Malignant Hepatic Solitary Fibrous Tumor

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Hepatic solitary fibrous tumors (SFTs) are mostly benign and rare because of information regarding the clinical symptoms, treatment, and prognosis of their malignant forms is currently lacking. A literature review concerning malignant SFTs revealed that there were a few cases where patients experienced abdominal right upper quadrant (RUQ) pain as their first clinical symptom, and metastases were found after being diagnosed with hepatic SFT. Here, we report a patient who was previously healthy without any clinical symptoms such as RUQ pain or weight loss, but had the appearance of a metastatic mass as the first clinical presentation before a primary hepatic SFT was detected (**J Liver Cancer 2019;19:143-148**)

Keywords: Solitary fibrous tumors; Sarcoma; Liver neoplasms

INTRODUCTION

Solitary fibrous tumors (SFTs) are rare mesenchymal neoplasms usually found in the pleural cavity.¹ However, they can also originate in other body parts, including the retroperitoneum, trunk, extremities, head, and neck. SFT are mostly benign.²

Hepatic SFT is rare and is reported to be benign.³ Only a few cases of malignant hepatic SFT have been reported, and right upper quadrant (RUQ) pain, weight loss, and loss of consciousness are some of the first symptoms to appear.^{4,5} According to the available literature, the skull base, lung, and vertebrae showed metastases after malignant hepatic SFT was diagnosed. Here, we report a case of malignant hepatic SFT

with metastatic subcutaneous mass as the first symptom in a previously healthy patient without abdominal or systemic symptoms, along with a literature review.

CASE REPORT

1. Clinical findings

In June 2017, a 69-year old woman was admitted to the hospital with a chief complaint of a mass in the right flank region. The patient was previously healthy without any past history, abdominal pain, anorexia, or weight loss findings. On physical examination, a 3×2 cm-sized, non-tender, oval-shaped mass was observed in the right flank subcutaneous region. Laboratory test results revealed elevated alkaline phosphatase (139 IU/L), gamma-glutamyltransferase (547 IU/L), aspartate aminotransferase (52 IU/L), and alanine aminotransferase (74 IU/L) levels, whereas carcinoembryonic antigen, carbohydrate antigen 19-9, and alpha-fetoprotein levels were within the normal range.

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2. Diagnosis, image, and pathologic findings

Abdominal computed tomography (CT) revealed a mass in the right flank region with relatively clear margins (Fig. 1A), and its depth and size were evaluated. An incidental finding of a 14×11×10 cm-sized heterogeneous enhanced mass was also observed in the right hepatic lobe (Fig. 1B). The mass was evaluated using magnetic resonance imaging (MRI). Early arterial enhancement findings were noted in the liver third-phase MRI arterial phase (Fig. 2A), while delayed progress enhancement findings were observed in the portal phase (Fig. 2B), which was interpreted as a suspicious hypervascular sarcoma.

Liver histological examination was performed using fine needle biopsy; the cells revealed similar morphology to that of spindled tumor cells with a typical “staghorn” vascular pattern of malignant SFT (Fig. 3A). For clinical staging, excisional biopsy of the flank mass was conducted; the histological analysis of the lesion was a “patternless” disposition with typical ectatic and irregularly shaped vessels (Fig. 3B). Additionally, in high power, tumor cells are ovoid to spindle shaped with relatively uniform and bland cytology, and increased mitotic activity was identified (Fig. 3C). The cluster of differentiation (CD) 34 immunohistochemical expression was strong and diffuse (Fig. 3D).

Figure 1. Abdominal computed tomography coronal view. (A) Heterogeneous intermediate density enhanced mass was observed in the right flank region (arrow). (B) An approximately 14×11×10 cm sized mass was accidentally detected in the liver.

Figure 2. Liver third phase magnetic resonance imaging axial view. Approximately 14×11×10 cm sized large intermediate signal intensity mass, peripheral enhanced rim with internal necrotic portion, peritumor bile duct dilatations from segment IV of the liver to the right hepatic lobe. (A) Arterial phase: early arterial enhancement. (B) Portal phase: delayed progress enhancement findings.

3. Treatment progress

Chest CT showed a suspected pulmonary metastasis (Fig. 4). The patient refused palliative surgery and thus, received three cycles of chemotherapy (CTx) that included adriamycin (30 mg on days 1-3), ifosfamide (2,355 mg on days 2-4), and mesna (1,256 mg IV 0 hours, 3 hours, and 6 hours after ifosfamide). Adjunctive radiation therapy was not administered. Despite CTx, the tumor rapidly enlarged and pulmonary metastases were detected with weight loss. The patient died in June, 2018.

Figure 4. Chest computed tomography findings with a small nodule in the left lower lobe of the lung, which was suspected to be metastasis (arrow).

Figure 3. Histological findings. (A) Histology of the liver shows similar morphology to spindled tumor cells with a typical “staghorn” vascular pattern (arrows) (hematoxylin and eosin staining [H&E], $\times 100$). (B) Histology of the right flank mass. The tumor cells are arranged in a “patternless” disposition with typical ectatic and irregularly shaped vessels (arrows) (H&E, $\times 100$). (C) Histology of the right flank mass. At high power, tumors are ovoid to spindle shaped with relatively uniform and bland cytology. Increased mitotic activity (arrows) is identified (H&E, $\times 400$). (D) CD34 immunohistochemical expression is strong and diffuse ($\times 200$).

DISCUSSION

The average age for the occurrence of hepatic SFT is 50 years (16-84) and SFTs are more common in female than in male (2.2:1). Because of their rarity, SFTs have no established classification, underlying predisposing factors, incidence, treatment, and prognosis.

Malignant hepatic SFTs are extremely rare and according to a literature review, only been five cases of malignant hepatic SFT have been reported.⁴⁻⁸ Sex, age, first clinical symptom, size of mass, location, treatment, time to metastasis, and prognosis of reported malignant hepatic SFTs are summarized in Table 1.

The average age of malignant hepatic SFT patients, including our case, was 50.6 years (24-69) and malignant hepatic SFT are more common in female than in male (2:1). The age range and sex distribution of malignant hepatic SFTs were similar to those of benign SFTs. Unlike benign SFTs, which frequently have no symptoms, malignant SFTs showed RUQ pain as its first symptom, and there were various cases with systemic symptoms, including weight loss and loss of con-

sciousness. However, in our case, the patient had no abdominal or systemic symptoms and she was admitted to the hospital with a painless metastatic subcutaneous mass as the chief complaint. The size of benign SFTs varied (5-30 cm) and, occurred in both the left and right lobes,³ but the size of the malignant SFT was frequently larger (14-32 cm) and was mostly found in the right lobe.

Resection was performed in most malignant SFT cases, and additional CTx was performed in some cases. In our case, when the patient was admitted, subcutaneous and lung metastases were already present; therefore, performing surgery was impossible. Thus, only CTx was administered. Many authors believe that postoperative adjuvant CTx and radiotherapy are helpful in unresectability or malignancy cases.^{6,7} Currently, the combination of doxorubicin and ifosfamide is the standard systemic CTx regimen for many soft-tissue sarcoma subtypes. There was a report of a malignant SFT case in which CTx showed a response.⁸ Archontaki et al.⁷ and we used CTx, including adriamycin, ifosfamide, and mensa; however, there was no response. Additional investigations in a controlled, prospective trial on the use of CTx

Table 1. Literature review of the malignant hepatic solitary fibrous tumors

Study	Year	Age (years)	Gender	Clinical presentation	Size (cm)	Lobe of liver	Treatment	Metastasis site	Time to metastasis	Follow up (months)	Prognosis
Yilmaz et al. ⁴	2000	25	Female	Epigastric mass, weakness, anorexia,	32×30×12	Right	Excision+ CTx	Vertebrae	1 month after surgery	6	Alive
Jakob et al. ⁵	2007	70	Male	RUQ pain, transient loss of consciousness	27×24×12	Right	Excision	Lung	9 months after diagnosis	12	Died
Korkolis et al. ⁶	2010	54	Male	No data	17×12×8	Right	Excision	Liver recurrence, skull base metastasis	8 years after diagnosis	96	Died
Archontaki et al. ⁷	2011	24	Female	RUQ pain, abdominal discomfort,	30×17×15	Right	Excision+ CTx	Skull base	Initial diagnosis	16	Died
Park et al. ⁸	2013	62	Female	RUQ pain, weight loss	20×15×10	Border on left lobe	Excision	No metastasis	No data	No data	No data
Our case	2018	69	Female	Metastatic mass of right flank	14×11×10	Right	CTx	Subcutaneous tissue, lung	Metastasis found first	12	Died

CTx., chemotherapy; RUQ, right upper quadrant.

and its regimen to treat malignant SFTs are warranted. There was a report of using radiotherapy as an adjunctive therapy for head and neck SFTs to prevent recurrence;⁹ however, no radiotherapy study has been conducted on malignant hepatic SFTs. Therefore, the effectiveness of radiation therapy for these tumors could not be assessed. Further studies are required to evaluate the effectiveness of radiotherapy as an adjunctive therapy for malignant hepatic SFTs.

In previous reports, metastatic sites were the vertebrae, lung, and skull base. Our case was metastasized to the subcutaneous tissue unlike the previous case. The time to metastasis after malignant hepatic SFT diagnosis varied from immediately after diagnosis to 8 years. When examining the subcutaneous mass, a hepatic mass was not suspected. This represents a rare case where the metastatic lesion was detected before hepatic SFT was diagnosed. The mechanism of how the tumor metastasizes from the liver to the subcutaneous tissue is unclear. Subcutaneous seeding has been reported after percutaneous liver injection. In this case, however, there was no iatrogenic procedures, including percutaneous injection, in which the subcutaneous metastasis was found before the primary liver lesion. Furthermore, non-iatrogenic subcutaneous metastasis may occur. Therefore, an asymptomatic subcutaneous mass may be considered as the first symptom of malignant hepatic SFT.

Usually, the prognosis of malignant SFT is poor. Yilmaz et al.⁴ mentioned that by excision and CTx, including cyclophosphamide and adriamycin, patients could survive up to 6 months; however, there was no long term follow up. All reports published since then mention a poor prognosis.

In hematological tests, benign SFTs usually show no abnormalities.³ Including our case, other studies about malignant SFTs reported that tumor marker and liver function test results were non-specific and could not be used to test for the suspicion of malignant SFT.

In radiological findings, SFT should be suspected if imaging reveals a solitary, highly vascular, well circumscribed, encapsulated mass that shows heterogeneous enhancement (owing to the varied density of the collagen component) in CT and MR images, especially if the enhancement is hypointense on the T2-weighted MRI and shows progressive en-

hancement in the delayed phase.¹⁰ However, because it is difficult to distinguish malignant from benign tumors radiologically, immunochemical evaluation should be used for diagnosis.¹¹

In our case, a similar morphology of spindled tumor cells with a typical “staghorn” vascular pattern was found in the liver histological findings. The tumor was well-circumscribed, with increased cellularity, a focal area of necrosis at low power, and increased mitotic activity at high power in the flank mass. Furthermore, CD34 immunohistochemical expression was strong and diffuse. Based on these characteristics, hepatocellular malignancy could be suspected. However, the CD34 antibody is not SFT specific and could be positive in both angiosarcoma and gastrointestinal stromal tumors.⁹ Because malignant SFTs share many features with other neoplasms, can occur at practically any site, and have no specific immunohistochemical profile, they can be extremely difficult to distinguish from other spindle cell neoplasms.¹² The diagnosis of malignant SFT was made based on the typical “staghorn” vascular pattern observed in the liver biopsy and the increased mitosis cell cytology of the subcutaneous biopsy.

In summary, malignant hepatic SFT is a rare neoplasm for which clinical symptoms, diagnosis, treatment, and prognosis are unclear. We report a case with a clinical symptom (painless metastatic subcutaneous mass) and metastatic course that are different from previous reports.

AUTHOR CONTRIBUTIONS

Conception and design: Hyo Young Kim

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Data analysis and interpretation : Min Jeong Lee

Drafting the article : Hong Il Kim

Critical revision of the article: Hyung Suk Yi

Final approval of the version to be published: Hyo Young Kim

Conflicts of Interest

The authors have no conflicts to disclose.

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