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CASE REPORT

Ruptured angiosarcoma of the liver treated by emergency catheter-directed embolization

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Abstract

Angiosarcoma is a rare primary malignant neoplasm of the liver with a poor prognosis. Here, we report a case of a patient with a ruptured hepatic angiosarcoma which was treated by emergency catheter-directed embolization, followed by left-sided hemihepatectomy.

Key words: Ruptured angiosarcoma; Liver; Embolization

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INTRODUCTION

Angiosarcoma (AS) is a rare tumor entity which comprises less than 1% of all sarcomas[1]. Although rarely observed, it is the third most common primary malignant tumor of the liver. The occurrence of AS in the liver shows a predelection for elderly males[2]. The exposures to vinyl chloride, arsenic, thorotrast and irradiation are associated with an increased risk for the development of AS of the liver and are considered as etiologic cofactors[3-5]. Clinical diagnosis is usually hampered by the unspecific clinical signs and symptoms. Patients reported have been found with pain, loss of energy, and weight, hemorrhage and extrusion[6,7,8]. The therapeutical options described are oncological liver resection and chemotherapy[6,7,9]. Liver transplantation has not been reported to be significantly beneficial in this subgroup of sarcoma patients so far[10]. The clinical course of AS, even after curative surgery and chemotherapy is aggressive with a poor prognosis has been reported[7,11,12].

Here, we report about the rare case of a patient with acute bleeding to the abdominal cavity by a spontaneously ruptured AS of the liver.

CASE REPORT

A 76-year-old man was referred to the hospital with acute abdominal pain. With the onset of pain the patient collapsed. The subsequent consultation lead to emergency admission to the department of surgery. Apart from a slowly progressive local prostate cancer which was already resected transurethrally thrice (5 years ago, 1 year ago and palliatively 1 month before the admission), no significant disease was reported. The patient neither reported any kind of abdominal trauma nor prior abdominal surgery. Medication comprised antihypertensive drugs, iodine and androgene blockers since 1999. Besides that the patient had controlled his diabetes with an insulin pump.

At physical examination of the conscious patient, the abdomen was distended and showed a diffuse pain at deep palpation without clinical signs for peritonitis. Vital signs showed a slightly elevated blood pressure (140/70 mmHg) and a tachycardia (120 heart beats/min). Emergency blood test including hemoglobin, white blood count, electrolytes and hemostasis parameters revealed a reduced hemoglobin with 6.9 g/dL. Besides that, infection parameters were elevated with leukocytes of 16.0/nL and a C-reactive protein of 75.4 mg/L. Cholinesterase and albumin were also lowered significantly. Hemostasis parameters were normal.

The ultrasound examination of the abdomen, performed as the primary diagnostic modality, showed free abdominal fluid and a pathological finding in the left lobe of the liver, diagnosed as a ruptured liver lesion, at that time suspicious of a liver cell adenoma due to a 5-year

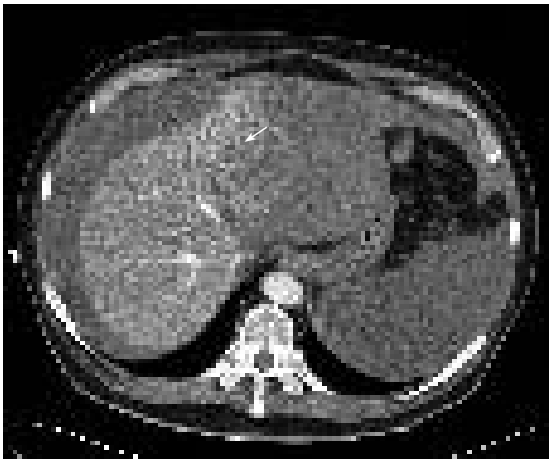


Figure 1 CT scan before embolization.

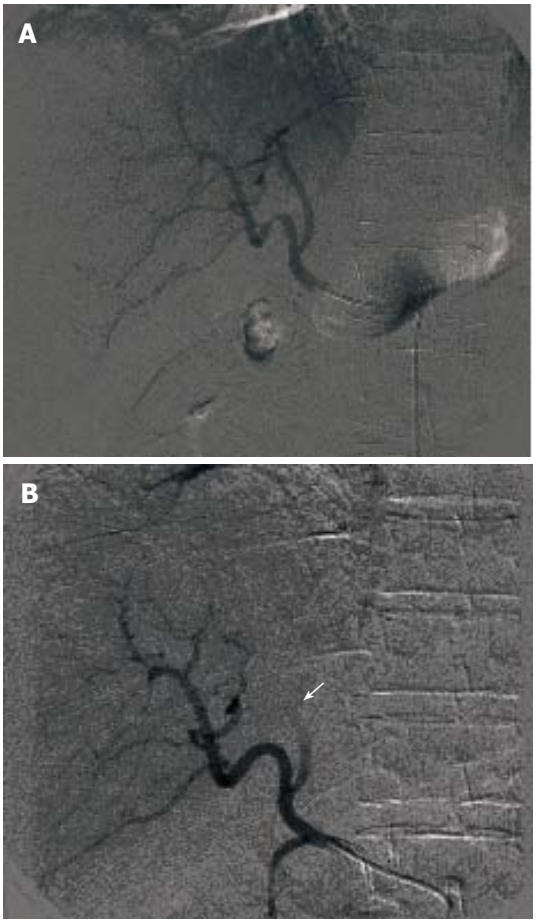


Figure 2 Angiography **A**: before embolization **B:** after embolization.

period of regular intake of androgene blockers. In order to identify the location of the active bleeding within the liver, an additive contrast enhanced computed tomography (CT) of the abdomen was carried out. The CT images confirmed a ruptured lesion of the left liver lobe with an ongoing active arterial bleeding located centrally within segments 2 and 3. In addition, a considerable amount of intra-abdominal blood (1-2 L) was diagnosed (Figure 1). The patient received blood transfusions (2 erythrocyte concentrates) and stayed hemodynamically stable. The interdisciplinary decision between radiologists and surgeons was made for therapeutic radiological intervention.

Subsequently, the patient was transferred to the radiological catheter room. The intervention was carried out by puncture of the right femoral artery and selective catheterization of the left hepatic artery. After cannulation of the left liver artery, the left lobe of the liver was completely and successfully embolized with 2 mL of embosphere 500-700 and 2 mL of embosphere 900-1 200. After intervention, there were no more signs for active bleeding, and blood pressure and heart rate stayed regular (Figure 2A, before embolization and Figure 2B after embolization). The patient was treated post-interventionally for 2 d at the intensive care unit before he was referred in a completely stable condition to the regular ward. Consecutively, elective surgery was scheduled to treat the abdominal hematoma and the ruptured lesion of the left lobe of the liver.

Preoperatively performed endoscopy of the upper GI tract and colonoscopy showed no substantial pathological findings (small axial hiatus hernia and a diverticulosis of the sigma without signs for inflammation).

Intraoperative findings

Surgery was performed 7 d after embolization. Explorative laparotomy revealed approximately 3 L of intra-abdominal hematoma without signs for active liver bleeding. Exploration of the left lobe of the liver revealed a ruptured hepatic tumor to the peritoneal cavity with a diameter of 12.5 cm which showed macroscopic characteristics of a hepatic adenoma. In order to treat the ruptured left lobe and to remove the liver tumor, a left sided hemihepatectomy was carried out. After resection, intraoperative sonography of the remaining liver parenchyma showed no pathological findings. Intraoperatively and during the early post-operative course, the patient received five erythrocyte-concentrates and two units of fresh frozen plasma. The post-operative course was uneventful and the patient could be discharged from hospital 19 d after the surgery.

Histopathologic findings

Histopathological examination of the specimen revealed a ruptured hematous hepatic malignancy of 12.5 cm diameter without sharp demarcation. The histopathological examination and the immunostaining diagnosed a tumor with endothelial proliferates along the liver sinusoids, large necroses and cell atypias consisting of solid and papillary tumor parts. Immunohistochemical staining for CD31, CD34, MIB-1 confirmed the diagnosis of a hemangiosarcoma. The final diagnosis was a ruptured AS of the left lobe of the liver with tumor-free resection margins at microscopic evaluation.

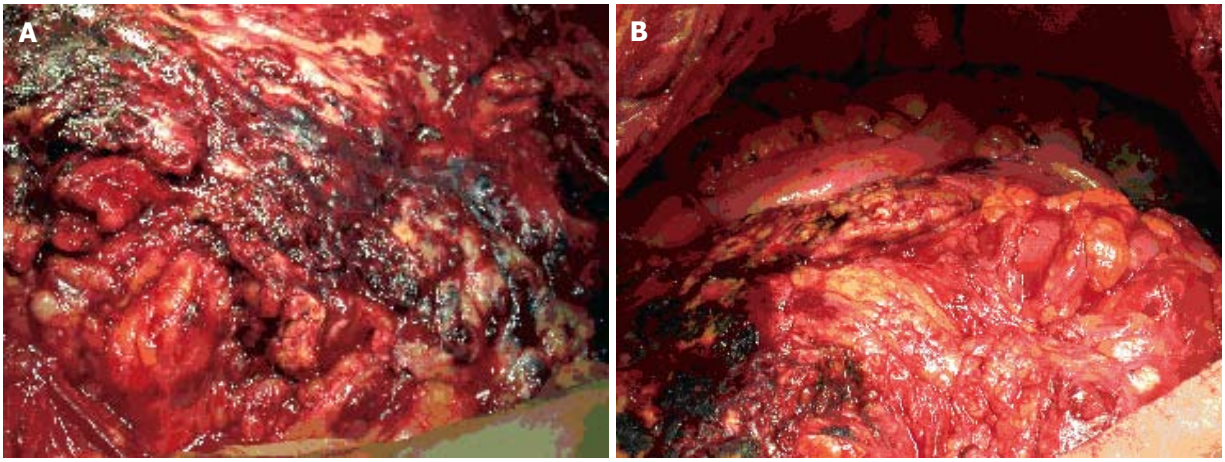
Postoperative course

Four weeks after primary surgery, the patient was readmitted to the hospital with the suspicion of recurrent acute intra-abdominal bleeding. A CT-scan showed free intra-abdominal fluid collection. An angiography showed small contracted vessels of the liver without proof of

Table 1 Case reports focusing on patients with hepatic AS undergoing surgery and/or embolization from 1995 to 2005

Reference	Year[1]	Number[2]	Age (yr)	Sex (M/F)	Clinical symptoms	Surgery	Resection margin	Additive Therapy	Metastasis at presentation	Emergency	Survival
Tordjman *et al*[27]	1995	1	34	M	?	No		Chemo-embolization	No	Yes	15 mo
Timaran *et al*[29]	2000	1	47	F	Right upper quadrant discomfort	Right hepatic lobectomy	Negative	No	No	No	Alive (120 mo postoperative)
Kirschstein *et al*[30]	2000	1	73	F	Abdominal pain	Right hepatectomy	Positive	No	Yes	No	6 wk
Hoppe *et al*[26]	2001	1	72	F	Pain, weight loss, hemodynamic instability	Liver segment resection	?	Preoperative embolization	No	Spontaneous rupture	2 wk
Ozden *et al*[10]	2003	1	54	F	?	Right hepatectomy + relaparotomy	Positive/ negative	Postoperative chemo-embolization	No	No	64 mo
Horger and Fendel[25]	2003	1	69	F	Right upper quadrant pain, bleeding	Right hepatectomy	?	Preoperative embolization	No	Spontaneous rupture	?
Almogy *et al*[8]	2004	2	33	F	Bleeding, right upper quadrant pain	Right hepatectomy	?	No	No	Yes	Died intra-operatively
			68	M	Bleeding	Right hepatectomy	Positive	Post-operative chemotherapy	No	Yes	7 mo

[1]Year of publication; [2]number of patients.



Figures 3 **A** and **B** Intraoperative pictures of peritoneal sarcomatosis.

active bleeding. The patient showed signs of hemorrhagic shock and received four erythrocyte concentrates and six units of fresh frozen plasma. Duplex-sonography showed reduced perfusion of the liver. Liver transaminases were elevated and the patient suffered simultaneously from a non-STEMI myocardial infarction without indication for acute catheter intervention.

In the following course the patient's abdomen became more and more distended with an aggravated pulmonary situation and progredient amounts of free intra-abdominal fluid. At this point, indication for explorative laparotomy was stated. Intraoperatively, multiple bleeding AS were found in the liver with massive peritoneal sarcomatosis (Figures 3A and 3B). Hemorrhage control of the diffuse bleeding could not be obtained surgically. The abdomen was closed and the patient was taken to the intensive care unit at basal infusion and kept on sedation and mechanical respiration. Few hours after the explorative laparotomy the patient died from persistent intra-abdominal bleeding from the angiosarcomatosis lesions.

DISCUSSION

Among malignant vascular tumors, AS is one of the most common subtypes diagnosed in patients undergoing surgery[13]. AS has a predilection for cutaneous sites, mostly in the head and neck region of elderly male patients[14]. AS also affects gastrointestinal organs[9,15-18] and hepatic AS is the second most common primary malignant neoplasm of the liver[19]. However, there have only been a few case reports available in the literature concerning primary hepatic AS over the past 10 years (Table 1).

The clinical course of AS is aggressive and prognosis is poor. In a study of 67 patients with AS, an overall 5-year survival of 35% has been reported[20]. Morgan *et al*[21] investigated 47 patients with cutaneous AS, outlining the

restricted prognosis and demonstrating a 5-year survival of 34%. Another analysis showed a median overall survival of 28.4 months in a cohort of 88 patients with AS of the scalp[14]. We observed a lethality of 65% in 43 patients who underwent surgery for AS with a median follow-up of 56 months[13].

AS presents with various unspecific clinical symptoms and a multilocular occurrence. Different sites of occurrence go along with a wide range of non-specific symptoms such as pain, swelling, extrusion, hemorrhage, or bowel obstruction[22]. Tumors of the skin and of superficial or deep soft tissue are usually biopsied preoperatively and thus, therapeutic decisions are made before surgery[13]. However, as also reported here, organotropic AS may be diagnosed consecutive to emergency treatment[23-26] or after the surgery for assumed benign disease. Thus, AS is often diagnosed unexpectedly after surgical procedures which do not meet oncological treatment standards.

To our knowledge, there are only two cases of hepatic AS reported to date, which have been treated by emergency catheter-directed embolization with consecutive liver resection (Table 1)[24,25]. Catheter-directed intervention is a useful method to cease acute arterial bleeding from the liver. The most common indication is traumatic laceration of the liver parenchyma[27]. Spontaneous bleeding and the formation of hematoma impede the clinical differentiation of the cause of the hemorrhage. In benign lesions (adenoma), a subsequent surgical resection of the affected parenchyma is curative. The catheter-directed embolization allows to perform a planned and well structured operation without the need of emergency liver surgery with high morbidity and lethality. In emergency cases with spontaneous bleeding, a differentiation of malignant or benign disease is impossible. Therefore, the final diagnosis is usually made by the histopathological evaluation of the resected specimen. At the time of the histopathological diagnosis, the prognosis of the disease becomes clear. In ruptured AS of the liver, the prognosis is devastating. Rupture in these cases leads to tumor cell spillage and consecutive diffuse angiosarcomatosis in the peritoneum. The angiosarcomatous lesions consecutively induce diffuse hemorrhage with subsequent loss of large amounts of blood. The acute bleeding from diffuse peritoneal angiosarcomatosis cannot be cured by surgical intervention and thus seems to be the leading cause for death in this rare subset of patients with AS. In an own observational series of 22 AS, 6 primary hepatic AS were found. Three of these patients died within 4 months and one patient 29 months after the diagnosis in spite of surgical intervention. The preliminary cause of death in the latter patients was peritoneal sarcomatosis with diffuse intra-abdominal bleeding[13].

The clinical course of the patient reported here shows that there is no effective treatment available till date either for cure or palliation of ruptured AS of the liver. The value of chemotherapy applied to the peritoneal cavity or systemically has not been clarified nor the value of experimental antitumoral strategies such as molecular therapies (e.g., with VEGF-antagonists) or hyperthermia. This clinical situation underlines the need for new therapy modalities and broader based clinical studies in patients with ruptured AS of the liver. An effort needs to be undertaken to include patients with ruptured AS of the liver after surgery into prospective trials. The opportunity to establish an international study group may, furthermore, allow a collection of tumor samples from AS in a reasonable number. Consecutive molecular analysis could help to establish targeted antitumoral therapies for these rare and extremely lethal malignancies.

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