OSTEOMYELITIS AND PYOGENIC ARTHRITIS IN PATIENTS WITH SICKLE CELL DISEASE: BAHRAIN EXPERIENCE

I Mannan Khan*

Objectives: Identify the most common aetiologic agent of osteomyelitis and pyogenic arthritis in children with a sickle cell haemoglobinopathy.

Setting: Paediatrics Department, Salmaniya Medical Centre, State of Bahrain.

Subject and Design: Chart review of all patients under the age of 14 years discharged with a diagnosis of sickle cell disorder and osteomyelitis or pyogenic arthritis between January 1988 through December 1993.

Method: Diagnosis was based on a positive culture of blood, pus or tissue / joint aspirate in the presence of clinical, radiological and or operative findings suggestive of osteomyelitis or pyogenic arthritis.

Results: Seven children with a sickle cell disorder and eight episodes of osteomyelitis and or pyogenic arthritis were identified in a review of 6 years experience.
Salmonella species was isolated from the blood, pus or tissue / joint fluid aspirate culture on 7 of the 8 episodes.

Conclusion: Salmonella species is the most common cause of osteomyelitis and pyogenic arthritis in children with sickle cell haemoglobinopathy in Bahrain. Bahrain Med Bull 1996;18(3):

Salmonella species is now generally recognized as the commonest aetiologic agent of osteomyelitis in patients with sickle cell haemoglobinopathies1-7. In the Middle East, several large series from Saudi Arabia have confirmed the predominance of Salmonella as the aetiologic agent of osteomyelitis and septic arthritis in patients with sickle cell anaemia2,3,5,6. Hence it appears rather surprising that these observations were not cited in the recent editions of text books of paediatrics and internal medicines10-12. In these texts Staphylococcus aureus is believed to be the most common cause of osteomyelitis in patients with sickling disorders. In a recent paper from USA, Epps et al suggested that Salmonella may not be the most common

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This study was carried out at the Paediatrics Department, Salmaniya Medical Centre, Bahrain to review our experience of bone and joint infection in patients with sickle cell disorders.

METHODS

Records of all patients less than 14 years of age admitted to Salmaniya Medical Centre between January 1988 through December 1993 with a discharge diagnosis of
a sickle cell haemoglobinopathy and osteomyelitis or pyogenic arthritis were reviewed. Criteria for inclusion in the study: (1) A positive blood, pus or tissue / joint fluid culture. (2) Clinical features suggestive of osteomyelitis / arthritis. (3) Radiological and or operative findings suggestive of osteomyelitis and or arthritis. The diagnosis of a sickle cell haemoglobinopathy was confirmed by haemoglobin electrophoresis.

RESULTS

During the period of the study there were 76 patients with sickle cell haemoglobinopathy treated for osteomyelitis and or pyogenic arthritis. However, only 16 patients fulfilled the criteria of diagnosis of the study. Of these 16 patients 7 were under the age of 14 years (Table) and formed the core of this study. These 7 patients had 8 episodes of osteoarticular infections. Four of the patients had SS and 3 SF. Mean age at the first attack of osteoarticular infection was 6.8 years, the youngest being 2.5 years old. There were 4 females and 3 males.

Table. Clinical and laboratory findings of children with sickle cell haemoglobinopathy and osteomyelitis/ pyogenic arthritis

<table>
<thead>
<tr>
<th>Case No</th>
<th>Sex/age</th>
<th>Organism</th>
<th>Blood</th>
<th>WBC (cmm)</th>
<th>ESR (mm/h)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M/8</td>
<td>Sal.gr.E</td>
<td>28000</td>
<td>117</td>
<td>68</td>
<td>Swollen, tender left knee and left hand. Knee aspiration negative. Osteo. left lower femoral metaphysis</td>
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<tr>
<td>2</td>
<td>F/6</td>
<td>Sal.ent</td>
<td>18600</td>
<td>112</td>
<td>72</td>
<td>Abscess over upper and lower Rt. tibial metaphysis. I&amp;D-pus. Osteotomy left radius-pus. Right knee jt. swollen and tender after 9 months. I&amp;D-pus, sterile. Arthritis of left knee jt. 2 years later. Joint aspiration - pus</td>
</tr>
<tr>
<td>3</td>
<td>F/5.5</td>
<td>Sal. typhimur</td>
<td>19000</td>
<td>125</td>
<td>75</td>
<td>Clinical picture of severe sepsis and DIC. Many bones and joints affected.</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>Citrobac.4000</td>
<td>45</td>
<td>Abscess over upper and lower Rt.</td>
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<tr>
<td>5</td>
<td>F</td>
<td>Sal.gr.C</td>
<td>60</td>
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<tr>
<td>4</td>
<td>F/13</td>
<td>Sal.gr.C 0</td>
<td>tibial metaphysis. Chronic osteo. Discharging sinus</td>
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<td>5</td>
<td>M/2.5</td>
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<td>73</td>
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<tr>
<td>Sal.gr.C</td>
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<td>9800</td>
<td>36</td>
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<tr>
<td>6</td>
<td>M/10</td>
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<td>70</td>
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<td>0</td>
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<tr>
<td>Sal.ent Sal.ent</td>
<td>12400</td>
<td>22</td>
<td>Pain and swelling over lumbar spine. Destructive changes in lumbar 4 vertebral body.</td>
</tr>
<tr>
<td>7</td>
<td>F/10</td>
<td></td>
<td>85</td>
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Sal.ent - Salmonella enteritidis, Sal.E - Salmonella group E  
Sal.C - Salmonella group C.

Clinical manifestations: At the time of admission to the hospital all the patients were febrile with body temperatures ranging from 38.0°C to 39.20°C (mean 38.50°C). Local pain and tenderness over bones and joints had been present in all the patients for a period ranging from 1 day to 3 weeks. Localized swelling was noted during 4 of 8 episodes, and pain with limitation of joint movements was present in 3 patients (2 of whom had arthritis). Multiple site involvement was observed during 5 episodes. One patient (No 3) presented with pain in the arm and abdomen. She vomited altered blood and on admission she developed severe sepsis with disseminated intravascular coagulopathy. Initial x-rays of bones were normal but within days many bones and joints were affected, needing aspiration of joints and decompression of bony abscesses. The constitutional symptoms and signs in most of the patients were mild at presentation and were initially thought to be due to vaso-occlusive crisis. Culture of pus from tibial abscess in patient No. 4 grew Citrobacter at the time of first admission to the hospital. She developed chronic osteomyelitis within a discharging sinus and Salmonella group C was cultured on 3 occasions during the following 3 years. She eventually recovered after decortication. The course of patient No. 6 was also interesting. She initially presented with fever and body ache. Blood culture grew Salmonella enteritidis. She apparently recovered after 2 weeks course of antibiotic. However, she was readmitted within 3 months with low grade fever and backache with soft tissue swelling over the lumbar spine. Spinal films revealed destruction of the body of lumbar 4 vertebra. Culture of the tissue fluid from the mass grew Salmonella enteritidis.

A Salmonella species was isolated from the blood and/or pus, joint fluid or tissue aspirate on 7 occasions during 8 episodes. Citrobacter was grown from the pus in one case (No. 4), during the first episode followed by isolation of salmonella C from pus on 3 occasions, during subsequent flare ups.

Polymorphonuclear leucocytosis was noted during 5 episodes. WBC count ranged between 4000/cmm to 28000/cmm with a mean of 14488/cmm. ESR was raised in all, ranging between 22 mm/hr to 117 mm/hr, with a mean of 71 mm/hr. Bandemia was observed in 3 patients. Absolute band cell count ranged between 1240 to 1900.
Management and Outcome: Prenatal ampicillin was administered on 6 occasions for a mean duration of 5 weeks (range 3 weeks to 8 weeks). During the initial 10 days to 2 weeks of treatment one or more antibiotics (Cefuroxime, Ceftriaxone, Cloxacillin, Fucidin) were also given in addition to ampicillin. Surgical drainage of the abscess was needed in 5 cases and joint aspiration was done in 3 cases. Two patients had more than one attack of bone/joint infection in the 2 years following the first attack. One patient developed chronic osteomyelitis which lasted several years. She eventually recovered after decortication.

DISCUSSION

Although Salmonella has been identified as the most common cause of osteomyelitis in patients with sickle cell anaemia, its exact frequency varies in different geographical areas where sickle cell anaemia is prevalent. In this series Salmonella was found to be the aetiologic agent of osteomyelitis and pyogenic arthritis in all of the seven patients. Salmonella septic arthritis is reportedly rare in patients with sickle cell disease. Syrogionopoulos et al identified Strep. pneumoniae in 5 out of 6 cases of septic arthritis in patients with sickle cell anaemia. Bennet and Namnyaak found Salmonella in 2 and Staph. aureus in 2 in their series of 4 cases of septic arthritis. Although there were only 2 patients with septic arthritis in our series (one with multiple bone and joint involvement) Salmonella was isolated in both cases. The absence of other organisms (Staph. aureus, Strep. pneumonia) in this series is noteworthy. Our experience is more in agreement with that of Al-Salam et al from the Eastern Province of Saudi Arabia.

The susceptibility of patients with sickle cell haemoglobinopathy to serious bacterial infection has been well known. These patients are also unusually susceptible to infection with Salmonella organisms. The peculiar susceptibility of these patients to infection with Salmonella organisms was first brought to notice by Hodges and Holt in the USA and Lambotte-Legrand in Belgium Congo in 1951. Various hypotheses have been proposed for the unusual susceptibility of the patients to infection with Salmonella. These include the following:

- Poor sanitation exposes infants and young children to frequent gastrointestinal infection with salmonella.

- Blood stream invasion by salmonella is facilitated by devitalisation of areas of bowel wall due to intravascular sickling in the intestinal blood vessels. Areas of infarcted bone are then infected by these blood borne organisms.

- Expanded marrow in sicklers with its increased oxygen demand and metabolic activity and sluggish circulation is vulnerable to infarction. Devitalised infarcted areas are prone to infection with salmonella which characteristically tend to linger in bone marrow after other sites have become sterile.

- Normally macrophages of the reticuloendothelial system eliminate salmonella from the body. In patients with sickle cell haemoglobinopathy macrophages are loaded with the breakdown products of the rbcs reducing their capacity to ingest and kill salmonella.

- Hepatic dysfunction and chronic haemolysis provide favourable conditions for salmonella to flourish.
Although statistically bone infarctions are much more common than osteomyelitis, in patients presenting with fever and tender warm, swelling over long bones, differentiation from osteomyelitis can be extremely difficult, as these findings are present in both conditions. As reported by others, the presence of mild constitutional symptoms in many cases of osteomyelitis in sicklers, make the problem of differentiation of osteomyelitis from bone infarction all the more difficult. About half the patients in our series had low grade fever and mild constitutional symptoms.

In this series of patients, polymorphonuclear leucocytosis was observed in all the 5 patients who had a positive blood culture. ESR was raised in all the patients. However, these findings have been described in patients with aseptic bone infarctions as well. Plain x-ray of the affected bone is of no help at the beginning of the illness in distinguishing osteomyelitis from bone infarction. Radionuclide imaging is being increasingly used in the separation of bone infarction from osteomyelitis. Tc99-Sulfur colloid bone marrow imaging and combination of bone scan and bone marrow scans have been used with good results. Recently combination of bone scintigraphy with either Gallium or labeled white cell imaging has been reported to give best results.

CONCLUSION

In this first ever investigation of the aetiology of Salmonella species is the most common organism responsible for osteomyelitis and pyogenic arthritis in children with sickling disorders in Bahrain. It is suggested that an antibiotic specifically effective against salmonella must be included in any treatment protocol for suspected osteoarticular infections in children with sickle cell haemoglobinopathies.

REFERENCES


