Radiology Case Reports 16 (2021) 3354–3358

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Case report

Transarterial chemoembolization for Kasabach-Merritt syndrome caused by hepatic angiosarcoma: A case report ☆

Ziyu Tang, master degree, Hong Hu, bachelor's degree, Yunguo Liao, master degree, Chao Li, master degree, Xing Deng, master degree, Shixiang Qiu, master degree*

Department of Interventional Radiology, Nanchong Central Hospital, Sichuan Province, China

ARTICLE INFO

Article history:
Received 21 July 2021
Revised 1 August 2021
Accepted 1 August 2021
Available online 29 August 2021

Keywords:
Kasabach-Merritt Syndrome
Hepatic angiosarcoma
Interventional radiology treatment

ABSTRACT

Hepatic angiosarcoma is a rare disease, and hepatic hemangiosarcoma with Kasabach-Merritt syndrome (KMS) is even rarer. Although there have been several reports about KMS caused by hepatic angiosarcoma, there has been no mention of successful treatment regimens for hepatic angiosarcoma with KMS. A 64-year-old female patient presented with right upper abdominal pain and multiple cutaneous purpuras for 10 days. Blood analysis revealed that hemoglobin, platelet and fibrinogen were significantly decreased, prothrombin time was prolonged, fibrinogen degradation products were increased. Contrast-enhanced computed tomography scan of the abdomen demonstrated a large mass in the right lobe of the liver, which is pathologically suggestive of hepatic angiosarcoma. Based on the above examination, the patient was diagnosed with KMS caused by hepatic angiosarcoma. Repeated transfusion of blood products could only temporarily improve the coagulation function of the patient. After transarterial chemoembolization, the patient experienced a long-term improvement of blood clotting, and the patient's survival increased by six months. Transarterial chemoembolization should be considered one of effective therapies for hepatic angiosarcoma with KMS.

Background

Hepatic angiosarcoma, originating from hepatic vascular endothelial cells, has a very low incidence and is highly aggressive and rapidly progressive. It is the most common primary malignant mesenchymal tumor of the liver in adults [1], accounting for approximately 2% of all primary hepatic malignancies [2].

Kasabach and Merritt first reported Kasabach-Merritt syndrome (KMS) in 1940, which is a rare but potentially life-threatening condition. The syndrome has the characteristics of thrombocytopenia, anemia, prolonged prothrombin time (PT), and hypofibrinogenemia [3]. Although there have been

☆ Competing interests: The authors declare that they have no conflict of interest.

* Corresponding author.
E-mail address: 18281796570@163.com (Z. Tang).

https://doi.org/10.1016/j.radcr.2021.08.004

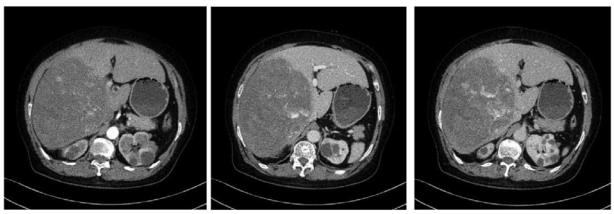

Fig. 1 – Contrast-enhanced CT of the abdomen (2 d after onset) demonstrated a large tumor in the right lobe of the liver with uneven enhancement in (A) arterial, (B) venous, (C) delayed phases.

some reports of KMS caused by hepatic angiosarcoma, there has been no mention of successful treatment regimens [4,5]. In this report, the patient was diagnosed with KMS caused by hepatic angiosarcoma and showed significant long-term improvement after transarterial chemoembolization (TACE).

Case presentation

A 66-year-old female patient came to our out-patient with the chief complaint of Right upper abdomen dull pain and multiple skin purpura for 10 days. The patient was admitted to hospital and received laboratory test and ultrasound examination immediately.

The abnormal blood analysis results were as follows: aspartate transaminase, 65 U/L (13-35U/L);hemoglobin, 76 g/L (110-150 g/L); platelet, 37 × 109/L (100-300 × 109 /L);PT, 15.6 s (9.0-14.0 s); fibrinogen, 1.5 g/l (2.0-4.0 g/l); International Normalized Ratio(INR), 1.35 (0.8-1.22); α-fetoprotein, 5.12 ng/mL (<13.6 ng/mL); carcinoembryonic antigen, 1.93 ng/mL (0-3.4 ng/mL); Carbohydrate antigen 19-9,61.89 (0-27 U/mL); Carbohydrate antigen 125, 54.58 (0-35 U/mL).

Abdominal ultrasonography revealed a huge neoplasm in the right lobe of the liver. A contrast-enhanced CT scan was obtained subsequently, which revealed a huge mass with heterogeneous enhancement in arterial, venous, delayed stages in the right lobe of the liver (Fig. 1).

Abnormal re-examine laboratory tests three days later as follows: platelet, 38 × 109 /L; PT, 16.4 s; fibrinogen, 0.34 g/L; FDP, 110.9 /ml (0-5 ug/ml); INR, 1.42. After 450 ml of fresh frozen plasma was injected, the coagulation function of the patient was significantly improved. Six days later laboratory tests

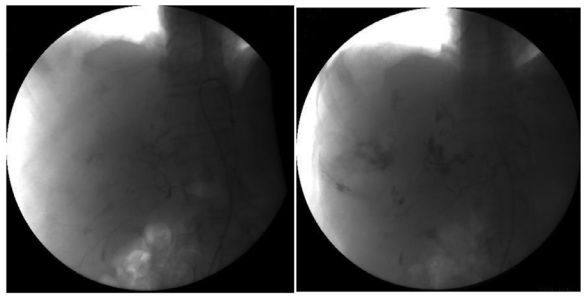

Fig. 3 – During TACE (2 wk after onset), (A)large tumor staining was visible. After TACE, (B) iodinated oil deposition was observed in the tumor.

showed as follows: platelet, 68 × 109 /L; fibrinogen,0.63 g/L; PT, 14.4 s, FDP, 103 ug/ mL, INR of 1.25.A CT-guided percutaneous liver biopsy was performed immediately. Hematoxylin-eosin staining showed abnormal proliferation of tumor cells. Immunohistochemical staining showed CD31(+), CD34(+), ERG (+), Ki-67 (positive cells,20%). (Fig. 2), Based on the above laboratory examination, CT examination and pathological examination results, the patient was finally confirmed to be hepatic angiosarcoma with KMS.

Two more intermittent transfusions of fresh frozen plasma or cryoprecipitate could rapid relief of coagulation, but the patient's coagulation deteriorated again after 2-3 days. Two weeks later, the patient's clotting function deteriorated further, abnormal laboratory results as follows: platelet, 48 × 109 /L, fibrinogen,0.22 g/L, PT, 36.7s, FDP, 85.4 ug/ mL, INR 3.12 and the patient's skin purpura scope was distinct increased. Infusion of blood products could only temporarily improve the patient's coagulation function, which deteriorated rapidly as the tumor progressed. Moreover, the patient's tumor volume was too large and the coagulation function was too poor to removed surgically. Therefore, after the patient received 400 ml of fresh frozen plasma and 10 units of cryoprecipitate in batches, we decided to perform TACE for this patient. During the intraoperative angiography, obvious tumor staining was visible. 5 ml Iodized oil, polyvinyl alcohol drug embolization microspheres (carrying epirubicin 80 mg) and Polyvinyl alcohol microspheres were used for embolization. After operation, iodinated oil deposition was observed in the tumor (Fig. 3). Nine days later after TACE, laboratory test as follows: platelet 237 × 109 /L; fibrinogen 1.95 g/L; PT, 12.8 s;FDP, 41.3 μg/ mL, INR 1.11. The patient's subcutaneous purpura was re-

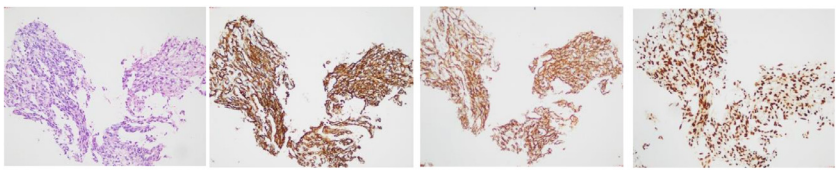

Fig. 2 – (A) Hematoxylin-eosin staining showed abnormal proliferation of tumor cells. Immunohistochemical staining showed (B) CD31(+), (C) CD34(+), (D) ERG (+).

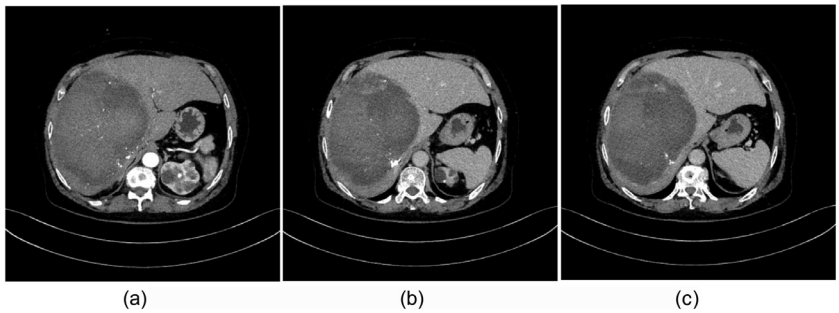

Fig. 4 – Abdominal enhanced CT (2 mo after onset) showed significant necrosis of the tumor in a wide range in (A) arterial, (B) venous, (C) delayed phases.

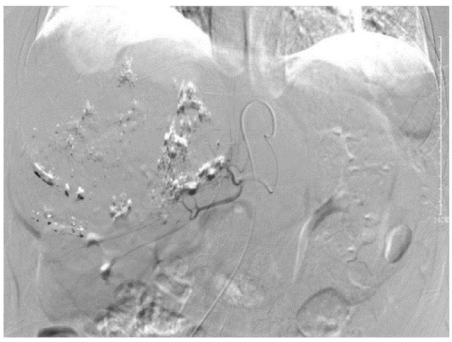

Fig. 5 – Intraoperative angiography of TACE (2 mo after onset) showed a small amount of dark staining of the tumor was visible.

lieved and after 3 days of observation, the patient's condition did not progress. the patient's clotting dysfunction was significantly improved and returned to normal, and the patient did not need to receive blood products to maintain life.

Two months later, the patient was admitted for a review, laboratory tests as follows: platelet 257 × 109 /L; fibrinogen, 3.89 g/L; prothrombin time, 11.8 s; FDP,32 ug/ml; INR, 1.03;the abdominal enhanced CT showed significant necrosis of the tumor in a wide range (Fig. 4). The patient underwent hepatic arterial chemoembolization again, during which a small amount of dark staining of the tumor was visible (Fig. 5), and a small amount of iodized oil, PVA HepaSphere were used for embolization. Six months later, the patient visited the clinic due to severe abdominal pain. CT examination revealed multiple metastatic lesions in the liver (Fig. 6). Laboratory tests as follows: platelet, 132 × 109 /L;fibrinogen, 1.35 g/L. PT, 14.3 s; FDP, 71 μg/ml; INR, 1.35; and the patient died of massive bleeding before the emergency hepatic artery embolization.

Discussion and conclusions

Hepatic angiosarcoma is the most common primary interstitial malignancy tumor of the liver and the third most common primary liver malignancy [6,7], but it is a low incidence tumor, which accounts for approximately 2% of all primary hepatic malignancies [4,8] and accounts for only approximately 5% of all angiosarcomas [2], with only approximately 200 confirmed cases each year worldwide [9]. Hepatic angiosarcoma is characterized by high degree of malignancy and rapid progression. The median OS time is only 6 months, and the 1-year survival rate is only 30.4% [2]. The main causes of death for hepatic angiosarcoma were liver failure, disseminated intravascular coagulation and massive bleeding caused by hepatic rupture [9].

Nosogenesis of liver angiosarcoma is still unclear, thorotrast, polyvinyl chloride, colloidal solutions of thorium dioxide, cerium (IV) oxide, radiation and arsenic, anabolic steroid and oral contraceptives may increase the risk of hepatic angiosarcoma development [2, 4, 6, 8–10], At the same time, There is no evidence that viral hepatitis contributes to tumor development [11]. However, the reported patients did not have any of these risk factors, suggesting that more remains to be discovered.

The clinical manifestations of hepatic angiosarcoma are varied, such as abdominal pain, abdominal distension, chest

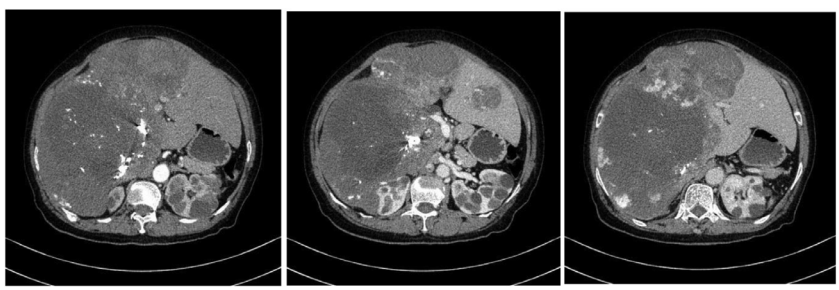

Fig. 6 – CT (6 mo after onset) examination revealed multiple metastatic lesions in the liver.

pain, chest tightness, low back pain, fever, jaundice, ascites, weight loss, fatigue, etc. There are also patients with ecchymatitis, melena or anemia in the lower limbs, uncontrollable bleeding after trauma, or even patients with no obvious clinical symptoms, the disease is not detected until the physical examination [2].

In most patients with hepatic angiosarcoma, the levels of serum tumor markers such as α-fetoprotein, carcinoembryonic antigen, Carbohydrate antigen 19-9, Carbohydrate antigen 125 did not increased [2].

Hepatic angiosarcoma CT typically presents an ill-defined mass with uneven density and a tendency to hemorrhage. Contrast-enhanced CT scan shows hypervascular, heterogeneously enhancing masses [2], arterial ring enhancement, continuous centriolar filling in the venous and late stages, possibly with an arteriovenous fistula, and finally uneven patchy enhancement, thus differentiating it from hepatic hemangioma with progressive homogeneous central enhancement addition. A few angiosarcomas showed heterogeneous enhancement, rapid early enhancement, well-defined boundaries, and indistinguishable from hepatocellular carcinoma [4,6,9].

Like most malignancies, hepatic angiosarcoma requires pathologic diagnosis to be definitive. On immunostaining, tumor cells showed positive vascular markers such as ERG transcription factors, CD31, CD34, factor VIII antigens and epithelial markers (Cam5.2 and CK7), among which ERG may be a more sensitive and specific marker for pathological diagnosis [10,12,13,14,15].

There is no standard treatment for primary hepatic angiosarcoma, Liver transplantation is contraindicated to hepatic angiosarcoma because of its high recurrence rate and poor survival [8], Surgical resection is considered to be the most effective treatment and may be curable, however, due to its invasive and multifocal nature, less than 20% of patients are suitable for radical hepatectomy [4,16]. TACE has been shown to be effective in unresectable intrahepatic masses, especially in ruptured bleeding masses [12,16,17], This is why we chose TACE to treat the patients in this report. Chemotherapy has limited survival in improving advanced hepatic angiosarcoma, and there is currently no recognized chemotherapy regimen and radiotherapy does not improve survival in patients with hepatic angiosarcoma. Targeted therapies such as sorafenib and bevacizumab have not shown good efficacy, and there are no reports on immunotherapy of hepatic angiosarcoma [16].

Hepatic angiosarcoma has a poor prognosis. Without treatment, the survival time of most patients is less than half a year [18,19], Even with treatment, only about 3% of patients survive longer than two years [4].

In 1940, Kasabach and Merritt first reported KMS, which mainly occurs in children with kaposiform hemangioendothelioma or tufted angiomas [3]. KMS is a rare but life-threatening complication of vasogenic neoplasms with clinical manifestations of anemia, thrombocytopenia, low fibrinogen, prolonged PT, and significantly increased FDP and D-dimer [4]. The basic pathophysiology of KMS is platelet trapping, activation and consumption within the tumor, with a prominent decrease in platelet level. Previously, KMS has only been reported in pedia with kaposiform hemangioendothelioma and tufted hemangioma [4], but several cases of adult hepatic angiosarcoma with KMS have recently been reported [20].

It has been reported that the mortality rate of KMS patients due to benign vascular disease is about 12%, even as high as 20% to 30% [21], while the mortality rate of KMS patients due to hepatic angiosarcoma, although no relevant data are available, is expected to be more higher, as the tumor itself is more difficult to treat than emangioendothelioma and tufted hemangioma .Though there have been some articles reported the merger of hepatic angiosarcoma with KMS, but those articles did not mention effective treatment. In this article, the rapid improvement in the coagulation function of the patient through transhepatic arterial chemotherapy embolization shows that it is an effective treatment for KMS caused by hepatic angiosarcoma.

Ethical statement

I certify that this manuscript is original and has not been published and will not be submitted elsewhere for publication while being considered by Diagnostic and Interventional Imaging. And the study is not split up into several parts to increase the quantity of submissions and submitted to various journals or to one journal over time. No data have been fabricated or manipulated (including images) to support your conclusions. No data, text, or theories by others are presented as if they were our own.

The submission has been received explicitly from all co-authors. And authors whose names appear on the submission have contributed sufficiently to the scientific work and therefore share collective responsibility and accountability for the results.

This article does not contain any studies with human participants or animals performed by any of the authors.

Patient consent

Informed consent was obtained from all individual participants included in the study.

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