Rare disease

Angiosarcoma of the liver as a cause of fulminant liver failure

Marco Montell García,¹ Raúl Romero Cabello,^{1,2} Raul Romero Feregrino,³ Mercado Atri Moises,⁴ Rafael Trejo Estrada,⁵ Padilla-Rodríguez Alvaro,^{6,7} Gama Moreno Manlio Gerardo,⁸ Romero Feregrino Rodrigo³

¹Department of Infectology, Hospital General de México, Mexico City, Mexico D F, Mexico

²Department of Microbiology and Parasitology, Faculty of Medicine, Universidad Nacional Autónoma de México

³Department of Infectology, Instituto para el Desarrollo Integral de la Salud (IDISA), Mexico City, Mexico D F, Mexico

⁴Endocrinology, Centro Médico ABC, México

⁵Gastroenterology, Centro Médico ABC, México DF, México

⁶Department of Pathology, Centro Médico ABC, México DF, México

⁷Department of Pathology, Universidad Panamericana, México

⁸Department of Nuclear Medicine, Centro Médico ABC, México

Correspondence to Dr Raul Romero Feregrino, draulromeroferegrino@hotmail.com

Summary

Primary liver sarcomas make up 2% of all malignant neoplasms of the liver; of these, angiosarcoma is the most common type. Primary liver tumours rarely cause fulminant hepatic failure (FHF), which is most frequently caused by non-neoplastic pathologies. In the case of neoplasms, the most frequent are lymphoma and metastatic carcinomas. We describe the case of a 76-year-old man who suffered from FHF as a result of a liver angiosarcoma and we present a review of the medical literature in which we found only two cases of liver angiosarcomas linked to FHF.

BACKGROUND

Primary sarcomas of the liver make up 2% of all malignant neoplasms of the liver. The most frequent type is primary angiosarcoma of the liver, comprising 50% of the cases, followed by leiomyosarcoma (17%) and fibrosarcoma (7%).^{1–4}

Some of the risk factors for the development of angiosarcoma are: exposure to thorium dioxide (thorotrast), which was used as a contrast medium in angiograms in the 1930s to the 1950s; use of androgenic steroids, diethylstilbestrol, exposure to vinyl chloride, arsenic, haemochromatosis, von Recklinghausen's disease and a history of radiation exposure.^{5–9}

The clinical presentation of our patient was fulminant hepatic failure (FHF). This is rarely caused by primary tumours or metastasis in the liver, which are most frequently caused by pharmacological toxicity and viral hepatitis. Less frequent causes include Budd-Chiari syndrome, Wilson's disease and autoimmune hepatitis.¹⁰ Among 4020 cases of FHF reported by Rowbotham *et al*,¹¹ only 18 (0.44%) were caused by tumour infiltration.

There are also some reported cases of FHF resulting from tumour activity in which the most frequent aetiological diagnoses were: Hodgkin's lymphoma, non-Hodgkin's lymphoma and metastatic carcinoma.^{11–20}

In the international medical literature, we found only two reported cases of FHF related to hepatic angiosarcoma.²¹ In this article, we discuss the case of a patient with hepatic angiosarcoma leading to FHF.

CASE PRESENTATION

The case is a 76-year-old man with a clinical picture at 15 days of evolution characterised by swelling of inferior

limbs, asthenia, adinamia and hyporexia as well as jaundice, coluria, nausea and disorientation. The patient reported having lost approximately 4 kg during the previous 3 months. A physical examination found clinical data showing hepatic encephalopathy, enlargement of the liver (hepatomegaly) which was slightly painful to the touch, jaundice of the integuments and an abdomen with shifting dullness. Laboratory results showed alteration in the liver function tests: total bilirubin: 20.5 mg/dl; direct bilirubin: 19 mg/dl; alanine transaminase 110 UI/l, aspartate aminotransferase 214 UI/l; alkaline phosphatase: 402 UI/l; albumin: 2.7 g/dl; ammonium: 81 µmol/l; coagulogram: INR—1.92; TP 21 seg.; TTPA 66 seg.

A computerised axial tomography of the abdomen was ordered. It showed that the liver had irregular contours, heterogeneous hepatic parenchyma, with diffusely distributed multiple hypodense focal lesions (figure 1). A positron emission tomography/CT was then ordered, which showed a significant increase in hepatic metabolic activity (figure 2). Treatment for hepatic encephalopathy was provided to the patient who responded partially. Given the alteration in coagulation times, it was decided to perform a transjugular biopsy of the liver.

The histopathological examination revealed fragments of residual liver parenchyma with minor cholestasis intermixed with extensive areas of necrosis, which alternated with areas of proliferation of malignant cells in a storiform pattern made up of spindle cells, ovoid nuclei, marked pleomorphism, fine even chromatin, with mild cytoplasm with poorly defined cell boundaries and frequent mitotic figures. Occasionally, the cytoplasm of the malignant cells formed small vascular lumen. A complete immunohistochemistry was performed. Tumour cells were

Figure 1 Abdomen contrasted TAC, shows multiple focal lesions in hepatic parenchyma.

strongly positive for the epithelial differentiation markers such as CD31, CD34 and factor VIII. This led to a definite diagnosis of hepatic angiosarcoma (figures 3–5). The patient died the month that he was diagnosed.

DISCUSSION

Hepatic angiosarcoma occurs with more frequency during the sixth decade of life, with a men-to-women ratio of 1.9:1. The clinical diagnosis is complicated because the signs and symptoms are non-specific—65% of the patients have clinical data related to the liver such as an enlarged liver (hepatomegaly), abdominal pain or ascites (as was the case with our patient); 15% suffer from acute abdomen and haemoperitoneum as a result of the rupture of the tumour; 15% have enlargement of the spleen or, sometimes, pancytopenia; and 9% present distant metastases.

Figure 2 Positron emission tomography shows ^{18}F -FDG caption in hepatic parenchyma.

Figure 3 Spindle cells proliferation in hepatic tissue.

In the case of our patient, the clinical presentation was of a FHF, which is defined by hepatic failure, manifested in encephalopathy or coagulopathy in a patient without previous liver disease and which develops within the first 2 weeks after the first symptom of liver disease, which is usually jaundice.

As indicated above, this was a relatively rare presentation of a primary neoplasm of the liver. In terms of laboratory findings, tests frequently show alterations in liver function with a predominantly cholestatic pattern. It is very rare to encounter to find an elevation of transaminases to more than double their baseline value, the α -fetoprotein is usually at normal values.

Clinical studies that are useful for the diagnosis are ultrasounds that show the areas of heterogeneous echogenicity, sometimes with data suggesting central necrosis; in the CT, one can observe areas of hypodensity in the hepatic parenchyma,³ which may alternate with other hypodense areas corresponding to haemorrhages.¹³

For a definitive diagnosis it is necessary to perform a biopsy. Because of the vascular nature of such tumours, a high incidence of haemorrhage as a complication have

Figure 4 Tissue section observed at $\times 40$, shows pleomorphism and one central mitosis.

Figure 5 Positive CD-31 immunohistochemistry in neoplastic cells.

been reported.^{3 5} For this reason, it is suggested that, when possible, a transjugular biopsy be performed. Our patient received this type of biopsy without complications. Unfortunately, sarcomas tend to have a poor prognosis and rapid progression: without treatment, life expectancy is 6 months and only 2% of patients live more than 2 years.^{22 23}

Treatment for angiosarcoma is still not well defined. Partial hepatectomy is indicated in cases in which the tumour is confined to a hepatic lobe and the rest of the parenchyma is normal.²⁴ However, it is rare for a patient with angiosarcoma to meet these conditions—there is only one reported case of survival for 10 years after a hepatectomy.²⁵

Currently, it is thought that the presence of angiosarcoma is a contraindication to liver transplantation, since those patients who received transplants incidentally or with therapeutic intentions did not demonstrate advantages for survival. The European Liver Transplant Registry reported one individual who survived for only 7 months among 17 patients with angiosarcoma receiving transplants. The use of chemotherapy has shown only limited improvement in survival rates.²⁶

CONCLUSIONS

Our patient arrived with the clinical data of FHE. Lacking a clear aetiology, one of the diagnostic possibilities to consider is a primary neoplasm of the liver. A biopsy is necessary to establish its nature.

Learning points

- This is the rare presentation of a very rare disease, and we did draw on the experience of many doctors of different specialties.
- During the progress of the case had to follow a diagnostic algorithm for the diagnosis, since this entity is rare.
- We had to get to know and respect the wishes of the patient about his treatment, he refused.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Bhati C**, Bhatt A, Starkey G, *et al*. Acute liver failure due to primary angiosarcoma: a case report and review of literature. *World J Surg Oncol* 2008;**6**:1–5.
2. **Miguelena JM**, Escartín J, Valenzuela MJ, *et al*. Histiocytoma fibroso maligno hepático: una rara variedad de sarcoma hepático. *Cir Esp* 2000;**68**:254–7.
3. **Lee SW**, Song CY, Gi YH, *et al*. Hepatic angiosarcoma manifested as recurrent hemoperitoneum. *World J Gastroenterol* 2008;**14**:2935–8.
4. **Padilla-Rodríguez AL**. Sarcoma indiferenciado (embrionario) del hígado. *Rev Med Hosp Gen Mex* 2002;**65**:168–72.
5. **Poggio JL**, Nagorney DM, Nascimento AG, *et al*. Surgical treatment of adult primary hepatic sarcoma. *Br J Surg* 2000;**87**:1500–5.
6. **Ligeti C**. Angiosarcoma of the liver associated with diethyl-ethyltestol. *JAMA* 1978;**240**:1510–1.
7. **Block JB**. Angiosarcoma of the liver following vinyl chloride exposure. *JAMA* 1974;**229**:53–4.
8. **Makk JL**, Creech J, Whelan G, *et al*. Liver damage and angiosarcoma in vinyl chloride workers. A systematic detection program. *JAMA* 1974;**230**:64–8.
9. **Monroe PS**, Riddell RH, Siegler M, *et al*. Hepatic angiosarcoma. Possible relationship to long-term oral contraceptive ingestion. *JAMA* 1981;**246**:64–5.
10. **Schilsky ML**, Shyoko H, Arnutt L, *et al*. ICU management of acute liver failure. *Clin Chest Med* 2009;**30**:71–87.
11. **Rowbotham D**, Wendon J, Williams R. Acute liver failure secondary to hepatic infiltration: a single center experience of 18 cases. *Gut* 1998;**42**:576–80.
12. **Emile JF**, Azoulay D, Gornet JM, *et al*. Primary non-Hodgkin's lymphomas of the liver with nodular and diffuse infiltration patterns have different prognoses. *Ann Oncol* 2001;**12**:1005.
13. **Ghosh P**, Fox IJ, Rader AM, *et al*. Fulminant hepatic failure as the initial manifestation of non-Hodgkin's lymphoma. *Am J Gastroenterol* 1995;**90**:2207–9.
14. **Zafrani ES**, Leclercq B, Vernant JP, *et al*. Massive blastic infiltration of the liver: a cause of fulminant hepatic failure. *Hepatology* 1983;**3**:428–32.
15. **Alexopoulou A**, Koskinas J, Deutsch M, *et al*. Acute liver failure as the initial manifestation of hepatic infiltration by a solid tumor: report of 5 cases and review of the literature. *Tumori* 2006;**92**:354–7.
16. **Harrison HB**, Middleton HM, Crosby JH, *et al*. Fulminant hepatic failure: an unusual presentation of metastatic liver disease. *Gastroenterology* 1981;**80**:820–5.
17. **Rajvanshi P**, Kowdley KV, Hirota WK, *et al*. Fulminant hepatic failure secondary to neoplastic infiltration of the liver. *J Clin Gastroenterol* 2005;**39**:339–43.
18. **Athanasakis E**, Mouloudi E, Prinianakis G, *et al*. Metastatic liver disease and fulminant hepatic failure: presentation of a case and review of the literature. *Eur J Gastroenterol Hepatol* 2003;**15**:1235–40.
19. **Tanaka M**, Watanabe S, Masaki T, *et al*. Fulminant hepatic failure caused by malignant melanoma of unknown primary origin. *J Gastroenterol* 2004;**39**:804–6.
20. **Kahraman A**, Miller M, Baba H, *et al*. Angiosarcoma of the liver as a rare cause of rapidly progressive liver failure. *Med Klin* 2006;**101**:746–50.
21. **O'Grady JG**. Treatment options for other hepatic malignancies. *Liver Transpl* 2000;**6**:S23–9.
22. **Locker GY**, Doroshov JH, Zwelling LA, *et al*. The clinical features of hepatic angiosarcoma: a report of four cases and a review of the English literature. *Medicine* 1979;**58**:48–64.
23. **Adson MA**, Beart RW. Elective hepatic resections. *Surg Clin North Am* 1977;**57**:339–60.
24. **Timaran CH**, Grandas OH, Bell JL. Hepatic angiosarcoma: longterm survival after complete surgical removal. *Am Surg* 2000;**66**:1153–7.
25. **Lerut J**. Liver transplantation and vascular tumours. *7th World Congress of the International Hepato-Pancreato-Biliary Association*. Edinburgh, UK, 2006.
26. **Dannaher CL**, Tamburro CH, Yam LT. Chemotherapy of vinyl chloride-associated hepatic angiosarcoma. *Cancer* 1981;**47**:466–9.

This pdf has been created automatically from the final edited text and images.

Copyright 2012 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Montell García M, Romero Cabello R, Romero Feregrino R, Atri Moises M, Trejo Estrada R, Alvaro P-R, Moreno Manlio Gerardo G, Feregrino Rodrigo R. Angiosarcoma of the liver as a cause of fulminant liver failure. *BMJ Case Reports* 2012;10.1136/bcr-2012-006417, Published XXX

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow