CASE REPORT

Diffuse cholangiocarcinoma presenting with hepatic failure and extensive portal and mesenteric vein thrombosis

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Accepted 4 June 2015

SUMMARY

A 64-year-old previously healthy man presented with a 4-week history of vague right upper quadrant abdominal pain. Imaging studies revealed extensive portal, splenic, superior and inferior mesenteric vein thrombosis with mosaic perfusion and wedge-shaped areas of liver perfusion abnormalities. An extensive thrombophilia workup including tests for factor V Leiden, prothrombin G20210A, lupus anticoagulant, paroxysmal nocturnal haemoglobinuria, protein C and S, homocysteine and antinuclear antibody titres were all negative. Other laboratory testing revealed an elevated alkaline phosphatase (340 IU/L). Surgical exploration and catheter-directed thrombolysis were not felt to be feasible given the extensive clot burden. He was started on anticoagulation therapy. Over the next 10 days, he required intensive care unit admission due to progressive hepatic encephalopathy and fulminant liver failure. He continued to decline and eventually died of multiorgan failure. Autopsy revealed extensive, diffuse intrahepatic cholangiocarcinoma that had almost entirely replaced his normal liver parenchyma.

chills, chest pain, nausea, vomiting, weight loss and any change in bladder or bowel habits.

His medical history was significant for hypertension (on treatment with atenolol and lisinopril). Otherwise, his surgical, family and occupational history was unremarkable. He was a lifetime non-smoker and denied any alcohol or illicit drug use. He had no risk factors for any sexually transmitted diseases including HIV, hepatitis B and hepatitis C. He denied any recent travel and any recent sick contacts.

The patient was haemodynamically stable on presentation (blood pressure 132/78 mm Hg, pulse 78 bpm, temperature 98 F, oxygen saturation 98% on room air) and in no acute distress at rest. Physical examination revealed a soft abdomen with localised tenderness in the right upper quadrant and a positive Murphy's sign. Respiratory, cardiovascular, neurological and other systemic examinations failed to reveal any abnormalities.

BACKGROUND

This case highlights the difficulty often encountered in establishing an aetiology for acute portal and/or mesenteric venous thrombosis. It also shows the occurrence of a very rare but aggressive form of diffuse intrahepatic cholangiocarcinoma in which the normal liver parenchyma is entirely replaced by invasive cholangiocarcinoma. In our case, this process was so widespread and diffuse that it was impossible to differentiate between normal liver parenchyma and tumour on imaging. A hepatic malignancy was not suspected antemortem because of lack of specific findings on contrast-enhanced CT imaging or ultrasonography of the liver.

CASE PRESENTATION

A 64-year-old Caucasian man with no significant medical history presented with a 4-week history of progressively worsening right upper quadrant abdominal pain. The pain began as a mild discomfort that worsened with activity and was relieved by over-the-counter pain medications. It gradually tended to worsen and be colicky in nature and also increased in severity, making it difficult for him to take a deep breath or perform any activity. He also noticed that the pain was worse after a meal and reported of early satiety. He denied any fever,

Figure 1 A triple-phase CT examination of the abdomen and pelvis showing heterogeneous and wedge-shaped areas of perfusion abnormalities in the liver.

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To cite: Vakil A, Guru P, Reddy DR (R), et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-209171

Figure 2 Autopsy specimen of the liver showing portal vein thrombosis along with extensive and diffuse intrahepatic cholangiocarcinoma entirely replacing the normal liver parenchyma.

INVESTIGATIONS

Initial laboratory studies showed a normal complete blood count. Electrolytes, pancreatic enzymes and markers of renal function were in the normal range.

Markers of liver function were abnormal with an elevated alkaline phosphatase (340 IU/L), elevated alanine aminotransferase and aspartate aminotransferase (301 U/L and 341 U/L, respectively) and a normal total serum bilirubin (1.5 ng/dL) and a normal ammonia level (19 µg/dL). His coagulation profile was within normal limits. An extensive thrombophilia workup (described earlier) was negative. Hepatitis panel was negative to show any evidence of acute, chronic or past infection with any of the hepatitis viruses.

A focused abdominal ultrasound failed to reveal any abnormalities.

A triple-phase CT examination of his abdomen and pelvis confirmed extensive portal, splenic, superior and inferior mesenteric vein thrombosis along heterogeneous and wedge-shaped areas of liver perfusion abnormalities (figure 1).

DIFFERENTIAL DIAGNOSIS

Portal and mesenteric vein thrombosis.

The most common underlying aetiologies include:

- ▶ Liver cirrhosis,
- ▶ Primary or secondary hepatobiliary malignancies (eg, hepatocellular carcinoma, cholangiocarcinoma, etc),
- ▶ Abdominal infections (eg, ascending cholangitis, cholecystitis or abdominal sepsis),
- ▶ Inflammatory conditions (eg, pancreatitis, inflammatory bowel disease, abdominal surgery, omphalitis, collagen vascular diseases),
- ▶ Myeloproliferative disorders,
- ▶ Thrombophilic conditions (eg, paroxysmal nocturnal haemoglobinuria, hyperhomocysteinaemia, inherited thrombophilia, oral contraceptive use),
- ▶ Extrinsic compression (pregnancy, tumour) or trauma.

TREATMENT

Surgical exploration and catheter-directed thrombolysis options were not felt to be feasible given the extensive clot burden and poor general condition. The patient was started on oral anticoagulation with oral warfarin and intravenous heparin.

OUTCOME AND FOLLOW-UP

Over the course of the next 10 days, the patient's general condition continued to deteriorate. He developed altered mental status. Laboratory values showed a marked increase in ammonia levels (220 µg/dL). He progressed to develop multiorgan failure leading to death. An autopsy examination revealed extensive and diffuse intrahepatic cholangiocarcinoma that had almost entirely replaced his normal liver parenchyma (figure 2). Extensive vascular invasion of the liver and focal lung metastasis with a lymphangitic spread were also found (figure 3).

DISCUSSION

Hepatobiliary carcinomas account for 15–24% of the cases with portal and mesenteric vein thrombosis.¹ In our review of the literature, we were unable to find a case of diffuse

Figure 3 (A) Histological examination showing complete replacement of the hepatic parenchyma by poorly differentiated carcinoma (H&E, ×200) coexpressing cytokeratin 7 (left inset, ×200) and cytokeratin 20 (right inset, ×200), compatible with cholangiocarcinoma. (B) The tumour showing marked nuclear pleomorphism (×400). Lymphovascular invasion was identified in the liver (C; ×200) and lung (D; ×400).

Learning points

- ▶ Portal and mesenteric venous thrombosis is a rare clinical entity that may present with non-specific symptoms.
- ▶ The most common underlying aetiologies include cirrhosis of the liver, primary or secondary hepatobiliary malignancies, infectious or inflammatory abdominal processes and myeloproliferative disorders.
- ▶ Underlying hepatobiliary malignancies may sometimes remain undiagnosed, therefore needing a high index of suspicion.
- ▶ Diffuse intrahepatic cholangiocarcinoma essentially replacing the entire liver is an extremely rare presentation and may not have the classic imaging or laboratory features typically seen in focal cholangiocarcinoma.

cholangiocarcinoma presenting in a rapidly fatal fashion with acute portal and mesenteric vein thrombosis. Portal venous thrombosis may be clinically silent and can be found incidentally when abdominal imaging is informed for other reasons.²

Symptoms may be very non-specific, ranging from abdominal pain, dyspepsia, nausea and vomiting to generalised weakness.³ Variceal bleeding may be seen in some cases due to the development of portal hypertension. Treatment typically involving anticoagulation with warfarin or low-molecular weight heparin has been found to be effective in the vast majority of patients.^{3 4} Surgical or catheter-directed clot removal is rarely performed.

Contributors All the authors were involved in researching for and writing of this manuscript. The first draft was written by AV and subsequently reviewed and approved by all the authors.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Janssen HL, Wijnhoud A, Haagsma EB, *et al.* Extrahepatic portal vein thrombosis: aetiology and determinants of survival. *Gut* 2001;49:720–4.
- 2 Qi X, Han G, He C, *et al.* CT features of non-malignant portal vein thrombosis: a pictorial review. *Clin Res Hepatol Gastroenterol* 2012;36:561–8.
- 3 Primignani M. Portal vein thrombosis, revisited. *Dig Liver Dis* 2010;42:163–70.
- 4 DeLeve LD, Valla DC, Garcia-Tsao G. American Association for the Study Liver Diseases. Vascular disorders of the liver. *Hepatology* 2009;49:1729.

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