

## CASE REPORT

### Childhood idiopathic myelofibrosis: a case report and review of literature

Noor-Fadzilah Z *MPath*, Leong C-F *FRCPE, FRCPA\**, Sabariah M-N *MPath\*\** and Cheong S-K *FRCPE, FRCPA\**.

*Faculty of Medicine and Health Sciences, Islamic Science University of Malaysia, \*Department of Pathology, National University of Malaysia, \*\*Department of Pathology, Universiti Putra Malaysia, Kuala Lumpur, Malaysia.*

#### Abstract

Idiopathic myelofibrosis occurs predominantly in older adults. It is very rarely seen in children. We describe a 3-year-old girl with Down's syndrome who presented with recurrent chest infections associated with anaemia and easy bruising. There was mild hepatosplenomegaly. Full blood picture revealed pancytopenia with leucoerythroblastosis with absence of circulating blast cells. Repeated attempts at bone marrow aspiration and trephine biopsy were unsuccessful. A trephine biopsy from the tibia showed depressed myelopoiesis and erythropoiesis, megakaryocytes with atypical morphology and increased bone marrow reticulin fibres, findings compatible with idiopathic myelofibrosis. She was treated symptomatically as she was clinically stable. Review of the English literature on-line yielded 46 reported cases of childhood idiopathic myelofibrosis with variable outcome from spontaneous remission to an indolent course with shortened survival. 6 cases evolved to another malignancy. 5 cases were associated with Down's syndrome.

**Keywords:** Idiopathic myelofibrosis, childhood, Down's syndrome, pancytopenia, leucoerythroblastic picture.

#### INTRODUCTION

Idiopathic myelofibrosis is also known as agnogenic myeloid metaplasia or myelofibrosis with myeloid metaplasia. The incidence of this disease is 0.5-1 in 100,000 population with a median age of 65 years. It is extremely rare in children<sup>1</sup>. It is characterized by anaemia, tear drop cells in the blood film, splenomegaly and bone marrow fibrosis in the absence of other pre-existing conditions such as chronic infections, chronic renal failure, primary marrow malignancy and metastatic diseases. There is extramedullary erythropoiesis, particularly in the spleen and liver. The disease is due to proliferation of a clone of cells arising from a multipotent myeloid stem cell. Proliferation of bone marrow fibroblasts with deposition of reticulin and collagen is secondary to the myeloid proliferation. Hepatosplenomegaly is a typical finding.

We report a young patient with Down's syndrome who has idiopathic myelofibrosis and a brief review of the English literature.

#### CASE REPORT

A 3-year-old Malay girl with Down's syndrome was referred for recurrent chest infections and easy bruising for a few months. She is known to have bronchial asthma and ventricular septal defect (VSD). There was no past history of chronic infections or other serious illnesses. She is the youngest of three siblings and there is no similar illness in the family. Clinically, she was pale with multiple bruises over the extremities. The vital signs were within normal limits. The cardiovascular and respiratory examinations were unremarkable. There was hepatosplenomegaly measuring 2cm and 5cm respectively below the costal margins. No significant lymphadenopathy was noted. She was unable to walk due to pain in the lower extremities.

#### Pathology

Full blood count showed pancytopenia with haemoglobin level of 8.2g/dL, white blood cell count of  $1.3 \times 10^9/L$  and platelet count of

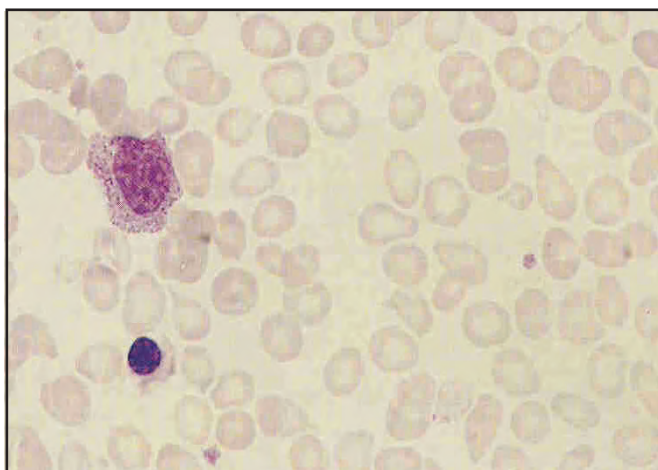


FIG. 1: Peripheral blood film showing anisocytosis, poikilocytosis (including tear-drop poikilocytes), a myelocyte and an erythroblast (leucoerythroblastic picture) X 400.

49 x 10<sup>9</sup>/L. Peripheral blood film revealed a leucoerythroblastic picture with the presence of a few tear-drop red cells (Fig. 1). No circulating blast cell was observed. A few attempts at bone marrow aspiration and trephine biopsy at the posterior iliac crests were unsuccessful. Finally, a trephine biopsy from the tibia revealed fibrosis of the bone marrow with reduction of the myelopoiesis and erythropoiesis (Fig. 2). Megakaryocytes were seen in clusters with abnormal morphology. The sinusoids appear distended. There was also an increase in bone

marrow reticulin fibres, supporting the diagnosis of myelofibrosis (Fig. 3). She was treated symptomatically as she was clinically stable.

**DISCUSSION**

Bone marrow fibrosis or myelofibrosis (MF) is a rare condition in children. Fewer than 100 cases have been described in the medical literature. Most cases are secondary to other disease processes such as malignancy, chronic renal failure and chronic infections. A search of the English literature on-line combining Pubmed,

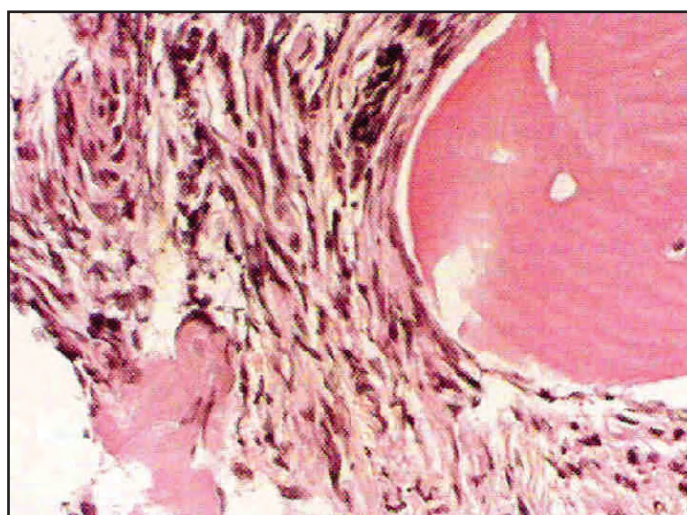


FIG. 2: Bone marrow trephine biopsy showing fibrosis of the marrow space with reduced haematopoiesis. Clusters of abnormal megakaryocytes (not shown) were observed among the fibrotic tissues. H&E X 400.

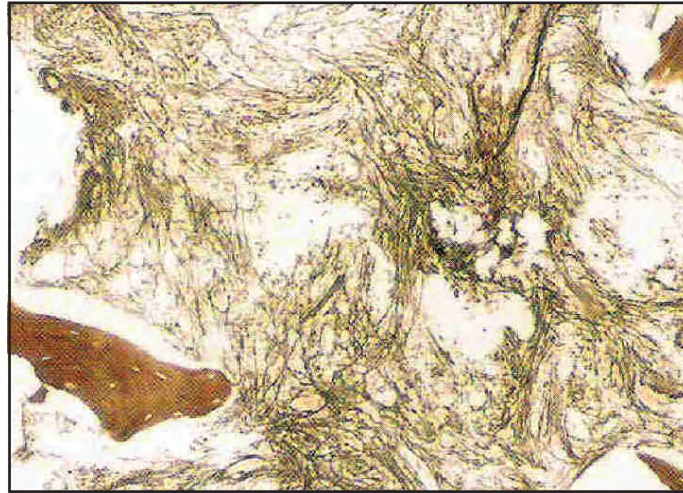


FIG. 3: Bone marrow trephine biopsy showing increased in reticulin deposition. Silver impregnation method X 200.

Google and Scopus search engines yielded 46 reported cases of idiopathic MF in children as of August 2009.<sup>2-23</sup>

Like our patient, 5 reported cases also have Down's syndrome.<sup>3,6,11</sup> The outlook was poor as they were reported to have shortened survival. Prognosis in our patient is therefore guarded. One patient actually progressed to acute leukaemia after 3 months.<sup>11</sup>

Idiopathic childhood MF is commonly observed prior to a diagnosis of acute leukemia or lymphoma.<sup>5,8,14,17,18</sup> The 6 reported cases suffered from acute lymphoblastic leukaemia, acute myeloid leukaemia or T-cell lymphoma. The transformation was reported within months after the diagnosis of MF. These 6 cases may represent a clonal disorder with genetic instability allowing a more aggressive malignancy to evolve.

Bone marrow aspirates are dry in the majority of patients. However, a bone marrow biopsy is essential for confirming the diagnosis. This is usually performed over the posterior iliac crest. Sternal aspirates are typically not useful obviously because of the high frequency of dry taps and inability to obtain a biopsy from this site. Another option is to obtain bone marrow aspirate from the tibia as it was done in our patient. Biopsy specimens reveal hypercellular or hypocellular marrow with increased megakaryocytes. Characteristic features include patchy hematopoietic cellularity and reticular fibrosis. The amount of reticulin deposition varies from field to field. Megakaryocytes may be present in clusters and may show dysplasia.

Distended marrow sinusoids, frequently containing intravascular hematopoiesis, are also observed. The bone marrow trephine biopsy classically demonstrates increased silver (reticulin) staining. Most of these features were observed in our patient. The bone marrow aspirate should be sent for cytogenetic analysis as it could reveal chromosomal abnormality. The presence of an abnormal karyotype is associated with a poorer prognosis. Unfortunately, cytogenetic analysis was not performed in our patient.

Apart from evolution to a malignancy, most of the childhood MF cases reported have an indolent course on supportive therapy. Long term survival is possible.<sup>19</sup> 2 cases<sup>7,21</sup> were reported to undergo spontaneous remission, one of which was for 16 years.<sup>21</sup> The disorder can be treated with allogeneic stem cell transplantation if there is a compatible sibling. Otherwise, unrelated stem cell transplant has been successfully carried out.<sup>23</sup>

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