Acute multifocal haematogenous osteomyelitis in children

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Abstract

Purpose Haematogenous multifocal osteomyelitis in children represents a dangerous form of osteomyelitis in which sepsis can develop quickly if it is not treated early. A retrospective analysis of 26 children with acute multifocal haematogenous osteomyelitis over a period of 5 years was undertaken in order to assess the clinical presentation, infective organism, laboratory investigations and risk factors involved.

Methods Children more than 1 year of age with two or more bones involvement presenting within one week from the onset of symptoms were included in this study. All of the children were evaluated by clinical examination, blood tests and local ultrasound.

Results The average age at presentation was 4.9 years and girls were affected more than boys, with a female to male ratio of 1.4. Lower limbs were affected in 92% of cases, and, specifically, the tibia in 73.1% of the patients. Blood culture was positive in 38.5% of our cases. The predominant microorganism isolated from surgical samples was *Staphylococcus aureus*, among which methicillin-resistant *S. aureus* (MRSA) was found in 50% of the patients. Surgical drainage of the pus was done in 24 cases, followed by appropriate antibiotics, and two cases were treated by conservative means. All of the children were successfully treated except for four, who developed chronic osteomyelitis and sequelae.

Conclusion We conclude that acute multifocal haematogenous osteomyelitis in children needs early diagnosis by a high index of clinical suspicion and adequate treatment

with timely intervention. The predominance of MRSA in our study shows the changing trend in its association with multiple bone involvement.

Keywords Multifocal osteomyelitis · MRSA · Anaemia · Surgical intervention

Introduction

Acute haematogenous osteomyelitis is most common in children and has the potential to cause life-long musculoskeletal deformities [1]. Haematogenous multifocal osteomyelitis in children represents a dangerous form of osteomyelitis in which sepsis can develop quickly if it is not treated early. In this fortunately rare form of the condition, acute infectious foci occur in several bones simultaneously as a result of haematogenous spread [2]. This pyogenic osteomyelitis begins in the metaphysis within a few days, with fever, local pain and signs of general sepsis. Chronic recurrent multifocal osteomyelitis (CRMO) should be distinguished from acute haematogenous multifocal osteomyelitis, which can occur acutely at several sites and trigger dramatic symptoms [2].

Through the use of appropriate diagnostic measures and intervention, this illness is treatable, with good functional results. In our retrospective study, we tried to assess the clinical presentation, infective organism, laboratory investigations and risk factors involved in this part of the world.

Materials and methods

In this retrospective study, we analysed 26 patients with acute multifocal haematogenous osteomyelitis. The data of

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patients presented to our department from January 2005 to June 2010 were collected. The patients more than 1 year of age up to 12 years of age were included in this study. Patients with the following diagnostic criteria were included in our study: (a) localised swelling, tenderness, redness or reduced mobility, (b) pus aspirated from bone, (c) growth of bacteria from blood or bone specimen. Patients presenting with more than 1 week of the onset of symptoms septic arthritis and recurrent infections were excluded from our study.

At emergency admission, clinical examination was done in all of the children, followed by blood tests, such as haemoglobin, white blood cell (WBC) count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and blood culture. The affected limb was immobilised in a splint. Ultrasonography of the affected sites was performed in order to diagnose subperiosteal abscess, further specifying the volume and precise location and differential diagnosis with respect to soft-tissue abscess.

Needle aspiration from the abscess and bones was done in all of the patients under sedation. The sample was sent for culture and sensitivity testing. The initial course of intravenous antibiotics were started empirically with ceftriaxone and gentamicin. Surgical intervention by means of incision, drainage and drilling into the medullary cavity of the affected bones was undertaken. Later, antibiotics were changed appropriately according to culture and sensitivity testing. Intravenous antibiotics were continued for 2 weeks, followed by oral antibiotics for another 4 weeks, with serial monitoring of the ESR and CRP.

Results

The clinical course of 26 children ranging from the age of 1 to 12 years was analysed. The average age at presentation was 4.9 years. Girls were affected more than boys, with a female to male ratio of 1.4. Lower limbs were found to be affected in 92% of the patients and, specifically, the tibia in 73.1% and the femur in 61.5% of the patients, respectively. The common sites involved were the proximal tibia (50%) and proximal humerus (46.2%), followed by the proximal femur (38.5%). In the upper limb, the humerus was involved in 65.4% of the patients. Scapula, ulna and phalanx were involved in one patient each (Table 1).

The average duration of symptoms at the time of presentation was 4.5 days (range 2–7 days). All of the patients presented with a history of fever, along with pain and swelling of the affected region. Involvements of the different bones were not simultaneous but were gradual over a period of 1–3 days. Distant foci of infection were not found in our patients.

The average haemoglobin level was 7.8 g% (5.9–11) showing anaemia in all of the patients. The average WBC count was 14,750/cmm and was found to be high in 88.5% of the patients. The ESR was found to be elevated in all of the patients, ranging from 26 to 86 mm/h, with an average of 55.1 mm/h. The average CRP was 21.8 mg/l, ranging from 6 to 40 mg/l (Table 2).

Ultrasonography showed subperiosteal abscess of the affected sites in 11 (42.3%) patients. Blood culture was positive in 10 (38.5%) patients and, of these, MRSA was found in seven patients. Microorganisms were isolated from pus culture in all of the patients in our study. *Staphylococcus aureus* was the most common organism isolated (78.1%) and MRSA was found in 13 patients. Other microorganisms cultured are shown in Table 3.

Two patients with durations of symptoms of 2 days were treated conservatively. Surgical intervention by means of incision, drainage of the pus and drilling holes in the affected bones was done in 24 patients (92.3%), followed by post-operative immobilisation. Malaria and scabies were associated with one patient each for which appropriate treatment was given. The ESR and CRP levels were normalised by 6–8 weeks. All of the patients were successfully treated except for four, who developed chronic osteomyelitis with sequelae. Amongst these, the tibia was involved in three patients and distal tibial growth disturbance was observed in one patient.

Discussion

Multifocal osteomyelitis is well recognised in the neonatal age group. Children less than 1 year of age were excluded from our study, as they may have a very high risk of association with perinatal infections. In our study, the average age at presentation was 4.9 years, which is comparable to a study by Labbé et al. [3], in which, among 43 children (9.5%) affected with multiple loci, the mean age was 5 years. Seventeen patients (65.4%) were found to be older than 3 years of age in our study. This may suggest increased involvement of acute multifocal osteomyelitis in older children also. Incidentally, we found that girls were affected more than boys in our study, contradicting the belief that boys will be affected more than girls in acute osteomyelitis.

Labbé et al. [3] showed that osteomyelitis was situated mainly in the lower limbs, 70% (all lesions) versus 20% for the upper limbs. The lower leg segment was the most frequently involved, amounting to 39.5% of all locations (tibia, 32.3%; fibula 7.2%). The femur and tibia accounted for 58% of all general locations. In upper limb involvement, the humerus was the most frequently affected segment (11.4%). Similarly, in our study, we found that the

Table 1 Clinical data of the patients

Case no.	Age (years)	Sex	Duration of symptom (days)	Bones involved
1	2	F	3	Lt proximal humerus and Rt proximal femur
2	2.5	F	4	Lt humerus and pandiaphyseal Lt tibia
3	1.5	F	3	Lt humerus and pandiaphyseal Lt tibia
4	5	F	7	Lt proximal humerus and Lt proximal femur
5	5	M	5	Lt proximal femur and pandiaphyseal Lt tibia
6	2	F	6	Lt distal femur and Rt proximal tibia
7	1	M	6	Rt proximal humerus and scapula
8	6	M	7	Lt proximal humerus and Lt distal femur
9	9	M	5	Rt proximal femur and Lt distal tibia
10	7	F	7	Lt proximal tibia and Rt proximal tibia
11	1.5	M	6	Rt proximal humerus, Lt distal humerus, Lt proximal femur and Rt distal tibia
12	11	M	3	Lt proximal humerus and Lt proximal tibia
13	7	F	4	Rt distal femur and Lt distal tibia
14	3	F	2	Rt proximal femur and Rt proximal tibia
15	6	M	3	Rt proximal humerus and Lt proximal tibia
16	5	F	3	Rt proximal femur and Lt proximal tibia
17	3	F	4	Lt proximal humerus and Rt proximal tibia
18	4	F	4	Rt proximal humerus, Lt proximal femur and Rt distal tibia
19	5	M	6	Lt proximal humerus and Lt proximal tibia
20	4	F	4	Rt distal humerus and Rt proximal tibia
21	4	M	7	Lt middle phalanx of the index finger and Lt distal femur
22	2.5	F	4	Lt proximal humerus and Rt proximal femur
23	7	F	5	Lt proximal humerus, Rt proximal tibia and Lt distal femur
24	9	M	3	Lt proximal femur, Lt proximal tibia and distal tibia
25	6	F	2	Rt distal femur and Lt proximal tibia
26	8	M	4	Lt proximal humerus and Rt distal ulna

Rt right, Lt left

Table 2 Investigations

Blood culture (positive)	10 (38.5%)
Pus culture (positive)	26 (100%)
	<i>Staphylococcus aureus</i> : 19 (73.1%)
	MRSA: 13 (50%)
Ultrasonography	Subperiosteal abscess: 11 (42.3%)
Haemoglobin level (g %)	7.8 (5.9–11)
TLC (/cmm)	14,750 (8,900–22,208)
ESR (mm/h)	55.08 (26–86)
CRP (mg/l)	21.77 (6–40)

MRSA methicillin-resistant *Staphylococcus aureus*, TLC total leukocyte count, ESR erythrocyte sedimentation rate, CRP C-reactive protein

lower limbs (64.9%) were more commonly involved than the upper limbs (35.1%). Among 57 bones involved, the common sites were the proximal tibia (50%) and the proximal humerus (46.2%), followed by the proximal

Table 3 Microorganisms cultured from surgical samples

Gram-positive organisms (73.3%)	Gram-negative organisms (26.7%)
<i>Staphylococcus aureus</i> : 19	<i>E. coli</i> : 2
<i>Streptococcus pyogenes</i> : 2	<i>Proteus</i> : 2
Enterococci: 1	<i>Klebsiella</i> : 1
	<i>Pseudomonas</i> : 1
	<i>Enterobacter</i> : 1
	<i>Acinetobacter</i> : 1

femur (38.5%). Osteomyelitis of the femur associated with tibia was seen in 11 (42.3%) patients and an association between the tibia and humerus was found in ten patients. Symmetrical involvement is a known fact in CRMO and, also, the study by Sichardt et al. [4] showed symmetrical acute multilocal involvement in children, but we did not encounter a similar trend.

All of our patients were incidentally found to have anaemia. The haemoglobin level was primarily associated with iron status in Indian toddlers; however, maternal haemoglobin level, family wealth and food insecurity were also important factors [5]. In these children, this nutritional anaemia may have contributed to low immunity, leading to multifocal bone involvement. As in most of the acute infections, the ESR and CRP levels were found to be elevated in all of our patients. Serial monitoring of these indicators were helpful in evaluating the response to treatment and follow up.

According to Wright et al. [6], ultrasonography is a proven method of identifying subperiosteal abscess in acute osteomyelitis. Ultrasonography was helpful in confirming the presence of subperiosteal abscess in those children with an appropriate history and localising signs in this study. We came across 11 patients (42.3%) in which there were subperiosteal abscess on ultrasonography. Bone scan and/or MRI would have been useful in the remaining cases, but, due to practical reasons, they could not be performed. Ultrasonography has proved to be essential: for early diagnosis by visualising the subperiosteal abscess, for surgical indication and for its non-invasive and easily reproducible character.

Staphylococcus aureus remains the most common aetiological organism in acute osteomyelitis in children. But, recently, MRSA has emerged as a major pathogen in acute osteomyelitis [7]. The emergence of MRSA in the community has increased the importance of culturing all collections in order to identify pathogens and to determine antimicrobial susceptibility. In the past 10 years, numerous outbreaks of community-based infection caused by MRSA in individuals with no prior medical exposure have been reported. Of concern has been the apparent capacity of community-acquired MRSA strains to cause serious disease in immune-competent individuals [8]. In $60\% \pm 70\%$ of all cases, the presence of pathogens can be demonstrated in the aspirate, as opposed to $40\% \pm 50\%$ in blood cultures [9, 10]. Blood culture was positive in 38.5% of cases, among which seven patients were MRSA-positive in our study. Saavedra-Lozano et al. [7] reported that only 23% of their patients were MRSA-positive in the blood culture in this study. Pus culture showed that 50% of the patients were positive for MRSA in our study. In our patients, the presence of organisms was higher (26 out of 26 patients) in aspirated sample compared with blood culture (10 out of 26).

In acute osteomyelitis of childhood, a rapid diagnosis and initiation of antibiotic therapy is necessary in order to prevent late sequelae. Appropriate antibiotic selection is critical for the successful treatment of acute haematogenous osteomyelitis. Depending on the clinical course (afebrile patient, considerably less local signs and

symptoms of infection) and laboratory data (decreased CRP level, ESR), 4–7 days after starting IV therapy, the antibiotic regimen may be continued by oral administration [10, 11] in acute osteomyelitis. Steer and Carapetis [1] recommended 3 days of intravenous antibiotics followed by 3 weeks of a high dose of oral antibiotics, provided there is no underlying illness, the presentation is typical and acute, and there has been a good response to treatment initially in the case of haematogenous osteomyelitis. Because of the varied presentations and clinical courses of acute haematogenous osteomyelitis, each case should be evaluated individually and followed closely [12].

In our study, patients who presented with a duration of symptoms of 2 days were initially given intravenous antibiotics and the clinical response was assessed after 24 h. These two patients responded well to intravenous antibiotics and conservative therapy continued. Clinical suspicion of the extent of involvement leads to surgical drainage in 24 patients under general anaesthesia, with drilling of the underlying cortex if necessary in order to remove the pus. Our patients received 2 weeks of intravenous antibiotics followed by 4–6 weeks of oral antibiotics. The duration of antibiotic therapy depends on the extent of infection and the clinical and laboratory responses. The need for longer and traditional duration of antibiotic therapy was necessary because of multifocal involvement in our patients.

Four of our patients developed chronic osteomyelitis, commonly involving the tibia in three patients. Among these, one patient had both tibial and humeral osteomyelitis and others had single bone involvement. Three patients were females and three had MRSA infection. The duration of symptoms in three patients was more than 5 days. One patient was found to be having growth disturbance of the distal tibia. Long-term follow up is needed in order to find out the sequelae in these patients. The drawback in our study is that bone scanning and MRI were not done, which would have detected many other sites of infection.

Conclusion

It is important to emphasise the fact that adequate and timely surgical intervention, along with antibiotics, is essential in the management of acute haematogenous multifocal osteomyelitis in order to minimise morbidity. Although many aetiological factors such as trauma, possible immunodeficiency or changing infective organisms could not be correlated definitely, the association of anaemia needs to be specially addressed in acute multifocal haematogenous osteomyelitis and needs further study to evaluate its role as a risk factor. The predominance of

methicillin-resistant *Staphylococcus aureus* (MRSA) in both blood and pus culture may suggest a changing trend in its association with multiple bone involvement and the focus on appropriate antibiotics therapy according to culture and sensitivity testing.

Conflict of interest None.

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