Miliary Tuberculosis With Tubercular Meningitis With Thrombocytopenic Purpura

S Verma, K Narayan

Citation

S Verma, K Narayan. *Miliary Tuberculosis With Tubercular Meningitis With Thrombocytopenic Purpura*. The Internet Journal of Pulmonary Medicine. 2007 Volume 10 Number 1.

Abstract

Disseminated Tuberculosis presenting with thrombocytopenia is a rare condition, especially in children. We describe a case of miliary tuberculosis with tubercular meningitis and thrombocytopenic purpura. An early suspicion to the diagnosis was made by clinical, radiological, pathological evidences and confirmed by the response to therapy. The patient was successfully treated with antituberculous chemotherapy and steroids.

INTRODUCTION

Hematologic abnormalities have been described in association with mycobacterial infections for almost 100 years. A comprehensive review of the literature reveals around 16 case reports documenting tuberculosis as a cause of severe hematologic conditions [1] .Tuberculosis should be considered a cause of immune thrombocytopenia in areas where tuberculosis is highly endemic. Here we report a spectrum of tuberculosis manifestations namely tubercular meningitis and miliary tuberculosis with thrombocytopenic purpura in a 13 year old child who was successfully treated with antituberculous chemotherapy.

CASE REPORT

A thirteen year old previously healthy female was admitted to our hospital with chief complaints of fever, loss of appetite since the last 25 days. She had severe headache and vomiting since the last six days, prior to presentation. Her parents had noticed some reddish spots on her arms and legs since one week. They denied any history of hematologic disorders or blood transfusions, and she was not receiving any drugs. The family history was nonc ontributory. Clinical examination revealed a febrile child(101 F) with pallor and icterus. Vitals BP-88/60mmHg,PR-130/min,RR-36/minute. Respiratory examination was normal except for fine crepitations present in the bilateral lung bases. Neck rigidity was present with a positive Kernig's sign and plantar response was withdrawal bilaterally. Abdomen was soft with mild hepatomegaly but no splenomegaly. Petechial rash was present on both the lower limbs and hands. A skiagram of the chest showed multiple micronodular lesions suggestive of military picture(Fig-1). Mantoux test with 5TU gave 22mm induration. Routine blood investigations Hb-7.9g%,TLC-4000/mm ^{3} ,DLC-P62L34E2M2%,platelet count 18000/mm ^{3} and a Normocytic normochromic blood picture with anisocytosis . LFT bilirubin total 2.0mg% with direct 1.2mg%,SGPT -84U/L,SALP-553U/L. Renal functions were within normal limits. ELISA for HIV was nonreactive. Bone marrow examination showed a normocellular bone marrow with a myeloid erythroid ratio(1.5:1). Megakaryocytes were seen in adequate numbers with almost absent platelet synthesis. No abnormal/neoplastic cell was seen. No granuloma was seen in the bone marrow. The child was not able to raise sputum and because of the poor socioeconomic status in the family, we did not do an antibody test for evaluating the cause for thrombocytopenia.CSF study showed a lymphocyte predominant fluid with TLC of 160 cells.The sugar, protein of the CSF sample was 35mg% and 80mg% respectively. No AFB was demonstrable and gram stain was not showing any organism. Taking into consideration her poor general condition, TB meningitis and the blood dyscrasia, she was started on steroids and we gave her 4 packed cell transfusions and 4 platelet concentrates.Deranged liver functions limited the full range of ATT and we had to start with streptomycin injection and ethambutol only. With normalisation of her LFT we added drugs in a stepwise manner within one week to put up a regimen of $S_{0.5}$ R_{300} H_{300} Z_{750}. In two weeks her Hb rose to 8.2g% and her platelet count reached 70000/mm ^{3} . The platelet count recovered to normal one month after therapy and her anaemia also improved with ATT. Oral steroids were withdrawn following this and ATT continued. The

initial regimen of SHRZ for two months was followed by $R_{300}H_{300}Z_{750}$ with a total duration of therapy of 9 months. There was no evidence of any recurrence in thrombocytopenia or hemolysis following this. The patient recovered fabulously with a complete clearing of the military picture, neurological signs, blood dyscrasias and a good weight gain of ten kgs.At present her Hb is 12g%,Total WBC count-6100/mm^3 ,Platelet count-1.5lakhs/mm^3 (Fig-2).

Figure 1

Figure 1: showing miliary picture

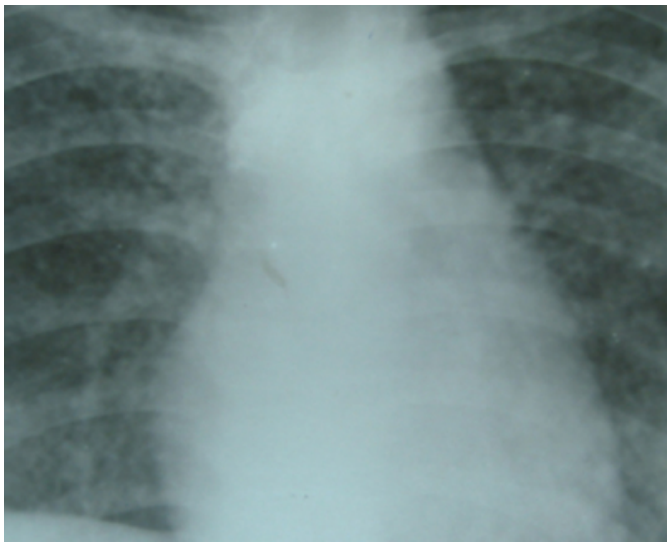
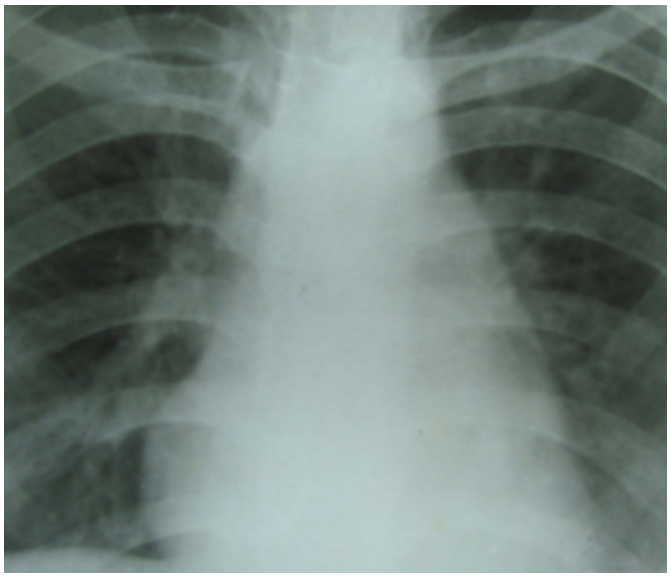


Figure 2

Figure 2: showing clearing of the lesions



DISCUSSION

Tuberculosis presenting with thrombocytopenic purpura is a rare association. About 16 case reports with 25 cases have been described in literature, though only a minority have been described in children [1] .Ours was a case of disseminated tuberculosis, which is defined as concurrent involvement of at least two non-contiguous organ sites of the body, or involvement of the blood or bone marrow by tuberculous process [2] .The various haematological abnormalities that present in tuberculosis include anaemia,leucocytosis,monocytosis,lymphopenia,leukopenia,thrombocytopenia,thrombocytosis,leukemoid reactions and pancytopenia [1,3] . TB-induced ITP is seen in all ages but is more common after the 3rd decade. Pulmonary TB is the most common clinical presentation and occurs in 33% of the patients, followed by 19% with either disseminated TB or lymphadenitis [4,5] .Thrombocytopenia in tuberculosis is thought to be secondary to cytotoxic antibodies directed against platelets. Other causes include production defect, hemophagocytic syndrome, disseminated intravascular coagulation,thrombotic thrombocytopenic purpura,hepatosplenomegaly resulting in platelet consumption and lastly drug induced especially rifampicin induced. It has been postulated that the anti-platelet antibodies generated in some cases of TB-related ITP are secreted by lymphocytes borne of a clonal proliferation that is set in motion by the host's exposure to the tuberculous pathogen [5] . Idiopathic thrombocytopenic purpura (ITP, also known as primary immune thrombocytopenic purpura) is an acquired disease of children and adults, defined as isolated thrombocytopenia with no clinically apparent associated conditions or other causes of thrombocytopenia. In our case, we excluded the adult ITP not only by basing on standard criteria [6] , but with response to steroids since thrombocytopenia did not recur after withdrawal of prednisolone. Also we excluded other causes of thrombocytopenia such as hemophagocytic syndrome, TTP, combined autoimmune cytopenias with history, clinical and laboratory findings, and examination of bone marrow aspiration and biopsy that were described in case presentation .The absence of recurrent thrombocytopenia after the withdrawal of corticosteroids and the poor response to immunomodulating therapies alone in most of the patients strongly support the etiologic role of TB in producing ITP and reinforces the need for antituberculosis therapy in patients with TB-related ITP. As highlighted in the American Society for Hematology's 1996 and British Hematology Society's 2003 guidelines for the diagnosis and management of ITP [7] , the absence of anti-platelet antibodies in no way invalidates the diagnosis of ITP. In fact, anti-

platelet antibodies are labelled as an “unnecessary” test for the routine evaluation to ITP. Although the most important therapy for infection-related thrombocytopenia is that directed at the underlying infection, treatment decisions for ITP remains controversial and may include single or combination therapy with corticosteroids, intravenous immunoglobulin (IVIg) according to degree of thrombocytopenia or hemorrhage. The child's sputum was negative for AFB,as TB in children are usually paucibacillary, with a poor yield of Acid fast bacilli [1] .Four drug antituberculous (ATT) regimen was prescribed taking into consideration the entire clinical scenario. Treatment decisions regarding the type of treatment have been variable. Some authors used ATT alone, ATT with IV gamma globulin or steroids [6,8,9] . In our case, corticosteroids were discontinued one month after therapy and the patient was discharged with only ATT and recurrent thrombocytopenia was not established after withdrawal of corticosteroid therapy. In conclusion, since the incidence of tuberculosis is currently increasing worldwide especially in developing countries and it may present with different hematologic manifestations, TB should always be recalled in case of immune thrombocytopenic purpura. To end up, further studies are needed in order to fully characterize the pathophysiology and immunological abnormalities in tuberculosis-related immune thrombocytopenic purpura.

CORRESPONDENCE TO

Dr. S K VERMAM Associate Professor Department of Pulmonary Medicine Chhatrapati Sahuji Maharaj Medical University, UP,Lucknow,India-226003 Phone No:919415783700 e-mail: drskverma@rediffmail.com

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Author Information

Sanjeev Verma, MD
Associate Professor, Department of Pulmonary Medicine, Chhatrapati Sahuji Maharaj Medical University(erstwhile King George's Medical University)

Kiran Narayan, MBBS
Junior Resident, Department of Pulmonary Medicine, Chhatrapati Sahuji Maharaj Medical University(erstwhile King George's Medical University)