Case Report

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Reversible gelatinous transformation of bone marrow – A rare and reversible cause of pancytopenia in tuberculosis

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Abstract:

A 68-year-old man presented with a low-grade fever for one month. He had loss of appetite and had lost 6 kilograms of weight in the last two months. He was evaluated and found to have miliary tuberculosis with pancytopenia. The bone marrow revealed Gelatinous transformation of bone marrow and there was no evidence of other causes of pancytopenia like histiocytic hyperplasia, maturation arrest, or infiltration of the bone marrow. The pancytopenia improved with anti-tubercular treatment showing the reversible nature of the disease. To conclude, multiple mechanisms can result in pancytopenia in tuberculosis. A bone marrow study can reveal most of them including rare causes like GTBM.

Keywords:

Pancytopenia, reversible gelatinous transformation of bone marrow, tuberculosis

Introduction

Gelatinous transformation of bone marrow (GTBM) is a condition that is featured by atrophy of the adipose tissue with deposition of an extracellular eosinophilic substance in the bone marrow resulting in ineffective hematopoiesis. The condition is commonly associated with states of severe malnutrition such as anorexia nervosa and starvation. Several other diseases are also considered to be related to GTBM including malignancy, connective tissue disorders, and infections. GTBM is usually reversible with treatment of the underlying disease. We describe a patient with pancytopenia due to GTBM which resolved completely with treatment of tuberculosis (TB).

Case Report

A 68-year-old man presented with a low-grade fever for 1 month. He had loss of appetite and had lost 6 kg of weight in the past 2 months. His medical history was unremarkable. He denied a history of high-risk behavior, any addictions and had no sick contacts. On examination, he had pallor, was febrile, and had normal blood pressure (with no postural hypotension). The rest of the examination was unremarkable.

Hemoglobin was 8.2 g/dl (normocytic normochromic), total leukocyte count 2960/ml, platelet count 29,000/µl, and erythrocyte sedimentation rate 35 mm in 1 h. Peripheral smear showed normocytic normochromic red blood cells, leucopenia, and thrombocytopenia but there were no immature or abnormal cells. Biochemical parameters were normal. HIV, hepatitis B, and hepatitis C serology were negative. Chest X-ray showed military mottling [Figure 1a]. Contrast-enhanced computed tomography of the thorax showed extensive lung nodules in the bilateral lung fields suggesting military TB [Figure 1b]. Bronchoalveolar lavage was positive for acid fast bacilli. Cartridge-Based Nucleic Acid Amplification Test of bronchoalveolar lavage was

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positive without rifampicin resistance. Bone marrow aspirate was hypocellular marrow with depletion of fat cells and showed amorphous eosinophilic material in the background [Figure 2a and b]. Bone marrow biopsy showed hypocellular hematopoietic elements with normal maturation and depleted fat cells. The intertrabecular spaces were filled with amorphous gelatinous extracellular material. Staining with Periodic acid–Schiff was positive but Congo red and reticulin were negative [Figure 2c-f]. Based on the histopathological features, the bone marrow was reported as GBTM. The patient was started on anti-tubercular treatment (isoniazid 300 mg, rifampicin 450 mg, pyrazinamide 1 g, and ethambutol 800 mg daily). After completing 2 months of anti-tubercular treatment, his pancytopenia improved.

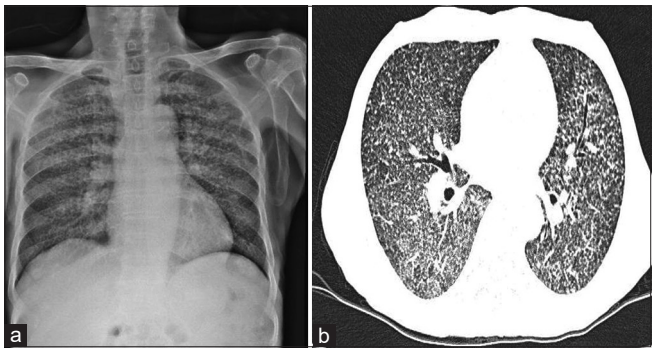

Figure 1: Chest X-ray showing military mottling (a). Contrast-enhanced computed tomography of the thorax shows extensive lung nodules in the bilateral lung fields suggesting military tuberculosis (b)

Discussion

Extrapulmonary gelatinous transformation of bone marrow can result in various kinds of hematological abnormalities. It can affect any of the cell lines and cause cytopenias or an increase in cell counts. Pancytopenia as a presenting feature of TB is rare. Pancytopenia associated with TB can be due to various mechanisms including overactive spleen, maturation arrest, or bone marrow fibrosis.[1]

GTBM has been linked to various underlying disease processes. Severe malnutrition as a result of anorexia nervosa or starvation is considered to be the common cause of GTBM.[2] Several malignancies (hematological and solid organ), infections (bacterial, viral, mycobacterial, and parasitic), connective tissue disorders, and other chronic diseases (chronic obstructive airway disease,

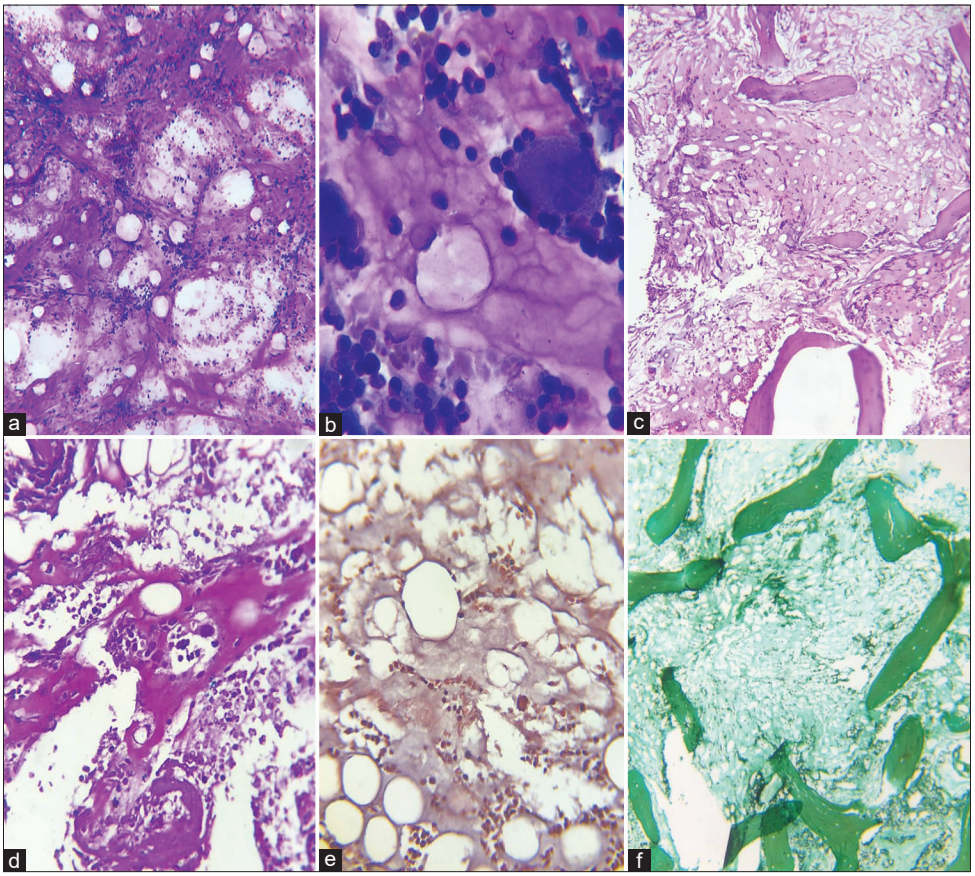

Figure 2: Bone marrow aspirate showing hypocellular marrow with depletion of fat cells and showed amorphous eosinophilic material in the background (a and b). Bone marrow biopsy showing hypocellular hematopoietic elements with normal maturation and depleted fat cells (c). The intertrabecular spaces were filled with amorphous gelatinous extracellular material. Staining with Periodic acid–Schiff was positive but Congo red and reticulin were negative (d-f)

dilated cardiomyopathy) were reported previously to be associated with GTBM.[2]

GTBM can result in cytopenias which are most commonly anemia. Bicyotopenia and pancytopenia also can be the initial presentation. Bone marrow examination shows characteristic findings such as hypoproliferation, adipose cell atrophy, and an extracellular gelatinous substance deposition in the bone marrow.[3] Bone marrow edema, necrosis, or amyloid can mimic the marrow findings of GTBM which can be diagnosed easily by suitable staining methods.

The underlying pathophysiology related to GTBM is not fully elucidated. Depletion of fat cells secondary to a state of severe catabolism, followed by deposition of a gelatinous substance containing hyaluronic acid-like material on the bone marrow results in GTBM.[4] The deposition of this gelatinous substance makes an unfavorable microenvironment in the marrow for hematopoiesis.[5] This can result in the loss of interaction between hematopoietic cells and cell-signaling molecules.[6] The fat cells in the bone marrow are needed to maintain hematopoietic progenitor cells.[2] Various mechanisms such as cytokine-mediated injury (interleukin 1, interleukin-2, and the tumor necrosis factor) are proposed, especially in infection-related GTBM.[7] Reversibility of GTBM has been described after improvement of nutritional state.[8] This may be explained by the occurrence of limited cell necrosis as cellularity in the marrow also decreases due to a lack of growth factors secondary to starvation.[9] Long-term outcomes and the prognosis of GTBM have not been well documented yet. The survival of patients having GTBM is dependent on the nature and stage of the underlying disease at the time of the diagnosis.[10]

This patient had miliary TB with pancytopenia. The bone marrow revealed GTBM and there was no evidence of other causes of pancytopenia such as histiocytic hyperplasia, maturation arrest, or infiltration of the bone marrow. The pancytopenia improved with anti-tubercular treatment showing the reversible nature of the disease. To conclude, multiple mechanisms can result in pancytopenia in TB. A bone marrow study can reveal most of them including rare causes like GTBM.

Compliance with ethical standards

All procedures performed in studies involving human participants were by the ethical standards of the Institutional and/or National Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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