CASE REPORT

Single-stage surgical management of pediatric chronic osteomyelitis using antibiotic-loaded bone filler: A single center prospective case series

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ABSTRACT

Osteomyelitis in children presents a significant clinical and surgical challenge. It is an acute or chronic infection of the bone. It predominantly affects preschool-aged children, with an estimated incidence of 8 per 100,000 children annually in high-income countries, with a male-to-female ratio of 2:1. Traditional treatments often involve multiple surgeries and prolonged systemic antibiotic use. Recent interest has focused on resorbable antibiotic-loaded bone fillers to minimize surgical interventions. The aim of this study was to evaluate the outcomes of single-stage surgical treatment for pediatric chronic osteomyelitis using local debridement and antibiotic-loaded bone filler. Twenty patients with Cierny-Mader type III chronic osteomyelitis were treated between March 2016 and March 2022. Clinical, radiological, and laboratory data were collected pre- and postoperatively, with a follow-up of up to 24 months. The cohort included 12 males and 8 females with a mean age of 11.1 years. The most commonly affected sites were the distal tibia, fibula, and femur. Staphylococcus aureus was the predominant pathogen (65%). All patients underwent successful single-stage procedures without need for further surgical intervention. Inflammatory markers normalized postoperatively, and all patients were infection-free at 1- and 2-year follow-up. No complications, wound issues, or growth disturbances were observed. A one-stage surgical protocol using local debridement and cemented antibiotic-loaded bone filler appears to be a safe and effective treatment for pediatric chronic osteomyelitis. (www.actabiomedica.it)

Key words: osteomyelitis, cemented antibiotic-loaded filler, orthopedics, pediatric orthopedics

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Introduction

Osteomyelitis in children presents a significant clinical and surgical challenge. It is an acute or chronic infection of the bone. It predominantly affects preschool-aged children, with an estimated incidence of 8 per 100,000 children annually in high-income countries, with a male-to-female ratio of 2:1 (1,2). Osteomyelitis can be classified by symptom duration: acute (<2 weeks), subacute (2 weeks to 3 months), and chronic (>3 months) (3). Most cases of pediatric osteomyelitis arise from hematogenous spread, commonly affecting the metaphysis of long bones due to its slow blood flow. The femur and tibia are frequently involved (4). Chronic osteomyelitis is a biofilm-related infection, where most pathogens are sessile and embedded in biofilm, making systemic antibiotic treatment challenging (5). Surgical management typically involves repeated debridement, delayed skin closure, and secondary reconstruction of bone defects (6-8). A traditional treatment strategy involves filling post-debridement cavities with antibiotic-loaded polymethylmethacrylate (PMMA) beads, which often necessitate a second surgery for removal due to biofilm formation. This challenge has spurred interest in resorbable, antibiotic-loaded bone void fillers (BVFs) (9,10). Calcium sulfate has been widely used as an antibiotic carrier, and its efficacy in bacterial eradication from bone defects has been demonstrated in several studies (11,12). To enhance bone formation and reduce fracture risk, hydroxyapatite has been added to create osteoconductive scaffolds (13,14). The aim of this study was to evaluate the outcomes of single-stage surgical treatment for pediatric chronic osteomyelitis using local debridement and antibiotic-loaded bone filler.

Methods

Patients presenting with Cierny-Mader (C-M) Type III (localized) chronic osteomyelitis (15), between March 2016 and March 2022 were eligible for recruitment. All patients underwent a single-stage procedure (Figure 1) and were preoperatively optimized to mitigate the impact of modifiable risk factors. Under tourniquet control, at least five deep specimens were obtained for microbiological analysis and two for histological examination before empirical intravenous antibiotics were administered. The necrotic bone was excised, and the defect was irrigated with physiological

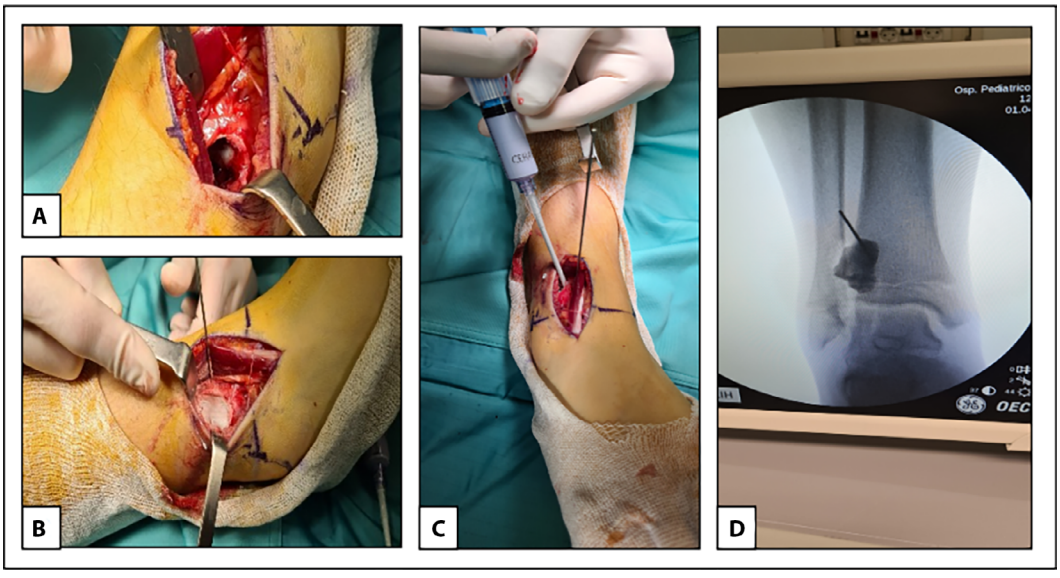

Figure 1. The surgical procedure. A) Surgical access and inspection of the site after curettage. B e C) Site filled with antibiotic-loaded filler. D) Intraoperative X-ray showing the site filled with cemented antibiotic-loaded filler.

solution. The defect was then filled with a bone filler, without the use of additional materials or antibiotic agents within the bone. Skin closure was performed during the same operation using VYCRIL 3.0 Rapid sutures. Clinical and epidemiological factors, preoperative and postoperative radiographs, and laboratory parameters, including white blood cell (WBC) count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and neutrophil percentage (NEU%), were documented. Appropriate oral or intravenous antibiotic treatment was administered for 6 to 12 weeks based on the infectious disease team's recommendations and the culture exam results. Patients were monitored for infection eradication at three-, six-, twelve-, and twenty-four-months post-surgery.

Statistical analysis

Statistical analysis was performed using GNU PSPP software. The Shapiro–Wilk test showed that the data were not normally distributed. A non-parametric test, the Mann–Whitney test was applied to evaluate significant differences in continuous variables. Nominal variables were grouped and cross-tabulated, with the chi-square test or Ficher exact test used for low-frequency variable comparisons, as appropiate. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 20 patients (11 males, 9 females) with a mean age of 11.1 years (range 9 to 13) were treated. All patients underwent clinical examination and laboratory tests upon admission. The mean admission temperature was 37.0 ± 0.4 ˚C. Nineteen patients (95%) were diagnosed with osteomyelitis of hematogenous origin, without prior surgical intervention. One patient (5%) was diagnosed with osteomyelitis secondary to an open fracture, requiring surgical treatment with external fixation. No patients had significant comorbidities, and no plastic surgery was necessary for skin closure. The average length of hospitalization was 6 days (range, 5 to 8 days). The most common infection sites were the distal tibia (6 cases), distal fibula (4 cases), and distal femur (3 cases). No patients had concurrent osteomyelitis and pyogenic arthritis. Postoperatively, laboratory biomarkers generally decreased, with ESR and CRP showing similar trends and normalizing within 6 days. Staphylococcus aureus was the most identified organism (13 patients, 65%). Group A beta-haemolytic Streptococcus was found in 6 patients (30%), and Escherichia coli was detected in 1 patient (5%) on cultural examination. All patients were reviewed at one- and two-years post-surgery. At one-year post-surgery, all patients were free of infection. At two years post-surgery, all patients remained free of infection without any complications. At the last follow-up visit, all patients had resumed daily living and sports activities, inflammatory markers were within the normal range, and no signs of growth arrest or disturbances were observed based on radiological and clinical assessments. All patients were pain-free at the last follow-up, and the range of motion of the affected extremity was comparable to the non-operated side in all but one patient. No statistically significant difference was found comparing different microbes' type and limbs nor sex, using Fisher exact test 2x3 (Table 2).

Discussion

The results of a single-centre study suggest that a total of 20 patients developed OM, 9 of whom were female and 11 males. As shown in Table 1, out of the 20 patients, 7 males and 6 females were infected with Staphylococcus aureus; 4 males and 2 females with group A beta haemolytic streptococcus; and only 1 patient (female) developed an Escherichia coli infection. This distribution was not statistically significant when calculating the p-value. With relation to the issue of localisation, it is evident that there were five infections affecting the upper limbs and fifteen affecting the lower limbs. In both localisations, Staphylococcus aureus was isolated in between 60 and 70% of cases. With regard to localisation, the calculated p-value also showed no significance (p-value > 0.005). Staphylococcus aureus was the most commonly isolated organism, in according with the litterature (26,37,38). Chronic osteomyelitis and infected non-union in skeletally immature patients are reported to cause several complications and morbidity (16-18). Since the transphyseal

Table 1. The table illustrates the distribution of the pathogens isolated in relation to patients' sex and the location of infection.

Variables		Type			Total	p-value
		Staphylococcus Aureus	Streptococcus Beta A	Escherichia Coli		
Gender						
Male	Count	7	4	0	11	(Fisher.e.t) 0.489
	Row %	63.6	36.4	0.0	100.0	
Female	Count	6	2	1	9	
	Row %	66.7	22.2	11.1	100.0	
Total	Count	13	6	1	20	
	Row %	65.0	30.0	5.0	100.0	
Limb						(Fisher.e.t) 0.723
Upper limb	Count	3	2	0	5	
	Row %	60.0	40.0	0.0	100.0	
Lower limb	Count	10	4	1	15	
	Row %	66.7	26.7	6.7	100.0	
Total	Count	13	6	1	20	
	Row %	65.0	30	5.0	100.0	

Table 2. The table illustrates the outcomes of the statistical investigation undertaken to ascertain the association between the variables by means of the Chi-square test.

Chi-Square Tests			
Tests	**p-Value**	**df**	**Asymptotic Sig. (2-tailed)**
Pearson Chi-Square	0.58	2	0.748
Likelihood Ratio	0.81	2	0.667
Linear-by-Linear Association	0.00	1	1.000
N of Valid Cases	20		

vessels persist until 15-18 months of age, infection in the metaphysis may spread to the epiphysis and result in concomitant septic arthritis (19,20). Cases in the literature indicate that this pathology is associated with limb length discrepancy, bone and soft tissue loss, and amputations (21-24). Therefore, prompt diagnosis and early treatment are essential for favourable outcomes (25). Diagnosing osteomyelitis in infants can be challenging due to less evident clinical manifestations compared to older children and adults. In our study, all patients presented with pain on acupressure and passive movements, limited range of motion (ROM) of the joint adjacent to the affected bone, and limb swelling and erythema in 55% of the cases. Goergens et al (26). found that most patients with osteomyelitis and septic arthritis exhibited mild infection symptoms. The most common symptom was refusal to move the affected limb (>90% of patients), while only 50% showed local swelling and 32% had no fever. Hence, normal temperature and laboratory parameters do not exclude the diagnosis of osteomyelitis. MRI and bone scintigraphy are recommended to detect infection evidence. One major challenge with osteomyelitis treatment is the potential intolerance to antibiotics, drug interactions, and poor patient compliance. Local antibiotic application can mitigate compliance issues and reduce reliance on systemic treatment. The local use of antibiotics directly in the bone is proven to be

safer than systemic administration (27,28). Definitive management of osteomyelitis and its sequelae require aggressive debridement, thorough cleaning, followed by reconstruction and appropriate antibiotic therapy (29,30). Managing osseous defects in chronic osteomyelitis patients is particularly challenging. Various bone reconstruction techniques have been reported, often requiring multiple surgical procedures (31). Antibiotic delivery systems, such as implanted antibiotic cement microspheres, do not provide mechanical support and may form fibrous tissue, complicating removal (32-34). Therefore, Resorbable calcium-sulfate-based antibiotic carriers have been developed to avoid the need for secondary removal (35). Canavese et al (36). investigated the surgical treatment of chronic osteomyelitis in children using antibiotic-laden cement (ALC) spacers, which were later removed, and bone substitutes (β-tricalcium phosphate) within the induced membrane, along with osteosynthesis as required. In our study, there were no issues at the surgical wound site, nor was there any loss of substance through wound secretions. Chronic osteomyelitis can sometimes mimic neoplasms both clinically and radiologically (37), making microbiological findings crucial for differentiation. Next generation metagenomic sequencing and other new diagnostic technologies could be useful in this context and warrant further investigation.

Our data on male-to-female ratios align with other publications (38). The lower limb was the most affected region, consistent with other studies (39). This study has some limitations. Firstly, the small sample size reduced the power of our statistical analysis. Secondly, the structure of the study and the inclusion of patients with different lesion sites introduced bias. Thirdly, the lack of a control group with other treatment options affected statistical efficiency. Nevertheless, this is one of the few single-centre Italian studies on the use of antibiotic bone filler for one-stage treatment of chronic osteomyelitis in children. Therefore, another limitation concerns the limited generalizability of our results.

Conclusion

This study supports the use of a single-stage protocol involving debridement and antibiotic-loaded bone fillers for treating pediatric chronic osteomyelitis. The approach demonstrated a low recurrence rate and minimized trauma by reducing the need for multiple surgeries. Further studies with larger cohorts are needed to validate these findings and establish this method as a standard treatment for pediatric chronic osteomyelitis.

Consent for Publication: informed consent was obtained from all subjects involved in this study

Conflict of Interest: Each author declares that he has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Authors Contribution: C.C. wrote the manuscript with support from G.Z., V.C., and M.M. contributed to patient follow up and support the review, L.D.B. contributed to data collection, statistical analysis, and writing—review and editing. A.G. was responsible for conceptualization, methodology, surgical procedures, and supervision. All authors read and approved the final manuscript.

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