation, since survival with observation alone for malignant schwannoma is poor (10).

Since discriminating between a schwannoma and malignant liver neoplasm is difficult, surgery is typically recommended. In order to better observe the difference in the treatment and prognosis between the benign and malignant primary hepatic schwannoma, the 30 patients were divided into two groups. In the benign group, 13/20 cases with liver tumors were located in the left lobe and 7/20 were distributed in the right lobe. The maximal diameter of the tumors reported varied between 2.3 and 30 cm. All patients in the benign group underwent surgical treatment and survived until the last follow-up, of whom 19 received complete resection. The tumor of the remaining patient was too large (the maximal diameter was 30 cm) to be removed surgically, so that patient underwent liver transplantation and no recurrence was observed during the follow-up of 4 months. In the malignant group (10 cases, including one semi-malignant case), the location of hepatic schwannoma in 6/10 cases was the right lobe and in 4/10 was both lobes. The size ranged between 2.6 and 30 cm. However, only 3 cases who underwent surgical resection survived at the last follow-up. The other 7 cases succumbed to mortality; 4 patients deteriorated prior to operation, and in the 3 cases with hepatectomy, 1 succumbed to liver dysfunction at 21 days postoperatively and 2 succumbed to recurrences at 18 and 23 months postoperatively. These results suggested that hepatic schwannoma must be resected regardless of the admission diagnosis of benign or malignant, since if schwannomas are benign, surgical treatment can lead to long-term survival and if malignant, enucleation should be oncologically adequate and once radical surgery is impossible, palliative resection is still recommended. To detect recurrence, a CT scan every 3 months for the initial 2 years, every 6 months for 2-5 years and annually thereafter, is generally recommended.

In conclusion, hepatic schwannoma is a rare benign disease with a good prognosis. However, this disease deserves attention with regards to the differential diagnosis of liver tumors. Preoperative diagnosis is highly difficult and complete resection is the mainstay for cure, with liver transplantation sometimes being necessary.

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