

## Physal Change after Tuberculous Osteomyelitis of the Long Bone in Children

Hsuan-Kai Kao, MD; Wen-E Yang, MD; Hsin-Nung Shih, MD; Chia-Hsieh Chang, MD

**Background:** Tuberculous osteomyelitis of the long bone in children is often neglected, and established transphyseal bone lesions are common. The purpose of this study was to evaluate the clinical outcomes of these patients.

**Methods:** Between January 1990 and December 2008, 19 patients (10 boys and 9 girls) with sustained tuberculous osteomyelitis of the long bone accompanied by physeal involvement were treated at our institute. The average age was 23.8 months (range, 10-58 months). All patients received surgical treatment and antituberculosis therapy for at least 6 months. The final radiographic and functional results were analyzed.

**Results:** All patients were followed up for an average of 61.8 months (range, 14-123 months). The most common site of infection was the distal femur (8 patients, 42.1%), followed by the proximal tibia (5 patients, 26.3%) and the distal tibia (3 patients, 15.8%). Most of the lesions were osteolytic, round to oval in shape, and showed marginal sclerosis. Some lesions were expanding or multiloculated. The periosteal reaction was minimal. Even in cases with extensive surgical curettage through the physis, the growth plate maintained its function and gradually remodeled. Clinical symptoms improved within 4-6 weeks. All bone lesions decreased in size in 3-6 months. Further, physeal bar formation was observed, but the extent was minimal. All transphyseal lesions healed gradually over a period of several years. Good remodeling of skeletal lesions was noted.

**Conclusions:** The diagnosis of tuberculous osteomyelitis of the long bone should be considered in every child with unexplained chronic limb pain or swollen limbs. The lesions are usually located in the metaphysis and easily cross the growth plate to the epiphysis. Surgical debridement is beneficial in both diagnosis and treatment. In patients with growth plate involvement, careful surgical debridement is recommended to eradicate infection since the risk of permanent physeal damage is minimal. The physis can heal gradually, and full range of motion of the adjacent joints can be maintained.

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**Key words:** tuberculous osteomyelitis, osseous tuberculosis, tuberculosis, osteomyelitis

Tuberculosis of the bone is rare in developed western countries, but it remains a serious prob-

lem in many developing countries. Tuberculous infection can affect any bone of the body. In about

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From the Department of Orthopedics, Chang Gung Memorial Hospital at Linkou, Chang Gung University College of Medicine, Taoyuan, Taiwan.

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Correspondence to: Dr. Chia-Hsieh Chang, Department of Orthopedic Surgery, Chang Gung Memorial Hospital at Linkou, 5, Fusing St., Gueishan Township, Taoyuan County 333, Taiwan (R.O.C.) Tel.: 886-3-3281200 ext. 2423; Fax: 886-3-3289582; E-mail: chiahchang@gmail.com

50% of patients, the vertebrae are the sites of skeletal involvement.<sup>(1)</sup> In Taiwan, the overall incidence of childhood tuberculosis is about 9.61/100,000 person-years.<sup>(2)</sup> The incidence of tuberculous osteomyelitis in children is uncommon, and the characteristics are different from those in adults. These lesions usually involve the metaphysis and can cross the physis of long bones.<sup>(3)</sup> The clinical findings are not specific. The only early symptoms are swelling and pain in the involved limbs. Therefore, it is often neglected or the diagnosis is delayed.<sup>(4,5)</sup>

With the introduction of effective multiagent chemotherapy, the requirement of surgical treatment of bone lesions has markedly reduced. Surgical debridement and curettage is indicated for cases with diffuse destruction.<sup>(6-8)</sup> It is well known that injury to growth plates may cause growth disturbance. However, in patients with tuberculous osteomyelitis, even after surgical curettage, the growth plate usually maintains the growth potential and heals gradually. This is very different from the physeal injury caused by trauma or pyogenic osteomyelitis.

It is unclear what extent of destruction by tuberculosis would cause early closure of the growth plate. The literature on this entity is scarce. The purpose of this retrospective study was to review our experience with such patients and to analyze the clinical presentation, growth plate remodeling, and long-

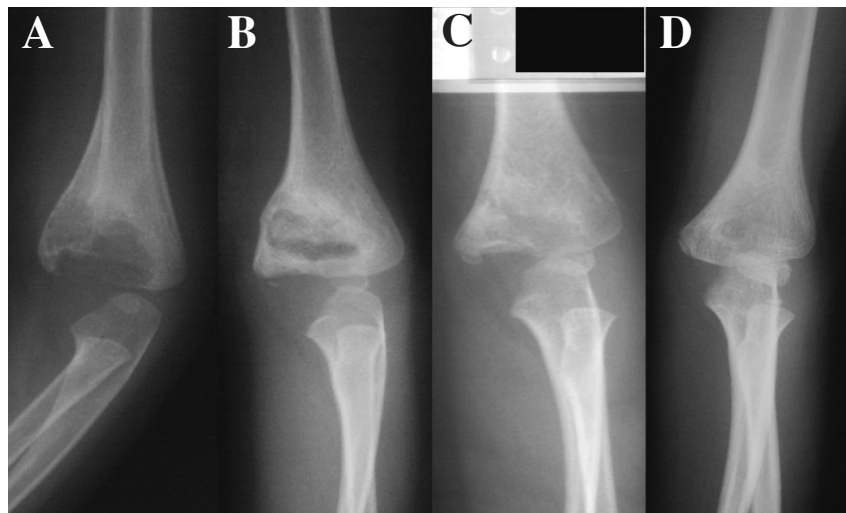
term outcomes.

## METHODS

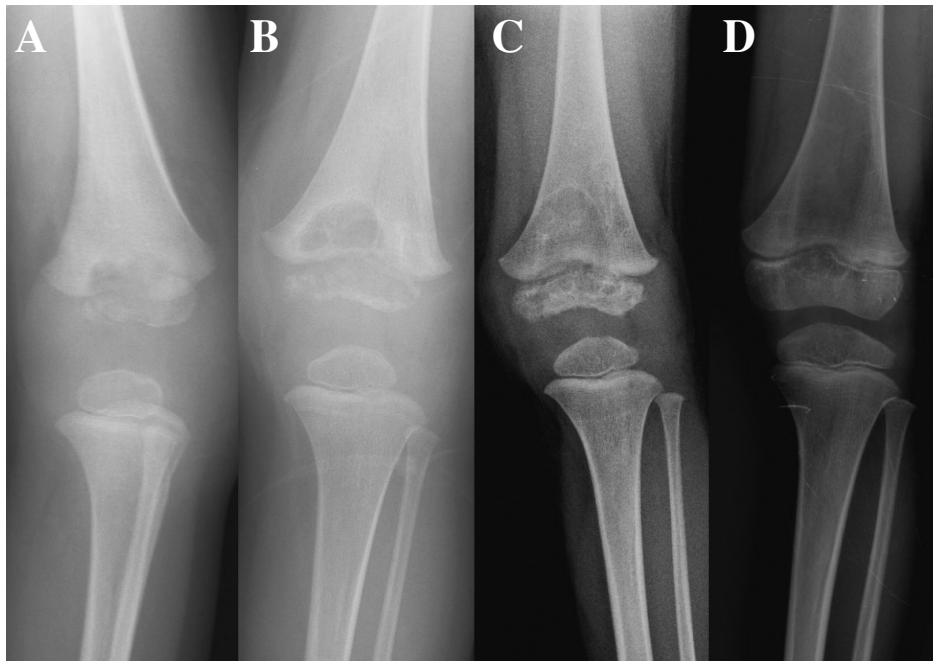
Between January 1990 and December 2008, 19 children younger than 18 years of age with sustained tuberculous osteomyelitis of the long bone with physeal involvement were diagnosed and treated at our institute. Patients with lesions that did not involve long bones or that primarily involved the joint synovium were excluded. The clinical records and radiographs were reviewed for data collection.

There were 10 boys and 9 girls. The children's ages ranged from 10 to 58 months (average, 23.8 months). All patients had been given Calmette-Guérin bacillus (BCG) vaccine in infancy. The chest radiograph and sputum culture for tuberculosis were performed in all patients and all tests showed negative findings. The most often noted clinical features were pain, swelling, tenderness, and limpness. No cases of multifocal lesions or pulmonary tuberculosis were present in our series. The physeal injury was confirmed by plain radiography (n = 16), magnetic resonance imaging (n = 2), and computed tomography (n = 1).

The involved sites were the distal humerus (n = 1, 5.3%) (Fig. 1), the proximal femur (n = 1, 5.3%), the distal femur (n = 8, 42.1%) (Fig. 2), the proximal



**Fig. 1** Case 4: A 21-month-old girl with an osteolytic lesion in the distal humerus. (A) The lesion extends from the metaphysis to the epiphysis. The growth plate is disrupted. (B) Six months after the operation, the lesion is sclerotic, and the growth plate has gradually remodeled. (C) One year after the operation, the growth plate remains uneven. (D) Five years after the operation, excellent remodeling is seen.



**Fig. 2** Case 18: A 24-month-old boy with an osteolytic lesion in the distal femur. (A) The lesion is located in the metaphysis and epiphysis of the distal femur. The growth plate is disrupted. (B) Four months after the operation, the growth plate has remodeled, and the margins of the lesion appear sclerotic. (C) One year after the operation, the lesion is healing gradually. (D) Three years after the operation, good healing is noted, except for a small residual cyst with sclerotic margins.

tibia (n = 5, 26.3%) (Fig. 3), the distal tibia (n = 3, 15.8%), and the distal fibula (n = 1, 5.3%). There was 1 patient with a discharge sinus from the distal femur (case 17). The average duration of symptoms before treatment was 2.4 months (range, 2 weeks to 6 months).

All patients received surgical debridement and curettage. After curettage, an allogenic bone graft was used to fill the bony defect in 2 patients (cases 4 and 7). The other 17 patients did not receive any type of bone grafting. The tuberculosis culture was performed and specimens were taken for pathohistological examination. After operation, oral antituberculosis drugs were administered for at least 6 months. The diagnosis was confirmed by positive acid-fast bacillus (AFB) smears, granulomatous inflammation with or without caseous necrosis in biopsy specimens or isolation of *Mycobacterium tuberculosis*.

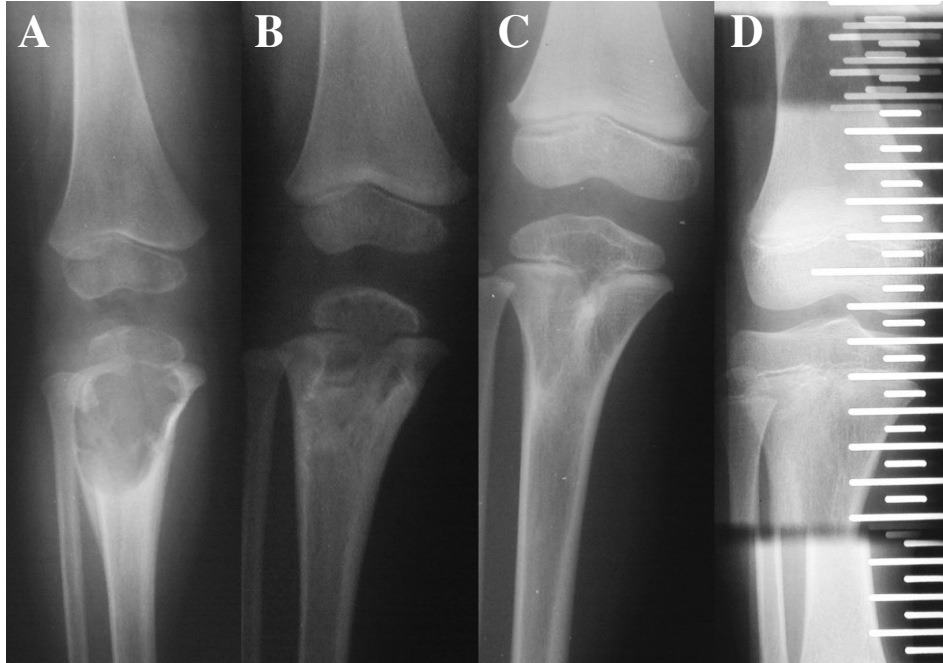
At the time of follow-up, all patients were queried about limb pain, range of motion of the adjacent joint, and any disabilities in the daily activities. All patients underwent routine anteroposterior and lateral radiographic examination of the involved

limbs. The size of the lesions and remodeling of the growth plate were evaluated. If the lesions involved the lower limbs, frontal scanography was carried out for leg-length measurement. A follow-up radiograph was made monthly for 3 months after the operation, then quarterly for 9 months, and annually thereafter. The final radiographic and functional results were analyzed.

## RESULTS

Nineteen patients were followed up for 14 to 123 months (average, 61.8 months). On radiographs, soft tissue swelling and osteopenia were seen in all patients. Most of the lesions were osteolytic, round to oval in shape, and showed marginal sclerosis. Some lesions were expanding or multiloculated. The periosteal reaction was minimal. The lesions were located predominately in the metaphysis and crossed the growth plate to the epiphysis.

The diagnosis was confirmed by pathohistological examination in all patients. *Mycobacterium tuberculosis* was cultured in 8 patients (42.1%) and



**Fig. 3** Case 2: A 23-month-old girl with a massive osteolytic lesion in the proximal tibia. (A) The lesion is located in the metaphysis and epiphysis of the proximal tibia. The growth plate has been disrupted. (B) Four months after the operation, the lesion is healing gradually. (C) Two years after the operation, physeal bar formation is noted. (D) Seven years after the operation, good remodeling is seen, with slight residual sclerosis.

acid-fast bacilli were identified in only 3 patients (15.8%).

There were 4 patients (cases 9, 10, 18, and 19) with sustained relapse of the infection, and surgical debridement was performed again for these patients. No patient received surgery more than twice. Cases 9 and 19 received revision surgery 1 month after the first surgery. They were not administered oral antituberculous drugs after the initial surgery because the diagnosis was unclear. In case 9, *Mycobacterium tuberculosis* was cultured from a specimen obtained from the first surgery; however, this result was obtained after 4 weeks. In cases 9 and 19, the pathohistological examination at the time of the first surgery revealed granulomatous inflammation with necrosis, but antituberculous drugs were not administered until the second surgery. Cases 10 and 18 received revision surgery at 9 months and 5 months, respectively, after the initial surgery. Standard antituberculous drugs were administered after the first surgery but the infection relapsed. The debridement and curettage were more radical in the second surgery. All lesions healed, uneventfully, after the

second surgery.

Lesions crossing the growth plate were also curetted. A large area of the metaphysis and epiphysis were curetted through the growth plate. The extent of physeal destruction was substantial after operation. All bone lesions decreased in size in 3 to 6 months. These lesions healed gradually and the growth plate regenerated over many years. The lesions became smaller and sclerotic during the healing period. Further, physeal bar formation was observed, but its extent was minimal. Eight patients experienced complete healing of the lesions and the other 11 patients showed a residual sclerotic shadow on the radiographs, but without clinical symptoms. The growth plate maintained its function and no growth disturbances occurred. All patients had a full range of motion of the adjacent joints. The clinical details are listed in Table 1.

## DISCUSSION

Tuberculosis is often thought of as an old disease. Because of advances in public health, tubercu-

**Table 1.** Clinical Data of 19 Patients with Tuberculous Osteomyelitis of the Long Bone

Case	Age (months) /Sex	Duration of symptoms (months)	Location	Pulmonary tuberculosis	Pathological confirmation	Culture confirmation	AFB confirmation	Follow-up (months)	Outcome
1	27/F	3	Proximal tibia	N	Y	N	N	123	Complete
2	23/F	6	Proximal tibia	N	Y	N	N	116	Sclerosis
3	40/M	2	Distal tibia	N	Y	Y	N	100	Complete
4	21/F	6	Distal humerus	N	Y	N	Y	98	Complete
5	27/F	2	Proximal femur	N	Y	N	N	76	Complete
6	13/M	1	Distal femur	N	Y	Y	N	67	Sclerosis
7	18/F	1	Distal femur	N	Y	N	N	66	Sclerosis
8	33/M	3	Proximal tibia	N	Y	Y	N	62	Sclerosis
9	31/M	2	Distal tibia	N	Y	Y	N	61	Complete
10	10/M	3	Distal tibia	N	Y	N	Y	57	Complete
11	10/F	0.5	Distal femur	N	Y	Y	N	55	Sclerosis
12	20/F	3	Proximal tibia	N	Y	Y	Y	50	Complete
13	16/M	2	Distal femur	N	Y	N	N	49	Sclerosis
14	14/M	0.5	Proximal tibia	N	Y	Y	N	37	Sclerosis
15	23/F	3	Distal fibula	N	Y	N	N	36	Complete
16	34/M	2	Distal femur	N	Y	N	N	36	Sclerosis
17	58/F	2	Distal femur	N	Y	N	N	36	Sclerosis
18	24/M	0.5	Distal femur	N	Y	Y	N	35	Sclerosis
19	11/M	3	Distal femur	N	Y	N	N	14	Sclerosis

Sclerosis: small sclerotic lesion on radiographs without clinical symptoms.

losis has been well controlled and is now a rare disease in developed countries. However, it remains a serious problem in many developing countries. In 75% of the patients, the focus of the infection is found in the lungs.<sup>(9)</sup> Skeletal tuberculosis is rare and constitutes only 1% to 3% of cases.<sup>(10,11)</sup> Because of the relative rarity of skeletal tuberculosis and non-specific early clinical findings, the diagnosis is usually considerably delayed. In this study, the average duration of symptoms before treatment was 2.3 months (range, 2 weeks to 6 months), which was not longer than that reported by other authors. Teklali et al. reported an average delay in diagnosis of 10 months (range, 10 days to 6 years), indicating the difficulty of making a prompt diagnosis.<sup>(12)</sup>

In this study, chest radiographs of all patients were evaluated and none had lesions of pulmonary tuberculosis. The families of the children were screened and there was only 1 child (case 3) whose grandfather had a history of tuberculosis infection. In the literature, 50% of the patients with tuberculous osteomyelitis have concomitant pulmonary tuberculosis.<sup>(13)</sup> However, in our series, tuberculous osteomyelitis was usually a primary and an isolated

lesion. This finding is consistent with that of Rasool et al. who reported that tuberculous osteomyelitis is rarely associated with pulmonary lesions.<sup>(9)</sup>

In our series, all patients had undergone BCG vaccination in infancy, because this is compulsory in Taiwan. However, BCG vaccination itself can cause osteomyelitis or a disseminated BCG infection.<sup>(14)</sup> The interval between BCG vaccination and disease presentation usually ranges from 5 months to 5 years.<sup>(15)</sup> Polymerase chain reaction was performed for only 1 patient (case 18) in our series at the Taiwan Centers for Disease Control: the test results confirmed BCG infection.

In our 19 patients, the most commonly involved site was the distal femur (8 cases, 42.1%), followed by the proximal tibia (5 cases, 26.3%) and the distal tibia (3 patients, 15.8%). The lower limbs appeared to be common sites of involvement in children, compared with the axial bones and pelvis in adults.<sup>(16)</sup> Most of the lesions were radiolucent, round to oval, with marginal sclerosis. Given its rich vascular supply, the metaphysis of long bones is the most frequent site of infection. In our series, the lesions were predominantly located in the metaphysis and crossed



the growth plate to the epiphysis. There are few reported cases in which the origin of osteomyelitis was in the epiphysis.<sup>(17)</sup> Radiographs of our patients showed that the radiolucent area in the metaphysis was larger than in the epiphysis. The main osteomyelitic lesion was thought to be in the metaphysis. These osteolytic bone lesions can represent benign, malignant, or infectious processes and require a broad differential diagnosis and astute observation for accurate diagnosis and timely treatment.<sup>(18)</sup>

In tuberculous osteomyelitis, positive rates of acid-fast bacillus smears are low. In our series, there were only 3 patients (15.8%) with positive results. Direct smears for acid-fast bacilli are relatively rapid and inexpensive but may produce false-negative results. Stains to identify acid-fast bacilli require the presence of at least 10<sup>4</sup> acid-fast bacilli per milliliter of specimen.<sup>(19)</sup> Isolation of *Mycobacterium tuberculosis* by culture is currently the gold standard for making a definitive diagnosis. This method may take 6 to 8 weeks to yield results and paucibacillary specimens may produce false negative results.<sup>(20)</sup> In our series, *Mycobacterium tuberculosis* was cultured in only 8 patients (42.1%). Because of significant false-negative rates of smear and culture, the materials obtained from the lesions were taken for pathohistological examination. If granulomatous inflammation with or without caseous necrosis was noted within the infectious bones, this would point toward the diagnosis.<sup>(21)</sup> All diagnoses were pathohistologically confirmed in our series. The initiation of antituberculosis treatment at the time of surgery was recommended to decrease the dissemination of disease.<sup>(16)</sup>

Surgical curettage was performed in all patients. The cystic cavity was curetted to remove granulation tissue and pus. Simultaneous curettage and bone grafting of the lesion were suggested by Kumar et al.<sup>(22)</sup> In our series, only 2 patients received allogenic bone grafting. Curettage without bone grafting was performed in the other 17 patients. All of them yielded good results. Resolution and bone remodeling were satisfactory in all patients. Currently, most authors agree that curettage alone is sufficient to yield favorable results.<sup>(3,9,23,24)</sup>

In cases in which the lesions were located in both the metaphysis and epiphysis, the surgery was performed with extreme care. We usually made an incision near the metaphysis and the lesion was

curetted. Then, the epiphysis was carefully curetted through the growth plate. The area of the growth plate injury was more severe after the operation. It is well-known that growth disturbances occur after trauma or disease involving the growth plates. However, the extent of growth plate injury that would cause its permanent injury is unknown. Makela et al. reported that destruction of 7% of the cross-sectional area of the growth plate caused permanent growth disturbance in rabbits.<sup>(25)</sup> The possible mechanism could be that progression of ossification of the epiphysis facilitated the formation of a bridging callus through the growth plate.<sup>(26,27)</sup> The physeal bar (bone extending from the epiphysis to the metaphysis) can cause complete or partial physeal arrest. Osterman et al. reported that growth disturbance could be prevented by bridge resection and filling the defect with a free fat graft.<sup>(28)</sup> Marsh et al. also reported that physeal bar resection could be performed using arthroscopic techniques. Even if up to 70% of the cross-sectional area of the physis was damaged, it could be treated successfully.<sup>(29)</sup>

In our patients, the growth plate damage was great after curettage. The osteolytic lesion healed gradually. The extent of physeal bar formation was minimal. The growth plate maintained its function and the remodeling process went on for many years. The length of the involved lower limb was equal to that of the opposite limb. Ohtera et al. reported that large lesions of the proximal tibia could be fully recovered.<sup>(30)</sup> In our series, not only the proximal tibia but also the distal humerus, distal femur, distal tibia, etc., yielded good results.

This study had several limitations. First, the patients in this study were not followed to skeletal maturity. Although the lesions showed good healing by the end of the investigation, we were unable to determine if any residual deformity was present when the patients achieved skeletal maturity. Second, most of the patients in this study underwent spot scanography examination instead of split scanography examination. We were unable to assess the mechanical axis and anatomical axis of the lower limbs. Third, with regard to the lesions that involved the upper limbs, we did not measure the limb length or angular deformity. The sequelae of tuberculous osteomyelitis in the upper limbs may be underestimated. Last, the number of patients in this study was small, and we could not identify significant factors

related to outcome.

In conclusion, orthopedic surgeons must consider tuberculous osteomyelitis in the differential diagnosis of bone infection. Low suspicion will result in delayed diagnosis and delayed treatment. The lesions are usually located in the metaphysis and easily cross the growth plate to the epiphysis. Surgical debridement is beneficial in both diagnosis and treatment. In cases of growth plate involvement, careful surgical debridement is recommended to eradicate the infection since the risk of permanent physeal damage is minimal. The growth plate can heal gradually, and the patients usually retain good function of the adjacent joints.

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## 兒童長骨結核性骨髓炎後生長板的變化

高軒楷 楊文一 施信農 張嘉獻

- 背景：** 兒童長骨的結核性骨髓炎經常被延遲診斷而造成病灶侵犯生長板。本研究的目的是分析這些生長板被侵犯的病患當初的症狀、接受的治療及最後的結果。
- 方法：** 從 1990 年到 2008 年，共有 19 位長骨結核性骨髓炎合併生長板侵犯的兒童在本院接受治療，平均年紀為 23.8 個月。所有的病患都有接受清創手術及至少六個月的抗結核菌藥物治療。其中 2 位病患於手術中有接受自體骨移植，其餘 17 位病患則無。最後分析生長板恢復的情形及鄰近關節的功能。
- 結果：** 19 位病患追蹤了 14 至 123 個月 (平均 61.8 個月)。最常受侵犯的位置是遠端股骨 (8 位, 42.1%)，接著是近端脛骨 (5 位, 26.3%)，接著是遠端脛骨 (3 位, 15.8%)。大部分的病灶都是骨溶解性的，圓形或橢圓形，邊緣有鈣化的現象。清創手術經常需要穿過生長板，而造成生長板進一步的傷害。而即使是接受大範圍的清創手術，生長板仍然可以保有生長的功能，逐漸恢復正常。
- 結論：** 若兒童有不明原因的肢體疼痛或腫脹，都應該把結核性骨髓炎列入鑑別診斷中。這種病灶經常發生在長骨的幹骺端，它很容易會穿過生長板而侵犯到骨骺端。外科手術對於診斷及治療是有幫助的。我們建議可以進行徹底的清創手術，即使手術本身會造成生長板破壞範圍變大，但永久性的生長板傷害是很少發生的。即使生長板有接受大範圍的刮除，它仍然可以逐漸復原，附近的關節仍然保有良好的功能。  
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**關鍵詞：** 結核性骨髓炎，骨結核，結核病，骨髓炎

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長庚醫療財團法人林口長庚紀念醫院 骨科；長庚大學 醫學院

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通訊作者：張嘉獻醫師，長庚醫療財團法人林口長庚紀念醫院 骨科部。桃園縣333龜山鄉復興街5號。

Tel.: (03)3281200轉2423; Fax: (03)3289582; E-mail: chiahchang@gmail.com