CASE REPORT

Chemoembolisation combined with percutaneous radiofrequency ablation in the treatment of primary angiosarcoma of the liver

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SUMMARY

Angiosarcoma of the liver is a rare disease; however, it ranks as the third most common primary liver malignancy. Diagnosis is difficult and prognosis is very poor. After the onset of clinical symptoms, the disease often progresses rapidly, decreasing the chances of curative treatment. We report the case of an 83-year-old male patient who presented with postprandial fullness. Upper abdominal ultrasound showed a hypervascular mass in segment 6 of the liver. The results of anatomopathological examination and immunohistochemistry were compatible with the diagnosis of primary angiosarcoma of the liver. Patient refused surgery (hepatectomy), and treatment was then initiated with transarterial chemoembolisation, followed by percutaneous radiofrequency ablation. The patient is currently cured based on clinical and radiological evidence. This case report is the first in the literature to describe the combined use of transarterial chemoembolisation with percutaneous radiofrequency ablation in the treatment of primary angiosarcoma of the liver.

BACKGROUND

We report a rare case of liver tumour. It is the first case report in the literature to describe an alternative and effective approach using transarterial chemoembolisation (TACE) combined with percutaneous radiofrequency ablation (RFA) in the treatment of primary angiosarcoma of the liver.

CASE PRESENTATION

An 83-year-old male patient presented with postprandial fullness and flatulence. He denied pain, fever, weight loss or jaundice and had no episodes of diarrhoea. The patient reported no history of viral hepatitis or alcoholism.

On physical examination, the patient was conscious, well oriented, eupnoeic, ruddy, hydrated, anicteric and afebrile. He had a flaccid and painless distended abdomen, RHA-positive, sudden negative decompression and free Traube's space without hepatomegaly. The patient had cardiac arrhythmia with use of a pacemaker.

Upper abdominal ultrasound showed a hepatic mass of 4.2×3.5×3.4 cm in the right lobe. A contrast-enhanced CT scan (figure 1) revealed a single calcified nodule measuring 4.0×3.6 cm and located in segment 6 of the liver, but no aetiology could be established. Upper gastrointestinal

endoscopy showed erosive gastritis. Diverticular disease of the colon was detected on optical colonoscopy.

Laboratory tests included: haemoglobin 13.6 g/dl, haematocrit 40.7%, leucocytes 7000/mm³, platelets 185 000/mm³, international normalised ratio 1.15, glucose 87 mg/dl, urea 43 mg/dl, creatinine 0.9 mg/dl, albumin 4.2 g/dl, aspartate aminotransferase 19 U/l, alanine aminotransferase 17 U/l, γ-glutamyltransferase 15 U/l, alkaline phosphatase 48 U/l, total bilirubin 0.65 mg/dl, direct bilirubin 0.26 mg/dl, indirect bilirubin 0.39 mg/dl, HBV surface antigen (negative), anti-HBs (negative), anti-HBc (negative), antihepatitis C virus (negative), carcino-embryonic antigen, carbohydrate antigen 19.9 elevated α-fetoprotein values within the normal range.

Ultrasound-guided biopsy showed a vascular neoplasm, consisting of angiosarcoma (figure 2).

Surgery (hepatectomy) was indicated for treatment of a single lesion; however, the patient and his family refused surgical treatment due to cardiac risk. Treatment was then initiated with hepatic TACE using drug-carrying microspheres (DC Bead microspheres Biocompatibles, Surrey, UK) plus doxorubicin (50 mg) (figure 3A). At 30 days, follow-up CT scan showed necrosis of approximately 85% of the lesion, but with an irregular residual area of viable tumour located in the peripheral region of the nodule. We then proposed the use of CT-guided percutaneous RFA (figure 3B).

The RFA procedure was performed with the patient under general anaesthesia and orotracheal intubation. A previous CT scan was used for procedure planning, when we decided on the best strategy to be adopted, the shortest route to the lesion and the safest needle path, that is, avoiding important organs/structures in the abdominal cavity, in our case, the hepatic angle of the colon and the gallbladder. With a single posterior puncture (retroperitoneal approach) of segment 6 of the liver, the multitined expandable electrode with continuous temperature feedback was placed at a distance of approximately 2.0 cm from the centre of the lesion. A single RFA needle with a 2 cm active tip (StarBurst electrodes; RITA Medical Systems, Mountain View, California, USA) was introduced, and the tip was advanced gradually into the centre of the target lesion under real-time CT guidance. An electrical circuit was thus established between the needle tip, the two grounding pads attached to

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Figure 1 (A) Axial CT scan showing a heterogeneous hypervascular nodule in segment 6 of the liver (arrow). (B) Coronal maximum intensity projection CT scan showing the hypervascular nodule.

the skin and the radiofrequency generator (Model 1500X; RITA Medical Systems). Two cycles of 10 min each with 5 min interval were performed. The mean effective temperature for RFA of liver tumours is around 100°C. Immediately after completing two cycles, contrast-enhanced CT scans were obtained, confirmed treatment success and ruled out any immediate complications. At 1 week, follow-up CT scan showed complete necrosis of the RFA-treated nodule (figure 4).

INVESTIGATIONS

Primary hepatic sarcoma is a rare tumour that includes a heterogeneous group of histological subtypes. Treatment of primary sarcoma of the liver is usually delayed for months due to vague abdominal symptoms and equivocal imaging findings.

Surgery is currently the treatment of choice for patients with primary hepatic sarcoma and may significantly prolong survival in a select group of patients with low-grade tumours.¹ Multimodality treatment has been used in extremity sarcomas to achieve superior local control and improve disease-free survival.²

Routine adjuvant chemotherapy for primary liver sarcoma, however, cannot be presently recommended. Following resection, patients diagnosed with primary liver sarcoma should be

referred to ongoing clinical trials. Other therapeutic options have been described in the treatment of primary liver malignancy, mainly hepatocellular carcinoma, including alcohol injections, RFA, cryoablation, chemoembolisation and combined approaches.

This case report is the first in the literature on combined treatments to describe the use of TACE with percutaneous RFA in primary angiosarcoma of the liver.

OUTCOME AND FOLLOW-UP

The patient has been followed up at 3 month intervals by contrast-enhanced CT of the abdomen, analysis of serum tumour markers and clinical evaluation, and was free of tumour recurrence and/or distant metastases at the time of the last follow-up scan. The patient is currently in excellent general health.

DISCUSSION

Angiosarcoma, a subtype of soft tissue sarcoma, is an aggressive malignant disease deriving from endothelial, lymphatic or blood vessels. Angiosarcoma occurs most commonly in the head and neck, followed by breast. The liver is ranked as fifth in the list of the most common sites of angiosarcoma.³

Figure 2 Microscopic analysis. (A) Immunohistochemistry—H&E staining. (B) Immunohistochemistry—CD31-positive—diffuse positivity.

Figure 3 (A) Superselective chemoembolisation of the tumour with parasitic vascularisation originating from the right hepatic branch. (B) CT-guided percutaneous radiofrequency ablation—patient in the left lateral decubitus position, retroperitoneal approach and radiofrequency needle tip placed within the nodule located in segment 6 of the liver.

Angiosarcoma of the liver is a very rare disease and occurs mainly in the elderly.⁴ Although symptoms are usually non-specific, abdominal distension and discomfort, weight loss and fatigue are commonly found in this condition.^{5–6} Symptoms such as jaundice, ascites and hepatomegaly are often associated with advanced disease and attributed to the replacement of normal liver parenchyma by tumour.⁷

Given the hypervascular nature of the tumour, it is difficult to radiologically differentiate liver angiosarcomas from other vascular tumours of the liver. Major differential diagnoses include hypervascular metastases, hepatocellular carcinoma and haemangioma. In contrast to hepatocellular carcinoma, angiosarcoma shows continuous progressive enhancement on delayed-phase images. Splenic metastasis and absence of cirrhosis or elevated α -fetoprotein levels may also indicate angiosarcoma rather than hepatocellular carcinoma. The immunohistochemical panel associated with histological aspects of vascular tumours has the following characteristics: predominantly architectural atypia with the formation of intercommunicating vascular channels with a patent lumen; non-significant cytological atypia; and non-reactive human herpes virus-8 expression.

Patients with liver angiosarcoma have a very poor prognosis with a median survival of 6 months without treatment. Even after treatment, only 3% of patients have been reported to live longer than 2 years.⁸ The reasons contributing to this

unfavourable outcome are complicated. First, because the symptoms of the disease are non-specific, its diagnosis is usually made too late, ruling out the possibility of complete tumour resection in most cases. Second, angiosarcoma of the liver usually presents with early metastasis to other organs, such as lung, spleen and bone, which further worsens the prognosis. At present, the standard treatment for liver angiosarcoma is surgical resection. Other approaches, such as chemotherapy and radiotherapy, have failed to show a conclusive survival benefit for patients with liver angiosarcoma,^{9–11} although chemotherapy plays a central role in the treatment of soft tissue sarcoma and radiotherapy plays a palliative role in liver metastases.¹² Likewise, liver transplantation is not deemed feasible for treatment of liver angiosarcoma because of its high recurrence rate and poor post-transplant survival.¹³

TACE is a widely used therapeutic modality for unresectable hepatocellular carcinoma and has an excellent antitumour effect.^{14–16} However, the efficacy of TACE remains controversial¹⁷ because hepatocellular carcinoma is sometimes resistant to TACE treatment. Hashimoto *et al*¹⁸ reported that TACE induced complete necrosis only in 50% of single nodular-type tumours.

While treatment of TACE-resistant hepatocellular carcinoma is a major clinical goal, RFA has been accepted as a safe and useful technique for the local treatment of this malignancy.

Figure 4 (A) Postcontrast axial CT scan immediately after the procedure showing complete absence of contrast enhancement (arrow). (B) Postcontrast coronal CT scan 1 week after the procedure showing complete necrosis of the nodule.

Chang *et al*¹⁹ found that RFA for incompletely treated hepatocellular carcinoma after TACE produced a relatively high complete ablation rate. Their findings are consistent with previous studies. Shibata *et al*²⁰ reported that complete ablation was achieved in 46 (96%) of 48 hepatocellular carcinomas (≤ 4 cm) treated with RFA, and Lencioni *et al*⁷ in 63 (91%) of 69 hepatocellular carcinomas (≤ 5 cm). Moreover, the side effects and the long-term impairment of liver function associated with TACE^{21 22} further supports the use of RFA rather than subsequent repeated TACE treatments.

Although primary angiosarcoma of the liver is a rare tumour, it can behave radiologically like other vascular tumours of the liver. In unresectable cases and/or patients with a contraindication to surgical treatment, there are other effective treatment options, such as TACE, RFA or even the combination of the two techniques.

Learning points

- ▶ Few cases of primary angiosarcoma of the liver have been reported.
- ▶ It is particularly difficult to identify this condition because its clinical presentation and laboratory and imaging tests are extremely non-specific.
- ▶ Although surgery is the definitive treatment, it is technically complex, and the neoplasm is often disseminated at the time of diagnosis, making resection impossible.
- ▶ Transarterial chemoembolisation combined with radiofrequency ablation is an excellent treatment option for patients in whom surgery is contraindicated and for those with single lesions larger than 5 cm.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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