Chronic Childhood Idiopathic Myelofibrosis in Down's Syndrome: A Case Report

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Abstract Idiopathic myelofibrosis a disease of elderly is rarely seen in children. A case of chronic idiopathic myelofibrosis in an 8 year old boy with Down's syndrome is reported here, who presented with progressive pallor and hepatosplenomegaly. Peripheral blood examination revealed pancytopenia, macrocytic anemia and tear drop cells. No blasts were found. Bone marrow aspirate yielded a dry tap and trephine biopsy showed marrow fibrosis with osteosclerosis. Focally megakaryocytes were increased in number with atypical morphology. No blasts were seen. Review of literature revealed 47 reported cases of childhood idiopathic myelofibrosis. Six cases were associated with Down's syndrome and only 3 of them had features of chronic idiopathic myelofibrosis without evidence of acute megakaryoblastic leukaemia.

Keywords Childhood · Down's syndrome · Idiopathic myelofibrosis · Osteosclerosis

Introduction

Primary myelofibrosis is a clonal myeloproliferative neoplasm characterised by proliferation of predominantly

megakaryocytes in bone marrow and is associated with reactive deposition of fibrous connective tissue [1]. Incidence of myelofibrosis is 0.5–1.5/1,00,000 [1]. Children are rarely affected with this condition. We report an 8 year old boy with Down's syndrome (DS) and chronic idiopathic myelofibrosis along with brief review of literature.

Case Report

An 8 year old boy, who had already been diagnosed with DS presented with gradually progressive pallor and fatigue for 6 months. There was no past history suggestive of any chronic infection or serious illness. General physical examination showed stigmata of DS, severe pallor, and petechiae and ecchymotic patches over trunk and extremities. On systemic examination, hepatosplenomegaly measuring 5 and 7 cm below costal margins, respectively was present. There was no icterus and no significant lymphadenopathy. Clinical diagnosis of myelofibrosis/kala azar was suggested. Blood counts revealed pancytopenia with hemoglobin 8.9 g/dl, white blood cells $3.6 \times 10^9/l$, and platelets $0.13 \times 10^9/\mu l$. Red cell indices were as follows: MCV 95.1 fL, MCH 31.1 pg and MCHC 32.7 gm/dl. Peripheral blood smear examination showed pancytopenia with presence of macrocytic red blood cells and few tear drop cells. Differential leukocyte counts showed lymphocytes 48%, neutrophils 43%, monocytes 3%, eosinophils 2%, band cells 1%, metamyelocytes 2% and myelocytes 1%. No blasts were seen. There were 6 nucleated red blood cells per 100 white blood cells. Repeated bone marrow aspirate yielded only dry tap raising suspicion of myelofibrosis. Trephine biopsy showed broad irregularly thickened bony trabeculae suggesting osteosclerosis (Fig. 1). The marrow spaces revealed fibrosis of bone marrow with

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suppression of erythropoiesis and myelopoiesis. Focally megakaryocytes were increased in numbers and had abnormal morphology. They showed clustering, variation in sizes, high nuclear cytoplasmic ratio, clumping of nuclei and coarsely clumped chromatin (Fig. 2). There were no blasts, granuloma or leishmania donovani bodies. There was grade 3 reticulin fibrosis in marrow (Fig. 3). Von Geison stain for collagen was negative. Immunohistochemistry for CD34 was negative suggesting absence of blasts. Liver function tests, kidney function tests, serum calcium, phosphorus and alkaline phosphatase were normal. HIV serology and antinuclear antibodies were negative. Chest X-ray was normal and Mantoux test was negative. Abdominal ultrasonography showed no other abnormality besides hepatosplenomegaly. Thus, final diagnosis of chronic idiopathic myelofibrosis with osteosclerosis was given. At the time of submitting this manuscript, i.e., after 3 months of diagnosis patient was clinically asymptomatic and not required any blood component therapy.

Discussion

Bone marrow fibrosis is an uncommon condition in children. Fewer than 100 cases have been described in the medical literature [2]. Most of them arise secondary to other disease processes such as vitamin D deficiency, renal osteodystrophy, systemic lupus erythematosus langerhans cell histiocytosis, tuberculosis, leishmaniasis, and malignant conditions especially acute megakaryoblastic leukaemia. Review of English literature yielded 47 reported cases of childhood idiopathic myelofibrosis [2]. Only six of these cases were associated with DS [2–5]. In recent times, it has become increasingly recognised that DS (trisomy 21) may predispose to various myeloid proliferations [1].

Fig. 1 Broad thick trabeculae suggesting osteosclerosis (H&E, 100×)

Fig. 2 Megakaryocytic clustering with atypical morphology (H&E, 400×)

Fig. 3 Grade 3 reticulin fibrosis with coarse fibres (Reticulin stain, 400×)

Furthermore, it has become apparent that an association exists between leukaemia and myelofibrosis.

There are two broad classes of primary myelofibrosis. Chronic idiopathic myelofibrosis is an indolent myeloproliferative neoplasm characterised by clonal hematopoiesis, splenomegaly and leukoerythroblastic peripheral blood smear. Whereas acute myelofibrosis of childhood is a fulminant disease in which splenomegaly is not observed and is associated with numerous bizarre megakaryocytes in marrow and presence of blasts. This condition is considered to be a variant of acute megakaryoblastic leukaemia in Down syndrome [1]. Out of six reported cases of myelofibrosis in DS, only three cases were of chronic idiopathic myelofibrosis. In the present case, symptoms were of gradual onset and there were no blasts on bone marrow biopsy. Marrow aspirates in these cases should be sent for cytogenetic analysis to look for GATA-1 mutation as these

are pathognomic for acute megakaryoblastic leukaemia of Down syndrome [1]. Unfortunately, cytogenetic analysis was not performed in our case.

These cases can evolve into malignancy or remain stable for long term. The only mode of treatment is allogenic bone marrow transplantation. This case is reported because of its rarity.

Conflict of interest None.

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