Myelodysplastic Syndrome With Tuberculosis Which Developed To AML - A Case Report

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Abstract:

A 60 year old male presented with pulmonary tuberculosis and moderate anaemia. He was on antitubercular treatment and haematinics. The anaemia remained refractory to treatment. But the patient developed recurrent deep vein thrombosis and pancytopenia, which subsequently transformed into acute myeloid leukemia (AML).The development of AML suggested that the haematological aberrations observed earlier were actually states of myelodysplastic syndrome (MDS). The significance of concurrently developing AML and MDS is discussed and reported here.

Introduction

A variety of haematological alterations ranging from various cytopenias to leukaemoid reaction[1] and even frank leukemia in association with tuberculosis have been reported[2]. The development of acute leukaemia from a state of pancytopenia in a case of pulmonary tuberculosis has not been reported so for. While pancytopenia in tuberculosis has been attributed to necrosis, mechanical replacement of bonemarrow[3]. Hyper-sensitivity to tuberculoproteins has been held responsible for the development of leukaemoid blood picture[4].

We are presenting a case which developed tuberculosis and myelodysplstic syndrome (MDS) almost simultaneously. The MDS subsequently evolved into acute myeloid leukemia (AML). A state of hypercoagulability in the form of recurrent deep vein thrombosis was also observed.

Case Report

A 60 year old male presented with complaints of cough and expectoration of six months' duration and a history of fever, off and on, malaise, fatigue and breathlessness for two months. He was a non-smoker and non-alcoholic. Physical examination revealed marked pallor. There was no jaundice, lymphadenopathy, purpuric spots or bony tenderness. Chest examination revealed an impaired percussion note in the left infraclavicular region with a slight increase in vocal fremitus and vocal resonance in the same area. Auscultation revealed bilateral vesicular breathing with minimal crepitations in the left upper zone. Examination of cardio-vascular and central nervous systems was normal.

The progress of the disease including clinico-radiological and haematological profiles is depicted in the accompanying charts,based on the clinical and investigation findings shown in the progress chart, a diagnosis of pulmonary tuberculosis was made and the anaemia was ascribed to tuberculosis. The patient was, therefore, put on anti-tubercular therapy and hematinics, After about two months, while the chest symptoms were slightly relieved, malaise, fatigue, breathlessness persisted. At this stage, as shown in the progress chart, the anaemia had progressed to pancytopenia, An occasional myeloblast was seen in peripheral blood and bone marrow biopsy revealed a border line increase in the number of myeloblasts. These changes indicated that the refractory nature of anaemia could have been Syndrome (MDS).

Six months later, however, the deep venous thrombosis reappeared and the patient was found to have developed full blown features of acute leukemia including the involvement of bones and lymphnodes. These are confirmed by bone marrow examination. The clinico-radiological and bacteriological evidences of active pulmonary disease were still there. Finally the patient died.

Discussion

The initial presentation of this case was that of active pulmonary tuberculosis with microcytic hypochromic anaemia as its manifestation of a chronic disorder and a common accompaniment of tuberculosis. The anaemia however, was not only refractory to treatment but progressed to

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pancytopenia and finally developed into acute myeloid leukemia while tuberculosis could not be fully controlled even after eight months of treatment,

Retrospectively, it appears that even at the initial presentation, when the haematological profile could not be considered adequate for the diagnosis of MDS, the patient probably had an impaired immune response which caused reactivation of a latent focus of tuberculosis, Subsequently, the anaemia was found to be refractory in nature and the development of pancytopenia with the appearance of myeloblasts in peripheral blood and their increased number in bone marrow suggested MDS. That state developed later into frank AML The MDS represents a pre-leukemic state in which a clonal abnormality of haemopoietic stem cell is characterized by a variety of phenotypic manifestations with varying degrees of ineffective haemopoiesis[5] and where cells have undergone only a proportion of the changes required for acquisition of the leukaemic phenotype[6]. Depending upon the presence of immature cells and blasts in peripheral blood and bone marrow, Bennett et al[4] have described 5 types of primary MDS which are.

(i) Refractory anaemia

(ii) Refractory anaemia with ring sideroblasts

(iii) Refractory anaemia with excessive blasts.

(iv) Refractory anaemia with excessive blasts in transformation.

(v) Chronic myelomonocytic leukaemia.

The possible relationship between tuberculosis and blood dyscrasias can be:

(i) Activation and dissemination of a latent tuberculosis focus due to loss of immune mechanism, particularly, cell mediated immunity in bone marrow failure and leukaemia.

(ii) Blood dyscrasias might be an unusual immunologic response to tubercular bacilli[3,7], or

(iii) The dyscrasias might be related to anaemia and the blast count in bone marrow was within the normal limits. A variable number of patients with MDS may progress to frank leukemia state depending upon the increase in the percentage of blasts, but the progression of the percentage of blasts, but the progression of a refractory anaemia with a normal blast count into leukaemia is unlikely[7]. The progression of refractory anaemia to the state of leukaemia in the present case might have been occurred accelerated by the tubercular infection. On the other hand, the existence of MDS might not have allowed the anti-tubercular drugs to be effective.

Aplastic anaemia and pure red cell aplasia have been reported in patients due to antitubercular drugs[8,5]. Figure-1 shows MDS film and bone marrow.

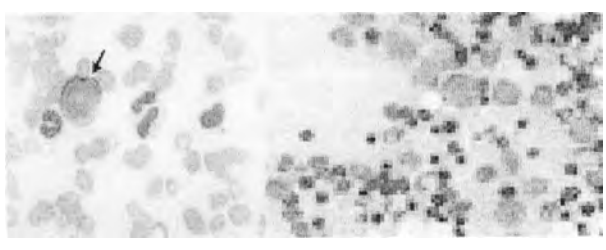

Figure - 1 MDS film and bone marrow

The anaemia in the present case, which subsequently proved to be refractory, was present even before the anti-tubercular therapy was stated.

Pancytopenia and a leukaemoid blood picture simulating acute myeloid leukemia have been described in association with disseminated tuberculosis[4]. Development of leukaemia in the present case was confirmed and the possibility of a leukaemoid picture was excluded as the patient developed hepatosplenomegaly, lymphadeno-pathy and punched out skeletal lesions. Further, the myeloblast count in bone marrow increased to 40 percent and there was pathologic evidence to tissue invasion (myeloblast in lymph node aspiration smears), thus satisfying the criteria described by FAB group[8]. Figure 2 shows increase blast cells count in the bone marrow.

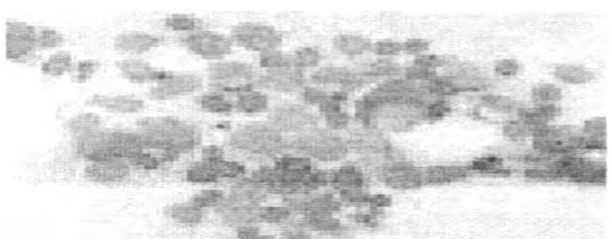

Figure - 2 Bone marrow slide of AML

Development of AML in this case confirmed the pre-existing myelodysplastic state which presented as deep vein thrombosis, refractory anaemia, and pancytopenia.

Myelodysplasticsyndrome With Tuberculosis

Clinical Chart

Haematologic profile

At the time of initial presentation

Anaemia: Microcytic hypochromic

TLC: 8600/Cumm,

DLC: P64,L29,M5,E2,B0,

Platelets: 357,000/Cumm

Bone marrow: Normocellular

M: E Ratio 5:1 normal maturation of myeloid and megakaryocyte series. Inadequate haemoglobinisation in normoblasts and normal iron stores.

At 2 months

Hb= 6.5 gm%

Anaemia: Normcytic hypochromic

TLC: 3500/Cumm,

DLC: P40,L54,M4,E2,B0,occasional myeloblast.

Platelets: 76,000/Cumm

BT= 3 Minuets, CT=3 Minutes, 50 Seconds,

PTI=75% PTTK=90% Urine and blood -negative for fibrine degradation products (FDP)

Bone marrow : Hypercelluler

M : E Ratio 3:1

Myeloblasts= 7% megakaryocytes, megaloblastoid erythropoiesis ringed sideroblasts and - ve iron stores.

At 6 months

Hb= 4 gm% Anaemia: Normcytic Hypochromic, TLC: 3800/Cumm, DLC: P38,L51, M5, E1, B0, myeloblast 5.

Platelets: 60,000/Cumm BT= 10 Minutes,, CT=10 Minutes; 20 Seconds, PTI=60%,

Bone marrow : Hypercelluer,

Myloblasts= 40% megakaryocytes, megaloblastoid erythropoiesis,- ve iron stores.

Bone pains +, Generalised lymphadenopathy. Hepatosplenomegly.

Lymph node aspiration cytology : 30% blasts.

To the best of our knowledge, pancytopenia evolving into frank leukaemia in association with tuberculosis has not been reported earlier, though, it is possible that cases of pancytopenia resulting in fatality, described in the earlier literature[6], might have been instances of myelodysplasia and death might have been caused by complications prior to the development of leukaemia, Furthermore, recurrent deep vein thrombosis due to hypercoagulable state or chronic DIC could be another manifestation of myelodysplastic state.

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