caused by nerve root compression and that bilateral empyema developed as a consequence of direct spread from the infected vertebrae.

A literature search showed one previous report of pleural effusion associated with osteomyelitis.⁴ In that case the effusion was small and not associated with respiratory symptoms. This is the first reported case of prominent pleural pathological features associated with shortness of breath occurring as the presenting feature of pyogenic vertebral osteomyelitis.

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Immune thrombocytopenia complicating pulmonary tuberculosis: case report and investigation of mechanisms

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Immune thrombocytopenia and pulmonary tuberculosis presented concurrently in a 20 year old Thai man as a bleeding diathesis. Intravenous immunoglobulin rapidly corrected the thrombocytopenia. Immunofluorescence and immunoblot studies with platelets and mycobacteria showed the presence of platelet surface membrane IgG.

Isolated thrombocytopenia is an uncommon complication of pulmonary tuberculosis.^{1,2} The pathogenesis is believed to be immune destruction of platelets, though only one previous report has provided evidence to support this hypothesis.³ We report a case of immune thrombocytopenia associated with tuberculosis and discuss mechanisms of platelet sensitisation.

Case report

A 20 year old Thai man presented with a four day history of recurrent mucosal haemorrhages and rectal bleeding with bright blood. He had been unwell for two weeks with a cough producing small amounts of purulent sputum, intermittent night sweats, fevers, and

rigors. In the preceding four months he had noted lethargy and a 9 kg weight loss. There was no personal or family history of tuberculosis. A drug and toxin exposure history was non-contributory. He had emigrated from Thailand in 1980. A chest radiograph in 1982 had been reported as normal.

On examination he was febrile and weighed 42 kg. Bilateral cervical lymphadenopathy was present, the glands ranging in size from 1 to 3 cm. There was no hepatosplenomegaly. He had numerous cutaneous petechiae and haemorrhages in the oropharynx and there was bright blood on rectal examination. Scattered early inspiratory crackles were heard over the left upper zone of the chest.

A chest radiograph showed patchy left upper lobe and right upper and middle lobe opacities. The platelet count was $5 \text{ (normal range } 140\text{--}400) \times 10^9/\text{l}$; the white cell count was $12.7 \times 10^9/\text{l}$ with a slight monocytosis. A microcytic anaemia of 11.7 g/l with a mean corpuscular volume of 73.3 fl was present. Haemoglobin E trait was noted. The erythrocyte sedimentation rate was 38 mm in one hour and the coagulation profile was within normal limits. Bone marrow biopsy showed a normal number of megakaryocytes and no evidence of mycobacterial infection. An autoantibody screen and an enzyme linked immunosorbent assay for HIV antibody gave negative results. Smears of sputum were positive for acid fast bacilli. Sputum cultures grew *Mycobacterium tuberculosis* sensitive to isoniazid, ethambutol, rifampicin, and pyrazinamide but resistant to streptomycin. Cultures of bone marrow were negative.

Intravenous immunoglobulin G (Intragam-CSL, Melbourne) infusion, 0.5 g kg/day , was started on day 1 and continued for four days. Antituberculosis chemotherapy with isoniazid 5 mg/kg , pyrazinamide 35 mg/kg , rifampicin 10 mg/kg , and ethambutol 25 mg/kg was started on the third day. Pyrazinamide and ethambutol were stopped after two months. Owing to problems over compliance isoniazid and rifampicin were continued for nine months.

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The platelet count returned to normal on day 4 of treatment and remained normal during chemotherapy. There was progressive radiological improvement with a weight gain of 10 kg. The lymphadenopathy had fully resolved after two months of treatment. Thrombocytopenia has not recurred.

Methods

Peripheral blood samples were collected from the patient before immunoglobulin infusion and at two month follow up. Platelets were assayed for surface membrane IgG and IgM by direct platelet suspension immunofluorescence testing,⁴ and positive reactions were graded on a 1+ to 4+ scale. Antiplatelet antibodies in serum samples were assayed by indirect platelet suspension immunofluorescence testing and immunoblotting.⁵ Antimycobacterial antibodies in the serum were sought against the patient's cultured mycobacteria by immunofluorescence on paraformaldehyde fixed and unfixed organisms and by immunoblotting. Sonicates of the cultured mycobacteria were prepared from whole and ground colonies in sucrose buffer with Triton X. The samples were run under reduced and non-reduced conditions on 7.5% continuous slab SDS polyacrylamide gels. Blotting was carried out in a Transblot Cell (Bio-Rad Laboratories, Sydney) according to the manufacturer's instructions. Standard lymphocytotoxic assays were performed to detect anti-HLA antibodies.⁶

Results

The direct platelet suspension immunofluorescence testing reaction was positive (1+) for platelet surface IgG at diagnosis and at follow up. Serum from the time of diagnosis gave a positive reaction to autologous platelets when assayed by indirect platelet suspension immunofluorescence testing. Diagnostic and follow up serum gave negative reactions to autologous platelets when assayed by immunoblotting. Serum also gave negative reactions to donor platelets (platelet suspension immunofluorescence testing and immunoblotting). Immunoblotting and immunofluorescence testing did not detect antibodies to solubilised *M. tuberculosis*. Antibodies against HLA antigens were not detected.

Discussion

This case provides compelling evidence of an immune basis for isolated thrombocytopenia complicating active pulmonary tuberculosis. Platelet surface membrane IgG was detected and the thrombocytopenia resolved rapidly with immunoglobulin treatment. The only previous direct evidence for immune thrombocytopenia was provided by Jurak *et al.*,³ who reported two patients with tuberculosis,

thrombocytopenia, and antiplatelet antibodies. They speculated that *M. tuberculosis* could stimulate a clone of B lymphocytes non-specifically and the lymphocytes might produce antibodies against autologous platelets.

The immunological results in our case differed from those of the previous cases³ in that, although IgG was bound to the patient's platelets, there were no circulating antiplatelet antibodies that reacted with normal donor platelets. This is not the pattern seen in idiopathic thrombocytopenic purpura, where antibodies generally react with normal platelets.⁷ This case is therefore very unlikely to represent the coincidental occurrence of idiopathic thrombocytopenia purpura.

The apparent IgG reaction with autologous platelets alone suggests that the target antigen is exclusive to the patient's platelets. Alternatively, the reaction may reflect non-specific binding to platelets by circulating immune complexes comprising IgG and mycobacterial antigens.⁸ These possibilities were tested by using an immunoblot system. No antibodies to autologous platelet or mycobacterial antigens were detected. The pathophysiology of the IgG-platelet interaction thus remains uncertain. As the immunoblot system used is largely limited to the detection of protein and glycoprotein antigens, our results do not exclude lipid or polysaccharide antigen-IgG interactions. The role of non-protein antigens should be considered in the investigation of future cases.

Severe thrombocytopenia complicating tuberculosis is uncommon but may be life threatening. It can, however, represent an acute reversible phenomenon, and high dose intravenous immunoglobulin treatment causes rapid correction of thrombocytopenia in this setting.

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