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A Case of Giant Undifferentiated Sarcoma of the Liver with Marked Regression after Transarterial Chemoembolization

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Abstract: Presented in this paper is a case of undifferentiated sarcoma of the liver (USL), especially for its therapy and angiographic findings. The patient, a 13-year-old girl was referred to our institute for a large low density mass of the liver revealed by computed tomography. The tumor occupied whole of the anterior and the medial segments of the liver. Angiographic evidence revealed elongation and stricture of the left branch of the portal vein. In addition, the occluded inferior vena cava (IVC) and development of intrahepatic collateral circulation between IVC and hepatic vein were seen. Based on these findings, we initially considered the tumor nonresectable and chose transarterial chemotherapy through the hepatic artery. Chemoembolization using the emulsion of Cisplatin (with the dose of 100 mg) and Lipiodol (5 m*l*) showed remarkable effects and allowed us to perform extended right trisegmentectomy of the liver.

Pathological examination of surgical specimen provided a diagnosis of USL.

However, the patient died of local recurrence 7 months after operation and the autopsy revealed no distant metastasis. This fact suggested a complete resection was the only way to cure this disease.

Key words: Undifferentiated sarcoma of the liver, Chemoembolization of Cisplatin and Lipiodol

INTRODUCTION

Undifferentiated sarcoma of the liver (USL) is one of rare mesenchymal tumors of the liver, and found predominantly in the pediatric group. While, USL is the fourth infrequency of malignant liver tumors in children, following hepatoblastoma, infantile hemangiosarcoma, and hepatocellular carcinoma[1)]. A high grade of malignancy and poor survival features are associated with this tumor, but the majority of its biological behavior remains unclear.

In this case, the tumor decreased in size after chemoembolization using Cisplatin (CDDP) and Lipiodol (LPD), it was then resected by extended right trisegmentectomy of the liver. We present this experience and discuss the treatment of USL.

A CASE REPORT

A 13-year-old girl visited a hospital with a sudden onset of epigastralgia and fever in February, 1990. She had been well and shown

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Table 1. Laboratory Data on admission

WBC 12000/μl RBC 346 × $10^4/\mu l$ Hb 9.5 g/dl Plt $48\times10^4/\mu l$
ESR 1h 56 mm, 2h 97 mm CRP 22.0 mg/dl
Tp 5.0 g/dl Alb 2.5 g/dl ChE 0.28 ΔPH
T-Bil 0.5 mg/dl
Alp 467 U/l LAP 153U/l γGTP 141U/l LDH 3810 U/l
GOT 47 U/l GPT 46 U/l BUN 11 mg/dl Cr 0.6 mg/dl
Nal 35 mEq/l K4.0 mRq/l C1107 mEq/l
HBsAg(−) Wa(−) AFP 10 ng/ml CEA 1.0 ng/ml
ferritin 377 ng/ml NSE 24.6 ng/ml
PT% 120% Fib 476 mg/dl

no previous weight loss until then. CT revealed a giant liver tumor, then she was referred to our institute on March 12, 1990. On physical examination, there was no anemia, jaundice, pathological lymphadenopathy, or any other abnormalities. However, the liver was palpable with slight tenderness, below the right hypochondria 7 cm in width.

Table 1 shows the patient's laboratory data. Evidence of inflammation can be seen in the white blood cell count, erythrocyte sedimentation rate, and C reactive protein value, and evidence of nutritional disorder was seen in the serum total protein and albumin values. The level of lactate dehydrogenase (LDH) and serum ferritin were very high and neuron-specific enolase (NSE) was slightly elevated, while the values of alphafetoprotein and other tumor markers were within the normal range.

X-RAY FINDINGS

CT (Fig. 1–A) showed a large low density area indicating malignant liver tumor with partial necrosis that occupied whole of the anterior and the medial segments, and expanded to a part of the lateral segment. The contrast medium enhanced the tumor well, and a non-enhanced low density area seen on

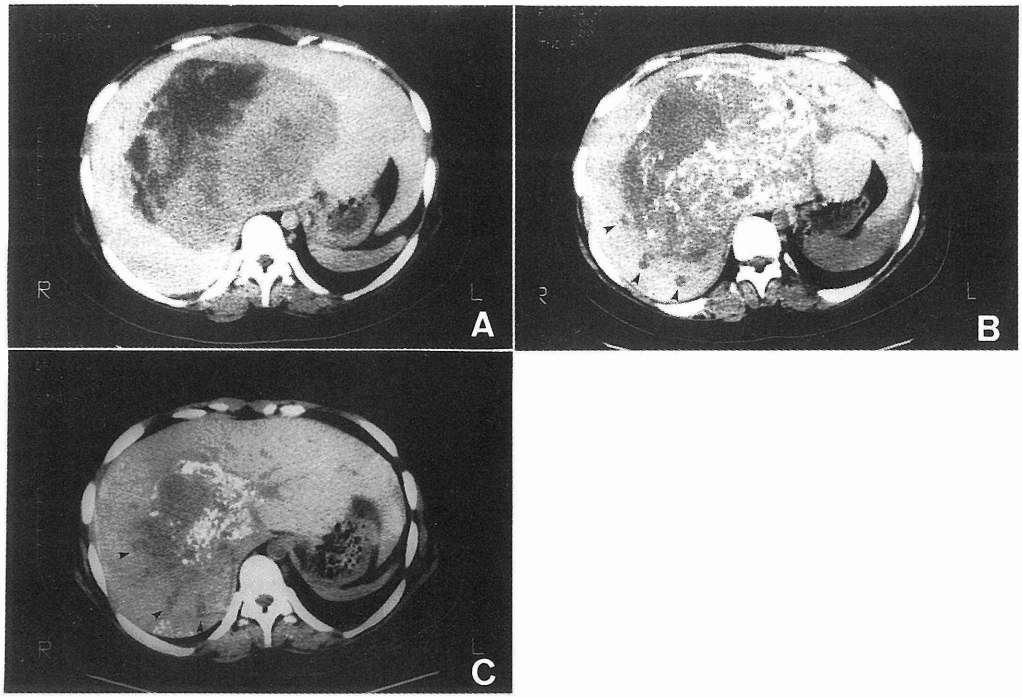

Fig. 1. Liver CT findings. A; contrast CT before chemoembolization indicating large liver tumor. B; 2 weeks after first chemoembolization, massive accumulation of lipiodol were observed. C; 2 months after chemoembolization, tumor regressed and compensatory hypertrophy of the left lobe of the liver was calculated as 30%. Black arrows indicate development of intrahepatic collateral circulations between the IVC and the right hepatic vein.

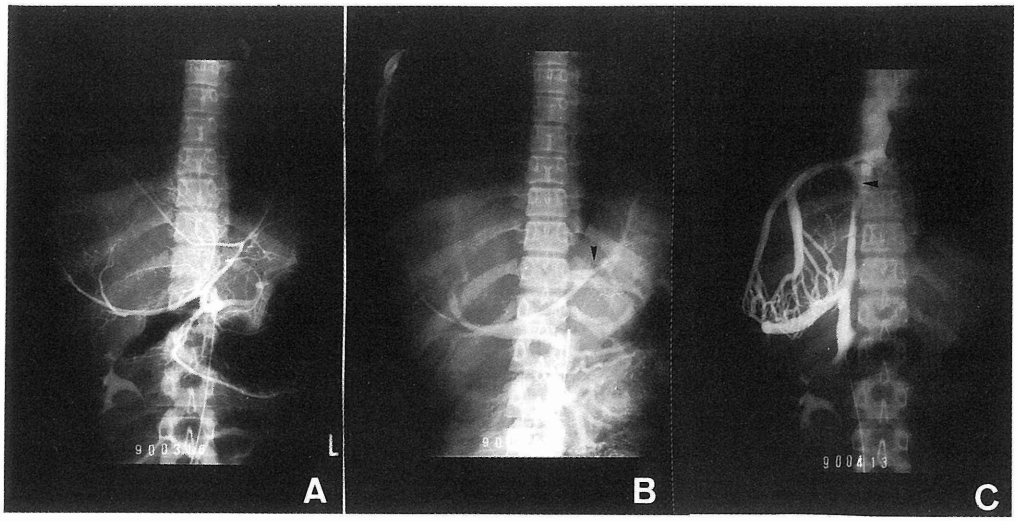

Fig. 2. Angiogram before chemoembolization. A; arteriogram. A few tumor vessels are supplied from the anterior and the medial segment branch of the hepatic artery. B; portogram, black arrow shows the stricture of the umbilical portion. C; venogram of IVC, black arrow shows the obstruction of IVC. Developed intrahepatic collateral circulations are seen.

the right half of the tumor indicated necrotic tissue.

The angiographic findings were as follows. An arteriogram showed severe dislocation of the right hepatic and middle hepatic arteries, and the tumor was slightly supplied from the anterior and the medial segment branches of the hepatic artery (Fig. 2–A). A portogram through the superior mesenteric artery showed elongation of the both main branches of the portal vein, and stricture at the umbilical portion (Fig. 2–B). The inferior vena cava (IVC) was obstructed and intrahepatic collateral circulations between an enlarged short hepatic vein and the right hepatic vein had developed (Fig. 2–C). Based on these findings, we considered that the tumor was nonresectable.

Chemotherapy and its effects

We started the local infusion chemotherapy under a suspected diagnosis of hepatocellular carcinoma with sarcomatous change from the finding of the needle biopsy. On April 13, an urokinase coated catheter was placed into the hepatic artery through the right femoral artery, and an injecting wedge was connected to Catheter Access^{R} (Nipro Co., Ltd., Osaka) that was implanted subcutaneously in the right lower abdomen. Initially, 20 mg of Adriamycin (ADR) was injected 5 times on April 13, 14, 15, 23 and 24, however that did not prevent tumor growth. We subsequently applied a 100 mg of CDDP with 5 ml of LPD twice on May 1 and 26. CT showed a massive accumulation of LPD but the tumor size was not changed 2 weeks after first chemoembolization (Fig. 1–B). However, 2 months later, CT showed marked tumor regression and hypertrophy of the left lobe of the liver. (Fig. 1–C). The angiographic findings after chemotherapy are shown in Fig. 3. The arteriogram showed that the dislocation of the both hepatic arteries had recovered (Fig. 3–A). The stricture of the umbilical portion was improved (Fig. 3–B). However, the length of occlusion area was extended and further development of collateral circulation was seen in venogram of the IVC (Fig. 3–C).

At this stage, IVC occlusion test was performed to determine whether the dilated short hepatic vein could be ligated. We could find the development of ascending lumbar vein and

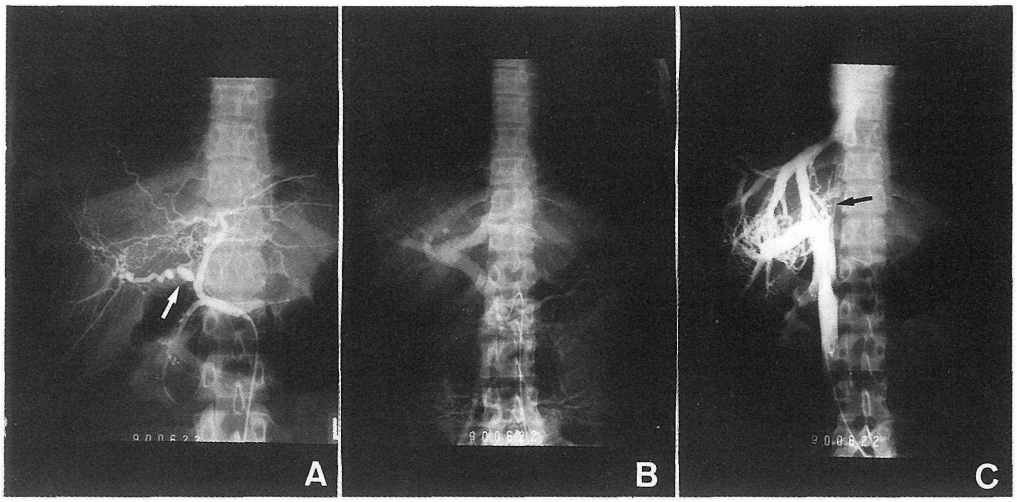

Fig. 3. Angiogram after chemoembolization. A; arteriogram, white arrow shows aneurythmic change caused by the cannulation. B; portogram. The stricture of umbilical portion was improved. C; venogram, black arrow shows further development of IVC occlusion.

collateral circulations from left renal vein to left phrenic vein (data is not shown). Furthermore, IVC pressure was not increased. These findings encouraged us to try resecting the tumor.

Operative findings

A laparotomy was performed on July 18, with an inverted T shaped skin incision in the upper abdomen, and a right thoracotomy was added in the ninth intercostal space. The tumor was located in the anterior and the medial segments under the diaphragma and extended to the lateral segment over the round ligament. Intraoperative ultrasonography revealed that the tumor expanded adjacently left hepatic vein. And that the caudal lobe was also occupied by the tumor. Occluded IVC and development of intrahepatic collateral circulations were also confirmed. Although an extended trisegmentectomy was performed, we could not resect curatively the micro residual tumor around the left hepatic vein. Finally, thrombosis was removed and blood flow was reconstructed in IVC.

Pathologic findings

The tumor, 11×9 cm in size, showed yellowish white and brown nodules with hemorrhage around that (Fig. 4–A). The brown nodules occupied in the left half of the tumor were necrotic tumor with lipiodol accumulation. Microscopically, the tumor was separated from normal liver by a pseudocapsule composed of fibrous tissue, non-tumorous atrophic hepatocytes and proliferative bile ducts. Dilated venules were seen in the Grisson's capsule of the non-tumor liver tissue. The tumor was composed of spindle, round and pleomorphic undifferentiated cells. The spindle cells were arranged like sarcoma (Fig. 4–B), and the pleomorphic cells have hyaline droplets and positively stained with periodic acid-Schiff (PAS). Immunohistochemical analysis showed the reactivity for Vimentin in the cytoplasm of 10% of spindle cells, but not for desmin, cytokeratin or S100. We diagnosed the tumor as undifferentiated sarcoma of the liver.

Postoperative course and autopsy findings

After 3 months of the surgery, CT revealed

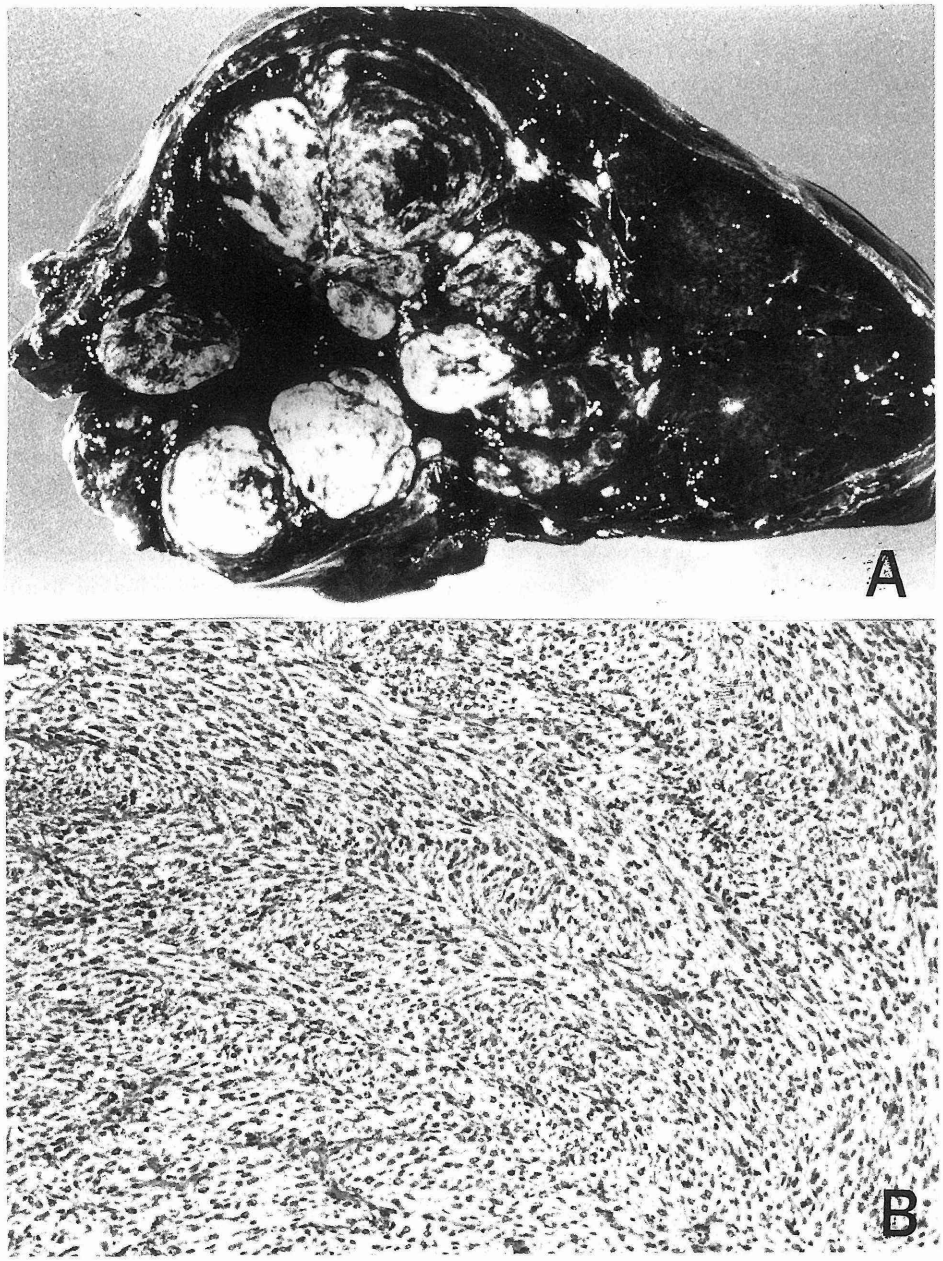

Fig. 4. Pathological findings. A; gross appearance, tumor consists of yellow or brown nodules. Brown ones are necrotic tissue with the accumulation of lipiodol. B; microscopic finding, spindle shaped cells are arranged like sarcomatous pattern. (H.E.stain × 500)

nodules around the hepatic vein. Despite of the CDDP and LPD therapy, the emulsion did not accumulate in the tumor, and had no effects. The patient died of hepatic failure caused by the tumor progression. The autopsy presented a large tumor replacing the left lateral segment of the liver, 9×10 cm in size, and compressing left hepatic vein. Non-

tumorous liver is suffered from the congestion and necrosis of central zone. There were only local recurrence on the liver and no distant metastase. Histological findings were as same as the operative specimen, and only Vimentin was positive on immunohistochemical analysis.

Discussion

Undifferentiated sarcoma was named by Stocker and Ishak in 1978 as an entity of mesenchymal sarcoma in which there were no differentiated components such as fibroblasts or lipoblasts[1].

Less than 30 cases have been reported in Japan[2] and about 80 reports in the world[3]. The majority of patients are between 6 and 10 years old. Because they have very few symptoms in the early stage, they were usually, found in an advanced stage with complaints of abdominal pain, abdominal mass, or ill-defined fever. Seventy percent of the published cases were already dead, and most of the living cases have recurrent lesions[4]. Recurrence is mostly local and there are a few reports of distant metastasis and peritoneal dissemination[5].

Our case showed typical clinical features, including lack of clinical symptoms in an operative stage, and few abnormalities in blood-serum examinations including tumor markers. These characteristics indicate a worse prognosis. Additionally, the absence of distant metastasis in the terminal stage can be noted. That is still controversial, because a few articles reported peritoneal dissemination[5][6], lung metastasis and bone metastasis[6]. However, our case showed no distant metastasis, despite extended local recurrence on autopsy findings. We found marked intrahepatic collateral circulation due to complete obstruction of the IVC. It seemed to be a special feature of an expanding giant tumor separated by normal hepatic tissue. We will discuss this finding below in association with surgical problem.

Special pathological findings of USL are the pseudocapsule including numerous bile ducts and cords of atrophic hepatocytes, spindle or pleomorphic tumor cells with PAS positive droplets in the cytoplasma, and the lack of components of differentiated mesenchymal cells[1]. However some reports described that the various components contained in USL, such as, rhabdomyosarcoma or hepatocellular carcinoma[7][8], making the origin of USL still unclear. It was reported that USL tissue was positive on immunohistochemical staining for cytokeratin and alpha-antitrypsin, suggesting relationship between USL and an epidermal component or malignant fibrous histiocytoma (MFH), respectively[5][6]. On electronmicroscopic study, USL cells have dilated endoplasmic reticulum and lysosomal inclusion bodies in the cytoplasm suggesting a relation to MFH[5][6]. Our case had typical histological features of USL with no other differentiated components. Furthermore, the immunohistochemical analysis showed positive staining only for Vimentin that supported a mesenchymal, rather than epithelial origin[6]. Unfortunately, we could not reveal the ultrastructural features in our case.

Regarding therapy for USL, complete resection was considered the only method to cure the disease, because neither radiotherapy nor chemotherapy has been reported effective[3].

Recently, it was reported that the combination chemotherapy using CDDP, ADR, and Cyclophosphamide (CPM) was effective for USL[3][7][9]. In one of these reports[9], the nonresectable tumor decreased and was resected after the chemotherapy, and the ensuing course was uneventful.

As local chemotherapy, an arterial infusion of anticancer drugs is most common for the nonresectable liver tumor in adult cases. Fortunately, our patient was grown up enough to use an implanted reservoir for transarterial infusion that allowed us to inject drugs repeatedly. Initially, we adopted ADR which has very wide spectrum in both carcinoma and sarcoma, but no effect was seen in our case. Subsequently, we tried the emulsion of CDDP and LPD that is often used in nonresectable hepatocellu-

lar carcinoma[10)11)]. The remarkable effect of this combination therapy allowed us to try the resection of the tumor. Although we could not determine whether the effect was caused by the embolization or cisplatin, such a combination seemed to be beneficial in view of increasing the effect of anticancer agents and reducing the toxicity for the patient.

In spite of the positive effect of the chemoembolization, tumor regrowth was seen in our case. On autopsy, however there was no distant metastasis. According to these findings, complete resection is considered the only method to cure our patient.

In the surgical site of this case, we discussed how to deal with the occlusion of inferior caval vein. In order to stop safely the intrahepatic bypass from the IVC to the hepatic vein during the extended trisegmentectomy, a biopump for V-V bypass seemed to be necessary[12)]. However, the preoperative occlusion test of IVC revealed the possibility of simple clamp of the IVC, and we could perform the extended trisegmentectomy without using a biopump.

Our experience in this case showed that an occlusion test of the IVC was a useful examination to simplify the surgical procedure for giant liver tumors.

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