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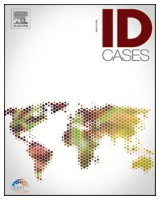

Case report

Case report of HIV associated arthritis

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ABSTRACT

Human immunodeficiency virus (HIV) infection is prevalent worldwide. Children living with HIV/AIDS form a vulnerable subsection and may frequently present with clinical symptoms in the first year of life itself. Besides its well-known signs and symptoms, HIV infection can have a wide spectrum of musculoskeletal manifestations. We report a case of a child with HIV infection with arthritis as a predominant presentation. The patient was anemic (Hb: 2.6 g/dl) and had features suggestive of inflammation, that is, highly elevated C-reactive protein (CRP) (161 mg/l), and erythrocyte sedimentation rate (ESR) (46 mm/h) values, accompanied with leukocytosis (12,100 cells/cu mm) and thrombocytoses (524,000 cells/ku mm). Urine culture showed Enterococcus spp. sensitive to linezolid and nitrofurantoin. A bone marrow aspiration and biopsy was done including culture for bacterial, mycobacterium and fungus. Treatment of arthritis in HIV-infected children can be challenging. It is crucial to recognize the arthritic manifestation of HIV infection in order to avoid delaying diagnosis and starting proper treatment.

Introduction

The HIV epidemic in India is the third worst in the world. HIV prevalence in India was predicted to be 0.3 % in 2016 [1]. Rare and recurring infections are typically seen in children who have been infected with the HIV. Arthritis is not a common presentation in children with HIV, contrary to reports from adult population. The most prevalent musculoskeletal symptom among individuals living with HIV infection is considered to be reactive arthritis. However, there have been reports of septic or HIV-related arthritis in children. It is crucial to recognize the arthritic manifestation of HIV infection in children in order to avoid delaying diagnosis and starting proper treatment.

Most of the arthritic manifestations of HIV disease are reactive, either due to HIV infection per se or secondary to opportunistic infections. Infectious arthritis is usually seen in children with significant immunosuppression, whereas inflammatory arthritis occurs early in the natural course of HIV disease. The first report of rheumatological manifestation of HIV infection was mentioned by Winchester R et al., from New York in their case series of 13 patients [2]. Autoimmune disease has been reported in the context of HIV infection since the origin of the HIV pandemic. Variable prevalence rates have been reported for musculoskeletal disorders in HIV-infected adults. However, data are scarce for the pediatric population. Human immunodeficiency virus (HIV) infection is prevalent worldwide. Children living with HIV/AIDS (CLHIV) form a vulnerable subsection, and may frequently present with clinical symptoms in the first year of life itself. Besides its well-known signs and symptoms, HIV infection can have a wide spectrum of musculoskeletal manifestations. Rheumatic manifestations can develop during any stage of the clinical course of HIV infection but usually in the later period. The commonly described rheumatic manifestations in HIV infection include arthralgia, HIV associated arthritis, painful articular syndrome, soft tissue rheumatism, reactive arthritis, undifferentiated spondyloarthropathy, septic arthritis, osteomyelitis, HIV related myalgia, polymyositis, Dermatomyositis, Diffuse Infiltrative Lymphocytic Syndrome (DILS), vasculitis like syndromes have also been described [3,4]. We report a case of a child with HIV infection with arthritis as a predominant presentation.

Case report

A 15-year-old boy presented with severe pain & swelling in the both lower limbs which hindered his ability to walk for 1 month. According to the patient, there was no history of trauma to the foot that could explain the onset of pain. The patient further complained of daily spiking fevers for 10 days and difficulty breathing for 1 day and no history of rash. He was taking over the counter medicines for above complaints. There was

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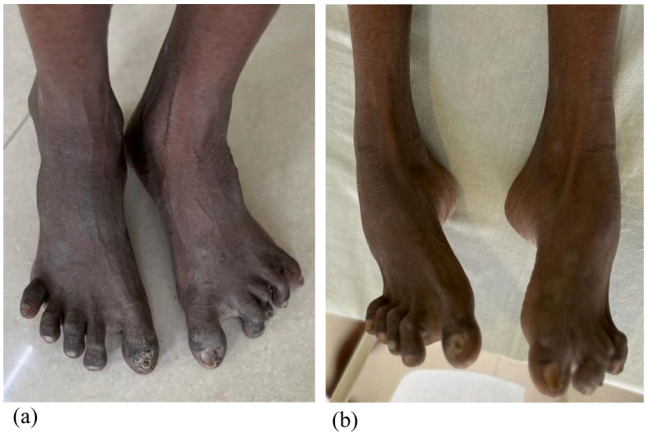
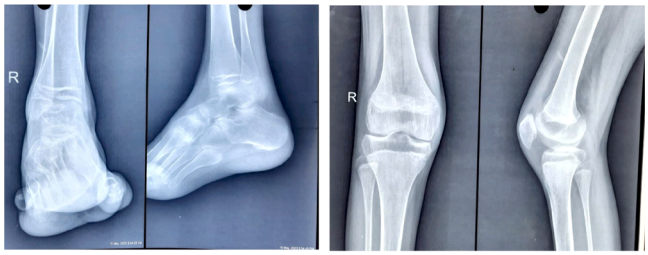
no family history of autoimmune diseases including JIA. Past history revealed cataract of left eye for which he was operated at 8 years of age and wearing spectacles for refractory error in other eye. The first episode occurred at the age of 12 years and recurrence of right and left ankle arthritis has since been reported relieved by NSAIDs administration. Review of the clinical history revealed that his father & mother had died at a young age of an unexplained illness. In view of family history, screening for HIV was carried out. The boy was found to be seropositive. Immunizations of the patient were all up to date (Figs. 1 and 2).

Physical examination revealed that he was underweight weighing 36 kg and was 166 cm in height. He had pallor and was febrile on admission (102 °F). On palpation bilateral cervical and inguinal lymphadenopathy with hepatosplenomegaly was noted. Local tenderness and swelling were detected in the left & right ankles with pes cavus deformity. other vital parameters were within range. Patient Bilateral knee joint tenderness was also detected. Initially, blood picture demonstrated that the patient was anemic (Hb: 2.6 g/dl) and had features suggestive of inflammation, that is, highly elevated C-reactive protein (CRP) (161 mg/l), and erythrocyte sedimentation rate (ESR) (46 mm/h) values, accompanied with leukocytosis (12,100 cells/cu mm) and thrombocytosis (524,000 cells/cu mm). General blood picture suggestive of macrocytic blood picture with retic count (3 %). Iron studies and serum vit B12 were normal. There was a decrease in serum ionic calcium levels (1.05 mmol/l) and serum vitamin D levels (10.6 ng/ml). Rheumatoid factor (RF), anti-nuclear antibodies (ANAs), ANTI-CCP and ASO titre was tested negative in the patient. Other parameters such as blood glucose, serum creatinine and blood urea, were found to be normal. Liver function tests apart from hypoalbuminemia (serum albumin: 2.9 g/dl), portrayed no abnormalities. Synovial fluid (ankle) was turbid yellowish colour and showed protein (5.6 gm %), total nucleated cells (1200 cells/cumm), mononuclear (55 %), polymorphs (45 %), macrophages (present) and negative for fungal, mycobacterial and malignant cells. Blood and synovial fluid cultures were sterile thereby excluding septic arthritis. Urine culture showed Enterococcus spp. sensitive to linezolid and nitrofurantoin. Ultrasound detected evidence of chronic cystitis and no other associated abnormalities. CECT abdomen suggestive of mesenteric and retroperitoneal lymphadenopathy with splenomegaly. Eye examination was normal. Bone marrow aspiration and biopsy was done including culture for bacterial, mycobacterium and fungus. It showed macrocytic picture without features of megaloblastic anemia, malignancy, granulomas or haemophagocytosis. Urinary histoplasma antigen and serum cryptococcal antigen was negative. Serum ferritin, LDH, fibrin degradation products (FDP) and triglyceride were within normal limit. After excluding all other possible diseases, a possibility of HIV associated arthritis or Juvenile Idiopathic Arthritis was made and the boy was started on anti-retroviral therapy (lamivudine, abacavir and lopinavir) with oral antibiotics. Naproxen was started and



(a) (b)

Fig. 1. (a) & (b) showing the foot deformity of both lower limbs.



(a) (b)

Fig. 2. (a) & (b):- Diffuse mild reduction in subtalar joint, intertarsal and tarsometatarssal joints noted with associated areas of periarticular sclerosis.

then oral prednisolone @ 1 mg/kg/day was added due to inadequate response and prednisolone tapered gradually in 3 weeks. Packed red blood transfusions were done. Naproxen was gradually withdrawn and methotrexate and folinic acid was added. Patient had improvement in his symptoms and continues to be on ART and was given physiotherapy for better mobility.

Discussion

A plethora of research efforts have been attempted to explore and address the diverse biopsychosocial challenges which shape the lives of children living with HIV/AIDS. However, musculoskeletal manifestations of HIV infection have not been prioritized and remain poorly defined. Rheumatological disorders in HIV-infected children appear to be relatively uncommon, and paediatric practice has been shaped by data generated in adult populations. While the number of children with advanced HIV/AIDS has declined substantively in the current era of universal ART, significant treatment gaps continue to affect children living with HIV. Arthritis can occur at any stage of HIV infected, although it has been described more commonly in advanced stages of HIV infection. Polyarthritis was the commonest presentation in the largest existing report of arthritis in HIV-infected children [5]. Existing literature has reported preferential involvement of the lower limbs, particularly knees and ankles, in both adults and children [5–7]. In their 2008 study, Yao et al. [8] reported that rheumatological manifestations were present in 9 % patients, with arthritis/arthralgia being the commonest (5.5 %), followed by septic arthritis (1 %), and osteomyelitis (0.9 %). Interestingly, our child presented with arthritis and was referred to our centre for rheumatological opinion and was being managed as JIA. He did not have any overt manifestation to suggest HIV infection. The unexplained death of a young parent prompted us to look for HIV infection. Thus, high index of suspicion should be entertained in children having arthritis with subtle clues to suggest HIV infection. Calabrese et al. [9] recommended that screening for HIV should be done routinely in rheumatology clinics for children presenting with arthritis. Although the pathogenesis of arthritis in HIV-infected individuals is not clear, the role of HIV in causation of arthritis has been implicated by some workers [10,11]. Treatment of arthritis in HIV patients can be challenging. Although some workers have shown an improvement in the arthritic symptoms with initiation of ART [12] others have found no difference in musculoskeletal symptoms before and after initiation of ART [5]. Arthritis in HIV patients has been treated with NSAIDs, systemic glucocorticoids, intra-articular corticosteroid injections (IACI) as well as disease-modifying anti-rheumatic drugs (DMARDS). HIV-associated arthritis is usually self-limiting and may occasionally require NSAIDs, IACI or oral, low-dose glucocorticoids. Methotrexate, which is a commonly used DMARD in children with inflammatory arthritis, was earlier reported to result in an increased incidence of opportunistic infections when used in patients with HIV infection however, recent studies do not support the same [13]. Based on limited experience therefore, it is suggested that methotrexate should not be initiated in patients with severe immune suppression and should be used

with caution and appropriate monitoring in patients with HIV infection [14]. Biological agents, including anti-tumor necrosis factor drugs are increasingly being used in rheumatology practice. However, their use has not been studied in patients with HIV infection. NSAIDs was initiated in the patient and he had no recurrence of joint symptoms after initiation of ART.

CRediT authorship contribution statement

Govind Pandey: Formal analysis, Investigation, Software, Supervision, Visualization, Writing – original draft, Writing – review & editing. **Tharuna Chandra:** Methodology, Project administration, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Kuldeep Singh:** Supervision.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Ethical approval

None.

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None.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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None.

Conflict of Interest Statement

None.

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