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A case report of primary fibrosarcoma of the liver

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Summary: A 75-year-old woman was admitted to our hospital complaining of right hypochondrial pain. Echo sonography and computed tomography demonstrated a large tumor with irregular internal density in the right lobe of the liver. Angiography revealed a moderately hypervascular tumor. She was treated with transcatheter arterial embolization. Three weeks later, the tumor ruptured. She died of accompanying acute myocardial infarction seven months after the onset of the illness. Autopsy revealed primary fibrosarcoma of the liver. The tumor appearance varied from firm whitish to soft myxomatous. A part of the tumor showed hemorrhagic necrosis. There was no intrahepatic metastasis. The tumor tissue was composed of spindle shaped cells and immunohistochemically stained with vimentin. *Gastroenterol Jpn 1990;25:753–757*

Key words: *fibrosarcoma of the liver; vimentin staining*

Introduction

Primary fibrosarcoma of the liver is a rare neoplasm. Since Jaffe[1] reported the first case in 1924, only 33 cases have appeared in the literature. Here we report a case of the disease which was diagnosed not only by light and electron microscopy but also by immunohistochemistry. In addition, we reviewed 34 cases, including our case, to clarify some clinical features of the disease.

Case Report

A 75-year-old woman was admitted to Mitsui Memorial Hospital on March 31, 1983 with compalints of right hypochondrial pain which lasted for two months. She had no history of alcoholism, hepatitis or exposure to any hepatotoxic substances. On admission, examinations of the head, the neck, the thorax, and the extremities were unremarkable. There was a tenderness on the right upper abdominal quadrant. The liver and the spleen were not palpable.

Laboratory data on admission showed normal liver function tests (**Table 1**). Serum alpha fetoprotein and HBs antigen were negative. Abdominal ultrasonography (US) with a real-time linear array scanner demonstrated a space occupying lesion, 8 cm in diameter, in the right lobe of the liver (**Fig. 1**). The lesion was sharply demarcated and the internal echo density was heterogeneous. Computed tomography (CT) of the abdomen demonstrated the tumor in the right upper anterior region of the liver. After bolus injection of contrast medium, the lesion was stained irregularly (**Fig. 2**). Angiography of the liver revealed a moderately hypervascular tumor (**Fig. 3**). There were compression and arch-like distribution of the arteries. There was no tumor invasion into the main trunk of the portal vein by US, CT or angiography. Because of her advanced age, we treated her with transcatheter arterial embolization

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Table 1 Laboratory data on admission

Peripheral blood			(normal range)
	(normal range)	LAP	57 U/l
WBC	8600/ul	γ-GPT	35 U/l
RBC	448 × $10^4/\mu l$	Total bilirubin	0.3 mg/dl
Hb	12.2 g/dl	TTT	3.1
Ht	40.7%	ZTT	7
Thrombocyte	40 × $10^4/\mu l$	Triglyceride	221 mg/dl
Protrombin time	87.5%	Glucose	111 mg/dl
Fibrinogen	377 mg/dl	ICG (15 min.)	5.1%
Blood chemistry			
Total prorein	7.8 g/dl	Serological Test	
Albumin	4.0 g/dl	AFP	2 ng/dl
Total cholesterol	202 mg/dl	CEA	1 ng/dl
Choline esterase	340 U/l	CA19-9	38 U/ml
GOT	25 U/l	HBs antigen	–
GPT	15 U/l	HBs antibody	–
LDH	294 U/l		
ALP	337 U/l		

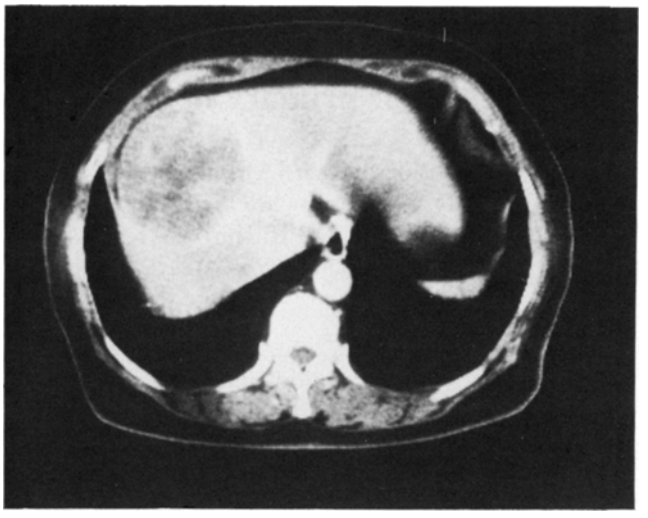

Fig. 2 CT showed a tumor stained irregularly after bolus injection of contrast medium.

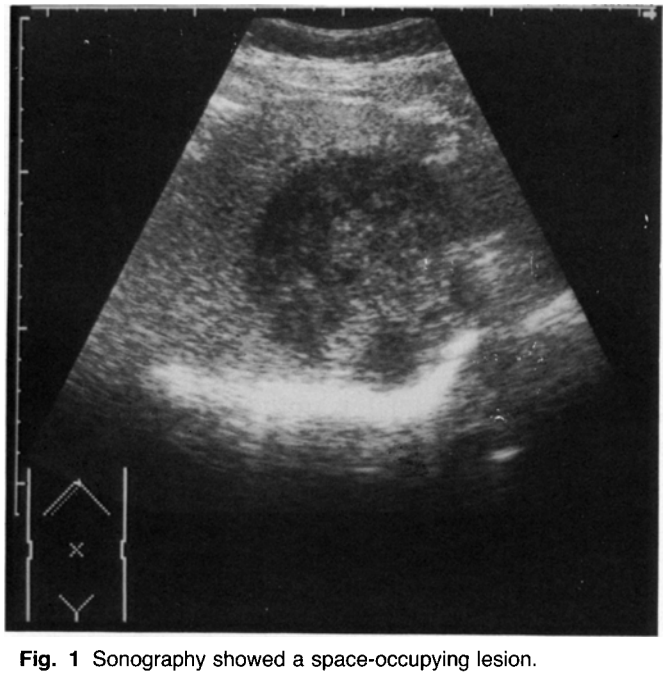

Fig. 1 Sonography showed a space-occupying lesion.

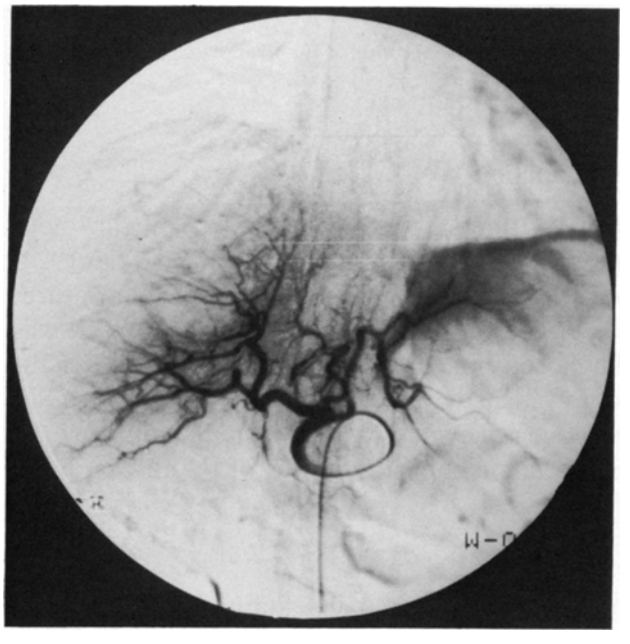

Fig. 3 Angiography revealed a moderately hypervascular tumor.

(TAE) on April 7. On April 28, she was admitted again with complains of severe right hypochondrial pain, abdominal distention and anemia. The ascites was bloody. Abdominal CT scan disclosed rupture of the tumor (**Fig. 4**). Fluid collected intraperitoneally and also in the subcapsular region of the liver. TAE was performed again to control hemorrhage of the lesion. She died of accompanying acute myocardial infarction on August 17, seven months after the onset of the illness.

Autopsy

Macroscopic findings

The liver weighed 3.3 kg. On the cut section, a large tumor mass, 14 × 14 × 12.5cm, was found in

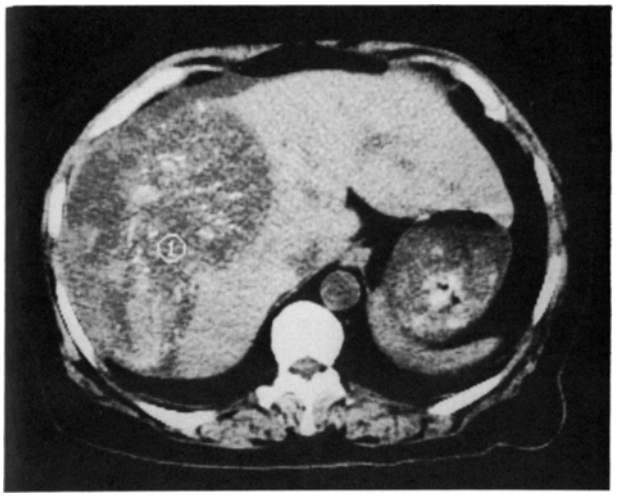

Fig. 4 CT showed rupture of the tumor Fluid collected intraperitoneally and in the subcapsular region of the liver. The density was that of water.

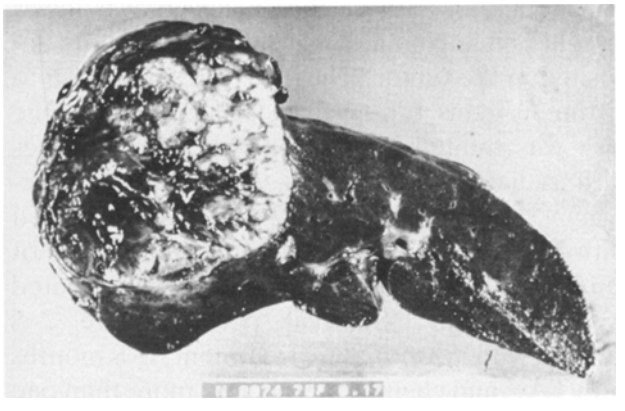

Fig. 5 At autopsy, a large tumor was recogniged in the right lobe of the liver.

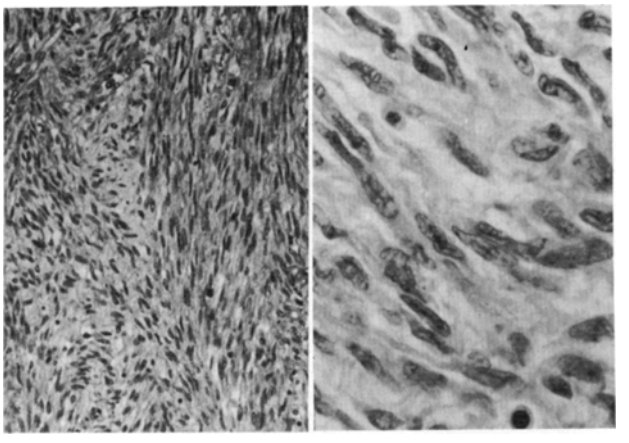

Fig. 6 The tumor cells were composed of spindle shaped cells (HE stain, left ×70, right ×210).

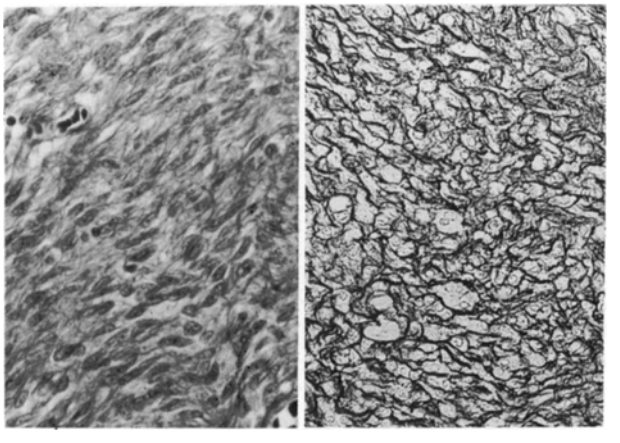

Fig. 7 Mallory staining showed abundant collagen fibers (left ×140). Silver staining revealed thick reticulin fibers (right ×140).

the right lobe of the liver (**Fig. 5**). It was well separated from the surrounding hepatic tissue without encapsulation. The tumor appearance varied from firm, whitish to soft, myxomatous, and approximately one half of the tumor showed hemorrhagic necrosis. There was no intrahepatic metastasis. Metastasis was found in the right lower lobe of the lung.

Light microscopic findings

HE stainng revealed that almost all the tumor cells were composed of spindle shaped cells (**Fig. 6**). Azan-Mallory staining showed abundant collagen fibers (**Fig. 7**, left). Silver staining revealed thick reticulin fibers enclosing individual tumor cells. These findings were compatible with the fibroblastic type of the sarcoma (**Fig. 7**, right). There was mild liver fibrosis.

Electronmicroscopic findings

Many spindle shaped tumor cells proliferated separately from each other within the loose connective tissue. There was no myofilament in the cytoplasm (**Fig. 8**).

Immunohistochemical reaction

Vimentin, a stroma marker, was positive, but

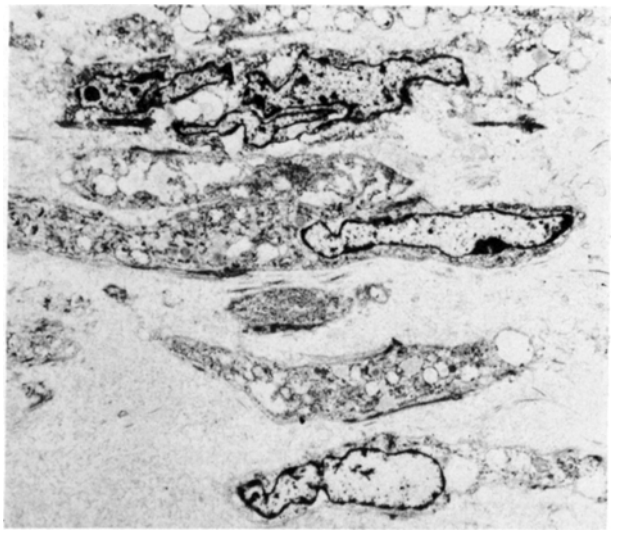

Fig. 8 Electron microscopically, the tumor cells proliferated separately from each other within the connective tissue (×800).

Table 2 Results of immunohistochemical examinations

Antibodies	Reactivity	Antibodies	Reactivity
1) Vimentin	+	11) Neuroendocrine marker	–
2) α-1-antitrypsin	–	12) Chromogranin	–
3) α-1-antichymotrypsin	–	13) Myelin basic protein	–
4) S-100 protein	–	14) Factor VIII related antigen	–
5) Lysozyme	–	15) Keratin	–
6) Desmin	–	16) Tissue polypeptide antigen	–
7) Myoglobin	–	17) Epithelial membrane antigen	–
8) Actin	–	18) Cytokeratin	–
9) Myosin	–	19) Carcinoembryonic antigen	–
10) Neuron specific enolase	–		

all other tests were negative, including α_1-antitrypsin, α_1-antichymotrypsin, S-100 protein, lysozyme, desmin, myoglobin, actin, myosin, neuron-specific enolase, neuroendocine marker, chromogranin, myelin basic protein, factor-VIII related antigen, keratin, tissue polypeptide antigen, epithelial membrane antigen, cytokeratin and carcinoembryonic antigen (**Table 2**).

Discussion

We reviewed the literature and discussed the clinical and pathological features of the tumor including our case. The age of the patients ranged from 8 to 75 years. The age peak was 50-60 years which included two-thirds of the cases. The male to female ratio was 2:1.

The most frequent complaints were abdominal distension and upper abdominal pain. Liver cirrhosis was recognized in 6 cases[1-3]. Hypoglycemia was noticed in 5 cases[5,6,19,28,29]. Intraperitoneal hemorrhage was accompanied in 4 cases[3,16,22]. The tumor was sharply demarcated and the internal echo density was heterogeneous in US. These findings suggested primary nodule-in-nodule hepatocellular carcinoma (HCC) or mixed-echo type hemangioma. CT demonstrated a low density area which was enhanced moderately and irregularly after bolus injection of the contrast medium. The enhancement was not so rapid as in HCC, nor was its so slow or high in density as in hemangioma. By angiography, vascularity of the tumor was moderate, and the tumor density was lower than in hemangioma. Lipiodol was markedly deposited in the tumor. These features may help to distinguish this tumor from other lesions. One case was treated with chemotherapy[11], 2 cases with radiation[3,19], 9 cases with surgical resection[6,7,9,10,12,21,27,29,30] and 2 cases were treated with TAE[16]. The effect of the treatment was not remarkable. The remaining 21 cases were treated symptomatically. Survival periods were 2–8 months with symptomatic treatment, 6–8 months with TAE and chemotherapy, and more than one year after surgical resection. Therefore, surgical resection would be the most preferable treatment, if possible. Diagnosis of the tumor was obtained pathologically. Additional immunohistochemical findings were most reliable for final diagnosis. In this case, reaction was positive for vimentin, which is a non-epithelial stroma marker. This finding indicatd that the tumor was sarcoma. Epithelial markers were negative, including α_1-antitrypsin, lysozyme, neuron specific enolase, chromogranin, keratin, epithelial membrane antigen, carcinoembryonic antigen, cytokeratin and tissue polypeptide antigen. S-100 protein, which is a marker of nerve cells was negative. Desmin, myoglobin, actin and myosin, which are specific markers of muscle cells were negative. Factor-VIII-related antigen which is a marker of

vascular endothelial cells was also negative in this case. In the present case, the final diagnosis of the disease was made by the light microscopic, electron microscopic and also immunohistochemical findings. Application of immunohistochemistry to the diagnosis of this tumor appears to be the first in the literature.

References

1. Jaffe RH: Sarcoma and carcinoma of the liver following cirrhosis. Arch Int Med 1924;33:330.
2. Alrenga DP: Primary fibrosarcoma of the liver. – Case report and review of the literature. Cancer 1975;36:446-449
3. Kaneko S, Kishioka S, Yamato K, et al: Primary fibrosacoma of the liver. Jap J Med Technology 1981;36:504
4. Hagino T, Tanno H, Suzuki T, et al: An autopsy case of primary fibrosarcoma of the liver that was diagnosed leiomyosarcoma with biopsy. Gastroenterology 1986;838-258
5. Oku A, Nishioka M, Miyamoto H, et al: An autopsy case of primary fibrosarcoma of the liver associated with hypoglycemia. Acta Hepat Jap 1982;23:1234
6. Kameya S, Sato R, Tamada M, et al: A case report of fibrosarcoma associated with severe hypoglycemia. Jpn J Gastroenterol 1985;82:513-517
7. Yoshiya K, Hirohashi N, Oishi G, et al: Fibrosarcoma of the liver capsule. Image Technology & Information Desplay 1986;18:429
8. Kasugai M, Shinagawa T, Tamano M, et al: Primary hepatic fibrosarcoma. Liver 1987;28:132
9. Cho C, Kakuya, H: Primary hepatic fibrosarcoma. J Jap Prac SUrg Soci 1955;16:175
10. Urano A, Kinouchi S: Primary hepatic sarcoma. Shinshu Med J 1956;7:94
11. Nishizato T, Ihara K, Onodera Y, et al: A case of primary fibrosarcoma of the liver.Acta Hepat Jap 1981;22:102-106
12. Shallow TA, Wagner FB: Primary fibrosarcoma of the liver. Ann Surg 1947;125:439
13. Ojima A, Sugiyama T, Takeda T, et al: Six cases of the rare malignant tumors of the liver. Acta Path Jap 1964;14:95
14. Steiner PE: Cancer of the liver and cirrhosis in Trans-Saharan Africa and the United States of America. Cancer 1960;13:1085
15. Iwasaki H, Enjoji M: Infantile and adult fibrosarcomas of the soft tissue. Acta Path Jap 1979;27:377
16. Fugii H, Katake K, Iwasa N, et al: Primary fibrosarcoma of the liver – Report of a case and review of the literture. Acta Hepat Jap 1976;17:852
17. Furukawa S, Kita T: Hepatic fibrosarcoma. Jap J Clin Med 1939;2:13
18. Schiff L: Disease of the liver. 2nd ed, JB Lippincott, 1963
19. Snapper I, Schraft WC, Ginsberg DM: Severe hypoglycemia due to fibrosarcoma of the liver. Maandscrift voor kindergeseekunde 1964;32:337
20. Bodker A, Boiesen PT: A primary fibrosarcoma of the liver. Case report. Hepato-gastroenterol 1981;28:218
21. Ninane J, Marlin D, Latinne D, et al: AIDS in two African children. – One with fibrosarcoma of the liver. Eur J Pediatr 1985;144:385
22. Cavallo T, Lichewiz B, Rozov T: Primary fibrosarcoma of the liver. Report of a case. Rev Hosp Clin Fac Med 1968;23:44
23. Baloulet G, Destombes P: A propos de quelques tumeurs mesenchymateuses hepatiques d'apparence primitive. Essai de classification et de diagnostic des tumers a cellules fusiformes du foie. Ann Anat Path (Paris) 1967;12:273
24. Edmondson HA: Tumors of the liver and intrahepatic bile ducts. Armed Forces Institute of Pathology 1958
25. Stout AP: Fibrosarcoma. The malignant tumor of fibroblast. Cancer 1948;1:30
26. Noordenbos W: Verwijdering van linker leverkwab wegens fibrosarcoma. Nederlands Tijdschrift voor Geneeskunde 1929;1:1021
27. Yamauchi Y, Kinoshita T, Nishijima Y, et al: Primary fibrosarcoma of the liver. Treated by the left lobectomy. Arch fur Japanische Chirurgie 1964;33:665
28. Gen E, Kusuyama Y, Saito K, et al: Primary fibrosarcoma of the liver with hypoglycemia. Acta Path Jpn 1983;33:177-182
29. Immerman SC, Seher SF, Khandekar JD: Causes and evaluation of tumor-induced Hypoglycemia. Arch Surg 1982;117:905-908
30. Walter E, Bodner E, Ledeker B: Primary fibrosarcoma of the liver. Wien Klin Wochenschr 1972;24:808
31. Totzke HA, Hutcheson JB: Primaty fibrosarcoma of te liver – Case report. South Med J 1965;58:238
32. Simpson HM, Baggenstoss AH, Stauffer MH: Prmary fibrosarcoma of the liver. A report of three cases. South Med J 1955;48:1177
33. Smith D, Rele SR: A case of primary fibrosarcoma of the liver. Postgraduate Med J 1972;48:62-63
34. Sugihara S, Kojiro M: Primary liver sarcoma. Nippon rinsho 1988;46:237