Primary Epiphyseal Osteomyelitis Caused by Mycobacterium Species in Otherwise Healthy Toddlers

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Background: Mycobacterial osteomyelitis involving only the epiphysis of a long bone is extremely rare, and its clinical and radiographic features remain unclear. The purpose of this study was to characterize mycobacterial epiphyseal osteomyelitis and to identify differences between its features and those reported for epiphyseal osteomyelitis caused by bacteria or unidentified pathogens.

Methods: We retrospectively reviewed the cases of eight children (five males and three females) who presented at a median age of nineteen months (range, twelve to twenty-five months). Clinical findings were compiled. Radiographs and magnetic resonance imaging (MRI) were used to determine local spread of the abscess outside the epiphysis during the disease course. At the time of the latest follow-up evaluation, the presence of limited joint mobility or growth disturbance was determined. Physeal damage was evaluated with use of MRI.

Results: Pathogens were identified through multiplex polymerase chain reaction. *Mycobacterium bovis* bacille Calmette-Guérin (BCG, Tokyo-172 strain) was identified in four patients; *Mycobacterium tuberculosis*, in three patients; and nontuberculous mycobacterium, in one patient. The lesion was located at the distal femoral epiphysis in six patients, at the proximal tibial epiphysis in one patient, and at the proximal humeral epiphysis in one patient. The abscess was confined to the epiphysis at the time of initial presentation but, over time, extended outside the epiphysis in seven cases. The lesion was initially located in the cartilaginous epiphysis in two patients, which could be diagnosed only on MRI. Seven patients worsened despite surgical drainage and medication, and five required additional surgery. At follow-up at a mean of 4.1 years (range, 1.3 to 7.8 years), focal physeal damage was evident in five patients, and clinical growth disturbance was evident in one patient.

Conclusions: In contrast to the reported benign features of epiphyseal osteomyelitis caused by bacteria or unidentified pathogens, mycobacterial epiphyseal osteomyelitis seems to have an unfavorable clinical course that tends to lead to physeal damage. MRI is useful for early diagnosis of a cartilaginous lesion and evaluation of abscess spread and physeal damage.

Level of Evidence: Prognostic Level IV. See Instructions for Authors for a complete description of levels of evidence.

Epiphyseal osteomyelitis has been considered to be secondary to the spread of infection from a metaphyseal focus, and therefore, thought to occur almost exclusively during infancy when the transphyseal canals are open. However, due to the vasculature of the epiphysis and slow blood flow in the epiphyseal sinusoids, an acute or subacute form of primary osteomyelitis involving only the epiphysis of a long bone can occur, regardless of age. Primary epiphyseal osteomyelitis has been considered to be secondary to the spread of infection from a metaphyseal focus, and therefore, thought to occur almost exclusively during infancy when the transphyseal canals are open. However, due to the vasculature of the epiphysis and slow blood flow in the epiphyseal sinusoids, an acute or subacute form of primary osteomyelitis involving only the epiphysis of a long bone can occur, regardless of age. Primary epiphyseal...
Osteomyelitis is usually caused by bacterial infection— *Staphylococcus aureus* is the most common pathogen—although sometimes, particularly with the subacute form of primary epiphyseal osteomyelitis, the pathogen may not be identified. Epiphyseal osteomyelitis caused by bacteria or unidentified pathogens usually responds promptly to antibiotics with or without surgical drainage, and has a favorable prognosis without long-term complications.

Mycobacterium is another pathogen of importance and the cause of musculoskeletal infections seen not only in developing countries but also in some developed countries where tuberculosis is endemic and routine neonatal bacille Calmette-Guérin (BCG) vaccination is still practiced. However, primary epiphyseal osteomyelitis caused by mycobacteria is extremely rare. To our knowledge, there are only four reports to date describing the clinical and radiographic features of mycobacterial primary epiphyseal osteomyelitis, observed in five cases; three of the cases were tuberculous osteomyelitis, one was BCG osteomyelitis, and one was nontuberculous mycobacterial osteomyelitis. A paucity of literature leads to inconsistent opinions on the outcomes and sequelae. We reviewed eight cases of mycobacterial primary epiphyseal osteomyelitis, of which seven cases had an unfavorable clinical course. We analyzed the cases to characterize clinical and radiographic findings, and to identify differences between the features of mycobacterial osteomyelitis and those reported for epiphyseal osteomyelitis caused by bacteria or unidentified pathogens.

### Materials and Methods

Our institutional review board approved this study. It was designed as a retrospective study investigating a series of eight consecutive patients with mycobacterial primary epiphyseal osteomyelitis who were treated in a tertiary children’s hospital (seven patients) or a tertiary general hospital (one patient) between 2005 and 2012. From our hospital database of septic arthritis and osteomyelitis cases (among patients who were eighteen years of age or younger), we determined that ninety-eight patients had presented with musculoskeletal infection during the study period. Fifty-seven of the patients presented with bacterial osteomyelitis, twenty-four presented with osteomyelitis caused by an unidentified pathogen, and seventeen patients presented with mycobacterial osteomyelitis. Fifteen patients had primary epiphyseal osteomyelitis. In two of those patients, the cause was ordinary bacteria; in five patients, unidentified pathogen; and in the remaining eight patients, mycobacteria. Cases in which the lesion involved both the metaphyseal and epiphyseal areas at initial presentation were excluded, even if the epiphyseal lesion was larger, because of the possibility of primary focus in the metaphysis.

The study population in this series included five boys and three girls with mycobacterial primary epiphyseal osteomyelitis. The median age at the time of symptom onset was nineteen months (range, twelve to twenty-five months). All patients were otherwise healthy and their immunocompetence—assessed through laboratory analysis including T-cell subset, immunoglobulins, and complements testing, human immunodeficiency virus antibody testing, and dihydroorotamide testing for chronic granulomatous disease—was normal. No children showed abnormal findings suggestive of pulmonary tuberculosis on chest radiographs through the course of the disease.

Mycobacterial species were identified through the molecular method using multiplex polymerase chain reaction (PCR), as has been previously described. In brief, mycobacterial colonies grown on the surgical specimens were analyzed through real-time PCR targeting the IS6110 region, a specific region of the *Mycobacterium tuberculosis* complex. The next step was to differentiate between the presence of the 77-base pair (bp) fragment only (*Mycobacterium bovis*) versus the presence of both the 77-bp and 53-bp fragments (*M. tuberculosis*) by real-time PCR targeting the senX3-regX3 intergenic region. If only the 77-bp fragment was present, further multiplex PCRs were performed to differentiate between *M. bovis* BCG (deletion at the region of difference [RD1]) and *M. bovis* (no deletion at the RD1). After confirming the presence of *M. bovis* BCG, further multiplex PCRs were performed to differentiate between the Tokyo-172 strain (deletion at the RD8 and RD14) and the Pasteur strain (deletion at the RD8).

We investigated the clinical features of the patients with respect to acute or subacute onset of presenting symptoms, laboratory findings, response to treatment, and complications. Radiographs and magnetic resonance imaging (MRI) were used for all patients to determine patterns of any abscess spread or growth disturbances caused by the damaged physisc.

### Source of Funding

There was no external funding source for this study.

### Results

Mycobacterial species were identified as *M. tuberculosis* in three patients and *M. bovis* BCG (Tokyo-172 strain) in

### TABLE I Initial Laboratory Findings at the Time of Symptom Onset

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age at Symptom Onset (mo)</th>
<th>Mode of Disease Onset</th>
<th>WBC (×10^3/L)</th>
<th>Neutrophil (%)</th>
<th>ESR (mm/hr)</th>
<th>CRP (mg/dL)</th>
<th>Pathogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>15</td>
<td>Subacute</td>
<td>10.6/35</td>
<td>34</td>
<td>0.33</td>
<td>BCG, Tokyo strain</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>18</td>
<td>Acute</td>
<td>19.1/32</td>
<td>21</td>
<td>0.74</td>
<td>BCG, Tokyo strain</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>25</td>
<td>Subacute</td>
<td>9.0/46</td>
<td>6</td>
<td>0.03</td>
<td>BCG, Tokyo strain</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>21</td>
<td>Subacute</td>
<td>8.3/42</td>
<td>14</td>
<td>0.55</td>
<td>BCG, Tokyo strain</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>20</td>
<td>Acute</td>
<td>12.5/55</td>
<td>21</td>
<td>0.68</td>
<td>M. tuberculosis</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>12</td>
<td>Subacute</td>
<td>9.7/31</td>
<td>16</td>
<td>0.32</td>
<td>M. tuberculosis</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>13</td>
<td>Subacute</td>
<td>9.4/16</td>
<td>2</td>
<td>0.05</td>
<td>M. tuberculosis</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>23</td>
<td>Subacute</td>
<td>8.4/66</td>
<td>40</td>
<td>0.52</td>
<td>Nontuberculous mycobacterium</td>
<td></td>
</tr>
</tbody>
</table>

*WBC = white blood cell, ESR = erythrocyte sedimentation rate, and CRP = C-reactive protein.*
four patients. In the remaining patient, nontuberculous mycobacteriosis was diagnosed; the specific pathogen was not further identified (Table I). In six patients, the lesion was located at the distal femoral epiphysis; in one patient, at the proximal tibial epiphysis; and in one patient, the proximal humeral epiphysis. Six patients (Cases 1, 3, 4, 6, 7, and 8) presented with subacute osteomyelitis characterized by an insidious onset of local symptoms including pain (six patients) and limited joint mobility (four patients), which lasted at least two weeks (range, two weeks to three months) without sudden aggravation of symptoms or systemic signs. The other two patients (Cases 2 and 5) presented with acute osteomyelitis characterized by rapid onset (four days and eleven days, respectively) of knee pain and disease progression with systemic signs, such as fever, malaise, and irritability. Soft-tissue swelling was observed in one patient with acute osteomyelitis (Case 2) at the time of the initial physical examination. Preoperative laboratory findings suggesting the severity of inflammation, such as the leukocyte count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP), were almost within the normal limits for the six patients with subacute osteomyelitis, and only a slight increase in the CRP and leukocytosis was observed in the two patients with acute osteomyelitis (Table I). For six patients, the epiphyseal lesion was identified at the time of presentation on both radiographs and MRI, but for two patients (Cases 1 and 7), the lesion was located at the cartilaginous epiphysis near the secondary ossification center and could be identified only on MRI (Figs. 1-A and 1-B).

Surgery was indicated when the abscess was large enough to necessitate decompression (four patients) and when local and systemic symptoms were not responsive to the empirical antibiotic treatment (four patients). Surgery was performed (by W.J.Y., I.H.C., T.-J.C., and Y.-H.Y.) with antibiotics administration for two patients with acute osteomyelitis, and two patients with subacute osteomyelitis who showed progressed infection and formation of a large amount of abscess in the epiphysis on MRI at the time of initial presentation. Empiric antibiotics were given to the remaining four patients as an initial treatment at a local clinic for at least seventy-two hours, but clinical improvement did not occur. These patients were referred to our hospital. Surgical drainage and curettage of the lesion was performed under C-arm fluoroscopy, with great care not to injure the physis and surrounding normal osteocartilaginous tissue of the epiphysis and metaphysis. A guide pin and then a 4.5-mm reamer were introduced to the center of the lesion directly from the side of the epiphysis. The abscess cavity was curetted and then irrigated gently with normal saline solution with use of a Nelaton catheter.

Postoperatively, all children were put on antimycobacterial combination chemotherapy, instead of ordinary antibiotics, as soon as the causative mycobacterial pathogen was identified by the multiplex PCR assay. A combination regimen of isoniazid,
rifampicin, and pyrazinamide was administered to the three patients with tuberculous osteomyelitis for an average of nineteen months (twelve months, fifteen months, and thirty months, respectively). A combination regimen of isoniazid and rifampicin was given to the four patients with BCG osteomyelitis for twelve months each. A combination regimen of isoniazid, rifampicin, and clarithromycin was administered to the patient with nontuberculous mycobacterial osteomyelitis for eighteen months. However, despite initial surgical drainage followed by medication, all but one patient (Case 7) demonstrated clinical worsening, such as increased swelling and spread of infection outside the epiphysis, enough to develop a subcutaneous abscess collection over time (Table II). Follow-up radiographic evaluation showed that the epiphyseal abscess had increased in size and

<table>
<thead>
<tr>
<th>Case</th>
<th>Metaphyseal Spread Through the Physis</th>
<th>Intra and Extra-Articular Spread</th>
<th>Complications</th>
<th>Follow-up Period (mo)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Present</td>
<td>None</td>
<td>None</td>
<td>33</td>
</tr>
<tr>
<td>2</td>
<td>Present</td>
<td>None</td>
<td>None</td>
<td>17</td>
</tr>
<tr>
<td>3</td>
<td>Present</td>
<td>None</td>
<td>Physal damage</td>
<td>25</td>
</tr>
<tr>
<td>4</td>
<td>Present</td>
<td>Present</td>
<td>Physal damage</td>
<td>16</td>
</tr>
<tr>
<td>5</td>
<td>Present</td>
<td>Present</td>
<td>Physal damage</td>
<td>52</td>
</tr>
<tr>
<td>6</td>
<td>Present</td>
<td>Present</td>
<td>Femoral shortening and valgus angulation</td>
<td>94</td>
</tr>
<tr>
<td>7</td>
<td>Present</td>
<td>None</td>
<td>None</td>
<td>93</td>
</tr>
<tr>
<td>8</td>
<td>Present</td>
<td>Present</td>
<td>Physal damage</td>
<td>64</td>
</tr>
</tbody>
</table>

Figs. 2-A through 2-D images of Case 6, tuberculous osteomyelitis of the distal femoral epiphysis in a boy with symptom onset at the age of twelve months. Fig. 2-A The epiphyseal lesion is located on the lateral aspect of the epiphysis (arrows). Fig. 2-B Despite surgical curettage and combination chemotherapy of isoniazid, rifampicin, and pyrazinamide for three months, the epiphyseal abscess extended to the metaphysis through the physis. Additional surgery for abscess drainage was performed.
extended to the metaphysis through the physis in five patients (Cases 3, 4, 5, 6, and 8). Septic arthritis secondary to the intra-articular spread of infection and abscess formation in the peri-articular soft tissues were found in five patients (Cases 1, 2, 4, 5, and 8) (see Appendix). Surgical drainage was repeated for the five patients who showed spread of the epiphyseal abscess to the metaphysis (Cases 3, 4, 5, 6, and 8). Infection was eventually controlled in all patients, which was determined by the absence of clinical symptoms and stationary or decreased osseous lesion(s) on follow-up radiographs, in addition to the normalization of ESR and CRP.

Follow-up MRI was obtained for the five patients with transphyseal abscess spread to the adjacent metaphysis. Focal physeal damage was evident on MRI in all five patients at follow-up at a mean of 4.1 years (range, 1.3 to 7.8 years). The damaged physeal area was replaced by elongated fatty tissue showing intermediate-to-high signal intensity on T1-weighted images and high signal intensity on T2-weighted images, but osseous bridge was not found in the damaged physeal area (see Appendix). Of the five patients who had physeal damage, one patient (Case 6), who had a focal lesion at the central and lateral portion of the distal femoral physis, demonstrated a genu valgum deformity at follow-up at 6.3 years without a notable leg length discrepancy (Figs. 2-A through 2-D). There was no evidence of limb shortening or angular deformity in the remaining four patients (Cases 3, 4, 5, and 8) at the time of the latest follow-up (2.1 years, 1.3 years, 4.3 years, and 5.3 years, respectively), but they are under close observation for possible later manifestation of growth disturbances.

Discussion

Mycobacterial primary epiphyseal osteomyelitis is a very rare condition, especially in regions without a high frequency of mycobacterial infection, and may be difficult to diagnose. The key to the diagnosis of mycobacterial epiphyseal osteomyelitis is a high index of suspicion, even for children with no complicating medical conditions that cause immunosuppression. Mycobacterium species should be considered as a possible causative pathogen of primary epiphyseal osteomyelitis, especially when infants and toddlers present with a history of BCG vaccination or pulmonary tuberculosis, and when symptoms are unresponsive to treatment with antibiotics. This study highlights that mycobacterial epiphyseal osteomyelitis often has an unfavorable clinical course including physeal damage.

After performing an extensive review of the literature, through a search of studies in English found in the MEDLINE, Embase, and Google Scholar databases, we identified twenty-two reports describing seventy-eight cases of primary epiphyseal osteomyelitis (see Appendix). Pathogens were identified in twenty-nine of the seventy-eight cases; twenty-three were bacterial, five were mycobacterial, and one was fungal. Pathogens
could not be identified in twenty-one cases, and the information on pathogen identification was not available for the remaining twenty-eight cases. In the twenty-three cases with bacterial epiphyseal osteomyelitis, Staphylococcus was the most common pathogen (twelve cases), followed by Streptococcus (five cases), Haemophilus (two cases), Salmonella (two cases), Pseudomonas (one case), and Kingella (one case). Of the five cases with mycobacterial epiphyseal osteomyelitis, three were caused by M. tuberculosis, one by M. bovis BCG, and one by non-tuberculous mycobacterium. Disease onset and progression were recorded in seventy cases; subacute osteomyelitis occurred in sixty-two (89%) of the cases and acute osteomyelitis in the remaining eight (11%) of the cases. One case of mycobacterial epiphyseal osteomyelitis showed a subacute course.

The site of involvement was noted in seventy-three of the previously reported primary epiphyseal osteomyelitis cases. The distal aspect of the femur was the most common site (forty-five cases [62%]), followed by the proximal aspect of the tibia (seven cases), the greater trochanter (seven cases), the proximal aspect of the femur (six cases), the distal aspect of the tibia (three cases), the proximal aspect of the humerus (three cases), the distal aspect of the humerus (one case), and the distal aspect of the radius (one case). Among the cases of mycobacterial epiphyseal osteomyelitis, three involved the distal aspect of the femur; one, the proximal aspect of the femur; and one, the distal aspect of the radius.

Age at symptom onset could be analyzed on the basis of the information from fifty-nine of the previously reported primary epiphyseal osteomyelitis cases; the mean age at symptom onset was 4.1 years (range, seven months to fourteen years). Mycobacterial epiphyseal osteomyelitis occurred at a median age of eight years (range, eighteen months to thirteen years). Our study examined an additional eight cases of mycobacterial primary epiphyseal osteomyelitis, which included three cases of tuberculous osteomyelitis, four cases of BCG osteomyelitis, and one case of nontuberculous mycobacterial osteomyelitis. Six of the cases involved the distal aspect of the femur, one case involved the proximal aspect of the tibia, and one case involved the proximal aspect of the humerus. Symptom onset was noted at a much younger age (median age, nineteen months [range, twelve to twenty-five months]) compared with age noted in the previous studies.

Epiphyseal osteomyelitis caused by bacteria or unidentified pathogen usually has a benign clinical course and heals without long-term complications. Cases of subacute primary epiphyseal osteomyelitis caused by bacteria or an unidentified pathogen can be treated by antibiotics with or without curettage. These infections respond promptly to treatment and heal even in the absence of positive cultures, and long-term complications, such as growth disturbances and joint sequelae, were not reported in any of the previous studies. Similar benign clinical courses of subacute primary epiphyseal osteomyelitis were reported in the studies in which the identification process for the pathogen was not clearly stated.

Acute primary epiphyseal osteomyelitis is reported much less frequently, with only eight cases identified in the literature. Six cases were caused by bacteria and one case, unidentified pathogen. There was no record of the pathogen information in one case. Seven patients were treated with antibiotics or without curettage, while the treatment details were not described for the remaining patient. Infection in these patients also healed well without long-term complications similar to that observed in the subacute cases, although joint involvement was found in four cases.

Primary epiphyseal osteomyelitis caused by mycobacterial species is extremely rare, and only five cases have been reported to date, based on our literature review. One patient with nontuberculous mycobacterial primary epiphyseal osteomyelitis showed a subacute clinical course, but we found no information regarding the clinical course for the remaining four patients. Of the five reported cases, treatment outcomes were noted in three cases; two cases healed well without complications, whereas one patient with BCG osteomyelitis in the femoral head developed a coxa magna deformity and subluxation of the femoral head. In the current study, subacute osteomyelitis occurred in six patients and acute osteomyelitis in two patients. Seven of the eight patients showed clinical worsening with spread of infection outside the epiphysis, regardless of subacute or acute clinical course, and five of them required a second operation. The epiphyseal abscess extended into the metaphysis through the physis with resultant physeal disruption in five patients, and one developed a genu valgum deformity due to partial physeal growth arrest in the distal aspect of the femur. Joint involvement and abscess formation in the periarticular soft tissues occurred in five patients. These clinical features were in sharp contrast with those of the reported primary epiphyseal osteomyelitis cases caused by ordinary bacteria or unidentified pathogens.

MRI has been used to differentiate epiphyseal lesions, but its role has not yet been established in epiphyseal osteomyelitis. In the current study, the epiphyseal lesions in two patients (Cases 1 and 7) were located initially at the cartilage near the secondary ossification center and were not evident on radiographs but were evident on MRI. We believe that MRI was useful in determining the surgical approach because it could clearly demonstrate the localization of the epiphyseal abscess and its route of spread through the physis or epiphyseal opening. Physeal damage was a frequently observed finding in the mycobacterial cases, and replacement of the lesion with fibrofatty tissue without the formation of a bone bridge was well demonstrated on MRI.

The prevalence of tuberculosis in our country is high, and routine BCG vaccination is still practiced for 99% of infants. In this regard, any infant or toddler with a history of BCG vaccination who presented with symptoms and radiographic features suggestive of bone and joint infection underwent single PCR testing to rule out tuberculous infection. If the single PCR test turned out to be positive, then multiplex PCR testing followed to identify the causative mycobacterial pathogen. Fine-needle aspiration cytology yields acid-fast bacilli (AFB) positivity in 28% to 64% of cases, and it can provide adequate histopathologic material for the diagnosis of skeletal tuberculosis. In our series,
surgical biopsy was performed in all cases. We suggest an algorithmic approach to the initial presentation of possible primary epiphyseal osteomyelitis (Fig. 3).

Primary epiphyseal osteomyelitis due to Tokyo-172 BCG vaccination was confirmed in four children. All of these children received BCG Tokyo-172 vaccination, and the same strain was detected in the surgical specimen with use of multiplex PCR assay. Therefore, hematogenous spread of the pathogen from the BCG vaccination site is the likely cause of the primary epiphyseal osteomyelitis. In the remaining four children with primary epiphyseal osteomyelitis due to M. tuberculosis or nontuberculous mycobacteriosis, the portal of entry of mycobacteria remains unclear. No child showed abnormal radiographic findings suggestive of pulmonary tuberculosis on chest radiographs. However, we cannot rule out that the portal of entry may have been through the pulmonary system, because we did not perform computed tomography (CT) or MRI of the chest or perform sputum culture in this series. It has been reported that 50% of patients with tuberculous osteomyelitis have concurrent pulmonary tuberculosis at the time of diagnosis.29

Our initial surgery was aimed at obtaining a pathologic specimen, decompressing the lesion by drainage, and preventing further damage to the remaining intact chondroepiphysis and physis by an enlarging abscess and chronic caseating granulomatous inflammatory tissues. In this regard, surgical drainage and curettage has a role in treating

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**Fig. 3**
Algorithmic approach to a fresh case of primary epiphyseal osteomyelitis. POE = primary osteomyelitis involving only the epiphysis of the long bone, OB = ordinary bacteria, FNAB = fine-needle aspiration biopsy, PCR = polymerase chain reaction, and ESR = erythrocyte sedimentation rate.
mycobacterial primary epiphyseal osteomyelitis. However, it is unclear why children in this series had an unfavorable prognosis despite our initial attempt of drainage and curettage. This may be due to the fact that the lesion was confined to the chondro-osseous epiphysis, which is poorly vascularized and so it would be poorly penetrated by chemotherapeutic agents, and that mycobacterial infection has much slower response to chemotherapy compared with bacterial infection. Moreover, we did not attempt to completely remove the lesion by curettage, for fear of iatrogenic damage to the remaining intact chondroepiphysis and physeis. In that sense, there is a high possibility of transfyseal extension of the lesion due to unresolved mycobacterial infection. However, we think our approach to mycobacterial primary epiphyseal osteomyelitis was moderate, considering the surgical benefits and risks. It should be noted that mycobacterial lesions cannot be completely eradicated by surgery alone, and that medical treatment should be the mainstay of treatment for tuberculosis7.

Certain limitations of this study require consideration. First, the retrospective nature of the study, with a small number of cases, may limit the generalization of our observations. Second, follow-up did not take place until patients reached skeletal maturity, in which case the occurrence of late-onset growth disturbances may have been underestimated. Nevertheless, this study is the largest case series of extremely rare mycobacterial primary epiphyseal osteomyelitis confirmed by molecular methods, and we believe that our cases clearly demonstrated different patterns in terms of the clinical course of the osteomyelitis compared with that of the reported cases of primary epiphyseal osteomyelitis caused by bacteria or unidentified pathogens.

We conclude that mycobacterial primary epiphyseal osteomyelitis tends to have an unfavorable clinical course, in contrast to the reported benign features of primary epiphyseal osteomyelitis caused by bacteria or unidentified pathogens. Physeal damage, which can frequently develop due to spread of infection, and late-onset growth disturbances should be carefully monitored during follow-up evaluations. MRI is useful in the early diagnosis of a cartilaginous lesion, decision-making for the surgical approach, and follow-up evaluation of physeal damage.

**Appendix**

Images of Case 5, tuberculous osteomyelitis of the proximal tibial epiphysis in a girl with symptomatic onset at the age of twenty months, and a table summarizing previously reported cases of primary epiphyseal osteomyelitis are available with the online version of this article as a data supplement at jbjs.org.

**References**