

Slide 3 - April 2006 / Cycle 28

Myelofibrosis

Please read this bit first

This CPD/ CEU exercise is designed to take approximately two hours as a small group exercise within your laboratory. The Thistle QA CPD No is: **MT00025**.

Please keep a register of those taking part in the exercise.

Each attendee should claim two CPD points for completing the questions correctly, by retaining a copy of the relevant Thistle QA Participation Certificate as proof of registration on a Thistle QA EQA.

FORWARD

The following clinical information may not match the slide exactly. We have decided to vary the clinical information as much as possible - for the sake of variety.

Scanned and edited from Essential Haematology by Hoffman, Pettit and Moss. Blackwell (2001).

Clinical features.

The predominant feature of myelofibrosis is a progressive generalized fibrosis of the bone marrow in association with the development of haemopoiesis in the spleen and liver (known as myeloid metaplasia). Clinically this leads to anaemia and massive hepatosplenomegaly. Confusingly, the condition has many names – idiopathic myelofibrosis; myelosclerosis; agnogenic myeloid metaplasia; or myelofibrosis with myeloid metaplasia (MMM).

The fibrosis of the bone marrow is secondary to hyperplasia of abnormal megakaryocytes. It is thought that fibroblasts are stimulated by platelet derived growth factor and other proteins secreted by megakaryocytes and platelets.

One-third or more of the patients have a previous history of Polycythemia Rubra Vera (PRV) and some patients present with clinical and laboratory features of both disorders.

Clinical features

1. An insidious onset in older people is usual with symptoms of anaemia.
2. Symptoms resulting from massive splenomegaly (e.g. abdominal discomfort, pain or indigestion) are frequent; splenomegaly is the main physical finding (Fig. 17.3b).
3. Hypermetabolic symptoms such as loss of weight, anorexia, fever and night sweats are common.
4. Bleeding problems, bone pain or gout occur in a minority of patients.

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Fig. 17.3 (b) Splenomegaly : enlarged spleens in male patients with myelofibrosis.

Myelofibrosis and chronic myeloid leukaemia are responsible for most cases of massive (>20cm) splenic enlargement in the UK and North America.

Laboratory findings.

1. Anaemia is usual but a normal or increased haemoglobin level may be found in some patients.
2. The white cell and platelet counts are frequently high at the time of presentation. Later in the disease leucopenia and thrombocytopenia are common.
3. A leucoerythroblastic blood film is found. The red cells show characteristic 'tear-drop' poikilocytes (Fig. 17.8).
4. Bone marrow is usually unobtainable by aspiration. Trephine biopsy shows a fibrotic, hypercellular marrow. Increased megakaryocytes are frequently seen. In 10% of cases there is increased bone formation with increased bone density on x-ray.
5. Low serum and red cell folate, raised serum vitamin B₁₂ and vitamin B₁₂-binding capacity, and an increased Neutrophil alkaline phosphatase (NAP) score are usual.
6. High serum urate, lactate dehydrogenase (LDH) and hydroxybutyrate dehydrogenase levels reflect the increased but largely ineffective turnover of haemopoietic cells. The serum LDH is normal in PRV.
7. Transformation to acute myeloid leukaemia occurs in 10-20% of patients.

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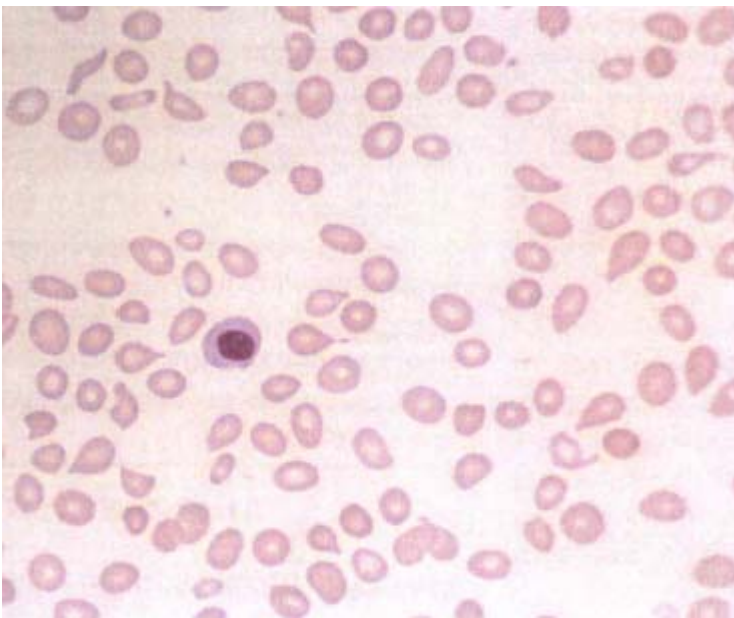


Fig. 17.8 Peripheral blood film in myelofibrosis. Leucoerythroblastic change with 'tear-drop' cells and an erythroblast.

Treatment.

This is palliative and aimed at reducing the effects of anaemia and splenomegaly. Blood transfusions and regular folic acid therapy are used in severely anaemic patients. Hydroxyurea may help to reduce splenomegaly and hypermetabolic symptoms. Splenectomy is considered for patients with severe symptomatic splenomegaly – mechanical discomfort, thrombocytopenia, portal hypertension, excessive transfusion requirements or hypermetabolic symptoms. Splenic irradiation is an alternative but usually provides relief only 3–6 months. Allopurinol is indicated in virtually all patients to prevent gout and urate nephropathy from hyperuricaemia. Allogeneic stem cell transplantation is currently experimental but may be curative for young patients.

The median survival is around 3.5 years and causes of death include heart failure, infection and leukaemic transformation. A haemoglobin level of less than 10g/dl, a white cell count of less than 4 or greater than $30 \times 10^9 / l$ and the presence of abnormal chromosome are associated with a worse prognosis.

CPD Questions.

1. What is the predominant feature of myelofibrosis ?
2. What would you say is the main characteristic of this slide ?
3. Discuss the clinical features of myelofibrosis.