

Bone marrow abnormalities in HIV infected children, report of three cases and review of the literature

Ira Shah, Anuradha Murthy¹

Pediatric HIV Clinic, and ¹Department of Pathology, B. J. Wadia Hospital for Children, Mumbai, Maharashtra, India

Bone marrow abnormalities in HIV infected adults include hypocellularity, myelodysplasia and poor marrow recovery. Data in children is limited. We report a series of three HIV infected with varied bone marrow abnormalities. First child was a 7-year-old boy with pulmonary tuberculosis, anemia, thrombocytopenia and bone marrow examination showed hypoplastic marrow. He succumbed to his disease within seven days of hospitalization. Second child was a three and a half year old girl who had severe anemia and her bone marrow examination showed dyserythropoiesis. Third child was a 7-year-old boy who had splenic abscesses and pancytopenia and bone marrow examination showed myelofibrosis with increased plasma cells. He also succumbed due to a fatal pulmonary bleed. Thus, advanced HIV disease in children can lead to bone marrow suppression in form of hypoplasia or myelofibrosis which can be fatal.

Key words: HIV, hypoplasia, myelofibrosis

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INTRODUCTION

Hematological abnormalities in HIV infected patients commonly are blood cytopenias. Anemia and neutropenia are generally caused by inadequate production due to suppression of bone marrow by HIV infection through abnormal cytokine expression and alteration of the bone marrow microenvironment. Thrombocytopenia is due to immune mediated destruction of platelets in addition to inadequate production.^[1] Other etiologies include drugs, secondary opportunistic infections, malignancies and nutritional deficiencies.^[1] We present a series of bone marrow abnormalities in HIV infected children who presented with anemia.

CASE REPORTS

Case 1

A 7-year-old boy presented with pain in limbs since two years, recurrent otorrhea since one year, cough since four months, breathlessness since eight days and edema of feet since two days. He was diagnosed as having pulmonary tuberculosis (TB) two months back and was on direct observed therapy (DOTS) for same. On examination, he was malnourished and had tachycardia, tachypnea with respiratory distress and hypotension.

He had severe pallor with anasarca and clubbing Grade III with generalized papular dermatitis with left ear purulent discharge and oral thrush. Systemic examination revealed cardiomegaly with gallop rhythm, hepatosplenomegaly and decreased air entry in left infrascapular region. HIV ELISA by two different kits was positive. Hemogram showed severe anemia (hemoglobin = 1.9 gm/dl) with thrombocytopenia (30,000.cumm), normal WBC count and ESR of 130 mm at end of one hour. X-ray chest showed left midzone and lower zone haziness and sputum for AFB on smear was positive. His serum biochemistry revealed hypoproteinemia, hypocalcemia, hypokalemia. Urine examination had 2+albuminuria and urine albumin/creatinine ratio was three. Ultrasound of abdomen showed hepatosplenomegaly with multiple abdominal lymph nodes. Bone marrow examination showed hypoplastic marrow with no megakaryocytes at all. There were no malignant cells. Echocardiography was normal. He was treated with IV antibiotics, antituberculous therapy, blood transfusion and dobutamine infusion; however he succumbed to his disease after seven days of admission.

Case 2

A three and a half year old girl presented with fever, cough and breathlessness since one year and skin

Address for correspondence: Dr. Ira Shah, 240 D. Walkeshwar Road, Malabar Hill, Mumbai 400 006, Maharashtra, India.

E-mail: irashah@pediatriconcall.com

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dermatitis since six months. Both parents were HIV infected and mother had died due to TB three months back. The child along with elder sister were diagnosed HIV infected recently by two different HIV ELISA kits. On examination, she was malnourished, had severe pallor with chalky white nails, chronic papular dermatitis and generalized lymphadenopathy. She had hepatosplenomegaly with cardiomegaly on systemic examination. Her investigations showed anemia (hemoglobin = 3.1 gm/dl) with normal WBC and platelet count. Reticulocyte count was 0.3% and ESR was 80 mm at end of one hour. Her direct Coombs test was negative. Urine showed 2+albuminuria. Bone marrow examination showed normocellular marrow with erythroid hyperplasia with mild dyserythropoiesis. She was treated with blood transfusion and advised regarding antiretroviral therapy which was refused due to non-affordability.

Case 3

A 7-year-old boy presented with injury to right elbow 25 days back while playing following which after 10 days, he developed pain in the right elbow with swelling and went to a doctor who diagnosed it to be a fracture and a plaster was applied. After two days, he had fever which subsided with Sulfamethoxazole/Pyrimethamine. At that time, his peripheral smear showed trophozoites and ring forms of plasmodium vivax. Subsequently increasing pallor was noticed was the past eight days. On examination, he was pale, had tachycardia with bilateral basal crepitations, cardiomegaly and hepatosplenomegaly with healed herpetic lesion over right groin. HIV ELISA positive and confirmed by western blot test. The child was treated with diuretics and blood transfusion. He developed severe abdominal tenderness with fever after two days. Ultrasound abdomen showed hepatosplenomegaly with splenic abscesses. CT abdomen also confirmed the same. He was treated with IV antibiotics but there was no improvement. He continued to have fever, abdominal pain and pancytopenia. His serial hemograms are depicted in Table 1. A bone marrow aspiration showed erythroid hyperplasia with increased plasma cells and biopsy showed myelofibrosis. No organisms were grown on bone marrow culture and it was negative for TEL/AML1 or MLL translocations or Monosomy 7. Hepatitis C and hepatitis B surface Antigen by ELISA were negative. He succumbed to a fatal pulmonary bleed and hematemesis.

Table 1: Hemogram of Case 3

| | Day 1 | Day 3 | Day 8 | Day 15 |
|-----------------------------|--------|--------|--------|--------|
| Hemoglobin (gm%) | 3.4 | 6.2 | 6.2 | 4.0 |
| WBC (cells/cumm) | 8,700 | 8,000 | 6,700 | 2,400 |
| Polymorphs (%) | 66 | 60 | 70 | 34 |
| Lymphocytes (%) | 27 | 34 | 27 | 62 |
| Platelet count (cells/cumm) | 50,000 | 55,000 | 49,000 | 14,000 |

DISCUSSION

The common bone marrow abnormalities in HIV infected adults reported are marrow hypocellularity, myelodysplasia and poor marrow recovery.^[2] Dysmegakaryocytopoiesis and dyserythropoiesis have been frequently reported.^[2] Similarly in our patients, dyserythropoiesis and dysmegakaryocytopoiesis were seen individually. Marrow hypoplasia is infrequent and is usually a terminal event of AIDS.^[3] Similarly, our first patient had AIDS and had a hypoplastic marrow on examination and his disease was fatal. However, the most characteristic and early bone marrow abnormality seen is in the megakaryocytes which may be responsible for early sclerosis of the bone marrow.^[4] However, such abnormalities were not seen in our patients. Plasma cells are also numerous and activated implying an immune response as was seen in patient 3.^[4]

Mechanisms leading to these changes include direct HIV effect on marrow progenitor cells, effect of drugs and other infective diseases along with alteration in IL-6 and G-CSF and malignancies.^[2] HIV infection affects hematopoietic processes possibly through abnormal expression of cellular genes and cytokines.^[5] The HIV-IC subtype which is commonly present in Indian population can directly infect CD34+ hematopoietic progenitors.^[6] This is supported by an African study which showed that HIV-infected children with severe anemia had 33% fewer CD34+ hematopoietic progenitors and 35% less erythroid progenitors in their bone marrow than uninfected children.^[7] They found that proportion of more mature erythroid precursor cells in bone marrow or peripheral blood (reticulocytes) did not differ between the two groups, suggesting that HIV-uninfected children had less efficient later stages of erythropoiesis than HIV-infected children suggestive that there is less dyserythropoiesis and apoptosis in HIV-infected children. Similarly in our case series, dyserythropoiesis was seen in only one patient whereas other forms of marrow suppression were seen in patients who died.

For treatment of these cytopenias, optimal treatment of HIV infection is essential. Treatment of opportunistic infections, stopping drugs leading to cytopenias are essential. Supportive care of anemia includes use of erythropoietin in addition to red blood cell transfusion. Therapy for neutropenia includes use of myeloid growth factors G-CSF and GM-CSF. Thrombocytopenia associated with bleeding due to decreased production will require platelet transfusions.^[1] ART in these patients may have a variable response as has been reported earlier.^[8] In our patients, those with advanced disease succumbed to their illness whereas the one with dyserythropoiesis did well on ART.

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