Original Article

Haematogenous Osteoarticular Infections in Paediatric Sickle Cell Trait Patients: A Reality in a Tertiary Centre in West Africa

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Abstract

Background: Sickle cell trait (SCT) affects at least 5.2% of the world population, and it is considered asymptomatic by medical practitioners. There is a paucity of data regarding SCT paediatric patients and haematogenous osteoarticular infections (HOAIs). In our practice, some children with SCT presented HOAIs. This study aims to describe the pattern of HOAIs in children with SCT admitted in our unit. **Materials and Methods:** A single-centre retrospective study of medical records of SCT paediatric patients treated for HOAIs between January 2012 and June 2019 was performed. The data extracted were epidemiologic (gender, age at diagnosis, history of haemoglobinopathy and ethnic group), diagnostic (time to diagnosis, type of infection and fraction of haemoglobin S [HbS] at standard electrophoresis of Hb), germs and complications. **Results:** Among 149 patients with haemoglobinopathy treated for HOAIs, 52 have SCT. The prevalence of SCT patients was 34.9%. Thirty-nine ($n = 39$) records were retained for the study. The average age at diagnosis was 7.18 ± 4.59 years (7 months–15 years). The Malinké ethnic group was found in 22 (56.4%) cases. The mean HbS fraction was 37.2% ± 4.3% (30%–46%). Septic arthritis and osteoarthritis involved the hip in 11 cases, the shoulder in 4 and the knee in 2. Osteomyelitis was acute in 5 cases (11.1%) and chronic in 16 (35.5%). None of the patients has multifocal involvements. Bacterial identification was positive in 17 cases (37.8%). *Staphylococcus aureus* was involved in 9 cases (52.9%), and in one case, it was *Mycobacterium tuberculosis*. This patient has abscess of the psoas. No patient was infected by human immunodeficiency virus. The sequelae were joint destruction ($n = 2$), epiphysiodesis ($n = 5$) and retractile scars ($n = 2$). **Conclusion:** Relatively infrequent in our daily practice, SCT patients present with HOAIs. These infections had characteristics that are not very different from the series of the literature.

Keywords: Children, osteoarticular infection, sickle cell trait

Introduction

Sickle cell disease (SCD), a hereditary disease with recessive autosomal transmission, is the most common haemoglobinopathy encountered worldwide, and sub-Saharan Africa bears the greatest load. Sickle cell trait (SCT) is the heterozygous conditions (haemoglobin AS [HbAS]) with one copy of the normal haemoglobin gene (HbA) and one copy of the sickle cell gene (HbS).[1,2] SCT affects at least 5.2% of the world population.[3] Its incidence greatly varies among different races and ethnic groups[4,5] and from state to state: 13.3% in Uganda,[6] around 20% in Cameroun,[7] 0.49% in the southern suburb of Beirut and 1.1%–9.8% in Brazil.[5] Three types of manifestations are seen in SCD patients: chronic haemolytic anaemia, vaso-occlusive crises and haematogenous infections. These infections affect many organs such as bones and joints, which are major targets in children. Carriers of the SCT are said to be asymptomatic by medical practitioners.[8-10] Because of this benign condition, there is a paucity of data available regarding haematogenous osteoarticular infections (HOAIs) in SCT patients. Few published studies reported some cases of HOAIs in SCT paediatric patients among their study population.[11-13] In our practice, some SCT patients are encountered presenting HOAIs. This study, therefore, aims at describing the characteristics of HOAIs in children with SCT admitted at Yopougon Teaching Hospital.

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Received: 01-08-2020 **Revised:** 10-09-2020 **Accepted:** 22-11-2020 **Available Online:** 16-02-2021

Access this article online

Quick Response Code:

Website: www.afrjpaedsurg.org

DOI: 10.4103/ajps.AJPS_114_20

How to cite this article: Yaokreh JB, Thomas HA, Ekobo PC, Kouamé GS, Kouamé BD, Ouattara O. Haematogenous osteoarticular infections in paediatric sickle cell trait patients: A reality in a tertiary centre in West Africa. Afr J Paediatr Surg 2021;18:62-6.

Materials and Methods

A single-centre retrospective study of medical records of children with haemoglobinopathy treated for HOAIs between January 2012 and June 2019 was performed. Included were all records of children with SCT (HbAS with A > S >30%). Incomplete or missing records and those of other genotypes were excluded. HOAI diagnosis was based on clinical, laboratory tests, imaging and bacteriological data. Acute osteomyelitis was associated with bone pains, fever and absence of chronic suppuration, whereas chronic osteomyelitis was associated with chronic suppuration with or without sequestrum or pathologic fracture or fistulae. Association of fever, pains, swelling of the joints, hypomobility of the limb, with the presence of suppurative fluid in the joints cavity defined septic arthritis. Osteoarthritis was associated with fever, pain, swelling, loss of joint flexibility, suppurative fluid in the joint cavity and metaphyseal or epiphyseal bone lesions. The data extracted were epidemiologic (gender, age at diagnosis, history of haemoglobinopathy and ethnic group), diagnostic (time to diagnosis, type of HOAI and fraction of HbS at standard electrophoresis of Hb), germs and complications. Bacteriological research included blood culture, needle aspiration or biopsy, swab of entry portal and cytobacteriological examination of pus [Table 1]. Testing for germs was done by standard techniques. For technical reasons, anaerobic germs were not tested. The polymerase chain reaction (PCR) was performed by five patients. Human immunodeficiency virus (HIV) serology was performed in all cases of HOAIs. The antibiotherapy strategy consisted of administered intravenous Amoxiclav® (100–150 mg/kg/24 h) or Ceftriaxone® (100–150 mg/kg/24 h) with or without Gentamicin® (3–5 mg/kg/24 h during 5 days via intramuscular route). The concerned member was also immobilised. Upper-limb immobilisation was the Mayo Clinic splint for the shoulder and a splint or cast for the forearm. For hip involvement, axial skin traction was performed, followed by hip cast for 4–6 weeks. In the lower limb, a splint or cast was applied, and the cast was windowed for local care or monitoring. Data were processed using Excel 2010 (Microsoft Office® 2010), and quantitative variables were presented as mean ± standard deviation.

Table 1: Demographic and clinical data

Variables	Number of cases (%)
Gender	
Male	24 (61.5)
Female	15 (38.5)
Age groups (years)	
<2	7 (17.9)
2-5	13 (33.3)
5-10	11 (28.2)
10-15	8 (20.5)
Ethnic group	
Akan	6 (15.4)
Krou	7 (17.9)
Malinké	22 (56.4)
Others	4 (10.3)
Known haemoglobinopathy	
Yes	14 (35.9)
No	25 (64.1)
Consanguinity	
Yes	26 (66.7)
No	13 (33.3)
Average consultation time±SD (days)	18.2±16.55
Type of infection	
Osteomyelitis	21 (53.8)
Acute	5 (12.8)
Chronic	16 (41)
Septic arthritis	6 (15.4)
Osteoarthritis	11 (28.2)
Abscess of psoas	1 (2.6)
Haemoglobin S fraction	
30-40	31 (79.5)
40-50	8 (20.5)
Antibiotic protocol	
Co-amoxiclav	11 (28.2)
Ceftriaxone	12 (30.8)
Ceftriaxone + gentamicin	5 (12.9)
Co-amoxiclav + gentamicin	10 (25.6)
Antituberculous drug	1 (2.5)

SD: Standard deviation

Results

Among 149 patients with haemoglobinopathy treated for HOAIs, 52 have SCT. The prevalence of SCT among sickle cell patients was 34.9%. The prevalence among patients with HOAI was 10.3% (52/502). Records were retained for the study [Figure 1]. The average age at diagnosis was 7.18 ± 4.59 years (range: 7 months and 15 years) with a male-to-female ratio of 1.8:1. The Malinké ethnic group was found in 22 (56.4%) cases. The mean HbS fraction was 37.2% ± 4.3% (range: 30%–46%). Septic arthritis was predominant in the age group of 0–5 years (n = 9). The patient characteristics are listed in Table 1. Septic arthritis and osteoarthritis involved the hip in 11 cases, the shoulder in four

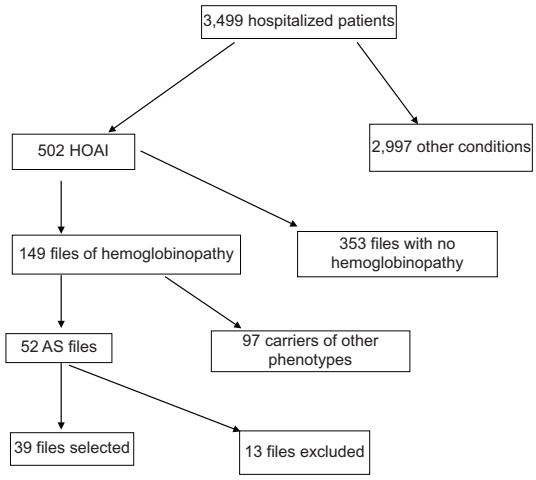

Figure 1: Flow charts of file selection

cases and the knee in two cases. Osteomyelitis was acute in 5 cases (11.1%) and chronic in 16 cases (35.5%) [Figure 2]. Osteomyelitis involved the femur (n = 7), tibia (n = 9), humerus (n = 4) and radius (n = 1). None of the patients has multifocal involvements. A pathogen was isolated in 17 cases (37.8%) [Table 2]. *Staphylococcus aureus* was involved in 9 cases (52.9%), and in one case, it was *Mycobacterium tuberculosis*. The patient with *M. tuberculosis* has developed the psoas abscess with vertebral osteolysis. He had a history of tuberculosis contagion and had a corset after surgical drainage [Figure 3]. No patient was infected by HIV. The treatment was surgical in 34 cases (75.5%). Among the patients with septic arthritis and osteoarthritis, 13 underwent surgical drainage, whereas the remaining 4 patients have needle aspiration. Chronic osteomyelitis cases were treated surgically either by sequestrectomy-drainage or by fistulectomy-drainage. The sequelae were joint destruction (n = 2), epiphysiodesis (n = 5), joint stiffness (n = 3), residual pain (n = 5), retractile scars (n = 2) and keloids (n = 3).

Discussion

The objective of this study was to describe the characteristics of HOAIs in SCT patients. This study has several limitations due to its retrospective nature. It was monocentric and the sample size was small. Identification of germs was limited. Anaerobic organisms have not been tested for technical reasons. Due to its high cost, the PCR, which has more diagnostic value than standard techniques, was only performed by five patients. Follow-up remains difficult because patients do not return for consultation once the infection has subsided.

HOAIs are one of the major causes of hospitalisation and morbidity among paediatric SCD patients.[4,5,7] However, there is a paucity of data of these HOAIs in SCT patients. The incidence of SCT varies from state to state.[4,5] It varies from 7% to 10% among African descendants in the USA[8,9,11,14-16] and 1%–40% in Africa.[11,17] There are no national data of SCT in Côte d'Ivoire.

The slave trade and migration of population were the common factors for SCT dissemination in America and Europe.[18] In our country, this trait remains disseminated, particularly in the Malinké ethnic group in which consanguineous marriages are cultural. These consanguineous marriages are favoured to eliminate social risk and to provide security to women and children by strengthening family ties and preserving wealth. Our findings are consistent with previous studies reporting that SCT varies among races and ethnic group.[4,5,19]

The lack of a national screening program and poor community awareness about SCT in our health system explains the fact that only a third of our patients had a known Hb status on admission. This was similar to the 29% reported by Nwadiaro *et al*. in Nigeria.[13] However, in the USA, despite neonatal screening, only 16% of Americans with SCT know their status in Ohio State.[2,20]

The early screening techniques such as isoelectric focusing or high-performance liquid chromatography are of very recent introduction in our hospital.

Traditionally, SCT has been viewed as a benign condition, a non-disease, partially protective against death from falciparum malaria[21,22] and without any of the painful episodes characteristic of the homozygous SCD.[23] However, most adverse events or complications have been reported: (1) fatal exertional heat illness with exercise; (2) sudden idiopathic death with exercise; (3) glaucoma or recurrent hyphema following the first episode of hyphema; (4) splenic infarction at high altitude, with exercise or with hypoxemia; (5) renal

Table 2: Causative microorganisms

Germs	Number of cases
Staphylococcus aureus	8
Staphylococcus meti-R	1
Salmonella spp.	4
Coagulase-negative *Staphylococcus*	1
Proteus mirabilis	1
Mycobacterium tuberculosis	1
Gram-negative	1
Total	17

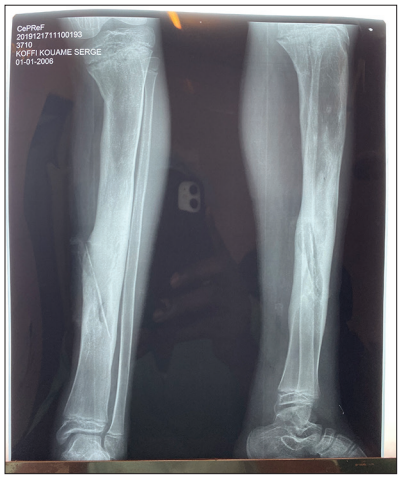

Figure 2: Chronic osteomyelitis of the tibia with sequestrum and proximal epiphysiodesis

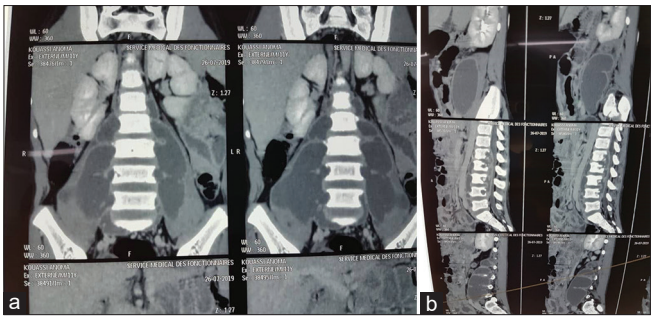

Figure 3: (a and b) A 13-year-old boy with spondylodiscitis (computed tomography scans show abscess of the psoas and vertebral osteolysis)

medullary carcinoma in young people; (6) isosthenuria with loss of maximal renal concentrating ability; (7) haematuria secondary to renal papillary necrosis; (8) bacteriuria in women; (9) bacteriuria or pyelonephritis associated with pregnancy and (10) early onset of end-stage renal disease from autosomal dominant polycystic kidney.[1,14,21,23,24] SCT might also increase the risk of venous thromboembolism.[25] Certain authors have reported that the risk of sudden death due to exercise stress was 30 times higher among black American soldiers with SCT.[1] Most are case reports and range from firemen dying during training exercises, a 6-year-old playing in the park, a teenager running forced participation in a juvenile justice boot camp and a 13-year-old running from the police.[1]

However, literature is poorer about data of HOAIs in SCT carriers. Few published studies reported some cases of HOAIs in SCT patients in their study population.[11-13] In Akakpo-Numado *et al*.[11] study in Togo, among 43 children who developed osteomyelitis, 11 (25.6%) had SCT. In the Tambo's series in Cameroon, of the 25 patients treated for septic arthritis, six (24%) had SCT.[12] Nwadiaro *et al*. have also reported musculoskeletal infections in SCT patients (8/24; 34%) in their study population.[13]

The clinical features and complications in SCT patients are not very different from those of common HOAIs in children. These HOAIs were characterised by a delayed diagnosis which remains common and multifactorial in sub-Saharan Africa: (a) first-intention trend to use prayer houses or traditional healers, (b) self-medication with street drugs, (c) diagnostic errors, (d) delayed referrals to definitive care centres and (e) lack of medical expertise outside tertiary centres. Because of late referrals, we resorted to surgery for fistulas and bone sequesters for all cases of chronic osteomyelitis. This management has a significant social and economic impact affecting families in our area where health insurance is lacking. Contrary to homozygous forms, none of our patients presented multifocal involvements.

The predominance of septic arthritis in the 0–5 years' age group confirmed the literature data, and the hip was more concerned.[26] On these toddlers, the metaphyseal vessel loop and epiphyseal vessel are connected via transphyseal vessels traversing across the growth plate. Therefore, spread of metaphyseal infection to the epiphysis and joints can occur via transphyseal vessels. This septic arthritis predominated where bone proximal metaphysis was intra-articular such as femur, humerus and radius.

Osteomyelitis predominated on the lower limbs and the most commonly involved sites are those with the fastest-growing metaphysis, where blood flow is rich but sluggish. Our findings are consistent with the literature data.[27]

In this series, the identification of germs was limited for practical and technical reasons. *S. aureus* was the predominant germ. SCD has classically been associated with *Salmonella* infections, but more series[26-28] noted a predominance of staphylococcal infections in both osteomyelitis and septic arthritis. This is believed to be due to its high adhesion capacity to bone through its surface receptors. The isolation of *Proteus mirabilis*, a commensal germ from the digestive tract and generally responsible for urinary and skin infections, could be explained by the presence of a skin portal of entry in this patient. The patient with *M. tuberculosis* had a history of tuberculosis contagion.

Early diagnosis and quick management is the best way to prevent extended bone destruction, joint damage and premature epiphysiodesis observed in this study. Early screening followed by family and patient education may provide additional value beyond the potential to inform or change reproduction behaviours, because these children are at risk of having a child with SCT or SCD.[2] Furthermore, we think that the possible occurrence of these adverse events above requires periodic monitoring such as annual ophthalmologist or nephrologist visit.

Conclusion

Relatively infrequent in our daily practice, SCT patients present with HOAIs. These HOAIs had characteristics that are not very different from the series in less developed countries in terms of late diagnosis and difficulties of germ research. First-line antibiotic must be directed against *S. aureus*. Further cross-sectional and prospective studies are necessary to well define the characteristics of these infections on SCT ground.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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