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Research Article

Skeletal Manifestations of Sickle Cell Disease, Role of Plain Radiograph in Predicting the Diagnosis and Management

Ahmed M. Abdelhai[1], Mohammed Hassan Babiker[2], Hassan Elbahri[3], Dafaalla Salih Altyar[4] and Hozifa Mohammed Ali Abd-Elmaged[5]*

[1]*Assistant Professor, Faculty of Medicine, University of Khartoum, Khartoum, Sudan*

[2]*MD Orthopedics and Trauma SMSB, Khartoum, Sudan*

[3]*Associate Professor, Faculty of Medicine, International University of Africa, Sudan*

[4]*Medical Student at Al-Zaiem Al-Azhari University, Khartoum, Sudan*

[5]*Assistant Professor, Faculty of Medicine, University of Khartoum , Kartoum, Sudan*

***Corresponding Author:** Ahmed M. Abdelhai, Faculty of Medicine, University of Khartoum , Kartoum, Sudan.

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Abstract

Introduction: The misdiagnosis of skeletal manifestation of sickle cell anaemia, Mostly bone Infraction as an infection, depending on the same clinical presentation and the x-ray findings.

Methodology: This is a descriptive prospective multi-centric hospital-based study. conducted in Khartoum, the Capital of Sudan in several hospitals, the study included 50 patients with SCA with skeletal manifestation. Which presented to hospitals during the study period.

Result: Sensitivity, specificity, positive predictive value and negative predictive value of final diagnosis (as osteomyelitis) were 46.7%, 90.9%, 87.5% and 94.7% respectively. The sensitivity, specificity, positive predictive value and negative predictive value of final diagnosis (as bone infarction) were 72%, 53.3%, 94% and 88.9% respectively, which significantly indicates low reliability of using X-Ray in the diagnosis of skeletal manifestations among SCD patients ($P < 0.05$).

Comparing between initial and final diagnoses realized the tendency to change from infection to infarction after initiation of treatment, which is mostly due to a lack of proper workup.

Radio-leucency was the most common X-Ray finding among the studied patients, followed by osteoscelerosis, joint destruction osteopenia and bone collapse.

Finally patients diagnosed with bone infarction, underwent bone debridement in their course of treatment before the definitive diagnosis as infarction and 82% of them were given a long course of antibiotics

Conclusion: We Note the necessity of clinical assessment and x-ray imaging in SCD workup, further imaging and investigation have to be done before diagnosing the patient as osteomyelitis and proceeding with aggressive management. In addition to radioisotope imaging which provides useful information about acute osteomyelitis.

Keywords: Sickle Cell Anaemia (SCA); Red Blood Cell (RBC); Sickling

Introduction

Sickle cell anaemia (SCA) is a one of Extra-vascular hemolytic Anemia, also it defined as term for haemoglobinopathies with a clinical feature of red blood cell (RBC) "sickling" . and it is autosomal recessive mutation B among Sudanese people has a lot of work done about it (reference), to clarify this disorder, and to know how to deal with its complications [1-3].

Osteomyelitis and Septic Arthritis are infections of bone and joints which are serious complications of sickle cell disease and important causes of hospitalization. That is caused mainly by Hematogenous in origin Bacteremia due to various Salmonella species, staphylococcus aureus and some Gram-Negative Organisms. The high frequency of infection in patients with sickle cell disease is due to several factors: Hyposplenism, impaired phagocytosis and complement dysfunction [4].

Bone Infarction (Osteonecrosis) is one most complications of Sickle cell anaemia that lead to Reduced blood supply to Bones, due to several factors such as the sucking of Red Blood Cells in the Bone Marrow. Infraction occurs in the medullary cavity and the epiphysis and often is the source of the painful bone, it has been described in essentially every marrow-containing bone. which may result in stasis of blood and sequestration of cells, ischemia, tissue hypoxia, and cell death. Ware HE [5] reviewed the prevalence of avascular necrosis (AVN) in a series of patients with sickle cell disease, using radiography and magnetic resonance imaging. They found AVN of at least one hip in 11 of 27 patients (41%) [5-7].

Epiphyseal ischemic necrosis in sickle cell anaemia is common, frequently seen in the femoral and humeral heads, and more often bilateral than avascular necrosis in other diseases [8].

Here, in our study we looked for two of the most disastrous skeletal complications of SCD which are bone infarction and bone infection, which are nearly similar in their clinical presentations, course of the disease, blood investigations, and imaging, but different in the treatment strategies.

From our practice, we realized that there is too much misdiagnosis of the most common bone infarction as an infection, depending on the same clinical presentation and the x-ray findings, without a proper workup. Treating a bone infarction as osteomyelitis in SCD patients, either medically or surgically, is as (to add insult to injury) because it is either a long course of antibiotics or debriding the already weak bone or joint, maximizing the patient's complaints

In another hand, missing a bone infection and diagnosing it as an infarction is another catastrophic problem. A neglected bone infection will result in significant patient morbidity and mortality.

Therefore; skeletal problems have to be well addressed, properly investigated and managed.

Methodology

Patients and design of the study

We registered 50 sickle cell anaemia patients with skeletal manifestation, Which presented to Several Hospitals with orthopaedics and paediatrics departments, in Khartoum, the Capital of Sudan. The Study is based on a descriptive prospective multicentric hospital. Due to the fact, that the current study dealt with a small study population, the study sample was selected using the total coverage technique, by which all SVD patients who fulfilled the inclusion criteria of the study were selected.

Data collection method and tools

All patients were interviewed, detailed history was taken, and then a physical examination was conducted. Also, X rays of the patients were studied, and the results were compared. Thus All data were collected, checklists were filled, and all the patients were followed throughout management to find out the accuracy of the initial diagnosis or any change in the final diagnosis.

Study technique

After taking a full history and a thorough examination, the x rays were taken, studied and compared. The initial diagnosis was then recorded. The patients then followed and their treatment plans were recorded too. The final diagnosis was obtained and compared to the initial diagnosis.

Sensitivity, specificity, and positive and negative predictive values of the x-ray are then calculated.

Data analysis

Data is entered in a master sheet and then analyzed using the Statistical Packages for Social Sciences (SPSS) version (19.0). Mean, and standard deviation was used.

Ethical considerations

Ethical approval was taken from the Medical Specialization Board. Permission for the study was obtained from the administration of the specialized orthopaedic centres.

Patients' personal information was confidentially treated.

Result

A total of 50 patients in the study were enrolled: 28(56%) Males and 22(44%) Females. Most of them, 19(38%) their ages ranged between 11-18 years and 9(18%) were aged less than 5 years.

The affected part of the body in 41(82%) was bone, 25(50%) was joint, and 10(20%) were soft tissues. Out of the 25 patients, their affected part was joint, the most common site was hipped in 21(42%) of the patients; shoulders in 6 (12%) small joints of hand and wrist in 6(12%), ankle in 5(10%) elbows in 2(4%), knees 4(8%) and small joint of feet 6(12%) (Table 2).

Out of the 41 patients, their affected part was bone, the most common site was the femur in 15(30%) of the patients, a small bone in the hands in 15(30%) small bone in the feet in 14(28%), spinal vertebrae in 10(20%) and humorous in 4 patients (Table 2). Bilaterally the most affected side reported by 21(42%) of the studied patients, followed by the Left side16 (32%), right side 15(30%) while the spine is reported in 9(18%) of cases.

The most common complaint at presentation was the pain reported by 44(88%) of the studied patients followed by stiffness 15(30%), swelling 12(24%), fever 7(14%), disability 5(10%) and discharging sinus 3(6%), 6(12%) patients just came for routine follow up.

The apparent finding on the exam was the tenderness reported by 32(64%) of the studied patients, followed by stiffness 18(36%), swelling 15(30%), decreased range of motion of the affected limb 12(24%), redness 5(10%), hotness 5(10%) and growth retardation 3(6%). about duration, The highest duration of complication was years reported by 24(48%) and the lowest was days by 5(10%) of the patients. The ability to the independent performance of daily activities was reported by the majority of 43(86%) of the patients, and about 7(14%) had some disabilities. Family history of SCD was reported in 22(44%) of the patients at the first-degree level and in 19(38%) at the second-degree level while 9 (18) has no family history of SCD.

Radio-leucency was the most common X-Ray finding among the studied patients found in 38(76%) of the patients, followed by osteoscelerosis 27(54%), osteopenia 15(30%), joint destruction 13(26%) and bone collapse 17(34%).

Initial diagnosis of the studied patients came as follows: osteomyelitis 22(42%), followed by septic arthritis 8(16%), bone infarction 6(12%), dactlitis6(12%) and joint vascular necrosis 8(16%). But On final diagnosis osteomyelitis in 11(22%), septic arthritis 3(6%), bone infarction 17(34%), dactlitis8(16%) and joint vascular necrosis 14(28%). SO Sensitivity, specificity, positive predictive value and negative predictive value of final diagnosis (as osteomyelitis) were 46.7%, 90.9%, 87.5% and 94.7% respectively. The sensitivity, specificity, positive predictive value and negative predictive value of final diagnosis (as bone infarction) were 72%, 53.3%, 94% and 88.9% respectively, which significantly indicates low reliability of using X-Ray in the diagnosis of skeletal manifestations among SCD patients ($P < 0.05$).

The most common types of treatment received by the patients were analgesia 50(100%), antibiotics 33(66%) and rehydration 23(46%).

Discussion

The clear finding on the examination was the tenderness reported by 32(64%) of the studied patients, followed by stiffness 11(22%), swelling 15(30%), decreased range of movement 12(24%), redness 5(10%), hotness 5(10%) and growth retardation 3(6%) and at low grade, included impaired joint motion, local heat, and erythema. Fever. The clinical features of long bone infarction in patients with sickle cell disease have not been well defined, and differentiation of bone infarct from osteomyelitis has accordingly been difficult. The most commonly affected bones were the humerus, tibia and femur [10].

Radio-leucency was the most common X-Ray finding among the studied patient-followed by osteoscelerosis, joint destruction osteopenia and bone collapse. there are some unique x-ray features in avascular necrosis of the femoral head, that it involves the epiphysis rather than the whole head, as in septic arthritis, which

Joint	N	%
Shoulder	5	10
Elbow	2	4
Wrist	3	6
Small joints of the hand	6	12
Hips	21	42
Knee	4	8
The Ankle	5	10
Small joints of the feet	6	

Table 1: Distribution of the patients according to affected site in joint.

Bone	N	%
Humorous	4	8
Radius	3	6
Ulna	3	6
Small bone of the hands	12	14
Femur	15	30
Tibia	4	8
Fibula	6	12
Small bone of the feet	14	28
Spine	9	18

Table 2: Distribution of the patients according to affected site in bone (n = 44).

Final diagnosis	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Osteomyelitis	46%	90.9%	87.5%	94.7%
Bone infarction	72%	53.3%	94%	88.9%

Table 3: Positive and negative predictive values, specificity, sensitivity (final diagnosis).

is referred to as the pattern of femoral head blood supply (Pictures 1,2) Also vertebral spine avascular necrosis results in bone fragility and compression, and appears in x-ray as codfish deformity.

Based on the Data that mentioned initial and final Diagnosis, When we compare them we realized the tendency to change from infection to infarction after initiation of treatment (Picture 1), but still, it is higher than the international reported ratio between infection and infarction, that is mostly due to lack of proper workup.

The most common types of treatment received by the patients were analgesia 50(100%), antibiotics 33(70%) and rehydration 23(46%). 8 patients (47%) of the finally diagnosed patients with bone infarction, underwent bone debridement in their course of treatment before the definitive diagnosis as infarction and 82% of them were given a long course of antibiotics (Picture 2). In Skaggs., *et al*. [9] study, seventy cases of bone infarction were diagnosed based on decreased uptake on the bone-marrow scan and abnormal uptake on the bone scan at the site of pain. Antibiotic administration was discontinued in sixty-six of the seventy cases after

the imaging results were obtained, and the bone pain resolved. In a local study, Doka [11] studied 148 SCD patient, he identified 44 patients with skeletal manifestations, 47% of them were diagnosed with bone and joints infections (compare to 5 out of 46 in the first study) and that reveal our high tendency to diagnosis bony lesions as infection.

Sensitivity, specificity, positive predictive value and negative predictive value of final diagnosis (as osteomyelitis) were 46.7%, 90.9%, 87.5% and 94.7% respectively. Sensitivity, specificity, positive predictive value and negative predictive value of final diagnosis (as bone infarctions) were 72%, 53.3%, 94% and 88.9% respectively (Table 3), which significantly indicates low reliability of using X-Ray in the diagnosis of skeletal manifestations among SCD patients ($P < 0.05$). There is no reference standard for diagnosing sickle cell-related osteomyelitis, and even the culture of biopsy specimens is not completely reliable [9]. The lack of a reference standard makes a comparison of imaging modalities difficult. Factors such as availability, local expertise, and suitability for the patient affect the choice of imaging modality used. The interpretation of radiologic findings must be part of a careful ongoing multidisciplinary assessment. Also, Sid Ahmed [12] conducted a case-control study to differentiate between bone infection and vasoocclusive crises, he divided the patient into 42 case groups with bone osteomyelitis and 42 control group with vasoocclusive crises: he identified that all cases of infection except one were having x-ray findings where are all infarction group have not, which is very strange and reveals the tendency of the treating doctors to diagnose the infection based on the x-ray findings. Furthermore, they found that in about 85% of the infection group the blood culture was negative, and even 83% of them were negative for swab culture. Inflammatory markers between both groups were no significant differences.

Conclusion

From our study, depending on x rays and clinical presentation alone as a definitive tool for diagnosis and differentiation of skeletal lesions in SCD patients is not enough, because of the similarity of the clinical signs and symptoms, and they-may findings. It is one of the most common malpractice, Leading to a high percentage of wrong diagnoses and management, which may be disastrous to the patient.

Picture 1: Left hip avascular necrosis.

Picture 2: Left humorous bone infarction.

Radioisotope imaging provides useful information about acute osteomyelitis. MRI is less reliable but better thanx-rays and its usefulness have to be studied.

MRI, ultrasonography and joint aspiration are very useful to differentiate joint effusion due to aseptic arthritis from infection.

Good workup before deciding on aggressive management is the rule, decreasing patient morbidity and iatrogenic complications.

So we recommend that Meticulous clinical assessment and x rays imaging are very important in SCD workup, but further imaging and investigations have to be done before proceeding with aggressive management. In addition, Radioisotope imaging provides useful information about acute osteomyelitis and can be a part of the routine workup of the suspected cases, to decrease the iatrogenic morbidity of the wrong diagnosis.

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