Liver abscess and disseminated intravascular coagulation in tuberculosis

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Summary

We report the case of a 55-year-old man with chronic renal failure, and a history of prolonged fever and jaundice. Radiological studies revealed a multiloculated irregular liver abscess. Mycobacterium tuberculosis was isolated from the abscess on smear and culture of aspirated pus. Haematological studies revealed the presence of disseminated intravascular coagulation. A detailed search failed to identify any reason for this other than the tuberculous infection. The treatment of tuberculous liver abscess and pathogenesis of disseminated intravascular coagulation in tuberculosis are discussed.

Keywords: liver abscess, tuberculosis, disseminated intravascular coagulation

Tuberculous liver abscesses are rare and are usually associated with foci of infection in the lung or gastrointestinal tract.¹ Isolated hepatic tuberculous abscesses are even rarer and only 14 cases have been reported in the English literature to date.² Diagnosis has been difficult in most instances and is usually made at *post mortem*.³ Development of disseminated intravascular coagulation is unusual in tuberculosis, although an association with miliary tuberculosis has been described.⁴ In this report, we describe a case of tuberculous liver abscess complicated by disseminated intravascular coagulation.

Case report

The patient was a 55-year-old Indian man who had been working in the pulmonary ward of the Chest Hospital in Kuwait for the previous 10 years. He had had hypertension and chronic renal failure due to chronic tubulo-interstitial renal disease since 1974. In February 1993, his serum creatinine was 720–750 $\mu\text{mol/l}$, with a creatinine clearance of 12 ml/min. He was admitted to the hospital in September 1993 with intermittent fever of one month duration. In addition he had a dry cough and recorded a weight loss of 5 kg during this period. Detailed clinical, biochemical, bacteriological, serological, mycobacterial, virological and radiological investigations failed to reveal any cause for the fever. He was advised to undergo a liver biopsy, even though the liver enzymes were normal, to search for any obscure granu-

lomatus disease. He refused the procedure and was discharged from the hospital.

He continued to have fever and was readmitted in November 1993 having had moderate melaena for two days prior to admission. On examination he was stuporous, anaemic, febrile (38.5°C), mildly volume depleted and acidotic. He had no evidence of cutaneous or other bleeding sites. His blood pressure was 130/80 mmHg. Examination of his respiratory system revealed basal fine crepitations posteriorly on the right side. Cardiovascular, gastrointestinal, neurological, musculoskeletal and optic fundus examination did not reveal any abnormal findings. Investigations done at this time revealed the following results: white blood cells $8.7 \times 10^9/\text{l}$, haemoglobin 7.1 g/dl, packed cell volume 19.9%, platelets $50 \times 10^9/\text{l}$, peripheral blood film showed schistocytosis and fragmented erythrocytes, prothrombin time 18 s (control 12 s) (INR: 1.59), partial thromboplastin time 85 s (control 30 s), thrombin time 20 s (control 18 s), fibrinogen 3.5 g/l (normal 2–4 g/l), fibrin degradation product 40 mg/l (normal < 10 mg/l), blood sugar 5.8 mmol/l, blood urea 42 mmol/l, serum creatinine 658 $\mu\text{mol/l}$, potassium 6.8 mmol/l, bicarbonate 10.2 mmol/l, sodium 130 mmol/l, chloride 106 mmol/l, serum amylase 500 IU/l, calcium 2.1 mmol/l, phosphorus 1.6 mmol/l, alkaline phosphatase 789 IU/l (normal: 35–85), aspartate transaminase 94 IU/l (normal 5–37), alanine transaminase 40 IU/l (normal 5–40), γ -glutamyl transaminase 108 IU/l (normal 7–64), and total bilirubin 29 $\mu\text{mol/l}$. Blood, urine, and throat swab cultures did not reveal any significant microorganism. Microbiological and virological studies of cerebrospinal fluid (CSF) were all negative for any pathogen. Chest X-ray revealed a few fluffy shadows in the right base. Computed tomography (CT) of brain did not reveal any abnormal findings. In view of his clinical picture, nationality and nature of work in a pulmonary ward, a trial of anti-tuberculous treatment with INAH, pyrazinamide and rifampicin was started. Bronchoscopic evaluation 48 hours later revealed inflammation of the right lower lobe and its bronchus. A bronchial lavage did not grow any bacteria, fungus or virus and smear revealed acid-fast bacilli. Upper gastrointestinal endoscopy revealed a bleeding duodenal ulcer which necessitated eight blood transfusions, and use of omeprazole and pepsidin. Disseminated intravascular coagulation

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was managed with fresh frozen plasma and platelet transfusions. In addition he was started on regular haemodialysis.

Ten days after admission (seven days after starting antituberculous treatment he was clinically icteric with tender hepatomegaly. The liver function tests then revealed total bilirubin 167 mmol/l (direct 88, indirect 79) and alkaline phosphatase 350 IU/l while aspartate transaminase and alanine transaminase were normal. His serum albumin was 32 g/l while prothrombin time and partial thromboplastin time had improved to 16 s (control 12 s) and 40 s (control 32 s), respectively. An abdominal ultrasonogram revealed a right lobe liver abscess with loculations and septations. The gall bladder, common bile duct, pancreas and spleen were normal. CT of the abdomen confirmed a liver abscess of 10 × 13 × 7 cm irregular, multiloculated and hypoechoic (figure). A percutaneous drain was done under ultrasound guidance after adequate correction of bleeding parameters and thick pus and necrotic tissue were obtained. A proper closed drainage was impossible since there were septations, loculations and poor breakdown of the lesion. A direct smear of this pus revealed numerous acid-fast bacilli. There were no bacteria or fungal hyphae and culture grew mycobacterium tuberculosis. He was continued on anti-tuberculous drugs because of apparent improvement in liver function tests except for bilirubin. Dialysis and other supportive measures like blood transfusions and parenteral nutrition were continued. In spite of these measures his clinical condition deteriorated. His liver function also worsened progressively and the laboratory results on the 30th day of admission revealed a total bilirubin of 435 µmol/l, direct bilirubin 162 µmol/l, aspartate transaminase 94 IU/l, alanine transaminase 40 IU/l, alkaline phosphatase 599 IU/l (heat stable being 436 IU/l), γ-glutamyl transaminase 95 IU/l, serum albumin 16 g/l and serum ammonia 102 µmol/l. Anti-hepatic coma measures were added to the therapeutic regime but his condition progressively worsened and he expired on the 34th day of admission.

Discussion

Diffuse liver involvement is frequently encountered in patients suffering from tuber-

culosis. A review of indexed literature since 1930 included 444 reported cases of tuberculosis of liver.⁵ Liver biopsy specimens show non-caseating granulomas in 25% of patients with pulmonary tuberculosis and 80% of patients with extrapulmonary tuberculosis.⁶ Three forms of tuberculous liver involvement are described (see box).³

Tuberculous liver abscess was probably first described by Bestowe in 1858.³ Leader *et al* collected 80 cases up to 1952¹ and Stevens³ concluded that less than 100 cases had been described up to 1987. Since then seven more cases have been described in english-language medical literature.^{2,5-10}

Tuberculous liver abscess is usually secondary to primary pulmonary or gastrointestinal involvement.² When there is no gut involvement, the route by which mycobacteria reach the liver could be the hepatic artery during systemic mycobacteremia from the lung. The immunologic status of the host and the load of bacilli are recognised as factors that influence the pathogenic pattern of infection. This could explain the occurrence of tuberculous liver abscess in our patient since uremia is an immuno-depressed state. Following the first description of AIDS, three cases of tuberculous liver abscess have been described in the literature.⁸⁻¹⁰ Tuberculous liver abscess occurs most frequently in children and in racial groups felt to have reduced natural immunity.³ Our patient fits into the latter high-risk group.

High fever, weight loss, right hypochondrial pain and hepatomegaly are the most frequently observed clinical findings.² Our patient had all four features. Jaundice is a rare manifestation in tuberculous liver abscess and may be caused by extra or intrahepatic obstruction.¹¹ Our patient had jaundice associated with a rise in alkaline phosphatase, similar to the case reported by Silverberg *et al*.¹³ No clear relationship exists between the degree of liver involvement and jaundice.¹² Tuberculous liver abscess is frequently confused with hepatoma, amoebic or pyogenic liver abscess and differentiation is frequently difficult such that one group labeled this entity as a 'pseudotumour' of the liver.¹⁴

Since the clinical findings are non-specific, the diagnosis of hepatic abscess is often made at autopsy or at laparotomy. There is no specific radionuclide imaging appearance that is characteristic.¹⁴ Ultrasonographic and CT finding of multiple septated ('honeycombed-like') liver abscess was described by Wilde and Kueh.⁵ Our patient had similar ultrasonographic and CT findings. Ultimate diagnostic confirmation

Figure CT scan of upper abdomen demonstrating irregular hypoechoic, multiloculated liver abscess (10 × 13 × 7 cm)

Liver involvement in tuberculosis

- diffuse involvement associated with miliary or pulmonary tuberculosis
- diffuse parenchymal involvement without any evidence of existing tuberculosis elsewhere (primary miliary tuberculosis of the liver)
- focal or nodular lesion in liver which may be multiple or solitary and present as tuberculoma or abscess

Treatment options in tuberculous liver involvement

- medical – oral antituberculous treatment
– local infusion of isoniazid and rifampicin 6 hourly through an indwelling catheter
- surgical – ultrasonographic or CT-guided aspiration and drainage of abscess
– open surgical drainage of abscess

is by demonstrating acid-fast mycobacterium in the aspirated pus or necrotic tissue on smear or culture, as in our patient. When this is not successful histological examination of the abscess wall may be required for confirmation.

Medical treatment of a tuberculous liver abscess is still a debated subject. Even though success has been reported with oral antituberculous drugs alone, prognosis is poor in most cases.^{6,8} Of interest is the formation of an abscess reported even after starting chemotherapy.² Gracey postulates that the thick fibrous tissues around the abscess and their large size may prevent antibiotics from reaching their target.¹⁵ Mustard *et al* have recommended local infusion of isoniazid and rifampicin every six hours through an indwelling catheter to overcome this problem.¹⁶ Even though surgical drainage was used earlier in management, presently either sonographic or CT-guided aspiration or drainage is found to

be equally successful.² Failure of treatment in our case was most probably due to inadequate penetration of drugs to the abscess region. However, drug-related hepatotoxicity may have contributed.

An association between miliary tuberculosis and development of disseminated intravascular coagulation, although rare, has been documented.¹⁷ The pathogenesis of disseminated intravascular coagulation is still not clear since mycobacteria are not known to produce either endotoxins or exotoxins that can initiate the clotting cascade. Initiation of disseminated intravascular coagulation by tuberculo protein in miliary tuberculosis is only a matter of conjecture.¹⁸ In our patient, the diagnosis of disseminated intravascular coagulation was based on low platelet count, prolonged prothrombin and activated partial thromboplastin time, increased fibrin degradation products and the presence of schistocytes and fragmented erythrocytes in the peripheral blood smear. Careful and detailed investigations had failed to detect any other type of infection. However, the presence of mycobacteria in pus aspirated from the liver and in bronchial lavage had confirmed disseminated tuberculosis. Liver functions were normal initially when the patient presented with disseminated intravascular coagulation and hepatic dysfunction developed only subsequently. Thus the causative relationship between disseminated intravascular coagulation and tuberculosis would seem highly probable in this patient.

1 Leader SA. Tuberculosis of liver and gall bladder with abscess formation. A review and case report. *Ann Intern Med* 1952; 37: 594–606.

2 Reed DH, Nash AF, Valabhji P. Radiological diagnosis and management of a solitary tuberculous hepatic abscess. *Br J Radiol* 1990; 63: 902–4.

3 Stevens A, Little JM. Isolated tuberculous hepatic abscess. *Aust NZ J Surg* 1987; 57: 409–11.

4 Mavligit GM, Bender RA, Crosby WHC. Disseminated intra-vascular coagulation in miliary tuberculosis. *Arch Intern Med* 1972; 130: 388–9.

5 Wilde CC, Kueh YK. Case report: tuberculous hepatic and splenic abscess. *Clin Radiol* 1991; 43: 215–6.

6 Desmidt P, Apfelbaum M, Holvoet J, Huben H, Haber I. Tuberculous (peri) hepatic abscess. *Acta Clin Belg* 1988; 43: 378–80.

7 Fernandez-Miyanda C, Perpina C, Kessler P, Torres N, Manjon P, de la Calle A. Hepatosplenic tuberculous abscesses in a patient with polyarteritis nodosa. *Am J Gastroenterol* 1993; 88: 1297–8.

8 Lupatkin H, Brau N, Flomenberg P, Simberkoff MS. Tuberculous abscesses in patients with AIDS. *Clin Infect Dis* 1992; 14: 1040–4.

9 Moreno S, Pacho E, Loez-Herce JA, Rodriguez-Creixems M, Martin Scapa C, Bouza E. Mycobacterium tuberculosis visceral abscesses in the acquired immunodeficiency syndrome (AIDS). *Ann Intern Med* 1988; 109: 437.

10 Weinberg JJ, Cohen P, Malhotra R. Primary tuberculous liver abscess associated with the human immuno-deficiency virus. *Tubercle* 1988; 69: 145–7.

11 Morris E. Tuberculosis of liver. *Am Rev Tuberculosis* 1930; 22: 585.

12 Charikli TS, Carmelita UT. Tuberculous liver abscess. *Tubercle* 1984; 65: 127–31.

13 Silverberg LF, Johnston C, Haber T. Tuberculous involvement of a polymicrobial liver abscess. *West J Med* 1984; 141: 682–5.

14 Dhekne RD, Moore WH, Long SE, Barron BJ. Tuberculous pseudotumor of the liver. *Clin Nucl Med* 1987; 12: 816–9.

15 Gracey L. Tuberculous abscess of the liver. *Br J Surg* 1965; 52: 442–3.

16 Mustard RA, Mackenzie RL, Gray RG. Percutaneous drainage of a tuberculous liver abscess. *Can J Surg* 1986; 29: 449–50.

17 Manzella JP, Kellog J, Sanstead JK. Mycobacterium tuberculosis bacteremia and disseminated coagulation. *JAMA* 1985; 254: 2741.

18 Eliopoulos G, Vaiopoulos G, Kittas C, Fessas P. Tuberculosis associated hemophagocytic syndrome complicated with severe bone marrow failure and disseminated intravascular coagulation. *Nouv Rev Fr Haematol* 1992; 34: 273–6.