CASE REPORT

Isolated hepatobiliary tuberculosis: a diagnostic challenge

Sathish Kandasamy,¹ Ramkumar Govindarajalou,²
Sunitha Vellathussery Chakkalakkoombil,² Prasanth Penumadu³

¹Department of
Neuroradiology, Sree Chitra
Tirunal Institute for Medical
Sciences and Technology,
Thiruvananthapuram, Kerala,
India

²Department of Radiodiagnosis,
Jawaharlal Institute of
Postgraduate Medical
Education, Pondicherry,
Pondicherry, India

³Department of Surgical
Oncology, Jawaharlal Institute of
Postgraduate Medical Education
& Research, Puducherry, India

Correspondence to

Dr Sunitha
Vellathussery Chakkalakkoombil,
drsunithapnair@rediffmail.com

Accepted 7 May 2018

SUMMARY

Hepatobiliary system involvement is frequently seen as part of disseminated tubercular infection. But primary isolated hepatobiliary tuberculosis with no evidence of tuberculosis elsewhere in the body is extremely rare. Isolated hepatobiliary tuberculosis can cause diagnostic dilemma as the clinical, laboratory and imaging features are non-specific in majority of the cases. We report the case of a 50-year-old woman who presented with hepatobiliary tuberculosis with no pulmonary or extra hepatic involvement. Liver function tests were abnormal and ultrasonography (USG), CT and MR cholangiopancreatography showed multiple focal lesions in the liver. The diagnosis of tuberculosis was confirmed by a USG-guided biopsy of the liver lesions. In endemic regions with the presence of supportive imaging findings, in the appropriate clinical setting, the possibility of hepatic tuberculosis should be considered and diagnosis has to be confirmed with histopathological examination.

BACKGROUND

Approximately 80% of all reported hepatic tuberculosis (TB) cases were due to systemic dissemination of tubercle bacilli.¹ Isolated liver involvement is an extremely rare entity, and it constitutes <1% of TB cases with <100 cases reported in the literature.² The radiological findings of hepatic TB are non-specific and these lesions can be misdiagnosed as neoplastic lesions or pyogenic abscess on imaging. Histopathological diagnosis is required for confirmation. Here we describe a case of isolated hepatobiliary TB without extrahepatic involvement with special emphasis on imaging features. Our patient also had portal vein thrombosis which is an extremely rare but reported association of hepatic TB.

CASE PRESENTATION

A 50-year-old woman presented with right hypochondrial pain associated with low-grade fever and weight loss for 7 months. No history of TB or any history of contact with a patient with TB. On examination, the patient was anaemic. There was no jaundice, organomegaly or palpable lymphadenopathy.

INVESTIGATIONS

Routine investigations revealed low haemoglobin of 7.3 gm/dL, elevated total leucocyte count of 12 700 cells/cu mm with a differential count of P62L30M6E1 and raised erythrocyte

sedimentation rate (ESR) (43 mm/hour). Liver function tests showed elevated total bilirubin (5.7 mg/dL) and direct bilirubin (3.2 mg/dL) levels, markedly elevated alkaline phosphatase (1881 IU/L) and borderline elevation of gamma-glutamyltransferase (111 IU/L). Aspartate aminotransferase (33 IU/L) and alanine aminotransferase (26 IU/L) were within normal limits. Levels of serum total proteins (5.1 g/dL) and albumin (1.7 g/dL) were low. Serological tests for HIV and hepatitis B were negative. Chest radiograph was normal (figure 1). Ultrasonographic (USG) evaluation of abdomen revealed multiple hypoechoic focal lesions and dilatation of intrahepatic biliary radicles in the right lobe of liver with a few enlarged periportal lymph nodes. Based on USG findings, hepatic abscesses, hepatic metastases or cholangiocarcinoma of right biliary tree were considered as probable diagnosis and further evaluation with CT was suggested.

Contrast-enhanced CT of the abdomen showed multiple hypodense lesions with heterogeneous enhancement, distributed along the portobiliary radicles with moderate intrahepatic biliary radicle dilatation in the right lobe. Thrombosis was noted in main and right and left branches of the portal vein with multiple periportal collateral venous channels (figure 2A,B). Multiple homogeneously enhancing lymph nodes were seen in periportal and upper retroperitoneal regions. Mild ascites was present.

As the focal dilatation of biliary radicles in the right lobe enhanced the doubt of cholangiocarcinoma, further evaluation with MR cholangiopancreatography (MRCP) was considered for detailed evaluation of the biliary tree. MRI of the abdomen with MRCP showed multiple linear and nodular T2 hypointense lesions showing restricted diffusion distributed along the portobiliary radicles in right lobe, and at porta with moderate intrahepatic biliary radicle dilatation (figures 3 A,B and 4 A–D). Common bile duct appeared normal in calibre. The hypointense signal intensity of lesions in T2-weighted sequences was a clue for suspecting tuberculous granuloma in MRI. But since the imaging findings in our case were not specific for any particular pathology, the patient was subjected to a USG-guided percutaneous Trucut biopsy of the lesions in the right lobe of liver and the histopathological examination revealed periportal granulomas composed of epithelioid cells, Langhans type of giant cells, lymphocytes and focus of caseous

To cite: Kandasamy S, Govindarajalou R, Chakkalakkoombil SV, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-223912

Figure 1 Chest X-ray PA view showing no abnormality.

necrosis consistent with caseating epithelioid granulomatous infection. Staining test for acid fast bacillus was negative. TB culture was not done in the biopsy specimen. TB-PCR was positive in the biopsy specimen.

DIFFERENTIAL DIAGNOSIS

Based on blood investigations which showed elevated total leucocyte count, raised ESR, reduced serum total proteins and albumin, raised bilirubin and markedly elevated alkaline phosphatase enzyme and on imaging findings which showed conglomerated focal lesions and dilated biliary radicles in the right lobe of liver with thrombosis of the portal vein and regional lymphadenopathy, two possibilities were considered, either granulomatous infection of the liver or cholangiocarcinoma involving the right lobe. As there were no features of pulmonary TB in chest X-ray or elsewhere in the abdomen, possibility of neoplasm was considered more likely than granulomatous infection initially. But later after MR imaging with hypointense T2 signal intensity pattern of the lesions and multifocal distribution of the lesions, suspicion of granulomatous infection was considered as a more probable diagnosis. Finally, a biopsy report confirmed the diagnosis to be TB.

TREATMENT

Based on the biopsy report of granulomatous infection and with positive TB-PCR in the biopsy specimen, a diagnosis of

hepatobiliary TB was made and she was put on antituberculosis treatment (ATT). The drug regimen included rifampin, isoniazid, ethambutol and pyrazinamide for first 2 months, followed by 4 months of rifampin and isoniazid.

OUTCOME AND FOLLOW-UP

After 2 months of initiation of ATT, the patient was evaluated with USG abdomen and there was subtle resolution in the size and number of hepatic focal lesions. The biliary radicle dilatation had also mildly reduced. The Patient tolerated the ATT well. Follow-up USG was done after completion of 6 months of ATT and there were no visible focal lesions or biliary radicle dilatation in the liver. Partial recanalisation was noted in the main and right and left branches of the portal vein. Liver function tests also were within normal limits.

DISCUSSION

The number of TB cases is on the increase worldwide since past few decades. The WHO estimates that 8.7 million people develop active TB disease and 1.4 million die from TB annually.^{3,4} The increase in HIV/AIDS cases all over the world together with emergence of multidrug-resistant strains of *Mycobacterium tuberculosis* are attributed as the major causes for resurgence of TB.⁵ Immunosuppression status has also contributed to the rise in extra pulmonary TB cases.³ The involvement of liver in hepatic TB can be in various patterns. Both hepatic parenchyma and biliary system may be affected. A review of literature showed multiple classifications of hepatobiliary TB by various authors.⁶⁻⁸ Our case had nodular type of parenchymal TB forming clusters associated with TB cholangitis as evidenced by the irregular dilatation of biliary radicles. Our patient also had portal vein thrombosis which though extremely rare is reported in cases of hepatic TB.

Despite the high involvement rate of the liver and spleen, radiological detection of hepatic involvement is less common because most lesions are below the resolution of cross-sectional imaging. Around 75% of patients with hepatic TB were found to have pulmonary TB in chest radiograph. But in our case chest X-ray was normal. Results of biochemical investigations like elevated liver enzymes were non-specific. A moderate to marked increase in the serum levels of alkaline phosphatase, along with normal or mildly increased serum bilirubin, is considered suggestive of hepatic TB; however, these findings are not specific and may occur in other conditions. Low serum albumin levels and hyperglobulinaemia have also

Figure 2 CECT of upper abdomen axial (A) and coronal multiplanar reconstruction (B) images showing multiple hypointense lesions with minimal heterogeneous enhancement (black arrows) distributed along the biliary radicles, dilated intrahepatic biliary radicles (bold white arrow) and thrombosis of the portal vein in the right lobe of liver (thin white arrows). CECT, contrast-enhanced CT.

Figure 3 MRI of the upper abdomen: T2 Trufi axial (A) and coronal (B) images showing dilated intrahepatic biliary radicles (black arrow) with multiple hypointense lesions distributed along the biliary radicles.

been described as suggestive of hepatic TB.⁹ This pattern of biochemical alterations was observed in our patient.

Isolated hepatobiliary TB results from tubercle bacilli gaining access to the portal vein from a microscopic tubercular focus in the bowel. Jaundice is caused by TB invasion and oppression of bile ducts and is easy to be confused with cholangiocarcinoma.^{1 2} Some patients with hepatobiliary TB may be associated with portal hypertension or biliary tract bleeding. Though our patient had features of portal vein thrombus with collateral venous channel formation, there was no feature of portal hypertension. In follow-up imaging, there was partial recanalisation of the portal vein and its major branches.

Diagnosis of hepatobiliary TB with imaging alone is inconclusive most of the time and histopathological diagnosis is required

to distinguish TB from lymphoproliferative disorder, metastatic deposits and other granulomatous diseases like sarcoidosis and fungal infection.

On CT, the classical liver tuberculoma appears as an unenhancing, central, low-density lesion owing to caseation necrosis with enhancing peripheral rim corresponding to surrounding granulation tissue. MRI of hepatic TB shows a hypointense nodule with a hypointense rim on T1-weighted imaging and hypointense, isointense or hyperintense with a less intense rim on T2-weighted imaging, and peripheral enhancement or internal septal enhancement on postcontrast MR. Though the findings of imaging methods are non-specific, USG, CT and MRI are very sensitive for the detection of hepatosplenic nodules. They can also assess the extent of involvement and

Figure 4 MRI of the upper abdomen: diffusion-weighted images (A and C) and ADC images (B and D) at corresponding levels showing restricted diffusion within the lesions distributed along the biliary radicles (white arrow).

associated findings such vascular involvement and lymphadenopathy etc.^{10–12}

Culture or microscopy of biliary fluid aspirate obtained with Fine Needle Aspiration Cytology or Endoscopic Retrograde Cholangio Pancreatography to look for acid fast bacilli or PCR of biliary fluid can also be done for diagnosis especially in cases of tuberculous cholangitis with biliary stricture and obstructive jaundice. Histopathological examination of liver tissue obtained by a biopsy is the most reliable diagnostic method. Ultrasound/CT-guided percutaneous liver biopsy is an adequate method of obtaining tissue for diagnosis. The presence of caseating granuloma is usually sufficient to establish the diagnosis. If the diagnosis is still in doubt, a laparoscopic liver biopsy is the next method of investigation to be opted. The histological picture of hepatic tuberculoma is usually that of a large epithelioid tumour composed of conglomerate tubercles with central caseation necrosis. Langerhans-type giant cells may be found in the granuloma and are surrounded by lymphohistiocytic cells, plasma cells and eosinophils. According to the literature, epithelioid granuloma formation can be demonstrated in 80%–100%, caseation in 33%–100% and positive AFB stains in about 60% of liver biopsy specimens, whereas biliary fluid cultures are often negative. PCR will be positive in around 57%–88% cases.^{13 14}

Management of hepatobiliary TB is with ATT using atleast four standard drugs. In cases with tuberculous liver abscess, percutaneous aspiration and drainage of the abscess is recommended in

addition to ATT. In rare situations for patients who present with obstructive jaundice not responding to ATT, biliary decompression by stent placement, percutaneous transhepatic biliary drainage or surgical decompression may have to be adopted.¹³

Contributors SK: data acquisition and drafting of manuscript. RG: revision, editing and final approval of manuscript. SVC: concept of manuscript, analysis and interpretation of data, revision and final approval of manuscript. PP: revision of manuscript and final approval of manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2018. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- Hickey AJ, Gounder L, Moosa MY, *et al.* A systematic review of hepatic tuberculosis with considerations in human immunodeficiency virus co-infection. *BMC Infect Dis* 2015;15:209.
- Karaosmanoglu AD, Onur MR, Sahani DV, *et al.* Hepatobiliary Tuberculosis: Imaging Findings. *AJR Am J Roentgenol* 2016;207:694–704.
- Glynn JR. Resurgence of tuberculosis and the impact of HIV infection. *Br Med Bull* 1998;54:579–93.
- Yu RS, Zhang SZ, Wu JJ, *et al.* Imaging diagnosis of 12 patients with hepatic tuberculosis. *World J Gastroenterol* 2004;10:1639–42.
- Rieder HL, Cauthen GM, Bloch AB, *et al.* Tuberculosis and acquired immunodeficiency syndrome—Florida. *Arch Intern Med* 1989;149:1268–73.
- Levine C. Primary macronodular hepatic tuberculosis: US and CT appearances. *Gastrointest Radiol* 1990;15:307–9.
- Reed DH, Nash AF, Valabhji P. Radiological diagnosis and management of a solitary tuberculous hepatic abscess. *Br J Radiol* 1990;63:902–4.
- Vanhoenacker FM, De Backer AI, Op de BB, *et al.* Imaging of gastrointestinal and abdominal tuberculosis. *Eur Radiol* 2004;14(suppl 3):E103–E115.
- Ferrari TC, Couto CM, Vilaca TS, *et al.* Localized hepatic tuberculosis presenting as fever of unknown origin. *Braz J Infect Dis* 2006;10:364–7.
- Ch'ng LS, Amzar H, Ghazali KC, *et al.* Imaging appearances of hepatic tuberculosis: experience with 12 patients. *Clin Radiol* 2018;73:321.e11–321.e16.
- Diallo I, Mbengue A, Gning SB, *et al.* Hepatosplenic tuberculosis simulating secondary malignant lesions with cholangitis. *BMC Res Notes* 2016;9:316.
- Kakkar C, Polnaya AM, Koteswara P, *et al.* Hepatic tuberculosis: a multimodality imaging review. *Insights Imaging* 2015;6:647–58.
- Chaudhary P. Hepatobiliary tuberculosis. *Ann Gastroenterol* 2014;27:207.
- Jain A, Chaturvedi R, Kantharia C, *et al.* Secondary sclerosing cholangitis in localized hepatobiliary tuberculosis simulating cholangiocarcinoma: a rare case report. *BMC Gastroenterol* 2017;17:126.

Learning points

- In endemic areas, tuberculosis (TB) should always be considered as a differential diagnosis in cases of multifocal lesions in liver with atypical imaging pattern.
- Isolated hepatobiliary TB is a strong mimic of primary or secondary liver malignancies.
- Symptoms and radiological findings are commonly non-specific and the ultimate diagnosis depends on tissue diagnosis demonstrating tuberculous granuloma with central caseous necrosis.
- TB being a curable condition, prompt diagnosis with a biopsy and appropriate medical management with suitable ATT regimen is important and lifesaving.

Copyright 2018 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.

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