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CASE REPORT

Secondary Myelofibrosis in a Case of Aplastic Anaemia – A Case Report

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ABSTRACT

Myelofibrosis following aplastic anaemia is rare. Here, we report a case in which a 25-year old patient with aplastic anaemia subsequently developed secondary myelofibrosis.

Key Words: Aplastic Anaemia, myelofibrosis, transfusion

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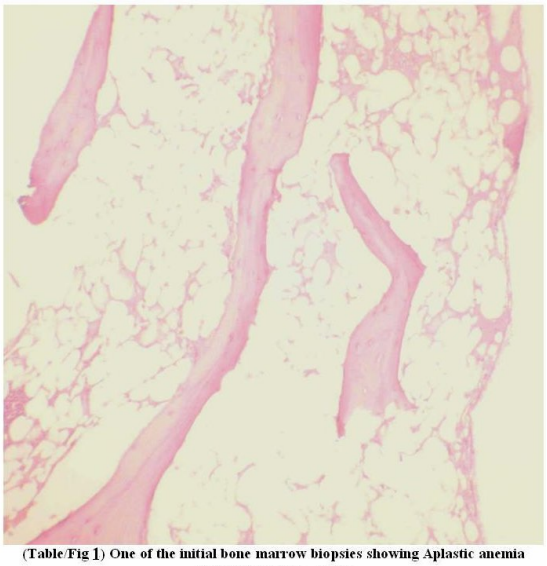
Pathological Findings

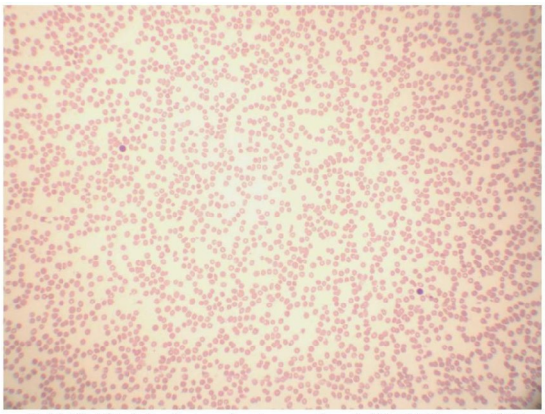
A 25-year-old male was admitted in our hospital in May 2008 with complaints of fever and pallor. He was a known case of severe aplastic anaemia [Table/Fig 1] on supportive blood product replacement therapy for the last 10 years and had previously received 3 courses of ATG and cyclosporine but was refractory. His HLA matched sibling donor was not available for bone marrow transplantation. He received more than 300 units of packed red blood cells over the duration of his illness. Deferasirox in a dose of 400 mg BD per day was given for iron chelation for the last 6 months, as his ferritin levels were 6500 ng/mL. On admission, his CBC was as follows- Haemoglobin of 10.0 g/dl, platelets: 17,000/µl and TLC: 3,200/µl (DLC – Neutrophils- 14%, lymphocytes- 82%, and myelocytes- 04%). His peripheral blood film showed pancytopaenia [Table/Fig 2]. His red blood cells were predominantly normocytic normochromic. His corrected reticulocyte count was 0.9 %. Leucopaenia and neutropaenia (absolute neutrophil count was 448/cmm) were seen with a mild left shift.His platelets were markedly reduced in number. His biochemical parameters were normal, including the liver function and renal function tests. A repeat serum ferritin was done and was 8730 ng/mL.The bone marrow aspiration smears were hypocellular with marked erythroid prominence and an M: E ratio of 1:7 . Erythropoiesis was mildly megaloblastic, with dyserythropoiesis. A marked paucity of myeloid cells and megakaryocytes was seen. Flowcytometric evaluation done to rule out Paroxysmal Nocturnal Haemoglobinuria did not show any deficient clone. His bone biopsy showed focal proliferation of fibroblasts with few patchy cellular areas showing mainly erythroid cells with paucity of myeloid cells and megakaryocytes [Table/Fig 3].Few haemosiderin-laden macrophages were seen.

One month later, on routine CBC follow up, one of the smears showed a leuco-erythroblastic picture. Shift to the left of the granulocytic cells with occasional blast cells was seen. Red cells showed presence of dacrocytes, with an occasional nucleated red cell in the periphery. A repeat bone marrow examination was done to rule out conversion to acute leukaemia. CBC findings were as follows- Haemoglobin-4.6 g/dl, TLC-1,600/µl (DLC – Neutrophils- 08%, lymphocytes- 83% and monocytes- 09%) and platelets-3000/cmm. Bone marrow aspiration and imprint smears were

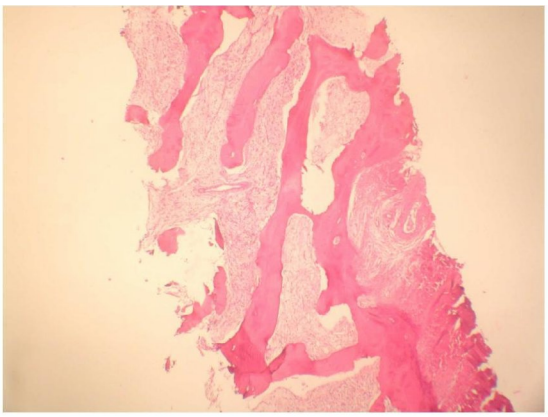
virtually acellular. The few cells that were seen were erythroid cells, lymphocytes and an occasional myelocyte. There was no apparent increase in blast cellsBone biopsy showed striking myelofibrosis with the laying down of the 3+-4+ reticulin. [Table/Fig 4], [Table/Fig 5] Enmeshed in this tissue, were several erythroid cells, plasma cells as well as many iron laden histiocytic cells, which stained positive for the Prussian blue stain. [Table/Fig 6, [Table/Fig 7] Massive iron overload was noted. Serum ferritin levels were done and were 8820 ng/L. However, no liver biopsy was done to quantify the iron content of the liver because of marked thrombocytopaenia. There was no enlargement of the spleen. Any foci of chronic infection, especially of tuberculosis or fungal infection were ruled out. Thus, the bone marrow aspirate and biopsy findings were reported as secondary myelofibrosis in a known case of aplastic anaemia, with associated iron overload.



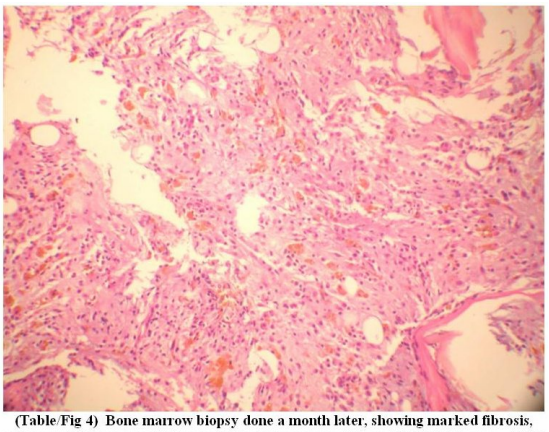
(Table/Fig 1) One of the initial bone marrow biopsies showing Aplastic anemia (Wright Giemsa – 10 X)



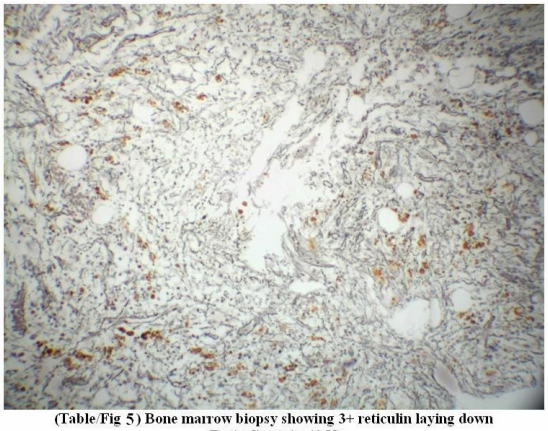
(Table/Fig 2)Peripheral smear showing pancytopenia (Wright Giemsa – 10 X)



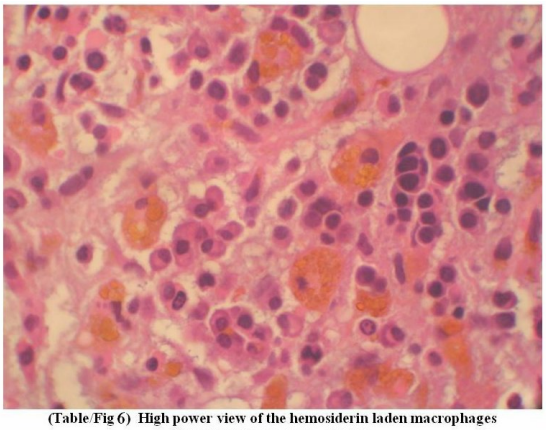
(Table/Fig 3)Bone marrow biopsy showing mild fibrosis and hypocellularity (Wright Giemsa – 10 X)



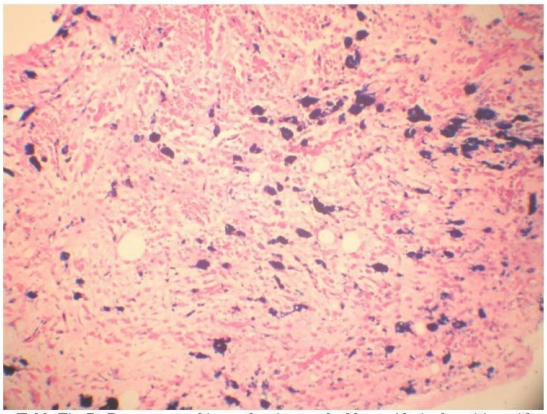
(Table/Fig 4) Bone marrow biopsy done a month later, showing marked fibrosis, patchy cellular areas with hemosiderin-laden macrophages. (Wright Giemsa – 40 X)



(Table/Fig 5) Bone marrow biopsy showing 3+ reticulin laying down (Reticulin stain 40 X)



(Table/Fig 6) High power view of the hemosiderin laden macrophages (Wright Giemsa stain – 100 X)



(Table/Fig 7) Bone marrow biopsy showing marked hemosiderin deposition with positivity for the Prussian blue reaction (Perl's stain – 40X)

Comment

Cases of aplastic anaemia subsequently converting to myelofibrosis, are rare. In 1989, Antonucci reported a case of benzene-induced myelofibrosis in a worker who had developed severe aplastic anaemia 20 years after using a paint remover containing benzene to strip paint from furniture. [1] Kaito et al described a patient with severe aplastic anaemia, who was treated with antilymphocyte globulin and within a year developed prominent splenomegaly and myelofibrosis [2]. Cases with aplastic anaemia terminating in acute myelogenous leukaemia associated with myelofibrosis, have also been previously described in literature. [3],[4].

In our case, the patient was suffering from and was being treated for aplastic anaemia for the past 10 years and subsequently developed myelofibrosis. However, no history of occupational exposure could be elicited in our patient. There was no laboratory evidence of an active focus of infection.The only additional feature that was seen, was an increase in haemosiderin deposits in two sequential bone biopsies, but no case reports resulting in marrow fibrosis due to iron overload from repeated blood product transfusions, have been reported.

Patients of aplastic anaemia are treated with blood products to maintain their haematological parameters and thus. do face a threat of iron overload on repeated transfusions. Iron overload from blood transfusion is seen in a wide variety of clinical conditions requiring repeated transfusions, such as thalassemic haemoglobinopathies, sickle cell disorders, and myelodysplasias. Mahachoklertwattana et al studied the effects of iron overload on the bone marrow in children and adolescents with ß-thalassemia disease on transfusions, and found that iron deposition in the bone impairs osteoid maturation and inhibits mineralization locally, resulting in focal osteomalacia [5].

Iron in transfusional overload is usually taken up primarily into parenchymal organs such as the hepatocytes, heart, anterior pituitary, and pancreatic B-cells rapidly and generation of free radicals is responsible for fibrosis of these organs [6]. Extensive literature search did not reveal any reports supporting the hypothesis that iron overload could have caused the bone marrow fibrosis in our case. The fact that the patient

developed secondary myelofibrosis in a long-standing case of aplastic anaemia is of interest, even though the cause for the transformation could not be ascertained.

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