Musculoskeletal Disorders in Sickle Cell Anaemia - Unusual Associations

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Abstract
Sickle cell anaemia coexisting with gout is a rare clinical association, as is gout and eosinophilia. This report records the second case of chronic tophaceous deposits in Sickle cell anaemia. The patient also had eosinophilia in association with gout. Skeletal fluorosis was an incidental finding in this patient. Treatment with packed cell transfusions, hydroxyurea and colchicine lead to the resolution of anaemia and symptoms of acute gout.

Introduction
Sickle cell anaemia (SCA) is an autosomal recessive disorder. The occurrence of gout with SCA is rare despite the high incidence of hyperuricaemia and impaired renal function.1 Despite extensive literature search, we came across only one published case of chronic tophaceous gout in association with haemoglobin SS disease.1-3 Gout in itself does not commonly present with eosinophilia except in Allopurinol hypersensitivity syndrome.4 The patient hails from an area endemic for fluorosis. Endemic fluorosis occurs due to the high fluoride content in drinking water and is also precipitated by renal dysfunction.5 It presented as compressive myelopathy in our patient.

Case Report
A 37 year old gentleman, a known case of SCA from Odisha presented with polyarthralgia and fever since three years and multiple nodular swellings on both hands and feet since 2 years. He also experienced tingling sensation in both legs since 18 months and progressive difficulty in walking since 10 months. Clinical assessment revealed poorly nourished, markedly pale, wheelchair bound patient. Multiple tophi were observed exuding chalky white material on all the fingers and toes (Figure 1). Tenderness, decreased range of movements, and deformities were observed in all the joints. Neurological examination revealed a sensory level, exaggerated lower limb reflexes and an ankle clonus, all suggesting a compressive myelopathy at T8 vertebral level.

At admission the haemoglobin was 5 g/dl, sickling test was positive with elevated levels of HbS, blood urea- 114 mg/dl, Creatinine -2 mg/dl and uric acid 12.4 mg/dl. Peripheral smear also confirmed SCA. FNAC from a firm swelling in the right thumb showed chalky material and numerous clusters of negatively birefringent needle shaped crystals surrounded by inflammatory cells. A radiograph of the chest revealed a chalky white appearance of bones, and a roentgenogram of forearm showed interosseous membrane calcification. MRI spine showed features of marrow sclerosis at the lower dorso-lumbar region; focal ligamentum flavum hypertrophy at D11 and D12, cord compression and signal changes suggestive of compressive myelopathy secondary to fluorosis.

SCA was managed conservatively with packed cell transfusions, folate supplements and hydroxyurea. The musculoskeletal manifestations were treated with colchicine, and subsequently, with Allopurinol.
Discussion

The increase in erythrocyte turnover associated with SCA is known to result in uric acid overproduction; hyperuricaemia occurs in patients who develop altered renal tubular function with diminished urate clearance. In contrast to hyperuricaemia gout is an uncommon complication of SCA. It is hypothesised that this infrequent association is due to circulatory impairment resulting from congestion and thrombosis of small vessels in the synovia. This prevents white blood cells from responding to chemotactic stimulus of the uric acid crystals. For gout to present acutely, the presence of polymorph nuclear cells is mandatory which may be impaired due to the vasculopathy and impaired generation of chemotactic factors. Also the activity of these cells is greatly reduced by the anaerobic conditions that are present in SCA. Another theory put forth is that aging and degenerative changes in joints play a role for urate crystallisation in joint fluids, only moderately supersaturated with urate. However patients suffering from SCA do not enjoy a lifespan long enough for this to occur. The rarity of this association may also result from a failure to recognise clinical gout, the symptoms of which may be blunted by chronic analgesic use or may closely resemble those of the acute sickle crisis.

Our patient not only presented with symptoms of acute gout confirmed by the presence of urate crystals in the joint fluid but also tophaceous deposits which is an extremely rare presentation and only one previous such case has been reported. During the course of investigation we came across two other interesting findings. Firstly, the patient had skeletal fluorosis as evidenced by the chalky white appearance of bones and interosseus membrane calcification seen on roentgenogram. At the time of presentation the patient had acute on chronic kidney disease. It is now established that diseased kidneys cannot handle fluoride excretion leading to fluoride toxicity and skeletal fluorosis even while consuming low levels of fluoride in drinking water. Since our patient was known to have SCA, the renal dysfunction was probably due to sickle cell nephropathy which predisposed the development of skeletal fluorosis as well as precipitated the gout. The aetiological cause of the compressive myelopathy was fluorosis of the spine. The second incidental finding was eosinophilia, another infrequent finding in gout. A clear correlation between the two has yet to be discovered especially in patients like ours, who have not received Allopurinol, as shown by prior studies.

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References