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Using the Existing Periosteum in the Treatment of Chronic Osteomyelitis in the Pediatric Age Group

Mohammad Al-Alwan MD[1*], Fadi Al Hiyari MD[1], Mohammad Al Sarayreh MD[1], Mohammad Al Ma'aitah MD[1], Ayat Al- Khasawneh MD[2]

[1]Orthopedic Department, Royal Rehabilitation Center, Amman, Jordan
[2]Princess Iman Laboratory Center, Amman, Jordan

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***Corresponding author:** Mohammad Al-Alwan
Orthopedic Department, Royal Rehabilitation Center, Amman, Jordan

Abstract **Original Research Article**

Background: The treatment of chronic osteomyelitis definitely needs a proper medical and surgical treatment, such as antimicrobial therapy according to established guidelines, and requires surgical intervention such as debridement and/or drainage, which has become particularly important in the last decade owing to the continued emergence of Community-acquired methicillin-resistant staph aureus (MRSA) which is resistance to all the β-lactam antibiotics. ***Methods:*** This is a retrospective study where we analyzed 23 cases of community-acquired MRSA chronic osteomyelitis presented to our orthopedic and trauma clinic at royal rehabilitation center between 2013-2021; All cases were started with broad-spectrum antimicrobial therapy, which is Vancomycin in addition to TMP–SMX or Rifampicin and multiple surgical debridements with removing all devitalized bone and the infected soft tissues and drainage procedures with preserving the thick periosteum were done in all cases. We used both the erythrocyte sedimentation rate (ESR) and the C -C-reactive protein (CRP) as acute inflammatory markers, which were checked twice weekly to monitor the outcome of the patients. ***Conclusion:*** MRSA osteomyelitis in the pediatric age group can be treated appropriately with surgery, which is the mainstay of therapy and antibiotic treatment based on international guidelines.

Keywords: MRSA osteomyelitis, Chronic osteomyelitis, Surgical debridement, Antimicrobial therapy, Pediatric age group.

INTRODUCTION

Osteomyelitis definition is an infection of bone and bone marrow caused by an infecting microorganism [5, 7, 17], while chronic osteomyelitis is the duration of the infection of the bone and marrow more than 3 months [5, 7,17], and most common microorganism is staphylococcus aureus. In the early 1900s, osteomyelitis patients had mortality and morbidity [1, 2, 3]. The pathophysiology of osteomyelitis is hematogenous, which is the most common; the microorganism is transported through the bloodstream, contiguous in which the microorganism transported from adjacent infected soft tissue and the direct-inoculation which results in penetrating insults, open fractures, or as post-operative complications.

In the hematogenous spread, the microorganism starts in the metaphyseal area of the bone due to the looping of the end arteries and venous pooling; in children older than 2 years, the physis acts as a barrier that prevents the spreading of the infection to the epiphysis, so it goes through the Volkman's canals to the subperiosteal space to create progressive inflammatory destruction which eventually damages the cortex of metaphysis and diaphysis. The most common symptoms of acute osteomyelitis include fever, pain, swelling, and hotness of the affected site, and with chronic osteomyelitis, the patient may complain of anorexia, loss of appetite, loss of body weight, and night sweating. Laboratory data is usually nonspecific; both CRP and ESR are usually elevated (97% and 91%, respectively), which is expected as both are acute inflammatory markers. However, Leukocytosis is only elevated in 35% of the cases [5, 7, 17].

By radiological work up, Plain X-ray is 50% sensitivity and 80% specificity [5,7,17], revealing the soft tissue swelling in the first 48 hours, the periosteal reaction after 5-7 days, and the osteolysis after 2 weeks. The CT scan shows gas on soft tissue view and the sequestrum on bone view. But MRI has the highest sensitivity, specificity and excellent views, which is the

osteomyelitis usually appears bright on T1 and dark on T2 [5,7,14,17].

The treatment of osteomyelitis includes broad spectrum antibiotics then can be shifted to culture sensitvity antibiotics. Also, surgical options include debridement and/or drainage of abscesses subperiosteally or soft tissue, bone, associated septic arthritis [3, 4].

The periosteum at the pediatric age group has a special anatomy which is thicker and has more blood supply than the adults which contributes in the growing of bone in width.

METHODS

We conducted a retrospective study and analyzed 23 cases of chronic osteomyelitis of pediatric age referred to our clinic at Royal Rehabilitation Center for further investigations and possible management between 2013- 2021. Twenty-three cases were referred to our center after 5-8 months of the beginning of the symptoms from another peripheral hospital. We excluded any patients older than 14 years old and the cases with acute hematogenous osteomyelitis from this study.

All cases underwent clinical assessment by history taking, physical examination, laboratory testing, and radiology assessment, followed by the medical and surgical plan. All patients started on the same antibiotics, Vancomycin and Rifampicin, by i.v. Route in the hospital according to the body weight, and all patients ordered radiological assessment by x-ray and MRI with IV contrast then underwent surgical intervention by making an incision over the affected bone and debridement of devitalized soft tissue then identifying the periosteum we open the periosteum by a sharp knife and elevated form the infected bone gently and preserving it; we do debridement of infected bone aggressively we do wash by three liters of normal saline then we close the preserved periosteum by absorbable sutures.

The patients followed up in the surgical ward by monitoring the temperature and pain assessment, laboratory markers (E.S.R., CRP) twice weekly and radiological assessment as a criteria for curing of the osteomyelitis.

The criteria for curing were subsiding of the clinical complaint (fever and pain), assessment of motion and weight bearing, laboratory markers (E.S.R, C.R.P), and radiological criteria (restoring bone continuity and consolidation).

RESULTS

All cases had pain and fever with local tenderness with erythema and swelling. Their laboratory findings showed elevated both ESR and CRP. The radiological studies (X- Ray, MRI) suggested of possibility of bone infection. By needle aspiration and bone biopsy confirmed the diagnosis of osteomyelitis and by cultures gave the infected organism is MRSA.

The mean age was 6.8 years, and the mean follow-up duration was 20 months. All 23 patients were treated by the same guidelines, by the same surgical team, and by the same antibiotic (Vancomycin and Rifampicin by i.v. route in the hospital and TMP+SMX with Rifampicin by oral as outpatients). Our treatment plans were based on the international guidelines [5,7,8,9].

Seventeen of the patients fulfilled the clinical criteria and the laboratory markers for cure in less than 8 weeks (mean duration for cure 4 weeks). The 6 cases of CRP and ESR were normalized after 16 weeks. The hospital stay ranged between 3-4 weeks, during which we did not face any drug reactions or side effects. Then, the patients were followed up in the clinic every 2-3 weeks, and after clinical and radiological healing was achieved, the patient was seen in the outpatient clinic at 3-month intervals. The mean clinical follow-up was 20 months, and the mean time to return to activities was 18 weeks (range 12 to 24 weeks).

DISCUSSION

As we mentioned in the introduction, osteomyelitis is an infection of the bone and bone marrow caused by bacteria. In general, osteomyelitis is considered a rare disease, as DiPoce *et al.*, reported an incidence of 6.0 per 1000 admissions in a children's hospital [14]. Staph aureus is the most common cause of osteomyelitis in all age groups, accounting for 70%-90%, and MRSA is becoming an increasingly major cause of Staph aureus infections (nosocomial and community-acquired), which accounts for 40%-60% of Staph aureus infections [1,6,12]. The prevalence of MRSA osteomyelitis increased from 0.4 to 1.5 per 1000 hospital admissions according to data collected from 33 different children's hospitals in the USA in a five-year period, while the rate of MSSA osteomyelitis remained stable in the same period of time [12].

Our 23 patients had the same findings in the physical examination on the day of admission, which revealed that they were in pain and febrile. Their physical exams were normal except for the musculoskeletal part, which showed local tenderness, swelling, erythema, and hotness. Laboratory findings showed increased WBC count, highly elevated ESR, and positive CRP results. The radiological studies (X-ray, MRI) suggest a high possibility of bone infection. After the admission, a needle aspiration and bone biopsy were done and sent for culture and histopathological examination before the antibiotic was started. After a couple of days, both tests showed that it was an osteomyelitis caused by MRSA. The patients were initially treated with cefazolin

according to the daily body weight dose, which was discontinued upon the return of culture sensitivity cultures.

Our treatment plans were based on international guidelines: 1. We provide analgesia and general supportive measures; 2. The affected part was rested in a splint or arm sling; 3. We identified the infecting microorganism and administered effective antibiotic therapy according to the culture's sensitivity report; 4. the pus was released as soon as detected; 5. we stabilized the bone if it has fractured by splint or external fixator; 6. we removed the avascular and necrotic tissue to eradicate the infection; 7. we restore continuity if there is a gap in the bone; 8. we maintain soft tissue and skin coverage; 9. once there is pus and bone necrosis, and the operative drainage was needed it was done again and again. [2,5, 9, 8, 17].

So, our treatment is divided into two components: the surgical treatment and the antibiotic treatment. The surgical treatment part, the mainstay of therapy, should be of the oncology approach. We make a longitudinal skin incision above the swelling, and after the delict dissection of soft tissue, we excise the entire sinus tract. If found, we incise the periosteum and elevate it 2-3 cm on each side. At this stage, we remove all the dead and infected tissue and bone (sequestrum) and wash the medullary canal with normal saline many times. At the end, we close the periosteum and the soft tissue loosely and the skin with non-absorbable interrupted sutures. This procedure could be repeated as needed, considering the blood loss, which requires close monitoring, and the operated limb is fixed by a splint or external fixator until the wound is healed and the bone is built again [9,12,7,15, 8, 17].

On the other hand, antibiotic treatment is given after the infectious pediatric consultation and should be used before, during, and after the surgical intervention. We treated our 23 patients during hospitalization with Vancomycin, which has been the drug of choice of parental therapy for MRSA, which has a bactericidal effect and is given slowly I.V. in a dose of 15 mg/kg/dose every 6 hours. The efficacy and safety of targeting through concentrations of 15-20 mg/mL in children require additional studies but should be considered in severe infections and recurrence cases. [3,6,9,10,12,13,16,17]. In literature, it is recommended to get the serum vancomycin concentrations of 15-20 mg/mL, and they recommend the 40-60 mg/kg/dose divided every 6 hours, and the maximum recommended dose is 100mg/kg/day or 6 g/day [20]. We also followed the kidney function of our patients twice weekly. Vancomycin is the primary choice for treating MRSA infections [2,12].

We added a second antibiotic with the vancomycin treatment inpatient and outpatient; we added Rifampicin to our patients as an adjunctive therapy, the dose of 400 mg twice daily for 3 months. It has a bactericidal activity, which reaches a high cellular level and can penetrate the biofilm. Still, it cannot be monotherapy due to the high possibility of developing microbial resistance [9]. We also followed the liver function of our patients weekly. The role of Rifampicin against MRSA is still under study, and more adequate clinical studies are needed [3,4,5,7,9,10,12,13,16,17]. The guidelines on shifting the route of antibiotics from parenteral to oral are unavailable [12]. For our patients, Two days before the patients' discharge, we shifted the antibiotic treatment of our patients to the oral antibiotic in combination with the parental therapy trimethoprim/sulphamethoxazole in a dose of 4 mg/kg twice daily in addition to the Rifampicin. Most CA-MRSA strains are TMP-SMX sensitive in Vitro, so it has become a good option for oral treatment [12]. The duration of therapy was varied for every patient, but it was between 8 weeks to 20 weeks. Although the optimal duration of antibiotic therapy is unknown, the literature recommends at least 8 weeks [4,9,12,13].

Regarding the outcomes, in 17 cases, we achieved the clinical criteria of eradicating the infection, which is resolution of fever and pain, restoration of motion and weight bearing, laboratory criteria (decreased E.S.R, normal C.R.P), and the radiological criteria of bone built again and restoring the bone continuity and consolidation of curing in less than 8 weeks. Six cases had an elevated C.R.P. for 20 weeks; after that, these cases with antibiotic treatment met the curing criteria. The literature showed that the curing rates of osteomyelitis are 68%-92% in general [13], and the recurrent rate is 20%-30% [3]. Meanwhile, the curing rate of osteomyelitis in children is 90% [3,4,9,12,13].

CONCLUSION

Dealing with these 23 cases of pediatric age group MRSA osteomyelitis opened our eyes to the treatment guidelines for MRSA infection. MRSA osteomyelitis in the pediatric age group can be treated appropriately with surgery, which is the mainstay of therapy and antibiotic treatment based on international guidelines.

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