Case Report

Fungal Osteomyelitis with Avascular Necrosis of Femoral Head in a Known Sickle Cell Anaemia Patient

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ABSTRACT

Fungal infection at the same site of an avascular necrosis (AVN) in sickle cell anaemia (SCA) is a rarity even though the incidence of deep fungal infection in recent time has been steadily increasing in immune-compromised, chronically ill and debilitated persons. The prevalence of AVN in SCA is approximately 10% while the burden of sickle cell disease in sub-Saharan Africa is highest globally. We present a 17year old SCA female with an AVN of right femur head and a concurrent African histoplasmosis.

Key Words: SCA, Avascular necrosis, Fungal, Osteomyelitis, Histoplasma duboisii

INTRODUCTION

The incidence of deep fungal infection in recent time has been steadily increasing especially in immune-compromised, chronically ill and debilitated persons. Also, previous non-pathogenic species have now been implicated in disease manifestations. However, the clinical manifestation is rather non-specific and depends on host factors thus resulting in delayed or mis-diagnosis.[1,2]Avascular necrosis (AVN) of the femoral head is not an uncommon complication of sickle cell anaemia (SCA)and results from intravascular sickling of red blood cells in the micro - circulation of the bone causing intramedullary sludging, stasis, thrombosis, destruction of vessel walls, oedema and progressive ischemia[3]however, fungal infection in association is uncommon.

The co-existence of fungal infection at the same site of AVN is novel and determining which disease preceded the other may be difficult because both pathologies are associated with a prolonged clinical course. We report a 17year old known sickle cell anaemia patient with AVN who had hemi-arthroplasty and incidental microscopic findings of *Histoplasma duboisii s*pores within the marrow of the right femoral head.

CASE PRESENTATION

A 17year old female student presented at the Haematology Clinic of ABUTH Zaria in 2015 with a 4 months history of persistent and worsening right hip pain of 5 years duration aggravated by walking. There was no history of trauma prior to the onset of the pain. Pain was burning in nature and associated with limitation of activity. She is a known sickle cell anaemia patient who was diagnosed in early childhood (following an alkaline electrophoresis) and has been attending the above clinic regularly. She was been managed conservatively on routine nutritional supplements and antimalarial prophylaxis medication. She had presented to the clinic twice for vaso-occlusive episodes (bone pain) in the preceding 12 months necessitating hospital admission but never had blood transfusion. In the past, she hadalso been treated separately for chronic osteomyelitis surgically in another hospital. She is neither hypertensive nor asthmatic. After a clinical examination an assessment of avascular necrosis of the right femoral head was made and this was confirmed by radiographic investigation (Pelvic X ray). She was counselled for cord decompression and prepared for bipolar hemi-arthroplasty surgery.

Her packed cell volume was 28.9%, serumelectrolytes, urea & creatinine and liver function tests were within range. Viral serological tests (HIV, HBsAg and HCV) were negative by a rapid antibody screen. She had manual partial exchange blood transfusion of 3 units of Haemoglobin AA fresh packed cells prior to the surgery. Intra-operatively, there was necrosis of the femoral head with an intact acetabulum. The hip was dislocated, femoral head osteotomised, marrow reared and a size 45 head bipolar prosthesis inserted with the wound closed in layers over drain. The specimen sent to the histopathology laboratory was a right femoral head measuring 6x6x4cm in dimensions with a weight of 50g. The cut surfaces after decalcification were spongy and solid. Microscopy showed avascular bony trabecula delimiting marrow spaces containing haematopoietic cells, granulomata composed of numerous oval spores of Histoplasma duboisii, epithelioid cells and giant cells containing spores.(Fig 1&2) The diagnosis of fungal granulomatous inflammation with AVN was madeand shewas placed on ketoconazole 200mg orally once daily for 6 months duration. She did very well post-operatively and was discharged on one leg crutch. A six months follow up at the clinic has been uneventful.

DISCUSSION

Deep (systemic) fungal infection is associated with pathogenic dimorphic fungi such as Histoplasma sp, Blastomycesdermatitidis, Paracoccidioidesbrasiliensis, Candida sp, Aspergillus sp, Cryptococcus neoformans and Coccidioidesimmitis amongst others and occurs as either endemic respiratory or opportunistic systemic infection in affected host.[1] The clinical manifestation also depends on the host immunity and mode of entry of the implicated fungus, though often asymptomatic, presentation is that of a chronic granulomatous inflammation due to prolonged clinical course.[1, 2]

The homozygous SCD, sickle cell anaemia (SCA) is the most common autosomal recessively inherited genetic disease affecting approximately 2% of Nigerians at birth[4,5]andsystemic manifestation include impaired growth and increased susceptibility to infections due to reduced host immunity. Osteomyelitis is a common infection in SCA and may affect any bone in the body. The commonly implicated pathogens in its causation are Salmonella sp, Staphylococcus aureus, Hemophilus influenza and Escherichia coli.[3]while a fungal pathogen is a rare occurrence. Fungal bone infection may be attributable to Blastomycesdermatitidis and Histoplasma duboisii, the causative organism in African Histoplasmosis, an intracellular parasite infecting the reticulo-endothelial phagocytic cells of the bone marrow with resultant granulomatous tissue response.[6] African histoplasmosis runs a prolonged clinical course and commonly involve the skin with osteomyelitis and may presents as ulcer, papule, nodule, abscess or fistula. [2, 6, 7]Other sites of involvement are the lymph nodes and lungs. Samaila et al in their study of cutaneous mycotic infections reported a frequency distribution of 37% for African histoplasmosis with one case having bony involvement that necessitated a maxillectomy.[2]This patient's medical history included surgical treatment for osteomyelitis, while the undetected thus, untreated causative organism could have been histoplasmaduboisii. Definitive diagnosis is by the identification of the spores in tissue biopsy as in this case. Effective anti- fungal treatment is also achievable with it raconazole, ketoconazole (which was used in index case) or amphotericin B.[7]

The clinical considerations in SCA include chronic haemolytic anaemia, chronic organ damage, anaemic and vaso-occlusive episodes with resultant avascular necrosis (AVN) due to infarction from intravascular sickling of red cells into the micro-circulation of the bone as seen in this patient.[3] The overall prevalence of AVN is approximately 10% and patients with SCA, alpha-thalassemia and those with frequent painful crises are at highest riskhowever, treatment is not standardized.[3,8]

Most patients have bilateral hip involvement and adolescents such as this patient with total head

involvement require either conservative or surgical intervention such asfemoral or pelvic osteotomy, core decompression, hip arthrodesis, and total hip arthroplasty. The pathologic changes in the femoral head in SCA consists of a spectrum of osteochondritis dissecans, coxa vara, spontaneous fracture and AVN which can be all be confirmed with radiological examination such as bone scan and X-ray. Another advantage is the identification of bone infection by these radiological examinations[9] with resultant early detection and culture to isolate a definitive pathogen.

To the best of our knowledge, this unusual case of AVN in a background of fungal granulomatous infection secondary to African Histoplasmosis has not been reported in documented literature. The identification of the particular pathogenic fungal spore or hyphae is important in diagnosis.

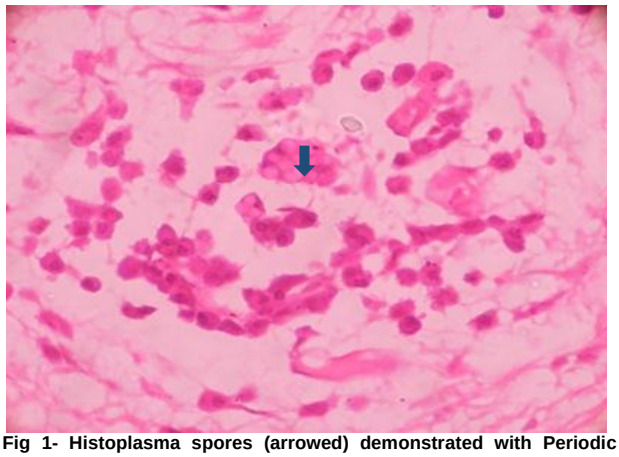

Fig 1- Histoplasma spores (arrowed) demonstrated with Periodic acid Schiff stain x400

Fig 2- Granuloma within marrow cavity delimited by bony trabeculae Giant cells (arrowed). H& E x100

Fig 2: Muitinucleated giant cells and fungal spores

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