

Primary Hepatic Leiomyosarcoma: a Case Report and Review of the Literature

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ABSTRACT

Background/Aim: Primary hepatic leiomyosarcoma is an extremely rare type of liver sarcoma with relatively poor prognosis, with about 50 cases having been reported in the literature. Potential origins of this tumor in the liver are the smooth muscle cells in the round ligament, intrahepatic blood vessels and intrahepatic bile ducts. There is no apparent sex predilection and there is a wide age range. The clinical presentation is not specific and the diagnosis depends on the expression of markers such as smooth muscle actin, desmin and vimentin by tumor cells.

Patients and Methods: Herein, we present a case of a bulky primary hepatic leiomyosarcoma in a 68-year-old female patient. The patient underwent resection of the exophytic mass en block with the hepatic segments III and IVB.

Conclusion: Surgical resection is the most effective among the treatment options.

KEYWORDS

hepatic; liver; leiomyosarcoma, primary

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INTRODUCTION

Primary hepatic sarcomas are rare tumors including various types, such as angiosarcoma, fibrosarcoma, liposarcoma, embryonal sarcoma, malignant fibrous histiocytoma, carcinosarcoma and epithelioid hemangioendothelioma (1). Primary hepatic leiomyosarcoma is another extremely rare type of liver sarcoma with relatively poor prognosis, with about 50 cases having been reported in the literature. Herein, we report a case of a bulky primary hepatic leiomyosarcoma in a 68-year-old female patient.

CASE REPORT

A 68-year-old female patient was referred to our department in order to treat a bulky liver tumor. The patient has been complaining for right upper quadrant heaviness and discomfort for 1 year. She underwent an abdominal ultrasound scan which revealed the presence of a hepatic mass located in the left lobe of the liver. Subsequently, she underwent an abdominal and thoracic computed tomography and an abdominal magnetic resonance tomography that confirmed the presence of a bulky, exophytic and heterogeneously attenuated mass

with irregular margins, originating from the hepatic segments III and IVB (Figure 1). The tumor was 13cm in diameter. The imaging studies excluded the presence of other primary sites. The patient had a medical history of chronic hepatitis B, type 2 diabetes mellitus and cholelithiasis. The patient's complete blood count test, biochemical tests and levels of carcinoembryonic antigen, alpha fetoprotein and cancer antigen 19-9 were within normal range.

The patient underwent resection of the exophytic mass en block with the hepatic segments III and IVB, from which the tumor appeared to be originated, along with cholecystectomy (Figure 2). The postoperative course was uneventful and the patient was discharged on the 7th postoperative day. The histopathological examination showed the presence of a whitish tumor, 13cm in diameter, with central cystic degeneration. The tumor was extended up to Glisson's capsule and up to 2mm from the resection margins. The neoplasm was a sarcoma made of large, atypical cells with abundant cytoplasm that occasionally were multinucleated (Figure 3A). The tumor included regions of spindle-shaped cells with fascicular arrangement and foci of osteoid production (Figure 3B). Extensive regions of necrosis were also present. No intracellular globules or entrapped bile ducts were detected. The neoplasm encased small blood vessels without infiltrating them. The mitotic count was 10 mitoses per 10 high-power fields (HPF). Furthermore, the immunohistochemical examination of the sarcoma revealed extensive expression of smooth muscle actin (Figure 3C) and limited expression of desmin (Figure 3D), but did not detect any expression of myoD1, myogenin, S-100 protein, c-kit or cytokeratins 7, 8, 18, 19 and 20, excluding diagnoses such as rhabdomyosarcoma, melanoma, gastrointestinal stromal tumor (GIST), carcinoma, etc. Therefore, a diagnosis of primary pleomorphic hepatic leiomyosarcoma was established.

The patient received six cycles of chemotherapy postoperatively with cyclophosphamide, doxorubicin and vincristine. Due to the presence of advanced tumor, she also received pazopanib, a multi-targeted receptor tyrosine kinase inhibitor, per os, which has been added as a treatment option for the

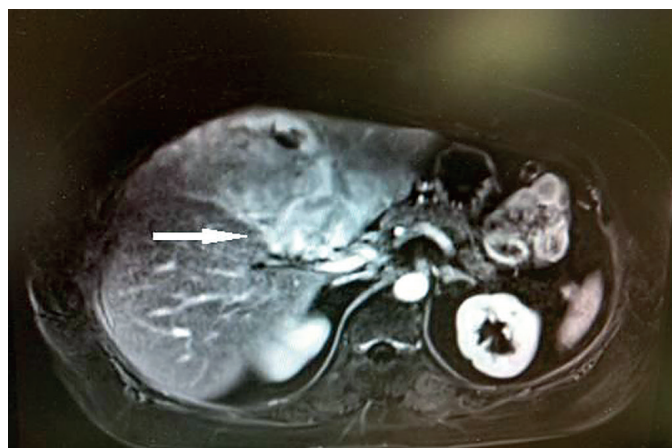


Fig. 1 Abdominal magnetic resonance imaging. The white arrow shows the liver tumor.



Fig. 2 Surgical specimen.

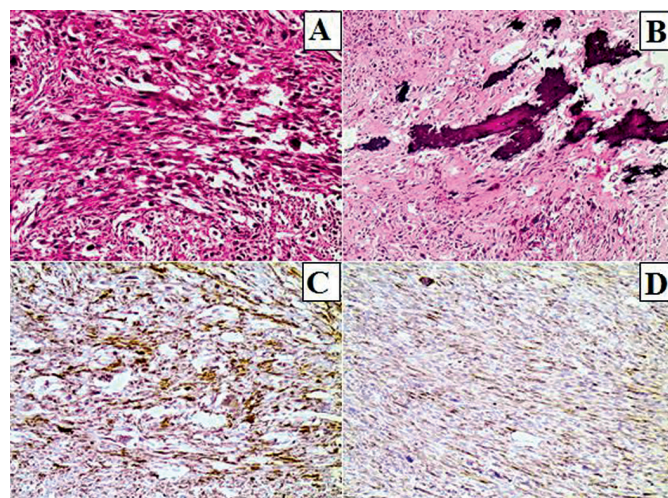


Fig. 3 Histological images. (A) Sarcoma made of large, atypical cells with abundant cytoplasm (hematoxylin-eosin stain). (B) Foci of osteoid production (hematoxylin-eosin stain). (C) Extensive expression of smooth muscle actin. (D) Limited expression of desmin.

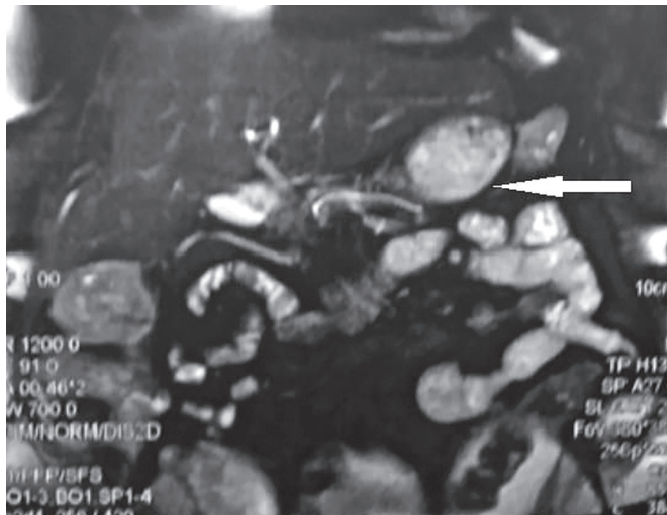


Fig. 4 Abdominal magnetic resonance imaging. The white arrow shows one site of recurrence.

advanced, metastatic and/or unresectable sarcomas, apart from liposarcomas (2, 3). An abdominal magnetic resonance tomography 18 months after the operation revealed four sites of recurrence, one between the liver and the first portion of duodenum, 5.5cm in diameter, other two at the front of pylorus, 3cm and 2.2cm in diameter, and another one at the front of the body of stomach, 2.1cm in diameter (Figure 4). The recurrent tumors were removed surgically, the postoperative course was uneventful and the patient was discharged from the hospital on the 7th postoperative day. She continued the per os treatment with pazopanib.

However, 3 months after the second operation, the patient presented melenas. An upper gastrointestinal endoscopy showed infiltration of the anterior wall of the first portion of duodenum by an ulcerated neoplasm. An abdominal computed tomography revealed three new sites of recurrence: one between the liver, the portal vein and the second portion of duodenum; another in contact with the anterior wall of the stomach and the first portion of duodenum, 5.5cm in diameter; and another arising from the mesocolon and reaching the abdominal wall (Figure 5). The patient received conservative treatment and continued the per os treatment with pazopanib. There was gradual progression of the disease and the patient died 37 months after the initial diagnosis from acute upper gastrointestinal bleeding due to infiltration of the duodenum by the tumor.

DISCUSSION

Primary hepatic leiomyosarcoma is an extremely rare malignant disease, with 50 cases having been reported in the literature so far, our case included (4–40). It is a malignant tumor that arises from smooth muscle cells (4, 8, 10–13, 15, 17, 19, 21, 22, 26, 28, 29, 31–33, 36–38, 40). Potential origins of this tumor in the liver are the smooth muscle cells in the round ligament (29, 31, 37, 38), the intrahepatic blood vessels and the intrahepatic bile ducts (15, 17, 22, 26, 29, 31, 32, 37, 38, 40). There is no apparent sex predilection, since there have been reported 23 (46%) cases of male patients (5, 9, 10, 12, 13, 15, 17, 19, 20, 24–26, 28–30, 32–35, 37) and 27 (54%) cases

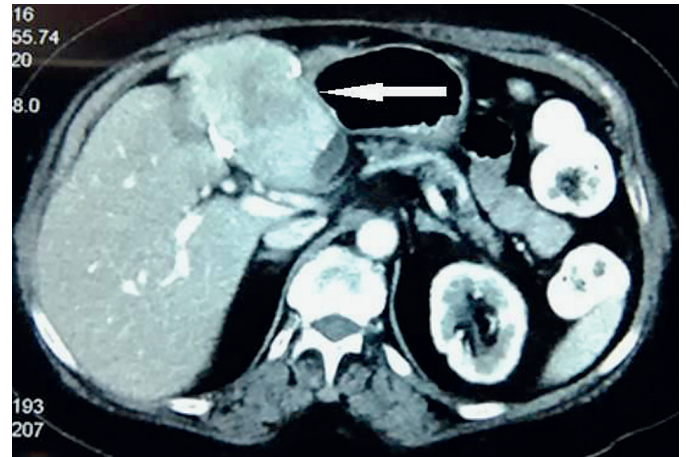


Fig. 5 Abdominal computed tomography. The white arrow shows one site of new recurrence.

of female patients, including our patient (4, 6–8, 11, 13, 14, 16–18, 21–23, 25, 27, 28, 31, 36, 38–40). The mean patients' age is 51.3 years and the median patients' age is 58 years. However, there is a wide age range, since the youngest patient was 5 months old (31) and the oldest patient was 86 years old (11), and the standard deviation is 18.6 years.

The underlying pathogenetic mechanisms have not been identified yet. However, there are some cases of primary hepatic leiomyosarcoma in immunosuppressed patients, two of whom had acquired immunodeficiency syndrome (32, 33). One of the patients with acquired immunodeficiency syndrome also had infection from Epstein-Barr virus (32). Another patient with primary hepatic leiomyosarcoma was under immunosuppressive treatment after renal transplantation (21). Furthermore, there are two cases of primary hepatic leiomyosarcoma in patients with chronic hepatitis, one with hepatitis C (19) and the other is our patient, who had hepatitis B.

Concerning the clinical image of primary hepatic leiomyosarcomas, they are often asymptomatic (21, 25, 30) or their symptoms are non-specific (4, 8, 10–12, 14, 16, 17, 19, 21, 23, 27–29, 31, 32, 34, 37, 38, 40). Abdominal pain or discomfort (4, 8, 11, 12, 14, 16, 17, 19, 22, 23, 27–29, 34, 37, 38), a palpable mass (4, 19, 22, 28, 29, 38), fever (17, 23, 28, 31, 32, 40), jaundice (39), anorexia (10, 12, 27, 28, 32), nausea or vomiting (31, 34) and weight loss (4, 8, 10, 12, 14, 16, 19, 28, 32, 37) are among the reported manifestations. A case with acute bleeding has also been reported (24). There is usually a single mass (4, 8, 11–13, 16, 18–25, 27–36, 38–40), although there are cases with two (25, 37), three (26) or even multiple tumors (15). The size of the tumor at diagnosis varies greatly (4, 8, 11, 12, 15, 16, 18–23, 25–35, 37–40) with the smallest tumor being 0.6cm in diameter (35) and the largest one being 30cm in diameter (11). The mean diameter of all the reported primary hepatic leiomyosarcomas is 10.3cm and the median diameter is 9.1cm, whereas the standard deviation is 6.7cm. The distribution of these tumors within the liver differs between the right and left hemiliver, with two thirds of them having arisen from the right hemiliver (4, 8, 11, 13, 16, 17, 19–22, 25–28, 31, 32, 34, 35) and one third from the left hemiliver (12, 18, 25, 26, 29, 30, 33, 36–40).

There is a number of data about radiological and histological findings of primary hepatic leiomyosarcoma in the literature. Ultrasonography usually shows a hypoechoic mass (15, 17, 19, 29, 30, 33, 37) or a mass with heterogeneous echogenicity (17, 22, 27, 30, 31, 37). Computed tomography usually reveals a hypodense (12, 17, 19, 21, 23, 27–33, 37, 39) and often heterogeneous mass (17, 21, 23, 31, 34) with inhomogeneous and often peripheral enhancement after administration of intravenous contrast (15, 17, 19, 23, 27–33, 40), which may show regions of cystic degeneration (27, 28, 31, 32). Magnetic resonance imaging displays on the other hand a usually heterogeneous mass that is hypointense in T1-weighted images and hyperintense in T2-weighted images (16, 19, 21, 37, 39, 40). Histological examination of primary hepatic leiomyosarcomas shows spindle-shaped cells with fascicular arrangement (4, 8, 10–12, 15–17, 19, 21, 22, 26–34, 36–38, 40). Immunohistochemistry reveals expression of smooth muscle actin (13, 15, 18, 19, 21, 22, 27–33, 36–38, 40), desmin (13, 15, 19, 21, 22, 27–34, 36–38) and vimentin (15, 17, 19, 22, 27–29, 31, 33, 37, 38, 40), whereas cytokeratins (22, 27–33, 37, 38), neuron-specific enolase (27–29, 32) and S-100 protein (19, 21, 27–34, 37, 38, 40) are not expressed.

Regarding therapeutic options for primary hepatic leiomyosarcoma, hepatic resection, in the form of wedge resection, segmentectomy, lobectomy or extended hepatectomy, was the preferred method for tumors without distant metastases (4, 6–8, 11, 12, 14, 16, 17, 20–23, 25, 26, 28–31, 33–36, 38). However, there were four patients with tumors confined within the liver who underwent liver transplantation (25, 27, 39). Some authors reported the addition of adjuvant chemotherapy consisted of various combinations of drugs (6, 8, 10, 23, 28, 30, 31, 35, 37, 39). Some of the administered chemotherapeutic regimens were the following: 1. vincristine, cyclophosphamide and dactinomycin (8); 2. cyclophosphamide, vincristine and actinomycin D (10); 3. doxorubicin (23); 4. folinic acid, fluorouracil, irinotecan (FOLFIRI) and bevacizumab (30); 5. mitoxantrone, cisplatin and fluorouracil (35); 6. ifosfamide and mesna (37). Radiotherapy has also been used as an adjuvant treatment along with chemotherapy in three cases (10, 23, 28). Finally, transarterial chemoembolization has also been used in one case (35) and transarterial infusion of epirubicin and carboplatin in another case (37). Survival rates are relatively low. On the basis of articles reporting survival data, median survival is 37.5 months and 5-year survival rate is 40% (4–12, 14, 17, 20–23, 25–38, 40).

In conclusion, primary hepatic leiomyosarcoma is a rare malignant disease with relatively poor prognosis. The most preferred type of treatment is surgical excision, which sometimes is combined with adjuvant chemotherapy and/or radiotherapy. However, very little is known about the effectiveness of the current treatment because of the rarity of the disease. More in-depth studies are needed to investigate and shed light on this uncommon clinical entity.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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