CASE REPORT

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Arthritis in Two Brothers: A Diagnostic Challenge

Rudrajit Paul, Biplab Gayen*, Prashant Kumar Mandal***, Bikas Ch Seth*, Sumit Sarkar***, Dipanjan Bandyopadhyay****, Sayantan Jana*****, Alamgir SK*******

Abstract

Arthritis or arthralgia may be caused by a variety of rheumatological and non-rheumatological disorders. Systemic disorders presenting only with joint symptoms may cause diagnostic confusion. We here present the case of a 24-year-old male from Eastern India who had prolonged history of joint pain and low back pain. He had visited numerous health facilities in the past and received varying treatment. He was finally diagnosed as sickle-beta disease with multiple bone infarcts. Genetic study revealed the classical HBB: c.20A>T mutation. The patient's brother was also found to have homozygous sickle cell disease, albeit with fewer symptoms. Musculoskeletal manifestations of sickle cell disease have been discussed at length.

Key words: Sickle cell disease; bone infarct; arthralgia; Eastern India.

Introduction

Joint pain or other symptoms related to the joints are common causes of hospital visit[1]. A recent study from India has shown that almost 10% of all primary healthcare visits are due to joint related symptoms and the trend rises with age[1]. Usually, when faced with rheumatological symptoms, clinicians tend to search for connective tissue disorders or similar diseases related to joints. But there are also a large group of other systemic disorders that may present with predominant arthritic symptoms.

Haematological disorders are responsible for a variety of joint-related symptoms[2]. In some of these cases like haemophilia or acute leukaemia, additional clinical features of the underlying disease help in accurate diagnosis. But there are some haematological disorders where, rarely, joint pain may be the most notable presenting feature for a long time. In such cases, diagnosis may be delayed considerably unless the index of suspicion is high and proper diagnostic procedures are planned. We here report such a rare presentation from Eastern India.

Case report

A 24-year-old male was admitted with recurrent low back pain and acute pain of right shoulder and knee. He had been suffering from arthritis of multiple small and large joints since 12 years of age. There was history of a few episodes of "acute arthritis" when he was admitted and treated with steroids and NSAIDs. The person had visited multiple hospitals all during India during the last 10 years. He had been variously diagnosed as juvenile idiopathic arthritis (JIA), rheumatoid arthritis and spondyloarthropathy. He had received DMARDs, steroids and NSAIDs in various combinations in the past. However, he never had a sustained remission of the symptoms.

The reason for the present admission was acute pain in the right shoulder and later, right knee. Both the joints were tender to touch. But there was no joint swelling or redness. The patient had restriction of movement of both joints. There was no morning stiffness. The pain was graded as 9/10 in a rating scale and there was partial response to ibuprofen. The patient did not have jaundice or fever. There was mild pallor. There was no visible deformity of any small or large joint. The patient also complained of a long-standing nagging low back pain which persisted throughout the day and was unrelated to activity or posture. There was no local vertebral tenderness or deformity. Spinal movement was normal in all directions. Sacro-iliac joints were not tender. The patient had no history of oral or genital ulcers, skin rash, photosensitivity, bowel disease or renal problems. He denied any addictions. There was no history of sexually transmitted diseases. He had never received blood transfusions. General systemic examination was normal except for mild non-tender splenomegaly. In family history, there was no consanguinity among parents. The patient had no history of contact with cattle or travel to areas endemic for Lyme disease.

The patient worked as an unskilled labourer but his occupation was jeopardised by the episodes of joint pain.

**Associate Professor, **Assistant Professor, ***Resident, ****RMO, Department of Medicine, *****RMO, Department of Medicine, Midnapore Medical College, Paschim Midinipur - 721 101, West Bengal.*

*******Professor and HOD, Department of Medicine, North Bengal Medical College, Paschim Midinipur - 721 101, West Bengal.*

Corresponding Author: Dr Rudrajit Paul, Associate Professor, Department of Medicine, Midnapore Medical College, Paschim Midinipur - 721 101, West Bengal. Phone: 9433824341, E-mail: r.paul.medicalcollege@gmail.com.

Initial laboratory reports revealed a haemoglobin of 8.7 gm/dl with normal leukocyte (6,100/µl) and platelet counts (2.4 l/µl). Differential count was normal. MCV was 68 fl and MCH was 19 pg. Renal and liver function tests were normal. ESR was 20 mm in the 1st hour and CRP was 4 mg/l. Serology for HIV, hepatitis B and C and dengue (for the current episode) were negative. Initial X-rays of shoulder and knee joints were normal. HLA B27 was negative; rheumatoid factor and anti-CCP were also negative. In view of the persistent pain in the joints, MRI scan of both shoulder and knee joint were done which revealed (Fig. 1) bone infarcts of various ages around the joints. An X -ray of the vertebrae was done which revealed (Fig. 2) cod-fish shaped vertebrae. Now, with the diagnosis of bone infarcts and a background of microcytic hypochromic anaemia, HPLC test of blood was done which showed (Fig. 3), sickle-beta disease (HbS: 70.3%; HbA2: 10.6%). Peripheral blood smear examination revealed (Fig. 4) sickle cells; when the blood sample was deprived of oxygen, there was universal sickling of the RBCs (Fig. 5). A genetic study was also done which revealed HBB: c.20A>T, which is the typical sickle cell disease mutation. Thus, in this patient, sickle cell crisis was responsible for the acute presentation with joint pain.

Family history of the patient revealed that his elder brother (29 years) also had history of arthralgia. The brother was summoned and examined. He did not have any splenomegaly. HPLC report showed HbS 71.8% and HbA2: 2.9%. Thus, he had classical sickle cell disease. None of the other family members had any similar symptom. The father had expired and the mother refused HPLC study.

The patient was explained about the diagnosis and its prognosis. He was advised on the measures to avoid a sickle cell crisis.

Discussion

Sickle cell disease (SCD) is a type of haemoglobinopathy

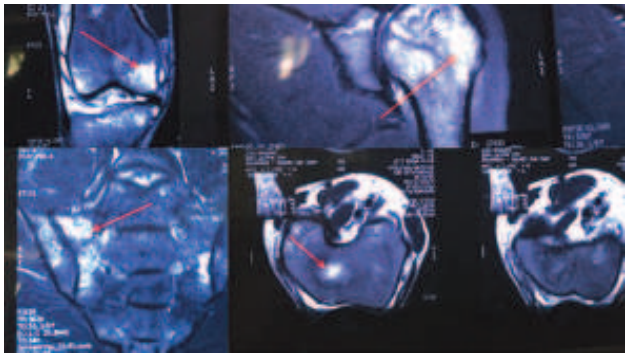


Fig. 1: *MRI scan of knee and shoulder joints of the patient showing areas of bone infarct and oedema (red arrows) in humerus head, femur, tibia and sacrum.*

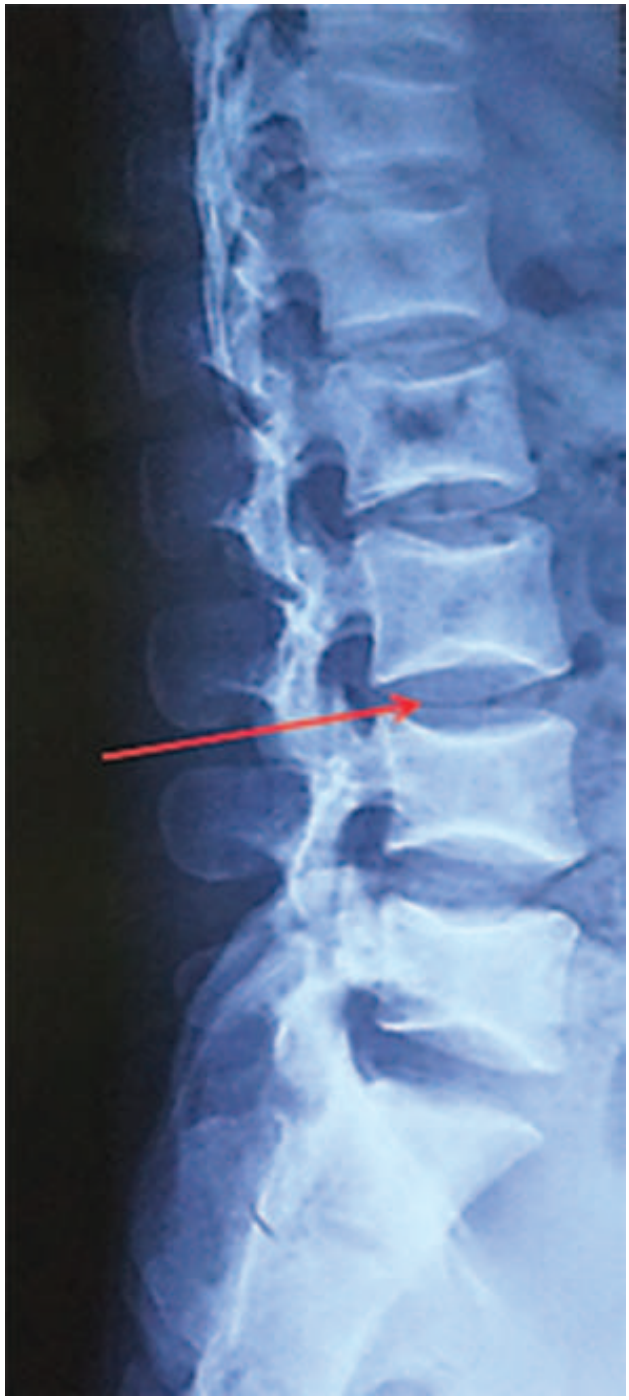


Fig. 2: *Vertebral X-ray of the patient (lateral view): red arrow showing the cod-fish vertebra.*

associated with vascular occlusion and consequent organ damage[3]. This is caused by an autosomal recessive point mutation in HBB (beta-globin) gene at codon 6 (new nomenclature: codon 7) which alters the biochemical properties of this protein, making it liable to polymerise and precipitate. There is upregulation of various adhesion molecules on the RBC membrane of SCD patients. This

causes endothelial activation and neutrophil recruitment[3]. Moreover, nitric oxide depletion due to haemolysis contributes to the final vascular occlusion and its deleterious consequences[3].

SCD may present with a variety of musculoskeletal pathology[2]. Dactylitis, avascular necrosis, vertebral collapse and non-inflammatory synovial effusions are some of the rheumatological manifestations[2]. Secondary osteoarthritis, diffuse osteopenia and osteomyelitis has also been reported[2]. All of these may cause considerable functional limitation and morbidity.

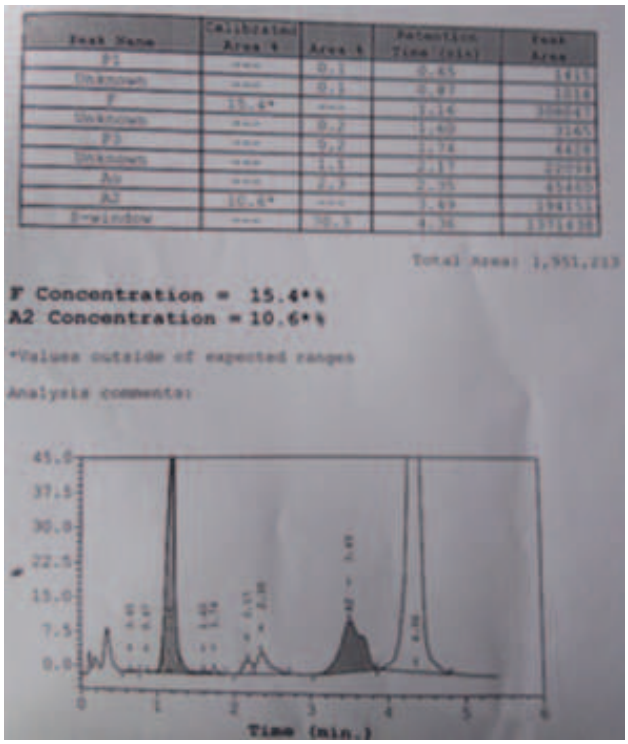
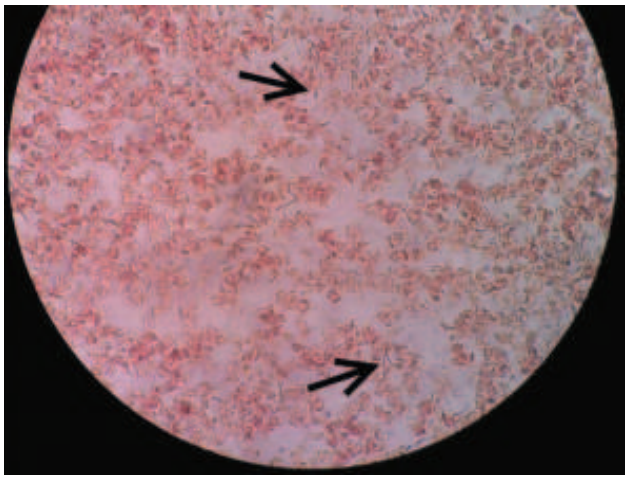


Fig. 3: *Haemoglobin electrophoresis report of the patient.*



Fig, 4: *(Picture courtesy: Dr Sayantan Jana): sickle cells in peripheral blood smear (arrows).*

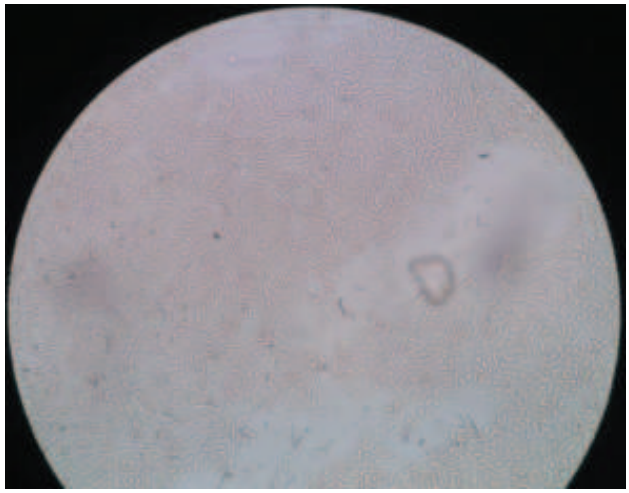


Fig. 5: *(Picture courtesy: Dr Sayantan Jana): universal sickling of the RBCs in deoxygenated sample: wet mount smear.*

Sickle cell disease is quite common in some parts of India. Carriage of the gene is presumed to be widespread in parts of Deccan plateau and Southern India[4]. In some specific communities, like tribal and ethnic minority populations, the prevalence is even higher, to the tune of 40%[5]. An epidemiological study among some of the rural communities in West Bengal depicted a prevalence of 0.56%[6].

Musculoskeletal symptoms and signs in known SCD patients are easier to manage. SCD patients presenting with arthritic features of the hip and back may have avascular necrosis and/or bone infarcts[7]. Acute bone pain in SCD may be due to bone infarct or acute osteomyelitis. MRI scan can help in differentiation of the two conditions[8]. Thus, early imaging for bone pain in SCD is necessary. But when the first presentation of SCD is with a joint symptom, the diagnosis is often delayed[9].

A case was reported from Qatar where a 10-year-old boy presented with recurrent back pain for one year before being admitted with severe pain, when he was diagnosed to have SCD[9]. In our patient, symptoms were present for 12 long years and he underwent a variety of treatments for presumed connective tissue disorders in this period. Such diagnostic delay is more likely if the patient only has arthritic symptoms as the sole manifestations of SCD.

Although a genetic disease, SCD may present with symptoms at any age[9,10]. A case was reported from India where a 23-year-old female presented with severe jaundice and intra-uterine fetal death as first manifestations of SCD[10]. The presenting features of SCD can be protean: anaemia, jaundice, hand-foot syndrome, acute chest syndrome or

splenic sequestration crisis are some of the commoner symptoms[10]. Since each of these individual symptoms have a wide differential diagnosis, the clinician is liable to be confused. However, missing the diagnosis of SCD can prove to be costly if the patient subsequently presents with stroke or splenic infarct.

Conclusion

We present this case to sensitize clinicians to this rare differential diagnosis of arthritis. Our patient did not receive a proper diagnosis for 12 years. Thus, haematological disorders should be included in the diagnostic algorithm of arthritis, especially in the young and when markers of inflammation are negative. Also, in certain population groups, where the prevalence of SCD mutations is known to be high, there should be a low threshold for testing for SCD by HPLC or genetic study. MRI imaging is a sensitive modality to pick up bone infarcts, which can point towards the underlying SCD. Hence, MRI imaging should be part of the initial work up in enigmatic cases of arthritis.

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