Case Report

Rare presentation of sickle cell anaemia with marrow necrosis precipitated by *Pandorea* sp., infection

Prabhu Kiran Vanka[1], Naval Chandra[1], Shantveer G. Uppin[2], Sohini Ganji[1], M. V. S. Subbalaxmi V[1]

Departments of [1]General Medicine, [2]Pathology, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India

Abstract

Bone marrow necrosis (BMN) is infrequently encountered in clinical practice and rarely reported in association with sickle cell disease (SCD). The occlusion of the bone marrow (BM) microcirculation with subsequent hypoxia and resulting cell injury has been thought to be the common underlying mechanism. Malignancy is the predominant cause in many studies. We present an unusual case of late-onset SCD whose initial presentation was BMN. The patient presented with fever with chills and bilateral thigh pain. Blood cultures grown *Pandorea* sp. Even after antibiotics according to sensitivity, fever continued. BM examination was done to send BM cultures. Cultures were sterile. Biopsy showed BMN which was an unexpected finding. As the patient was from tribal area, haemoglobinopathy was suspected and haemoglobin (Hb) electrophoresis was sent which suggested SCD. Thus, a high index of suspicion must be borne in mind, particularly in high SCD-prevalent areas, to identify and prevent this rare complication.

Keywords: Bone marrow necrosis, myelonecrosis, Pandorea infection, sickle cell anaemia

Address for correspondence: Dr Naval Chandra, Additional Professor, 4th Floor, Old Building, Department of General Medicine, Nizam's Institute of Medical Sciences, Punjagutta, Hyderabad - 500 082, Telangana, India.
E-mail: naval31@yahoo.co.in

INTRODUCTION

The aetiology of bone marrow necrosis (BMN) is diverse, and malignancy, especially haematopoietic in origin, is the most common underlying disease of BMN. Sickle cell disease (SCD) is an uncommon cause seen in <2% of cases.[1] SCD presenting for the first time with BMN at a later age is rare and hence we report the present case. The precipitating cause in this patient was *Pandorea* sp., bacteraemia. It was previously isolated from the respiratory tract of cystic fibrosis patients and is an uncommon, multidrug-resistant pathogen.[2] It was not previously isolated from a sickle cell patient, and it may be the first case report to our knowledge.

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CASE REPORT

An 18-year-old male patient presented with complaints of high-grade fever with chills and rigors for 10 days, non-bilious vomiting 1–2 episodes per day for 10 days and lower limb muscle pain for 5 days. There were no history of rashes and bleeding manifestations. There was also a complaint of slight yellowish discolouration of the eyes for 5 days. There were no similar complaints in the past. At the age of 4 years, he had fever and swelling of both hands, which were managed with oral medication. He was also transfused two units of packed red blood cell at that time. There was no history of blood transfusions in the family members.

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On examination, the patient was moderately built and nourished. Pallor and icterus were present. There were no clubbing, cyanosis, lymphadenopathy and pedal oedema. The patient was febrile and had tachycardia and tachypnoea, with a blood pressure of 110/70 mmHg. Cardiovascular, respiratory, neurological, musculoskeletal and per-abdomen examinations were normal.

On investigation, haemogram showed haemoglobin (Hb) of 6.7 g/dL and total leucocyte count of 23,500 cells with neutrophilic predominance. Peripheral smear showed normocytic normochromic red blood cells [Figure 1] and neutrophilic leucocytosis. Reticulocyte count was 0.5%. Erythrocyte sedimentation rate was 150 mm at the end of first hour. Liver functions tests revealed serum glutamic oxaloacetic transaminase of 56 IU/mL, serum glutamic-pyruvic transaminase of 67 IU/mL, alkaline phosphatase of 546 IU/mL, total bilirubin of 6.7 mg/dL and conjugated bilirubin of 2.6 mg/dL. Renal function tests and serum electrolytes were normal. Serum lactate dehydrogenase was elevated (1799 IU/L). We suspected malaria in view of fever with haemolysis. We started the patient on antimalarials and also antibiotics empirically after sending blood cultures. Two units of blood transfusions were given. Fever spikes did not decrease even after 48 h of therapy. Smear for malaria parasite and strip test for malaria were negative. Blood cultures showed growth of *Pandorea* bacteria in all the four culture bottles, which is a very rare and highly resistant pathogen, sensitive only to imipenem, trimethoprim-sulfamethoxazole and cefoperazone-sulbactum. The patient was started on imipenem. The patient's fever spikes reduced in severity but persisted even after 14 days of therapy. Repeat blood cultures were sterile. Serum procalcitonin levels were decreased. In view of persistent fevers, we did bone marrow (BM) examinations to exclude infiltrative disorders and also to do aspirate cultures. BM aspirate Gram's staining showed plenty of pus cells but no organisms. Acid-fast staining, aerobic cultures, fungal staining and Xpert MTB/RIF all were negative. BM aspirate cytology was normal. BM biopsy showed myelonecrosis [Figure 2]. As we could not get the aetiology, we reviewed the history; the patient revealed that he lives in a city but he was from a tribal area. In view of the tribal background, haemolysis, thigh pains and blood transfusion history during childhood, the patient was suspected to have any haemoglobinopathy and Hb electrophoresis was done. It was suggested of homozygous sickle cell anaemia. Hb electrophoresis also done for his brother and sister revealed that they both are sickle cell traits. The patient was treated with adequate hydration and haematinics. His fever spikes gradually subsided and hence discharged in a stable condition to follow up regularly.

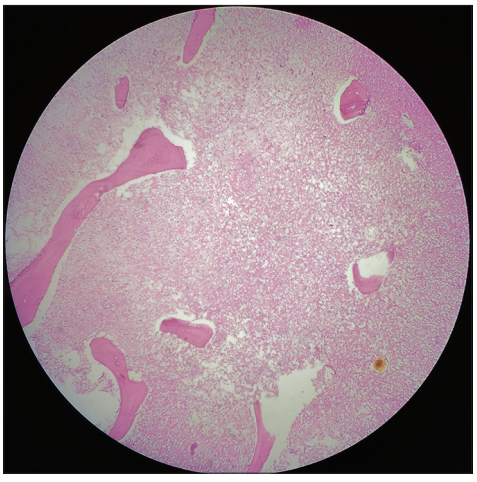

Figure 1: Bone marrow trephine biopsy specimen showing marrow necrosis (Hematoxylin and eosin, ×40)

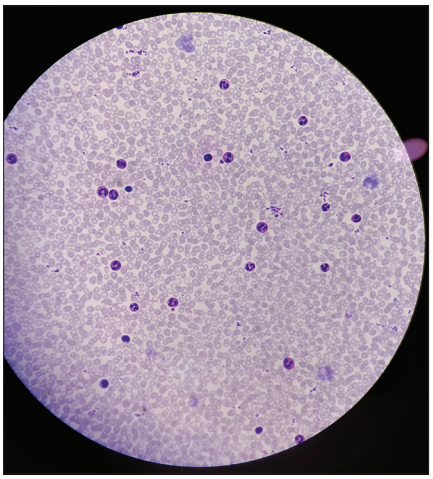

Figure 2: Peripheral blood smear (×100; oil immersion) showing normocytic normochromic red blood cells and neutrophilic leucocytosis. No sickle cells were seen (Giemsa, ×1000)

DISCUSSION

BMN is infrequently encountered in clinical practice. The incidence of BMN varies from 0.3 to 37% among different reports.[1] Such variability in the results could be attributed to the difference in the type of specimens examined (*in vivo* or postmortem), pathologist experience and diagnostic criteria used (the incidence was reduced to 0.3%–12% when only those biopsies with more than half BM involvement by necrosis were included).[1] BMN is defined as necrosis of hematopoietic tissue and stroma with preservation of cortical bone.[3,4] It has been identified with various clinical conditions including malignancy, infection, autoimmune disease, chemotherapy, Disseminated intravascular coagulation (DIC), anorexia nervosa, antiphospholipid syndrome and SCD.[1,3-8]

Although the first case of BMN was reported in an SCD patient, the association of BMN with SCD was reported in only 2% of the cases.[3] One possible cause of the paucity of this association is that BM examination is not commonly done during sickle cell crisis.[5] In a study[4] it was observed that one of the six patients with SCD has some degree of BMN during painful crisis; usually, these patients have full recovery.[4] It has been found that patients with genotype SS were at low risk for BMN and paradoxically, those with mild phenotypes were at higher risk of this catastrophic complication.[5]

In our case, the first clinical disease presentation of SCD was BMN with persistent fevers at the age of 18 years. He was not suspected to have SCD prior to this presentation. He had never complained of bone pains and Hb electrophoresis had never been previously performed. In addition, the initial disease presentation with the development of extensive BMN is rarely reported in literature.[6-8] Having a mild SCD phenotype, the limited family history and lack of neonatal or later screening for haemoglobinopathies all contributed to the late diagnosis of SCD and postponed interventions that could possibly prevent life-threatening complications of the disease such as BMN. We missed the diagnosis as the patient presented with infection and blood culture-grown *Pandorea*. However, as the fever did not decrease even with antibiotics, we did BM examination to send them for cultures. BM biopsy showed extensive BM necrosis, but the cause was not known. on reviewing patients history we found that he belongs to tribal community, in whom the incidence of hemoglobinopathies are comman and we, retrospectively diagnosed the patient to have sickle cell anaemia leading to BMN based on Hb electrophoresis. This highlights the importance of reviewing the history during the evaluation of cases. This case presentation emphasises the importance of SCD screening, especially in high-prevalent areas and need for follow-up of patients as catastrophic complications could occur irrespective of the disease phenotype.

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Conflicts of interest

There are no conflicts of interest.

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