

CASE REPORT

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Prognosis of transphyseal hematogenous osteomyelitis in children: three case reports and a literature review

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Abstract

Background Transphyseal hematogenous osteomyelitis (THO) has been considered a potential cause of severe sequelae due to its damage to the growth plate. It has been reported that growth disturbance would take place if the area of involvement exceeds 7%. However, the growth plate seems to have more potential to recover and regain normal function.

Case presentation We report three cases of hematogenous osteomyelitis (HO) in children (ages 9 weeks, 4 years, and 13 years respectively) with significant physeal involvement. All patients underwent surgical debridement and antibiotic therapy. Follow-up assessments demonstrated full recovery, with normal knee movements, no pain and equal limb length. Complete recovery of the physeal plate morphology and normal subsequent development were observed.

Conclusions THO in children may have the chance of complete recovery after proper treatment, suggesting that the physeal plate has a great potential for self-recovery.

Clinical trial number Not applicable.

Keywords Physeal plate, Transphyseal hematogenous osteomyelitis, Prognosis, Children, Osteomyelitis

Background

Hematogenous osteomyelitis (HO) is a common pediatric infectious disease, in which timely treatment generally leads to favorable outcomes [1]. However, in some rare cases, infection can cause damage to the physeal plate, which is referred to as the transphyseal hematogenous osteomyelitis (THO). A previous retrospective study indicated that 25.7% of pediatric hematogenous osteomyelitis involved the growth plate [2]. THO in children

appears to be more common in those older than 18 months and is often caused by acute infections [3]. It predominantly occurs at the distal tibia and is mainly caused by Methicillin-Sensitive *Staphylococcus aureus* and *Klebsiella kinga* [2]. Another study showed that among the 10 patients with physeal-associated osteomyelitis, 8 exhibited growth disturbances [4]. Animal studies have shown that damage exceeding 7% of the physeal cross-sectional area may significantly increase the risk of subsequent limb growth disturbance [5]. Large-scale retrospective studies are lacking in clinical research. Favorable outcomes in THO cases are typically seen in subacute infections with low-virulence pathogens and older children [6–8]. Overall, current research on THO often emphasizes the severity of its long-term sequelae [9–11]. In this

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study, we report three cases of THO, all of whom made a full recovery. The clinical characteristics and prognosis of these cases are discussed in detail.

Case presentation 1

A 4-year-old boy was admitted to a primary care facility with right knee pain, swelling, and limited range of motion. He experienced a sprain before the onset of symptoms but became pain-free after a few days of immobilization. Subsequently, he developed a fever of 38°C without any signs of upper respiratory infection. The primary care facility treated him with a 7-day course of oral first-generation cephalosporin, which partially relieved his symptoms. However, the intermittent knee pain persisted for about three weeks, and the patient visited our hospital for further treatment.

Physical examination revealed tenderness, mild swelling, and restricted flexion and extension of the right knee, with no erythema or flare around the joint. Significant laboratory findings included a white blood cell count of $9.0 \times 10^9/L$, an erythrocyte sedimentation rate of 65 mm/h, and a C-reactive protein (CRP) level of 27.6 mg/dL. The blood culture was negative. MRI of the right distal femur revealed a longitudinal, translucent lesion with a well-defined border across the growth plate (Fig. 1-A) and THO was suspected. The lesion accounts for 6.7% of the growth plate area in the coronal plane.

Surgical treatment was performed 30 days after the onset of symptoms. Joint aspiration found purulent fluid and the patient underwent abscess drainage and curettage of the lesion, along with irrigation of the joint

cavity. The infected area started from the metaphysis, went down across the growth plate of distal femur, extended distally until eroding the cartilage and breaking in to the joint space. One-fifth of the growth plate of the distal femur was involved. No bone grafting, bone cement, or local antibiotics was used. Microbiological analysis identified Gram-positive *Staphylococcus aureus*. The diagnosis of THO in the distal femur with septic knee arthritis was made.

Postoperatively, the patient received cefmetazole sodium at the dose of 0.5 g twice daily for one week and was discharged when his white blood cell count and CRP levels returned to normal. At the 2-year follow-up, clinical and radiographic evaluations confirmed complete healing, with no signs of growth arrest (Fig. 1-B.C.D). Physical examination showed no limitation in the range of motion of the affected knee and equal limb length.

Case presentation 2

A 9-week-old boy was admitted to our hospital with decreased active motion and swelling of his left knee joint, along with mild restriction in passive flexion and extension for approximately 20 days. His temperature was normal, and there was no history of trauma or upper respiratory infection. Physical examination revealed swelling of the left knee joint with normal skin temperature. The knee was flexed at 30 degrees, with restricted extension and pain (crying and resistance) during flexion. Laboratory investigations found normal white blood cell count of $9.7 \times 10^7/L$ and normal CRP level of 4.85 mg/L. MRI revealed that the lesion extended across

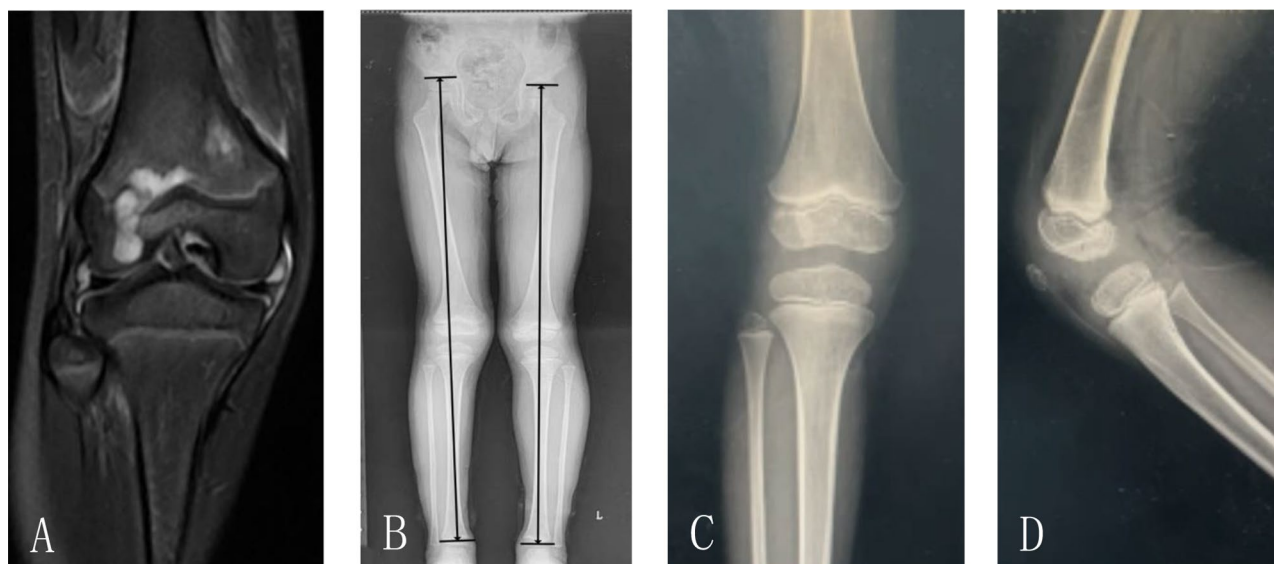


Fig. 1 A 4-year-old boy diagnosed with transphyseal hematogenous osteomyelitis of the distal right femur underwent both preoperative and follow-up imaging studies. **A.** Preoperative knee MRI T2-weighted images revealed a lesion disrupting the lateral physis of the distal femur. **B.C.D.** Postoperative full-length X-rays and anteroposterior and lateral views of the distal right femur showed symmetrical alignment of the lower limbs, with the affected side approximately 0.6 cm longer than the unaffected side, and no evidence of growth disturbances

the epiphyseal plate of the distal femur, with the destructive area occupying 25.1% of the total growth plate area in the coronal plane, accompanied by significant knee joint effusion (Fig. 2-A). Upon admission, the patient was started on empirical broad-spectrum antibiotics (i.v. oxacillin, 0.1 g twice daily).

The patient was diagnosed sub-acute THO and septic arthritis. Under aseptic conditions, 5 ml of yellow-green pus was aspirated from the knee joint for culture, which yielded negative result. The patient underwent arthroscopic washout, drainage of the abscess, and curettage of the lesion. During the surgery, yellow-white purulent tissue was observed within the knee joint. After debridement, a cavity was found in the femoral cartilage, and the infection had spread through the growth plate from the distal femoral ossification center, involving the metaphysis. The cavity was left unfilled and a cast was used for immobilization after surgery. The bacterial culture yielded negative results. Due to significant clinical improvement, the antibiotic regimen was continued for two weeks and the patient was discharged after normalization of white blood cell count and CRP levels. MRI scans of the knee joint were performed six months and one year postoperatively. Initially, a “bone bridge” formed in the growth plate, but it did not impede growth and gradually moved away from the growth plate as the bone grew (Fig. 2-B). By the one-year follow-up, the growth plate and epiphysis had almost returned to their normal shape (Fig. 2-C). Two years after surgery, during a follow-up outpatient visit, physical examination of this child showed the limbs were of equal length, with no angular deformities and no restriction in the range of motion (Figure-D).

Case presentation

A 13-year-old boy was admitted to our hospital with swelling, erythema, and pain in the left knee for one day. His temperature was normal, but he had a history of minor knee trauma two months before onset of the symptoms. Physical examination revealed swelling of the left knee joint with normal skin temperature. The knee was flexed at 20 degrees, with restricted extension and pain during flexion. Laboratory results showed a white blood cell count of $9.31 \times 10^7/L$, an elevated erythrocyte sedimentation rate of 100 mm/h, and a CRP level of 85.8 mg/dL. The blood culture was negative. MRI revealed extensive subcutaneous and bone marrow edema, with localized involvement of the medial epiphyseal plate of the proximal tibia (Fig. 3-A). The destruction area of the growth plate accounted for 14.3% of the total. He was diagnosed THO of the left proximal tibia.

Upon admission, the patient received empirical antibiotic treatment (i.v. cefazolin, 0.5 g twice daily) and soon underwent surgical treatment. The lesion extended proximally across the epiphyseal plate into the epiphysis, with complete involvement of the tibial tuberosity epiphysis. The knee joint was not involved. After debridement, a cavity approximately $6.0 \times 5.0 \times 5.0$ cm in size was left, and antibiotic-laden bone cement (40 g polymethylmethacrylate with 2 g vancomycin) was applied for anti-inflammatory treatment and mechanical support. Intraoperative pathogen culture identified Gram-negative *Staphylococcus*. Postoperatively, the organism was sensitive to cefazolin (M.I.C. ≤ 0.12). The patient continued the current antibiotic regimen for two weeks and was discharged once his white blood cell count and CRP levels normalized.

Two years post-surgery, the child's height had increased by approximately 13 cm since the initial visit. Physical

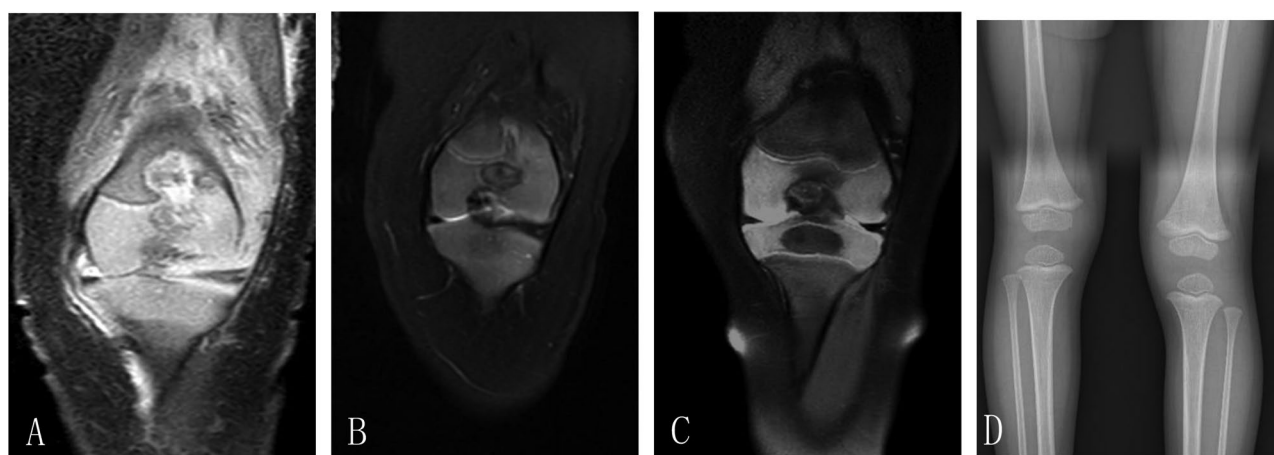


Fig. 2 A 9-week-old boy diagnosed with transphyseal hematogenous osteomyelitis of the distal left femur underwent both preoperative and follow-up imaging studies. **A.** Preoperative MRI showed that the lesion was hyperintense on sagittal T2-weighted images. The hypersignal shadow was seen in the metaphysis and epiphysis. **B.** Sagittal T2 MRI image of the knee 2 months after operation. **C.** Sagittal T1 MRI image of the knee 1 year after operation. **D.** The anteroposterior X-ray of both knees taken 2 years postoperatively showed no evidence of growth arrest in the lower limbs

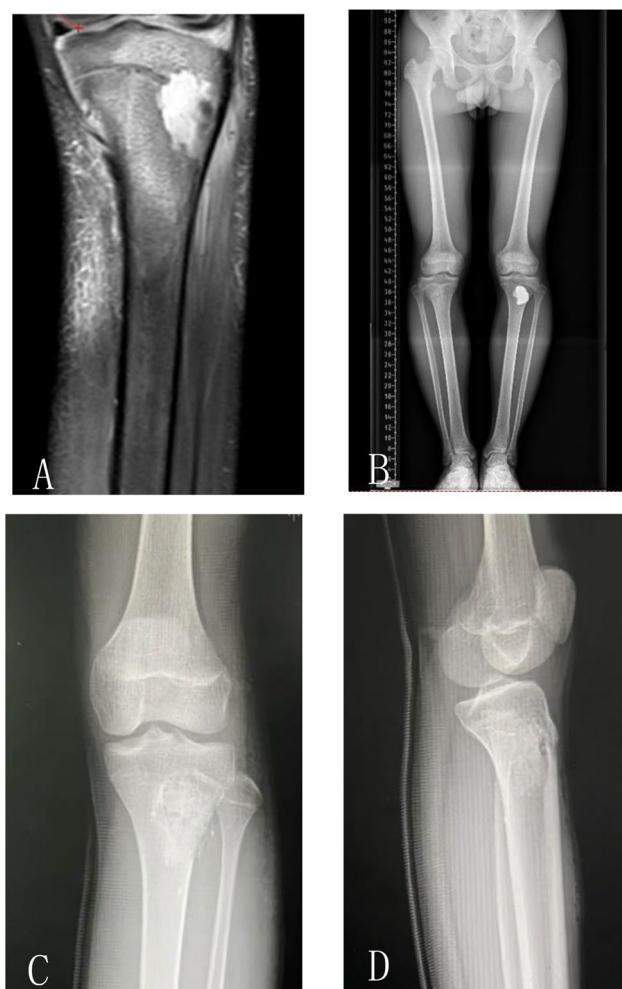


Fig. 3 **A.** Preoperative MRI revealed a hyperintense lesion on sagittal T2-weighted images, indicating complete transgression of the growth plate. **B.** Full-length X-rays taken 2 years postoperatively showed no evidence of growth arrest in the lower limbs. **C** and **D.** X-rays of the knee joint in both the anteroposterior and lateral views, taken after the removal of the bone cement, showed no evidence of growth arrest in the lower limbs

examination revealed that the limbs were of equal length, with no angular deformities and no restriction in the range of motion. Full-length radiographs of both lower limbs and the anteroposterior and lateral views of the left knee showed good recovery. The growth plate and epiphysis had almost returned to their normal shape (Fig. 3-B), followed by bone cement removal (Fig. 3-C,D).

Discussion and conclusions

HO in children predominantly affects the metaphysis of long bones. This is primarily due to the slow blood flow within the metaphyseal vascular loops that allows bacteria to settle [1]. Some researchers suggest that between birth and the first two years of life, blood vessels directly connect the metaphysis to the epiphysis. These vessels permit bacteria to traverse the growth plate and invade

the epiphysis, leading to growth plate destruction. In older children, however, these vessels gradually disappear, making the growth plate an effective barrier against bacterial invasion [3, 12–14]. However, this study reports two cases of THO, including a 4-year-old and a 13-year-old child. This indicates that the barrier sometimes can also be destroyed and THO is still a possibility in children older than age two.

Prognostic factors of THO include the extent of physal damage, bacterial virulence, and age [2, 3, 6–8, 15, 16] (Table 1). However, no clinical studies have reported a specific threshold for predicting prognosis. Animal studies have shown that damage exceeding 7% of the physal cross-sectional area significantly increases the risk of subsequent limb growth disturbances [5, 6]. This threshold is currently used in predicting the likelihood of a favorable prognosis. However, in our report, despite physal damage far exceeding this threshold, their limb growth remained unaffected. This finding challenges the threshold of 7% and indicates that aside from the percentage of involvement, there might be other factors that influence the recovery of physal morphology and development.

Bacterial virulence may be one of the factors, with lower bacterial virulence correlating with less physal damage [7, 16]. Bogoch [7] reported six cases of Brodie abscesses that crossed the physis, none of which left growth disturbance after treatment. This was attributed to the low virulence of the pathogens which possibly reduced the impact on their growth potential. However, Eli Ezra's study of eight cases of Brodie abscesses found that five children older than five years with subacute THO experienced favorable recovery, while three older children developed varying degrees of growth disturbance [6]. This suggests that not all patients with subacute infections have favorable outcomes, leading to the suggestion that older age might be associated with a lower risk of growth disturbances.

Our cases also demonstrated surprisingly favorable outcomes. In Case 1 and Case 2, both involving young children, serial MRI scans revealed that soon after subsiding of the inflammation, a lesion with the bottom at the physis and ossified edge in the metaphysis formed at the site of THO, previously regarded as a temporary "bony bridge". With the growth of new bone from the physis of the distal femur, the lesion extended proximally and the ossified edge gradually diluted and merged with nearby metaphyseal bones. Physis at the bottom of the lesion regained continuity and developed at the same speed as nearby, leaving no sign of permanent bony bridge. This suggests that physal damage due to THO has a strong potential of self-repair and do not necessarily result in poor prognosis.

Table 1 Overview of prognostic factors and outcomes in transphyseal hematogenous osteomyelitis

Study/Au- thor (Year)	Study Design	Population	Sample Size	Surgery	Prognostic	Conclusion
Bogoch et al. (1984)	Case series	Children with Brodie abscess	6 pediatric patients	4- Incision and drainage 2-None	Functional re-covery, healing of bone	The good prognosis is attributed to the low virulence of the infecting organism, the host's immune response, and the modification of the infection through antibiotic therapy.
C. Tudisco et al. (1991)	Case series	Children with chronic osteomyelitis	4 pediatric patients	4-Incision and drainage	Growth arrest	Chronic osteomyelitis-induced damage to the growth plate may be irreversible.
Wes Peters et al. (1992)	Case series	Children with acute osteomyelitis	6 neonates	4-Incision and drainage 2-None	Growth arrest	Neonatal infection-induced growth plate damage can have catastrophic sequelae.
Eli Ezra et al. (2002)	Case series	Children with Brodie abscess	8 pediatric patients	8-None	Functional re-covery, healing of bone	No difference in treatment or outcome between patients with lesions confined to the epiphysis and those involving the physis and adjacent metaphysis.
Emal Wardak et al. (2009)	Case series	Children with acute osteomyelitis	4 pediatric patients	4-Incision and drainage	Growth arrest	Narrowing of the growth plate is a risk factor for future growth disturbance, with children over eight years more likely to be affected.
Andrea Cossio et al. (2019)	Case report	Children with Brodie abscess	1 pediatric patient	Incision, drainage, and filling of the bone defect with BAG-S53P4 granules	Functional re-covery, healing of bone	BAG-S53P4 could be a suitable and safe bone substitute in the treatment.

THO presents significant controversy regarding prognosis in pediatric patients due to its distinct pathogenesis and clinical presentation, which differ from primary epiphyseal osteomyelitis. Despite recent advances, controversies remain regarding the age distribution, mechanisms of infection spread, and prognosis of THO. Currently, there are no specific treatment protocols or guidelines for THO. We have largely adhered to the strategies outlined in traditional literature, including timely antibiotic usage and surgical debridement upon diagnosis. Considering the diversity of age, site of involvement and time elapse between onset of symptoms and surgery, we believe that the good outcome of the three cases should be explained by the great remodeling potential of the growth plate in children, rather than any specific skills of diagnosis or treatment.

This study has several limitations. While longer follow-up until skeletal maturity is needed to fully assess the prognosis of THO, the follow-up duration in our cases was limited to 2 years. The small sample size also limits the universality of the findings. Future studies should increase the sample size and compare cases with and without complications to better understand the prognostic factors.

In conclusion, we provided three cases of THO that gained full-recovery of the physeal plate morphology and function. THO in children may have the chance of complete recovery after proper treatment, suggesting that the physeal plate has a greater potential for self-recovery than previously thought. Further research is needed to

explore the mechanisms underlying this self-recovery, as well as the characteristics of physeal plate damage that could potentially lead to permanent dysfunction.

Abbreviations

CRP	C-Reactive protein
MRI	Magnetic resonance imaging
THO	Transphyseal hematogenous osteomyelitis
HO	Hematogenous osteomyelitis

Acknowledgements

Not applicable.

Author contributions

Tianjing Liu designed the overall study. Peng Ning and Shuting Lin conducted a systematic literature search and drafted the manuscript. Zhixin Yang contributed to sourcing images and drafting sections of the article. All authors critically revised and approved the final manuscript."

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Data availability

The data that support the findings of this study are available from Shengjing Hospital of China Medical University, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Shengjing Hospital of China Medical University.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee at Shengjing Hospital of China Medical University, with approval number 2022PS1046K. Written informed consent was obtained from individual or guardian participants. The

study followed the ethical standards set by the Declaration of Helsinki and other relevant guidelines.

Consent for publication

We confirm that written informed consent for publication of the case series titled “Prognosis of Transphyseal Hematogenous Osteomyelitis in Children: Case Series and Literature” has been obtained from the parents or legal guardians of the children involved. This consent covers the inclusion of any individual details, images, and other relevant data presented in the manuscript.

Competing interests

The authors declare no competing interests.

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