

Splenic tuberculosis associated with monoclonal gammopathy of undetermined significance and pericarditis

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Tuberculosis usually affects the respiratory system, but it may present atypically involving multiple systems, extrapulmonary systems, and manifest as a protein disorder. Here we report a case of splenic tuberculosis associated with monoclonal gammopathy of undetermined significance, and pericarditis. The diagnosis, confirmed by a plugged biopsy of the spleen, precluded the need for splenectomy in this patient and allowed prompt initiation of treatment, thereby avoiding the complications of tuberculous pericarditis and splenic infection.

Introduction

Tuberculosis (TB) usually affects the respiratory system, but it may present atypically involving multiple systems, extrapulmonary systems and manifest as protein disorders. Hong Kong sees more than 5700 new cases of TB per year, according to the Centre for Health Protection.¹ The diagnosis is based on finding acid-fast bacilli in a smear or culture and/or the presence of caseous granulomas in a tissue specimen. Here we report a case of splenic TB associated with monoclonal gammopathy of undetermined significance and pericarditis.

Case report

A 52-year-old non-smoking housewife who was born in Hong Kong presented with malaise, exertional dyspnoea, and weight loss in May 2006. She had a history of hypertension and was put on a beta-blocker. She also complained of poor appetite, an intermittent fever and night sweats. She denied having any cough, haemoptysis or gastro-intestinal symptoms, and had reached the menopause 6 months earlier. Pallor and moderate splenomegaly were noted on physical examination. She had no lymphadenopathy, other organomegaly, or signs of endocarditis, and her chest was clear.

Preliminary blood tests found a hypochromic microcytic anaemia with a haemoglobin level of 68 g/L. Iron studies revealed an anaemia of chronic illness with iron levels of 3.3 $\mu\text{mol/L}$, total iron binding capacity of 29.6 $\mu\text{mol/L}$ and ferritin of 589 pmol/L. Her white blood cell count was raised to $12.9 \times 10^9/\text{L}$ with a neutrophilia; her erythrocyte sedimentation rate (ESR) was elevated to 90 mm/h and the C-reactive protein (CRP) was 90.4 mg/L. Her liver and renal biochemistry tests were normal except for a hypoalbuminaemia of 32 g/L with a reversed albumin/globulin ratio of 1.2. Her prothrombin time was prolonged to 13.7 s, while the activated partial thromboplastin time and platelet count were both normal. Her electrocardiogram showed low voltage in the chest leads and the chest X-ray revealed cardiomegaly. An abdominal ultrasound showed splenomegaly with multiple hypoechoic lesions. An echocardiogram revealed a pericardial effusion 1.6 cm thick with no vegetation noted (Fig 1). A computed tomographic (CT) scan of the thorax and abdomen revealed a pericardial effusion and splenomegaly with multiple hypoenhancing areas measuring 1 to 2 cm. An upper endoscopy and a colonoscopy were performed and no abnormalities were found.

She was investigated further for a possible infective cause of her illness. Blood, sputum, and urine were all negative for bacteria and acid-fast bacilli on both smears and mycobacterial cultures. Her serum was negative for anti-HIV antibodies, anti-hepatitis C virus antibodies and the hepatitis B surface antigen. No malaria parasites were seen and serological testing for brucellosis and salmonella were negative, as was Widal's test. The Mantoux test was positive with an induration measuring 2 cm.

Serum protein electrophoresis (SPE) detected an immunoglobulin A lambda monoclonal band of 4.2 g/L but other immunoglobulin levels were not suppressed. The urine sample was negative for the Bence Jones protein. A bone marrow aspiration and trephine biopsy showed atypical plasmacytosis (12%) with a reverse lambda-to-kappa ratio.

Key words

Multiple myeloma; Pericarditis;
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與未知臨床意義的單株免疫球蛋白增高和心包膜炎有關的脾結核

結核病普遍影響呼吸系統，但也可能牽涉多種系統、肺外的系統，以及演變成蛋白病變。本文報告一宗與未知臨床意義的單株免疫球蛋白增高和心包膜炎有關的脾結核案例。我們使用脾穿刺活檢為病人確診，並證實毋須進行脾切除術和及早進行醫治，以避免出現延遲確診結核心包膜炎和脾感染的嚴重併發症。



FIG 1. Pericardial effusion demonstrated by a transthoracic echocardiogram

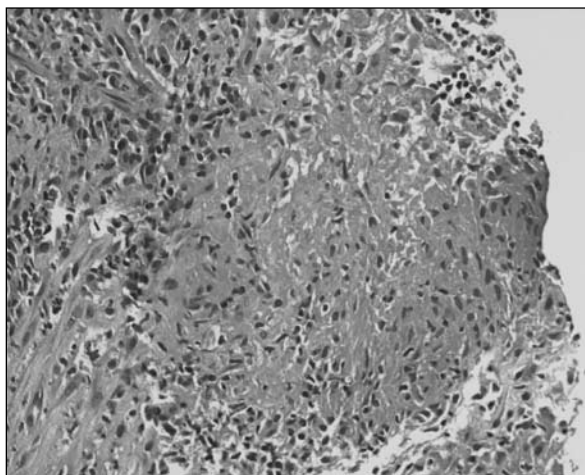


FIG 2. Histology of the splenic biopsy: epithelioid granuloma with focal necrosis and polymorphic infiltrates in a fibrotic stroma

The overall picture was compatible with monoclonal gammopathy of undetermined significance (MGUS). The skeletal survey was normal and tumour marker levels were unremarkable. Tests for autoimmune markers, including anti-nuclear factor, rheumatoid factor and anti-nuclear cytoplasmic antibodies, were all negative.

A pericardiectomy and biopsy was performed to

look for tuberculous involvement of the pericardium. No definitive pathological diagnosis could be made from the biopsy and fluid specimen. A positron emission tomography scan showed splenomegaly with multiple metabolically active masses, a right middle lobe lung lesion, mediastinal lymph nodes and diffuse increased red marrow uptake. Despite the above investigations, no conclusive diagnosis had been arrived at, so, in view of the prolonged prothrombin time, a plugged splenic biopsy was performed. During the procedure, an introducer set was passed into the spleen using targeted ultrasound, then an 18-gauge Temno (Bauer; Via del Fosso, Italy) needle was inserted into the splenic lesion through the introducer and a biopsy was taken. After taking the biopsy, the tract created by the introducer was embolised with gelfoam to achieve haemostasis.

A histological examination of the biopsy revealed a few epithelioid granulomas with focal necrosis and polymorphic infiltrates in a fibrotic stroma (Fig 2). No Langerhans' giant cells were seen. Ziehl-Neelsen staining found no acid-fast bacilli. There were no fungal organisms or evidence of malignancy. Immunohistochemical staining for kappa and lambda light chains did not show any light chain restriction in the small number of plasma cells present. The provisional diagnosis was disseminated TB with spleen and pericardial involvement. She was treated with anti-TB therapy (isoniazid INH 300 mg daily, ethambutol 800 mg daily, pyrazinamide 2 g daily, and rifampicin 600 mg daily) from 1 July 2006. The fever subsided 2 days after treatment. Prednisolone 60 mg daily was prescribed for 3 months to treat the presumed tuberculous pericarditis.

The inflammatory markers, namely ESR, CRP, all returned to normal levels. Her spleen decreased in size to just 4 cm below the costal margin. A CT scan of the abdomen performed 4 months later showed a decrease in the splenomegaly. An echocardiogram performed 4 months after treatment showed minimal pericardial effusion and no evidence of constrictive pericarditis. A repeated SPE showed the monoclonal band was static. She was given a four-drug anti-TB regimen for 5 months, then this was changed to rifampicin and isoniazid from 1 December 2006. Overall, the anti-TB regimen was given for 9 months.

Discussion

In disseminated TB, which is defined as involvement of two or more non-contiguous extrapulmonary organs, seeding of every organ in the body is possible. Tuberculosis can spread to other parts of the body such as the spleen in this case, from dissemination of advanced pulmonary or miliary disease, following either a haematogenous route via the portal vein, or direct swallowing of infected sputum or contaminated food.² As a result, the presentation of disseminated

TB can be variable and poses a diagnostic challenge.

The differential diagnosis for a patient with pyrexia of unknown origin, a pericardial effusion and splenomegaly comes from three disease categories: infection, malignancy, and autoimmune diseases.

Our patient had no autoimmune markers suggesting autoimmune diseases. The presence of paraprotein and plasmacytosis in the bone marrow biopsy prompted further investigation for haematological malignancies such as multiple myeloma and lymphoma but the diagnostic criteria for multiple myeloma were not fulfilled.³

Our patient's paraprotein may have developed for various reasons. Firstly, MGUS is associated with chronic inflammation, although there is no established pathogenesis. It is postulated that patients with diseases stimulating increased production of immunoglobulins over a long period, such as leprosy, sarcoidosis, hepatitis C viral infection, and collagen-vascular disease, may develop a superimposed monoclonal gammopathy.⁴ Although polyclonal gammaglobulinaemia is common in TB, an association with MGUS is rather rare. Secondly, TB may increase antigenic stimulation which confers a higher risk of developing multiple myeloma.⁵ Approximately 10% of patients with MGUS will develop multiple myeloma in 20 years' time.⁶ Therefore, it is possible that the MGUS has preceded the development of multiple myeloma in this patient. Finally, the paraprotein could be a coincidental finding. Thus, it will be interesting to follow this patient's progress, to see if the monoclonal band will disappear now that the TB has been treated or whether she develops multiple myeloma later on.

An image-guided percutaneous biopsy of the spleen can provide a specific diagnosis in most

patients with focal splenic lesions.⁷ Nonetheless, in a 10-year review, 10% of patients had bleeding complications requiring emergency splenectomies.⁸ Those with abnormal coagulation parameters or vascular tumour lesions are at highest risk. Imaging may not always identify the vascular nature of the lesion before the procedure.⁸ When performing a liver biopsy in patients with impaired coagulation, there is evidence that a plugged percutaneous liver biopsy carries a minimal risk of bleeding.⁹ Data from animal models suggest that using a plugged splenic biopsy can also reduce bleeding complications.¹⁰ The advantages of plugged splenic biopsies are that the high yield enables specific diagnosis, and they pose a lower risk of bleeding complications, allowing patients with impaired coagulation to undergo such procedures. An alternative is a diagnostic laparoscopic biopsy of the spleen. Although this is more invasive than the percutaneous route and has to be performed under general anaesthesia, it can establish the diagnosis and has the additional advantage of securing haemostasis and arresting bleeding under direct vision should this occur. This is particularly useful if the splenic masses are small, multiple and not uniloculated, circumstances in which an image-guided percutaneous biopsy may have a lower yield.¹¹ A laparoscopic procedure is also preferable in institutions where invasive interventional radiology expertise is not available.

In conclusion, we present a rare case of splenomegaly, pericarditis and MGUS due to disseminated TB. Confirmation of the diagnosis by plugged biopsy of the spleen precluded the need for splenectomy in this patient and allowed prompt initiation of treatment, thereby avoiding the undesirable complications of tuberculous pericarditis and splenic infection.

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