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Radiological Evaluation of Osteonecrosis of the Femoral Head in Homozygous Sickle Cell Disease

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SUMMARY

Objective: Avascular necrosis (AVN) is an ischaemic injury of the femoral head. Femoral osteonecrosis (avascular necrosis) is one of the numerous complications of sickle cell disease. The aim of this study was to evaluate osteonecrosis in sickle cell disease (SCD) patients using plain radiographs.

Methods: A cross – sectional study was done among consenting homozygous sickle cell disease patients between the ages of 14-50 years. Plain radiographs' of bilateral hip bone in –anterior-posterior and lateral views of participants were taken. The radiographs were evaluated and reported. The descriptive data was analysed in percentages.

Results: The participants consisted of 84 subjects out of which 39 (46.4%) were males and 45 (53.6%) females. The mean ages obtained were 22.38±7.42 and 24.92±7.88 years for males' and females' respectively. A total of 9 (10.7%) had femoral head deformity, while 75 (89.28%) had normal femoral head. A total of 37 (44%) had hip pain at the time of study, while 49 (56%) had no hip pain.

Conclusion: Femoral osteonecrosis prevalence of 10.7% was obtained amongst sickle cell disease using plain radiograph.

INTRODUCTION

Haemoglobin S (HbS) is a mutant of Haemoglobin A in which valine substitutes for glutamic acid at the 6th position of the β-globin gene on chromosome 11. Haemoglobin S gene is common in the black race. HbS polymerizes and causes sickling of the erythrocyte under conditions of low oxygen tension or reduced blood flow. The sickled erythrocyte obstructs micro-vasculation impairing tissue oxygenation (ischemia), predisposing to necrosis and tissue death.

Avascular necrosis (AVN) is an ischaemic injury of femoral head. Femoral osteonecrosis (avascular necrosis) is one of the numerous complications of sickle cell disease. The need for joint replacement is delayed by early diagnosis and appropriate intervention of femoral osteonecrosis. However, most patients present late in the course of the disease. Without treatment, the process is almost always progressive, leading to joint destruction within 5 years.[1]

Diagnosis

Plain radiographs are a necessary first step in the diagnosis of osteonecrosis. In addition, MRI should be obtained if clinical suspicion of the diagnosis is high but radiographs are negative. In advanced stages of the disease involving a minimal subcohondral fracture, CT scanning is useful in accurately identifying the presence of a subchondral collapse where MRI is often insufficient. The zenith of the diagnostic algorithm of osteonecrosis is a good quality radiographic antero-posterior and frog leg laterals of the hip. However, MRI's sensitivity is up to 100% compared with plain radiographs or bone scanning.[2] Stages 0 and 1 are missed by plain radiographs. A delay of 1-5 years may occur between the onset of symptoms and the appearance of radiographic abnormalities. Normal radiographic findings do not necessarily mean that disease is not present. Magnetic resonance imaging (MRI) is the most sensitive and specific diagnostic tool of osteonecrosis. MRI is useful for very early lesion with a diagnostic

sensitivity and specificity of greater than 90% based on histology and eventual progression.[3]

Computed tomography (CT) also has a role in diagnosing osteonecrosis. It has 55% sensitivity in detecting osteonecrosis a value similar to what is obtainable for planar nuclear medicine imaging.[4,5] CT scans are also insensitive for detecting stage 0 and 1 AVN, but are excellent for detecting femoral head collapse, early degenerative joint disease (DJD), and the presence of loose bodies.

Single-photon emission computed tomography (SPECT)

SPECT images reflect vascular integrity. Early in the disease, SPECT scans may demonstrate an avascular focus; such findings are missed with MRI unless contrast is used. Collier found a sensitivity of 85% for SPECT.[6] With triple-head high-resolution SPECT, Lee *et al* reported a sensitivity of 97%.[7]

Staging of osteonecrosis

Ficat and Arlet,[8] and Steinberg *et al*(1995)[9] developed staging systems, the former based on radiological findings alone and more recently, the latter which incorporated MRI and scintigraphic findings. Stage 0 is pre-clinical and pre-radiologic, avascular necrosis is suggested only if it has already been diagnosed in the contralateral hip. Stage 1 is preradiologic it is defined by normal findings on radiographs and positive findings on MRI or bone scintigraphy. It represents the early resorptive stage. Late in this stage, plain radiographs may show minimal osteoporosis and/or blurring and poor definition of the bony trabeculae.

Stage 2 represents the reparative stage before flattening of the femoral head occurs. It may extend for several months or longer. Demineralization becomes evident. It may be generalized or patchy or appear in the form of small cysts within the femoral head. Patchy sclerosis appears after demineralization, usually in the superolateral aspect of the femoral head. Stage 3 is an early collapse of the femoral head. A linear subcortical lucency, representing a fracture line, is present immediately beneath the articular cortex. It may extend into the articular cartilage at the supero-lateral aspect of the femoral head. This is termed the crescent sign. Stage 4 progressive degenerative disease is represented by further flattening of the femoral head which occurs with loss of its smooth convex contour. Ultimately, the superior femoral fragment, representing the articular surface and the immediate subchondral bone, may become separated from the underlying femoral head or depressed and compacted into the femoral head. Severe collapse and destruction of the femoral head leads to progressive degenerative joint disease (DJD) with joint space narrowing, marginal osteophyte formation, and subchondral cyst formation.

Despite the reported limitations of the plain radiographs in diagnosing osteonecrosis, it is the most readily available, affordable and easy to use and interpret in developing countries. While the import of CT scans, MRI, and scitigraphic studies is appreciated, they are expensive and available in only few centres in Nigeria. Radiologic evaluation of osteonecrosis in homozygous sickle cell disease patients highlights the prevalence of osteonecrosis vis-à-vis the commonest stage of presentation. This will be most beneficial to physicians engaged in the management of sickle cell disease in Nigeria in order to nip the process in the bud from progressing to total joint destruction.

PATIENTS AND METHODS

This was a cross – sectional study using adults/ adolescent between the ages of 14-50 years homozygous sickle cell disease patients attending the sickle cell clinic of the Lagos State University Teaching Hospital, Ikeja from June 2013 to September 2013 recruited consecutively after obtaining the Institution's Ethics and Research Committee's approval.

Plain radiographs' of bilateral hip bone in anterior-posterior and lateral views of consenting participants were taken. Participants were asked to fill structured questionnaires containing demographic data and questions like previous history of trauma, hip pain, history of alcohol intake, HIV positivity, use of steroid and those who could neither read nor write, were assisted to obtain the data. Radiological characteristics were evaluated and reported by the 4 radiologist in the team (one of the authors). An inclusion criterion was patients with haemoglobin phenotype of SS in steady state attending adult sickle cell clinic of the hospital.

Exclusion criteria were patients with haemoglobin phenotype SC and other participants on steroids, HIV infected, and alcoholics.

Statistical assessment

The descriptive data were given in percentages and as mean ± standard deviation (SD). Chisquared test was used for the analytic assessment. The differences were considered to be statistically significant when the p value obtained is less than 0.05.

RESULTS

A total of 84 subjects were studied consisting of 39 (46.4%) males and 45 (53.6%) females. The overall mean age was 23.71±7.72 years, majority 83.3% (70) were single while 7 (8.3%) were married, 2 (2.4%) separated and 5 (6%) were non respondents. Majority of the study population 53 (63.1%) had no previous history of trauma while 29 (34.5%) had history of trauma. A total of 9 (10.7%) had femoral head deformity. Joint space was normal in more than half of the patients, 46 (54.8%), reduced in 26 (31%) and increased in 12 (14.28%). There was sclerosis of the hip joint in 22 (26.2%) while 54 (64.3%) had no sclerosis had normal lucency while 19 of 84 (22.61%) had reduced lucency. A total of 37 of 84 (44%) had hip pain at the time of study while 49 of 84 (56%) had no hip pain.

Only 9 of 84 (10.7%) had femoral head deformity, while 75 of 84 (89.28%) had normal femoral head. A total of 8 of 84 (9.5%) could not have a frog leg view while majority 68 (81%) had a frog leg view. The minimum age of males was 14 years and maximum 45 years, mean age was 22.38±7.42 years. (10.3%) of the males had femoral head deformity, while 32 of 39(89.74%) had normal head.

Only (28.2%) of males had sclerosis while 25 of 84 (64.1%) had no sclerosis. About 25 of 39 males (64.1%) had normal joint space, 10 of 39(25.6%) males had reduced joint space, while 1 of 39(2.6%) had increased joint space (Table

ii). Osteonecrosis prevalence of 10.3% 4 of 39 was obtained in males. Of the total study population of 84 subjects, 4 males (4.8%) had femoral head deformity, while 38% had normal head. Only 13% of males had sclerosis; 25 male (29.8%) had no sclerosis. 29.8% (25) of the male subjects had normal joint space, 11.9% had reduced joint space while only 1 male in the study population (1.2%) had increased joint space. The mean age of females was 24.92+7.88 years. Minimum age was 14years and maximum 46years. Only 6% of females in the total study population had femoral head deformity while 35 of them (41.7%) had normal femoral heads. About 13.1% (11 females) had sclerosis while 29 females (34.5%) had no sclerosis. 35 females (41.7%) had normal radiolucency while there was reduced radiolucency was seen in 10 of the females (11.9%). A total of 21 females of the total study population (25%) had reduced joint space and only 3 females (3.6%) had increased joint space.

The mean age of female was 24.92±7.88 years. Minimum was 14 and maximum 46 years. Only 5 of 45 (11.1%) had head deformity while 35 of 45 (88.8%) had normal head of femur. About 11 of 45 (24.4%) females had sclerosis while 29 of 45 (64.4%) had no sclerosis. Over 70% of the females 35 of 45 (77.85%) had normal luscency while luscency was reduced in 10 of 45 (22.2%) of females. A total of 21 of 45 females (46.7%) had reduced joint space while 3 of 45 (6.7%) had increased joint space (Table I). Majority 36 of 45 (80%) had normal 5 frog leg view, 9 of 45 (20%) could not have frog leg view. Osteonecrosis prevalence of 11.1% (5 of 45) was obtained for females.

This study could not establish a statistically significant relationship using pearson's Chi square between AVN and history of trauma/hip pain. Figures 1 and 2 show stages 3 and 4 of osteonecrosis reported in this study.

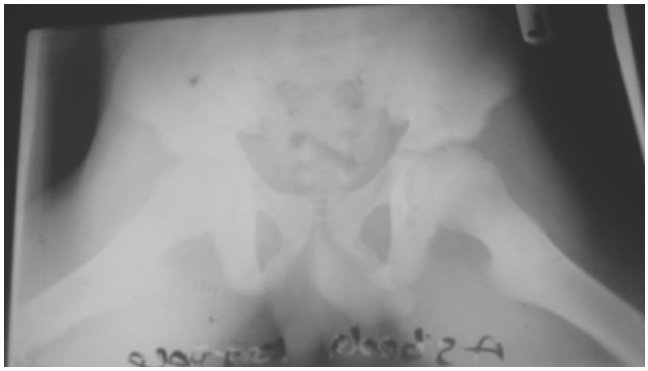

Figure 1: Stage 3 of osteonecrosis

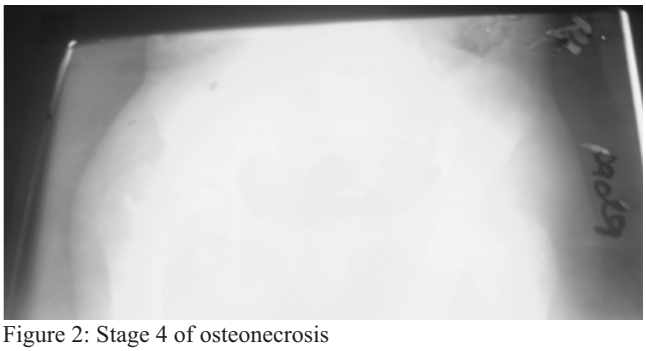

Figure 2: Stage 4 of osteonecrosis

DISCUSSION

Osteonecrosis could be traumatic or non-traumatic. Non-traumatic causes include steroid use,[10] alcoholism,[11] systemic lupus erythromatosus,[12] and exposure to radiation,[13] cytotoxic agents14 or sickle cell disease [15]. A substantial percentage (34.5%) of our study population apart from being sickle cell disease patients also gave previous history of trauma which could accelerate development of osteonecrosis. Osteonecrosis in SCD affects femoral heads most commonly followed by the head of humerous, knee and small joints of the hands and feet.[16] More than half of patients with femoral heads osteonecrosis have bilateral disease, and over 74% of those with affected shoulder, also developed osteonecrosis of the femoral head.[17]

A prevalence of 10.7% was obtained in this study, compared with 20.9% reported by Milner *et al*,[17] as against 15.9%,[15] prevalence found amongst Nigerians with haemoglobinopathy in 2007 , however prevalence obtained in our study was very similar to 10% reported by Paul *et al*.[18] Powers *et al*,[19] reported 20% prevalence amongst adult HbSS patients. All reports were based on plain x-ray of the hip. Plain x-ray findings were mottled attenuation of the epiphysis, sub-chondrial luscency, flattening and collapse of articular surfaces. Followed by narrowing of the joint spaces, articular sclerosis and osteophyte formation.[20]

Akinyoola *et al*,[21] found a mean age of presentation among Nigerians of 23.7±4.9 years. This is very similar to results obtained in this study for males' 22.38±7.42 years and females as 24.92±7.88 years. However, Powers *et al*[19] reported a median age of 31 years. More than half of the patients had normal joint space, 31% had reduced joint space expected in osteonecrosis and about 14.28% of the patients had increased joint space, the increased joint space reported could be as a result of fluid collection, a feature of osteomyelitis or septic arthritis. Of the 84 adult patients with HbSS referred to an orthopedic clinic in Yaoundé 18% had Osteomyelitis [22] while 7% had septic arthritis. The most common site of osteomyelitis is the femur, followed by tibia and humerous [23].

Despite low sensitivity of plain x-ray, Milner *et al* [17] studied 2590 adult HbSS patients and reported that 47% of the patients with hip disease were asymptomatic at the time the radiological diagnosis was made. A prevalence of 41% was obtained by Ware *et al* [24] amongst adult HbSS patients using MRI. Also, using MRI, a high prevalence of 27% was reported by Adekile *et al* [25] in children.

A higher prevalence is expected with a more sensitive MRI compared with plain x-ray, because as well reported, magnetic resonance imaging (MRI) is the most sensitive and specific diagnostic tool of osteonecrosis[2]. MRI is useful for very early lesion with a diagnostic sensitivity and specificity of greater than 90% based on histology and eventual progression.[2,26] Prevalence is dependent on method of diagnosis, the higher the sensitivity of the method, the higher the prevalence. Early disease is best diagnosed with MRI, because plain x-ray does not detect early disease.[27] Cost and availability informed the choice of plain x ray and the sample size used by the authors. The prevalence obtained would have been higher if MRI was used. The mechanisms responsible for the

pathogenesis of osteonecrosis in SCD are multifactorial.

A common denominator to the development of AVN of the femoral head is decreased blood flow to the femoral head leading to bone ischemia and death.[28] Mechanical blood vessel interruption, thrombotic intravascular occlusion, and extravascular compression are usual mechanisms causing osteonecrosis.[29] However, Akinyoola *et al* [21] attributed impaired plasma fibrinolytic activities as an important factor in the pathogenesis. Vascular occlusion can be caused by local thrombi, fat emboli, nitrogen bubbles, or abnormally shaped red blood
cells like in SCD.[30]

Symptomatic AVN has a very high probability of progression, almost half of our study population (44%) were symptomatic, i.e had hip pain. Hernigou *et al's*[31] reported that 75 of 92 symptomatic hips among 64 adult patients with HbSS had no radiographic collapse at presentation but 65 had progressed to collapse within 5 years with an average time of collapse of 42 months for stage 1 and 30 months for stage 2.

This study could not establish a statistically significant relationship using pearson's Chi square between AVN and history of trauma/hip pain.

CONCLUSION

AVN prevalence of 10.7% was obtained amongst SCD using plain radiograph while almost half of the patients were symptomatic. Efforts should be made to use MRI in diagnosing AVN in SCD in order to make early detection of the condition.

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Conflict of Interest

Research was self-funded, no conflict of interest declared.

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