Reduction of Tear-Drop Poikilocytes in a Case of Myelofibrosis Following Splenectomy

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ABSTRAK

Mielofibrosis adalah sejenis penyakit mieloproliferatif kronik yang dicirikan dengan pembengkakan limpa, anemia leukoeritroblastik, poikilositosis berbentuk air-mata (tear-drop poikilocytosis) dan fibrosis sumsum tulang. Pembedahan splenektomi dilakukan untuk pesakit yang memerlukan transfusi darah yang kerap ataupun pembengkakan limpa yang amat besar sehingga mengakibatkan gejala-gejala yang memilukan serta trombositopenia yang teruk akibat hipersplenisma.

Seorang wanita berumur 56 tahun telah didiagnos menghidap penyakit mielofibrosis primer pada tahun 2000 dan dirujuk ke Hospital UKM untuk rawatan selanjutnya bagi kekerapan transfusi darah yang semakin meningkat dan juga kerana pembengkakan limpanya yang teruk. Beliau juga telah mengalami kolesistitis akut sebanyak dua kali pada masa yang lampau. Pemeriksaan menunjukkan paras hemoglobin 6.4g/dl, kiraan sel darah putih : 23.4x10^9/l, kiraan platelet : 163x10^9/l dengan gambaran leukoeritroblastik dan poikilositosis berbentuk air-mata (tear-drop poikilocytosis) pada filem darah periferi. Bacaan alkalin fosfatase neutrofil (Neutrophil alkaline phosphatase NAP score) adalah 184/100 neutrofil. Ujian ultrasound pada abdomen menunjukkan splenomegali yang teruk, dan juga terdapat batu karang pundi hempedu yang multipel. Memandangkan kekerapan transfusi darah yang semakin meningkat dan juga gejala splenomegali yang teruk, pembedahan splenektomi dan kolesistektomi telah dilakukan. Pemeriksaan filem darah periferinya selepas splenektomi menunjukkan penurunan poikilositosis berbentuk air-mata (tear-drop poikilocytosis) dan juga kehilangan gambaran leukoeritroblastosis. Kami percaya bahawa limpa memainkan peranan yang penting dalam pembentukan poikilositosis berbentuk air-mata (tear-drop poikilocytosis) dan leukoeritroblastosis, tetapi mekanisma yang terlibat masih tidak jelas.

Kata kunci: mielofibrosis, penurunan poikilositosis berbentuk air-mata dan anemia leukoeritroblastik.

ABSTRACT

Myelofibrosis is a chronic myeloproliferative disorder characterised by splenomegaly, leukoerythroblastic anaemia, tear-drop poikilocytosis and marrow fibrosis. Splenectomy is indicated for patients requiring frequent transfusions or massive splenomegaly causing distressing symptoms and severe thrombocytopenia secondary to hypersplenism.

A 56 year-old lady diagnosed to have primary myelofibrosis in year 2000 was referred to HUKM for further management of her increasing requirement of blood transfusion and

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massive splenomegaly. She has had two episodes of acute cholecytitis. Investigations done in our hospital showed that her hemoglobin level was 6.4g/dl, white cell count of 23.4x10^9/l, platelet count 163x10^9/l and peripheral blood showing leukoerythroblastic picture and tear-drop poikilocytosis. Leukocyte alkaline phosphatase score (NAP) was 184/100 neutrophils. Ultrasound of the abdomen showed massive splenomegaly with multiple gall stones. In view of the frequent transfusion requirements and symptomatic massive splenomegaly, splenectomy and cholecystectomy was performed. A review of her peripheral blood picture, post-splenectomy, showed marked reduction of the tear-drop poikilocytosis and leukoerythroblastosis. We believe that the spleen plays an important role in their formation, but the exact mechanism remains unclear.

Keywords: Myelofibrosis, reduction of tear-drop poikilocytes & leukoerythroblastosis

INTRODUCTION

Myelofibrosis is a clonal myeloproliferative disease characterised by proliferation of predominantly granulocytic and megakaryocytic series in the bone marrow, associated with marrow fibrosis and extramedullary hemopoiesis. Peripheral blood dacrocytosis and leukoerythroblastic features are characteristic findings of myelofibrosis especially at the fibrotic stage. The pathogenesis of tear-drop poikilocytes and leukoerythroblastosis have been attributed to a variety of mechanisms from marrow fibrosis, extramedullary dyserythropoiesis or to the physical difficulties of red cells in traversing the tiny sinus wall apertures in the spleen.

In 1977, DiBella et al had suggested that the spleen plays an important role in tear-drop poikilocytes formation after comparing the number of tear drop poikilocytes in patients with myelofibrosis before and after splenectomy. However, no subsequent studies were performed to look into the mechanisms involved in the formation of tear-drop poikilocytes and leuko-erythroblastosis. Manoharan et al (1998) described the effect of chemotherapy on the reduction of the extramedullary haemopoiesis and liver and spleen size as well as the reduction of tear-drop poikilocytes. Indirectly, this finding supported the theory that the spleen plays an important role in the formation of tear-drop poikilocytes. In this case report, we would like to highlight these peculiar findings that give insight to the possible mechanisms and the role of the spleen in the formation of tear-drop poikilocytosis and leukoerythroblastosis in myelofibrosis.

CASE REPORT

A 56 year-old lady was diagnosed to have primary myelofibrosis in 1999 in a private hospital. She was on regular follow-up with that hospital until the year 2002 when she was referred to Hospital UKM for the management of her increasing requirement of blood transfusion and massive splenomegaly.

On physical examination, she was found to be afebrile. Her vital signs were normal. Examination of the cardiovascular system showed that she was in congestive heart failure with hepatosplenomegaly (liver 10cm, spleen 18cm below the costal margins). Laboratory investigations showed the following results: haemoglobin 6.7g/dl, WBC 24.6x10^9/l, platelet 153x10^9/l. Liver and renal profiles were normal, serum lactate dehydrogenase was 2425 U/l, serum uric acid 648μmol/l. In view of the worsening of the disease, she was started on low dose Busulphan (1mg daily) and was on regular follow-up. In July 2002, she developed two episodes of acute cholecystitis. Investigations done showed that her hemoglobin was 6.4g/dl, white cell

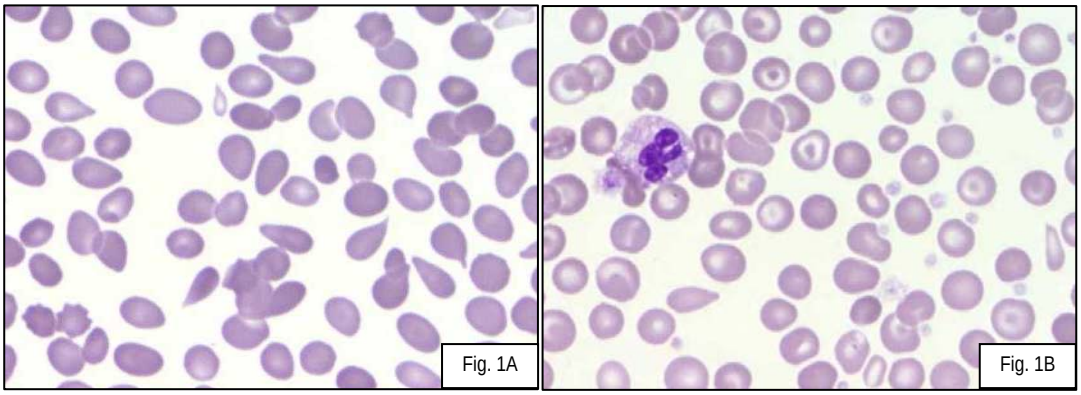

Figure 1(A)is the peripheral blood film of this patient before splenectomy showing numerous tear-drop poikilocytes as compared to 1(B) which is the peripheral blood film taken after splenectomy demonstrating marked reduction in tear-drop poikilocytes. (Wright stain, x 400)

count of $23.4x10^9$/l, platelet count $163x10^9$/l with leukoerythroblastic picture and tear-drop poikilocytosis (Fig 1A). Leukocyte alkaline phosphatase score (NAP) was 184/100 neutrophils. Ultrasound of the abdomen showed massive splenomegaly with multiple gall stones. In view of the frequent transfusion requirement and symptomatic massive splenomegaly, splenectomy and cholecystectomy was recommended. Following the operation in November 2002, she recovered without much complication. Review of her blood picture post splenectomy showed disappearence of the tear-drop poikilocytosis and post-splenectomy changes (Fig 1B). On the subsequent follow-ups, patient's peripheral blood films showed persistent reduction of the tear-drop poikilocytes with appearance of target cells, schistocytes, spherocytes and persistence of nucleated red cells.

DISCUSSION

Various mechanisms were postulated to be involved in the formation of tear-drop poikilocytes in myelofibrosis. One of it is the ineffective erythropoiesis in the bone marrow or extramedullary sites such as the liver and the spleen, and the other postulated mechanism is that these red cells become distorted or fragmented in their passage through the myelofibrotic marrow or the abnormal splenic channels. Leblond and Weed (1975) with their scanning electron micrograph observations in patients with myelofibrosis had concluded that the spleen plays a major role in the tear-drop poikilocytes formation. Following that, DiBella et al (1977) carried out a small study on the effect of splenectomy on tear-drop poikilocytosis in 13 patients with myelofibrosis; they found that the average number of tear-drop poikilocytes per 1,000 RBCs in the pre-splenectomy smears was 42 (range, 15 to 112), compared with 11 tear-drop poikilocytes in the post-splenectomy smears (range, 6 to 20)(P = less than .001). Based on this fourfold decrease in the number of tear-drop poikilocytes post-splenectomy, they had again concluded that the spleen plays an important role in the formation of tear-drop poikilocytes. The postulated mechanisms in which the spleen may play a role in the formation of these tear-drop poikilocytes are: (i) the

distortion of erythrocytes in their passage through the splenic sinusoids; (ii) the production of distorted erythrocytes by extramedullary sites in the spleen or a combination of both. Futher review of the literatures did not reveal any other reports on the study of mechanisms of how the spleen causes tear-drop poikilocytosis.

Manoharan et al (1988) studied the effect of chemotherapy on tear-drop poikilocytes and other peripheral blood findings in myelofibrosis; the observed improvement of haemoglobin levels and red cell morphology with decreasing spleen size and splenic fibrosis after a course of chemotherapy. This study further supports the notion that spleen plays an important role in the red cell changes in myelofibrosis. However, the pathogenesis of the formation of tear-drop poikilocytes remains unclear. It would be interesting to look into the exact mechanism of the formation of tear-drop poikilocytes as well as leukoerythroblastosis in myelofibrosis.

In this case, we have highlighted the interesting findings of reduction of tear-drop poikilocytes post-splenectomy and reinforced the important role of the spleen in the formation of tear-drop poikilocytes in myelofibrosis.

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