Isolated Hepatic Inferior Vena Cava Thrombosis in a Case of Tuberculosis

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Abstract

The report describes a case of pleuropulmonary tuberculosis developing isolated inferior vena cava thrombosis with raised anticardiolipin antibodies and antinuclear factor during the course of antitubercular therapy with diagnostic implications.

Key Words: Pleuropulmonary tuberculosis, Isolated hepatic IVC thrombosis, Raised anticardiolipin antibodies, Antinuclear factor.

Introduction

Infections can possibly cause venous thrombosis by local invasion of surrounding tissues, compression, direct endothelial damage, and of late are known to produce a transient hypercoaguable state1.2. Tuberculosis is still a common disease in the developing countries like India. There are reports to indicate that it may be a risk factor for deep vein thrombosis2. Acute phase reactants, haemostatic changes, and also transient increase in anticardiolipin antibodies have been attributed to link inflammation with deep vein thrombosis in pulmonary tuberculosis2. Treatment with antitubercular drugs and low molecular weight heparin has been shown to resolve the deep vein thrombosis1-2.

Case history

A 50 yr. old postmenopausal lady had complained of episodes of low grade fever since 1½ years associated with symmetric polyarthralgias involving small and large joints and weight loss. Initially she had received symptomatic treatment from her village medical practitioner. In October, 2002, she was diagnosed to have right lower zone pulmonary parenchymal infiltration and exudative pleural effusion with lymphocytic predominance (pleural fluid protein 4.6 gm%, 97% lymphocytes). In the absence of sputum production and refusal to permit a pleural biopsy, but keeping in view that she stayed with her daughter-in-law who had sputum smear positive pulmonary tuberculosis, she was given antitubercular therapy (rifampicin, isoniazid, ethambutol, and pyrazinamide; protocol 2RHZE + 4RH). She became afebrile within fifteen days with resolution of her polyarthralgias and gained weight for the first time since her illness started.

However, 5 months later in March, 2003, she presented to our hospital with complaints of dyspnoea on effort, vague pain over right side of chest, and increasing prominence of veins over her abdomen. She denied any history of recent prolonged travel and had not taken HRT. She had never had any episodes of DVT in the recent past or childhood. There was no family history of recurrent thrombosis. There was no recent /past occupational exposure to asbestiform fibres. She was a non-smoker, non-alcoholic, but a non-vegetarian. On examination, she was afebrile, had no pallor, oedema, skin rash, clubbing, lymphadenopathy, or arthritis. Her vitals signs were within normal limits. Homan's sign was negative. Her breasts were supple. She had signs of volume loss of her right hemithorax with stony dullness and diminished breath sounds. Cardiovascular examination was essentially normal. Superficial abdominal veins and veins on her back were markedly dilated with flow below upwards. There was no organomegalgy/abdominal mass.

Her haemogram (Hb 12.9 gm%) and her platelet count (1,85,000/mm³) were normal. Plasma glucose, liver, and renal functions were normal. Her Mantoux test was strongly positive (15x20 mm). Her chest radiographs showed right sided multiple encysted pleural effusions with rib crowding and fibroinfiltrative lesions in the left
mid-zone. Her CT (thorax) revealed multiple encysted empyemas with air-fluid level on the right side (post attempted aspiration by a physician prior to admission). There was no bronchopulmonary or mediastinal mass (Fig. 1). Abdominal ultrasonography revealed 7 cm long large thrombosis of the hepatic IVC extending till the IVC-RA junction with normal patent intrahepatic veins and portal vein (Fig. 2). There was a small amount of free fluid in the pelvic gutter. There was no organomegaly or enlargement of retroperitoneal and porta-hepatic lymph nodes. The uterus and ovaries were normal. Ultrasound compression test of both lower limbs showed no thrombosis of femoral, popliteal, and tibial veins. Echocardiogram was normal. Ultrasound guided right intercostal tube drainage was done. The pleural fluid was again exudative with lymphocytic predominance (proteins 7.7 gm%, 65% lymphocytes). Pleural biopsy was attempted but failed to reveal any tissue. Pleural fluid analysis for malignant cells did not show any cellular atypia.

Elisa for HIV, VDRL, and Ham’s test for PNH were negative. Protein C and S activity was low normal (protein C-79% and protein S-76%; normal activity values: protein C: 70-140%, protein S: 70-123%). S. fibrinogen was increased (498 mg%, normal: 175-400 mg%). Anticardiolipin antibodies were mildly raised (IgM 14 mpl U/ml, IgG 15 gpl U/ml, normal: IgM < 10 mpl U/ml, IgG < 11 gpl U/ml). Antinuclear factor was low positive: 1.6 AI (negative < 1.0 AI, low positive 1.0-2.0 AI, high positive > 2.0 AI). However, anti ds DNA antibody and rheumatoid factor were negative.

She was started on unfractionated heparin (5,000 units IV bolus followed by 5,000 units s/c 8 hrly) and antitubercular treatment (rifampicin and isoniazid) was continued. 10 days later warfarin was added with a 4 day overlap with the INR aimed at 2.0. Her intercostal drainage subsided and ICD was removed. On account of entrapment of the right lung, thoracotomy with decortication was planned. However, on the 15th day she had sudden breathlessness with hypotension and died possibly due to massive pulmonary embolism. A post mortem study was not possible.

Discussion

Tuberculosis as a disease with a wide variety of clinical presentation is well known. Recently, the association between inflammation and acute phase reactants with haemostatic changes is thought to result in hypercoagulable state that may cause deep vein thrombosis in cases of severe pulmonary tuberculosis. Such cases may have thrombocytosis, elevated plasma fibrinogen, fibrin degradation products, tissue plasminogen activator (t-PA) and inhibitor (PAI-I) with depressed antithrombin III levels. Fibrinogen is seen to rise within the first 2 weeks of therapy and then normalise.
within 12 weeks, which, coupled with impaired fibrinolysis may result in deep vein thrombosis. Another hypothesis favouring a hypercoaguable state in tuberculosis is the increase in concentration of C4 b-binding protein (C4b BP), an acute phase reactant which binds protein S in plasma. Protein S is a cofactor for activated protein C mediated cleavage of Factor VIIIia and Factor Va. Also, experimentally peripheral blood mononuclear cells in tuberculosis can produce IL-1 and TNF-α, the latter causing down regulation of protein C/protein S during sepsis.

Deep vein thrombosis can be the presenting feature of tuberculosis. Extensive deep vein thrombosis up to hepatic IVC in adult tuberculosis has been described from our institution earlier in which thrombosis was attributed to IVC compression by matted retroperitoneal lymph nodes given the normal levels of protein C and S, AT-III level, and antiphospholipid tests. However, Manuel Casanova-Roman et al from Spain have reported transient elevation of protein S and anticardiolipin antibodies in a 4 yr. old boy with pulmonary tuberculosis and DVT and observed that two or more anomalies in the anticoagulation system are necessary for causing venous thrombosis. Such patients presenting acutely with DVT respond well to antitubercular treatment and anticoagulation. Also, the levels of protein S and anticardiolipin antibodies are seen to return to normal during the course of antitubercular treatment.

Exudative pleural effusion sequelled by shrunken hemithorax, as in our case, is commonly due to tuberculosis in developing countries like India. Our case had somewhat Poncelet's disease-like onset (polyarthralgias) which is known to have immunological basis. Isolated hepatic IVC thrombosis was seen to occur 6 months after antitubercular treatment was started despite constitutional improvement albeit residual pleural fluid encystment and shrunken hemithorax. In addition to elevated plasma fibrinogen and anticardiolipin antibodies, there was a low normal protein C and S activity. Also, low positive antinuclear factor qualified by a negative anti ds DNA antibody was noted in our case. It is possible that the mildly elevated plasma fibrinogen and anticardiolipin antibodies may be regressing towards normal after initial elevation. But then the late onset thrombosis remains unexplained. Interestingly, late onset thrombosis during course of antitubercular treatment seems to occur at unusual sites such as hepatic IVC, as in our case, and portal vein, as in the case of abdominal tuberculosis with hepatic hilar lymph nodes.

Thus, tuberculosis can not only be associated with deep vein thrombosis, but also isolated venous thrombosis at unusual sites like hepatic IVC. In addition, the increased levels of anticardiolipin antibodies and antinuclear factor in such cases, raise the issue of close differential diagnosis of collagen and antiphospholipid disorders.

References