Myelofibrosis

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Myelofibrosis with myeloid metaplasia (MMM) is a chronic myeloproliferative disorder characterized by progressive fibrosis of the bone marrow and extramedulary hematopoeisis(1). It is primarily a disease of adults(2,3). Very few cases in pediatric age group are reported(4,5). It is the rarity of this disease in pediatric age group which prompted us to report this young child who had all characteristic features of MMM.

Case Report

A 2½-year-old male child was admitted to Kalawati Saran Children's Hospital, New Delhi with the complaints of progressive enlargement of abdomen and lump in the abdomen for 1½ years duration. He had never had bleeding and had not required blood transfusion. The physical examination revealed a thin built boy (Grade III PEM of IAP classification) who was mildly anemic, had pedal edema and small cervical, axillary and inguinal lymphnodes. There was no evidence of bleeding. Abdominal examination showed splenic enlargement of 16 cm and hepatomegaly of 5 cm below costal margin.

His investigations showed hemoglobin from 10-11 g/dl, except in the terminal stage when it decreased to 4.4 g/dl. The TLC was between 22000-39000/mm^3. Platelet count was 70000/mm^3. The peripheral blood smear showed leucoerythroblastic blood picture with presence of immature WBCs (myeloblasts, myelocytes and metamylocytes) and nucleated red cells. The red cells were normocytic and normochromic and showed features of dyserythropoeisis (presence of tear drop cells and pencil shaped cells). Reticulocyte count was 4.4%. Leucocyte alkaline phosphatase score was normal and raised on two separate occasions. Bone marrow aspiration smear showed hyperplasia of all three elements. Fetal hemoglobin was 0.6%. Direct and indirect Coomb's tests were negative.

On the basis of above investigations myelofibrosis was suspected and for confirmation of diagnosis, bone marrow biopsy and lymphnode biopsy were done. Bone marrow biopsy showed patchy areas of hypocellularity and hypercellularity. There was megakaryocytic hyperplasia. Fibroblastic proliferation with reticulin laying down (*Fig. 1*). was seen which was confirmed on special stain for reticulin. Van Geison staining showed collagenization. Lymphnode biopsy showed areas of myeloid metaplasia (extramedullary hemopoeisis, *Fig. 2*).

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Fig. 1. Photomicrograph (10 × 10) of bone marrow biopsy showing hypercellular area and increased reticulin with condensation in some (→) areas (Reticulin stain).

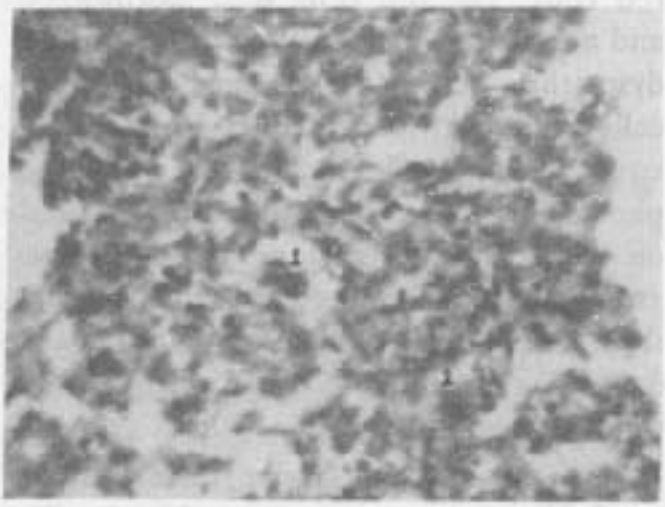

Fig. 2. Photomicrograph of lymphnode biopsy (10 × 40) showing an area of extramedullary hematopoeisis (focus of normoblast, 1 and a megakaryocyte, 2).

To rule out secondary causes of myelofibrosis, renal function tests were done which were normal. Radiological skeletal survey was normal except growth arrest lines. Serology for toxoplasma was negative. Investigations for tuberculosis (*X*-ray chest, Mantoux and BCG diagnostic tests, gastric lavage for acid fast bacilli and lymphnode biopsy) were negative.

During his hospital stay he acquired bronchopneumonia for which he was treated with broad spectrum antibiotics. For myelofibrosis he was started on oxymethalone and was given a blood transfusion. He died after 35 days of hospitalization to resistant chest infection.

Discussion

MMM is also described as agnogenic myeloid metaplasia or chronic myelosclerosis. The diagnostic criteria of MMM include anemia with nucleated red cell precursors and tear drop cells, immature leucocytes in the peripheral blood, evidence of extramedullary hematopoeisis and fibrosis of the bone marrow, the last two features being essential for diagnosis(2,4). Adults over the age of 50 years are usually affected, however MMM is known to occur in young adults and rarely in pediatric age group. From India, Rani *et al*. have earlier reported MMM in a 6-year-old child(5). Other reports from India mainly included adult patients(6).

Progressive spleen and liver enlargement are almost invariably present in MMM. Other clinical features include lymphadenopathy, petechiae and fever(3,6,7). The peripheral smear is characteristically described to show leucoerythroblastic blood picture with presence of immature granlocytes and nucleated erythrocyte precursors. The anemia is usually present with RBCs showing features of dyserythropoeisis in the form of tear drop cells. Leucocyte count is variable but nearly half of the cases have leucocytosis. One third to half of the cases have thrombocytopenia and platelets tend to be large and misshapen(2-

4,7). When associated with leucocytosis, clinical and peripheral blood picture may be difficult to differentiate from chronic myelogenous leukemia(8). These clinical and hematological abnormalities in children may be seen in variety of conditions in children like tuberculosis, severe hemolytic anemias, congenital infections and osteopetrosis(4).

Causes of secondary myelofibrosis include leukemia, lymphoma, rickets, chronic renal failure and systemic lupus erythymatosus. If these conditions are excluded, then it is termed as idiopathic or primary, myelofibrosis(4). In the present case, these clinical conditions were excluded and hence we believe that he had primary myelofibrosis.

Treatment of MMM has usually been unsatisfactory. Apart from blood transfusion and supportive care; androgens, corticosteroids with or without busulphan, splenic irradiation and splenectomy have produced variable results in adults(7). High dose intravenous methylprednisolone had produced complete remission in pediatric patients in a recent report(9). 1,25-dihydroxy Vitamin D_3 which inhibits the collagen synthesis promotor megakaryocytes and thus decreases the fibrosis of bone marrow has also been found useful for treatment of MMM in adults and children(10,11). Reversal of fibrosis and clinical improvement in primary and secondary myelofibrosis has been described after allogenic bone marrow transplantation(12,13).

Prognosis generally is poor, though long term survival upto 5-15 years is reported. Younger age at diagnosis, absence of thrombocytopenia and constitutional symptoms point towards better prognosis. Splenic size usually does not influence the prognosis(1,8,14). Leukemic transformation is known to occur in 5-12% of cases(8).

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Knowledge and Practices Regarding Diarrhea in Rural Mothers of Haryana

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Prevention of diarrheal deaths by promoting the use of oral rehydration salt (ORS) is one of the components of the child survival strategy enunciated by the UNICEF. According to an UNICEF estimate, of the expected five million annual diarrheal deaths only one million are at present being prevented by oral rehydration therapy (ORT) whereas 2.5 million potential lives could be saved by ORT(1). Thus, it becomes imperative that we assess the current usage rate of ORS and make efforts to improve the same.

This study was conducted with this aim and also to use the information generated in constructing an educational campaign for prevention of diarrhea and diarrheal deaths.

Material and Methods

This study was done in two villages–Garhkhera and Atali (population 3000 and 5000, respectively) of Haryana, which fall in the field practice area of Centre for Community Medicine, AIIMS.

One hundred and forty five mothers with under five children were selected by stratified random sampling (with reference to caste) from both the villages. All the mothers were interviewed by the investigator using a pretested schedule having 25 questions. These questions covered various aspects of diarrhea and ORT, such as mother's definition of diarrhea, dietary practices in diarrhea, *etc*. The demographic particulars of the families were also recorded. All the mothers answered the question. The interview was done in June-July 1988. Each interview lasted for about half an hour, and apart from a few, the rest were done in one sitting.

Results

The characteristics of the study population is shown in *Table I*. This population

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