Chondro-Osseous Growth Abnormalities after Meningococcemia

A Clinical and Histopathological Study*

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ABSTRACT: **The cases of nine children who survived the acute stage of meningococcal septicemia and secondary disseminated intravascular coagulation were reviewed. All of the children had major orthopaedic problems as a result of the acute disease. Detailed histological studies were performed on specimens of bone and cartilage, obtained when these patients had either acute amputation for gangrene or subsequent revision for a chondro-osseous deformity.**

In the specimens that were obtained from the children who had acute gangrene, the histological changes included small-vessel thrombi, osteonecrosis, subperiosteal new-bone formation, cortical disruption, cellular disorganization in the physis, and medullary inflammation. These findings were compatible with a combination of inflammation (acute osteomyelitis) and ischemia.

In the specimens that were obtained during revision of the amputation, three years or more after the initial infectious or ischemic process, the clinically relevant findings involved the epiphyses and physes. The growth plates showed variable permanent ischemic damage. Bone bridges connecting the epiphysis and metaphysis were observed in various stages of formation, including several early bridges with involvement of only the physis and metaphysis. Endosteal and cortical bone, in contrast, showed complete recovery with no evidence of permanent ischemic damage.

We concluded that children who survive meningococcal septicemia are at high risk for complex orthopaedic problems, both acute and chronic. The disseminated intravascular coagulation and focal infections of the acute phase are primarily responsible for the vascular injuries to the growing chondro-osseous tissues. Ischemic changes also selectively involve the physeal circulation, but may take several years to adversely affect longitudinal and transverse growth of bone.

Meningococcemia associated with disseminated intravascular coagulation is a life-threatening illness. While improved medical management has considerably enhanced the rate of survival for affected children, the rate of mortality may still be as high as 15 to 20 per cent[7,10,12,24]. Diffuse vasculitis, thrombosis, hemorrhage, and necrosis may occur in any organ system, including the skeleton[7,24]. Children who survive often are left with long-term sequelae, particularly the effects of the vascular injuries.

Several case reports have documented the clinical and radiographic findings that are associated with the vascular insults to the developing skeleton; these findings have included radiographic irregularities in the epiphysis or metaphysis; physeal injuries, such as angular deformity, premature closure, and physeal bars; and limb-length discrepancy[1,2,4,6,8,16-21,23]. Amputation is common for severe, acute injury to the chondro-osseous and contiguous soft tissues[2,3,5,9,11].

We followed the cases of nine patients who survived an acute episode of meningococcemia and had an array of orthopaedic problems. Specimens of chondro-osseous tissue were obtained from these patients in both the acute and chronic phases of the disease. The microvascular (ischemic) and inflammatory (infectious) nature of the acute disturbances to bone and cartilage and the microvascular nature of the chronic damage to the physeal cartilage were documented. To our knowledge, this is the largest published series of patients who had musculoskeletal sequelae of meningococcemia, and the first in which the associated histopathological manifestations have been documented.

Materials and Methods

Clinical

The study comprised nine children who ranged in age from one month to fifteen years when the disease first developed (Table I). Four of the children (Cases 1, 2, 3, and

* No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article. No funds were received in support of this study.

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TABLE I

CLINICAL DATA

Case	Age at Onset of Acute Disease (Yrs. + Mos.)	Sex	Acute Amputation*	Reason for Referral	Age at Referral (Yrs.)	Age at Last Follow-up (Yrs.)	Operation during Follow-up†				
							Stump Revision†	Reamputation	Osteotomy	Excision of Bar	Other
1	2 + 9	M	Bilat. BKA	—		8	See text				
2	1	M	Bilat. BKA; all R fingertips	—		7	Bilat. BKA (1)		Prox. end of R tibia (4)	Prox. end of R. tibia (4)	Capping of dist. end of tibia with prox. end of fibula (2)
3	4 + 6	F	R BEA	—		13	R BEA (5)				Epiphyseodesis, dist. end of L femur (10)
4	15	F	Bilat. transmetatarsal	—		25		Bilat. transmetatarsal to tarsometatarsal (15)			L talocalcaneal arthrodesis (23)
5	4	M	Bilat. BKA; bilat. BEA	Prosthetic fitting	7	10	See text				
6	1 + 10	F	None	Limb-length discrepancy; valgus, L knee	5	14			Prox. end of L tibia (6) Prox. end of L tibia (7) Prox. end of L tibia (9) Dist. end of R tibia (10)	Prox. end of L tibia (6) Prox. end of L tibia (7)	Epiphyseodesis, dist. end of L fibula (3) Epiphyseodesis, dist. end of R tibia and fibula (5)
7	0 + 1	M	None	Valgus, R knee	2	13			Dist. end of R femur (5) Prox. end of L humerus (11)	Dist. end of R femur (5)	Epiphyseodesis, prox. end of L humerus (11)
8	1 + 5	F	R AKA; L BKA; R ring fingertip	Valgus, L knee	3	8	L BKA (2,3,5)		Dist. end of L femur (5)	Dist. end of L femur (5)	
9	1 + 4	F	R foot, fifth ray	Limb-length discrepancy; varus, R knee	7	10			Dist. end of L tibia (8)	Prox. and dist. end of R tibia (4) Dist. end of L tibia (8)	

* BKA = below-the-knee amputation, BEA = below-the-elbow amputation, and AKA = above-the-knee amputation.
† Numbers in parentheses = age in years.

4) were treated by one of us (J. A. O.) during both the acute illness and subsequently and were followed to the time of writing. The other five children were seen, in three Shriners Hospitals, for orthopaedic problems that developed months to years after the acute disease. The details concerning the acute phase of the disease in these five patients were obtained from records of other hospitals. The reasons for referral included the need for fitting a prosthesis (Case 5), angular deformity and limb-length discrepancy (Cases 6 and 9), and angular deformity alone (Cases 7 and 8).

Eight of the nine children were less than five years old when the meningococcemia initially developed; they were still under our care at the time of writing. The ninth patient (Case 4) was fifteen years old; she was the only patient who had follow-up beyond skeletal maturity.

Illustrative Case Reports

CASE 1. Meningococcemia with disseminated intravascular coagulation developed in this boy when he was two years and nine months old. He was hospitalized for seventy-two days. Gangrene developed in both legs, necessitating mid-diaphyseal below-the-knee amputations. Each amputation had to be revised acutely because of continued necrosis of the skin and muscles. Eventually the wounds were closed with multiple split-thickness skin grafts.

Four months after he was discharged from the hospital, the child needed a revision of both amputation sites for distal overgrowth of bone and continued problems with coverage of the skin.

Progressive deformity of the proximal part of the left tibia became evident one year after the acute disease, secondary to premature closure of the physis of the tibial tuberosity. An anterior osseous bar acted as a tether to cause bowing of the proximal part of the tibia. The normal posterior inclination of the proximal articular surface of the tibia diminished progressively, so that the epiphysis of the proximal part of the tibia actually dislocated behind the femoral condyles (Figs. 1-A and 1-B). Because of the deformity and persistent problems with wear of a prosthesis over scarred soft tissues, a disarticulation at the knee was done three years after the acute disease. Closure of the lateral aspect of the growth plate of the distal part of the right femur by an osseous physeal bar caused progressive valgus deformity of the distal end of the right femur (Fig. 1-C). Resection of the physeal bar and osteotomy were done to realign the limb.

At the most recent follow-up, at the age of nine years, the boy walked well with bilateral prostheses, but he had persistent problems with the soft tissues of the right leg and may need a disarticulation at the right knee. A recent test for human immunodeficiency virus was positive; this can be attributed to the transfusions that were necessary at the time of the acute disease.

CASE 5. A four-year-old boy who had meningococcal septicemia and disseminated intravascular coagulation was hospitalized for fifty-eight days. Ischemia and gangrene developed in all four extremities. He had bilateral amputations of the forearm just distal to the elbow and of both legs distal to the knee. Multiple débridements, revisions, and skin-coverage procedures were necessary in the acute stage of the disease.

Chronic problems with the soft tissues of both legs delayed the functional use of prostheses. The child had a disarticulation at each knee, three

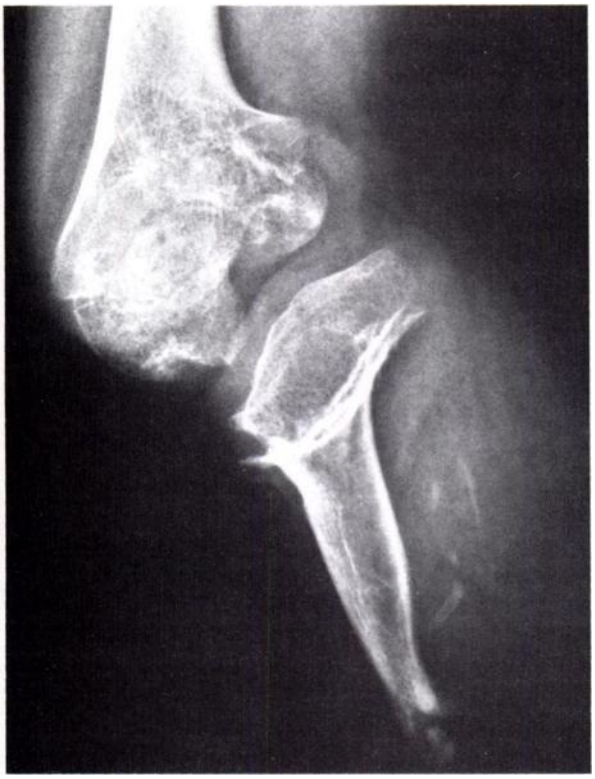

FIG. 1-A

Figs. 1-A, 1-B, and 1-C: Case 1.
Fig. 1-A: Anteroposterior radiograph of the left knee, made at the age of five, showing a severe irregularity of the distal end of the femur and angulation of the proximal tibial physis.

and four years after the acute disease. Because of overgrowth of bone and problems with coverage of the skin, a revision of the amputation of the left forearm was done.

At the latest follow-up, at the age of ten years and five months, the patient could walk using bilateral knee-disarticulation prostheses, and he was receiving physical therapy and rehabilitation services.

Histopathology

Amputation specimens, obtained from six to fifteen days after the onset of the disease, were examined to assess the effects of the acute phase of the disease. The specimens included four legs after below-the-knee amputations, two toes, one distal part of the forearm and hand after a distal amputation of the forearm, and three fingers. Specimens for cultures were obtained from the marrow of the below-the-knee amputation specimens.

Specimens also were examined to assess the effects of the chronic phase of the disease, three years or more after the initial meningococcemia. Three remnants were obtained from the proximal part of the tibia after conversion of a below-the-knee amputation to a disarticulation at the knee, and one radio-ulnar segment was obtained from a revision of a below-the-elbow amputation. Each specimen was examined both radiographically and histologically.

Results

Clinical

As already mentioned, all nine patients had an array of skeletal lesions and deformities when they were seen by us for treatment. All had radiographic evidence of multiple physeal disturbances (Fig. 2). Thirty-two bones were observed to have had major injury to the physis, manifested as either partial or, less commonly, total premature closure. The partial premature closures were always associated with progressive angular deformities, some of which needed sur-

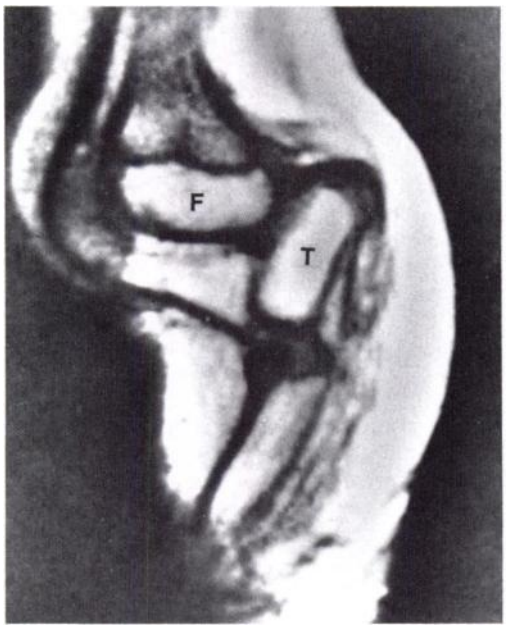

FIG. 1-B

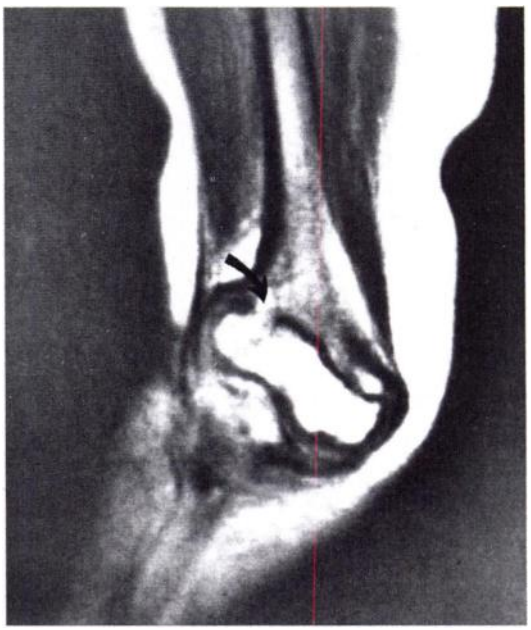

FIG. 1-C

Fig. 1-B: Magnetic resonance image, made in the sagittal plane, showing the relationship between the distal femoral epiphysis (F) and the proximal tibial epiphysis (T). The proximal tibial epiphysis has progressively migrated nearly 90 degrees from its original horizontal position, due to injury to the anterior aspect of the growth plate at the tibial tubercle. (The histological appearance of this area is seen in Figs. 5-B and 5-C.)
Fig. 1-C: Magnetic resonance image of the right residual limb, made in the coronal plane after below-the-knee amputation. A physeal bar (arrow) is seen in the lateral aspect of the distal femoral growth plate, and there is resulting valgus deformity.

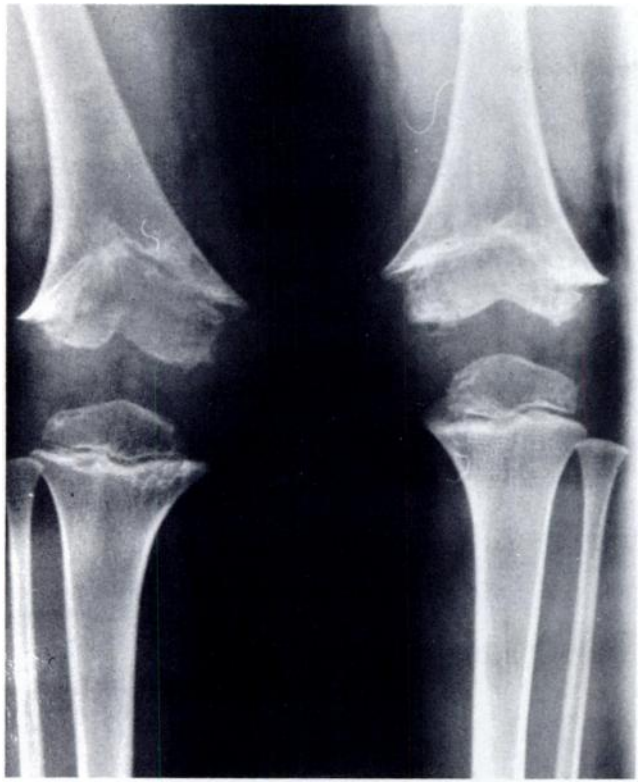

FIG. 2

Case 7. The anteroposterior radiograph of both lower limbs shows injury to the growth plates at the distal ends of both femora and the proximal parts of both tibiae. These growth plates were thought to be unaffected for four years after the acute disease. The distal aspect of the right femur had a progressive valgus deformity that necessitated excision of the physeal bar and a corrective osteotomy when the child was five years old.

gical correction (Table I). Clinically important shortening (more than 2.5 centimeters) was present in three limbs (Cases 3, 7, and 9). At least two of these patients (Cases 3 and 9) will be future candidates for limb-lengthening.

The anterior portion of the growth plate in the proximal part of the tibia showed signs of involvement and premature closure in four patients (Cases 1, 2, 5, and 9). Progressive growth disturbance in this region produced a recurvatum deformity of the proximal part of the tibia, including the articular surface, that created cosmetic and functional problems and necessitated surgical intervention. In one patient (Case 1), the deformity progressed to the point that the left proximal tibial epiphysis turned 90 degrees and subluxated behind the distal end of the femur (Figs. 1-A and 1-B). The right tibia was duplicating this process at the time of writing.

A bone bridge was identified and was surgically excised in seven growth plates (six patients). Only four of these excisions were considered successful.

Seven of the nine patients needed at least one amputation, for a total of twenty amputated limbs. Acutely, there were three below-the-elbow amputations (Cases 3 and 5), one above-the-knee amputation (Case 8), seven below-the-knee amputations (Cases 1, 2, 5, and 8), two transmetatarsal amputations (Case 4), and seven amputations of one or more fingers or toes (Cases 2, 8, and 9). All of the amputations needed at least one surgical revision during either the acute or chronic stage of the disease, and most needed more than one. In the acute stage, revision was needed for progressive ischemic changes in the soft tissues, while in the chronic stage, it was usually done because of overgrowth of bone or problems with soft-tissue coverage. Three below-the-knee amputations (Cases 1 and 5) were converted to a disarticulation at the knee, and another such operation (Case 1) was planned. The two transmetatarsal amputations (Case 4) needed conversion to tarsal-metatarsal amputations. Skin loss necessitating grafting in areas other than the sites of the amputations occurred during the acute stage in four patients (Cases 4, 6, 7, and 9). Some of these grafts were revised in the follow-up period.

All six patients who needed prosthetic devices had problems related to them, because of the extensive soft-tissue deficiency accompanying the skeletal injury. The loss of healthy muscle, fat, and skin was addressed by split-thickness skin-grafting, but the skin became densely adherent to underlying bone and did not withstand the rigors of prosthetic wear very well.

Histopathological

Acute Phase

All of the specimens showed diffuse involvement secondary to a combination of intravascular coagulopathy and acute inflammation from the meningococcemia (all specimens were positive for *Neisseria meningitidis* on culture).

FIG. 3-A

Figs. 3-A, 3-B, and 3-C: Case 1.

Fig. 3-A: Proximal end of the amputation specimen that was obtained six days after the onset of the disease. The patient had previously had a débridement of gangrenous toes and areas of cutaneous gangrene. Note the elevated subperiosteal new bone (white arrow) and cortical erosion (black arrow).

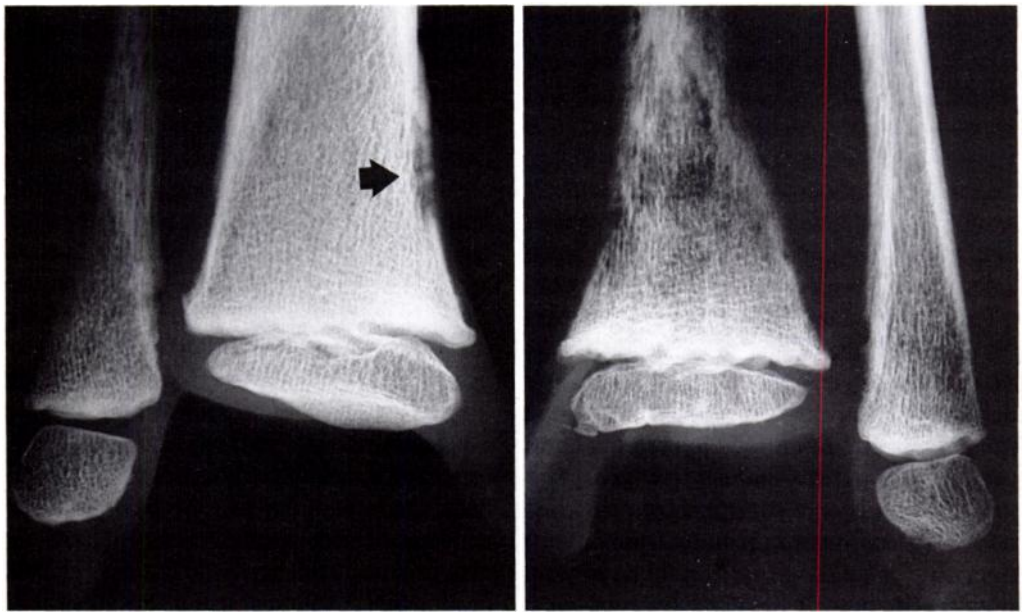

FIG. 3-B FIG. 3-C

Anteroposterior radiographs of amputation specimens obtained from the right (Fig. 3-B) and left (Fig. 3-C) sides, showing erosion of the cortices (arrow) due to inflammatory destruction. One side was more seriously involved than the other.

This led to major histological changes that variably involved the medullary cavity, diaphysis, metaphysis, epiphyseal ossification center, cartilage-canal system, and physis.

Figures 3-A, 3-B, and 3-C show extensive subperiosteal new-bone formation with multiple erosions of the original diaphyseal cortex. In the medullary cavity, there was loss of cellular components in and around the trabecular bone, and extensive but highly variable inflammatory-tissue response in the trabecular spaces, replacing many of the normal marrow elements. Some of the small vessels in the trabecular regions were occluded, and there was perivascular inflammation. The areas of the subperiosteal space that did not show active new-bone formation often had areas of fibrinopurulent exudate that elicited cortical erosion and elevation of the periosteum.

Vascular involvement also was variable, especially in the cartilage-canal system (Fig. 4). There were some areas of uninvolved cartilage canals, but nearby canals sometimes contained exudate that filled the extravascular space and caused occlusion of the vessels, without a marked cellular inflammatory response. Other areas showed vascular thrombosis with occlusion of the vessels. The involved vessels were particularly associated with the germinal zone of the physis or with the periphery of the unossified cartilage. In areas with extensive involvement, occlusion from intravascular thrombosis and perivascular cellular inflammation were both present.

The acute lack of vascularity evidently had an effect on the physis, which showed variable damage, manifested mostly by separation of columns of cells. The disease had been active for six to fifteen days before amputation was performed. Involvement was variable, and some areas that were a few millimeters away from the cellular separations did not exhibit the same disruption of columns of cells.

Chronic Phase

One of our major objectives in studying the specimens that were obtained several years after the onset of the disease was to assess the effects of long-term ischemia on chondro-osseous growth, including the formation of bone bridges.

Each of the three tibial specimens showed evidence of arrested growth. The specimen from the proximal aspect of

FIG. 4

Cartilage canals between the growth plate and the secondary ossification center of the distal aspect of the tibia are filled with fibrinous clot (arrow), and the vessels are totally occluded (× 20).

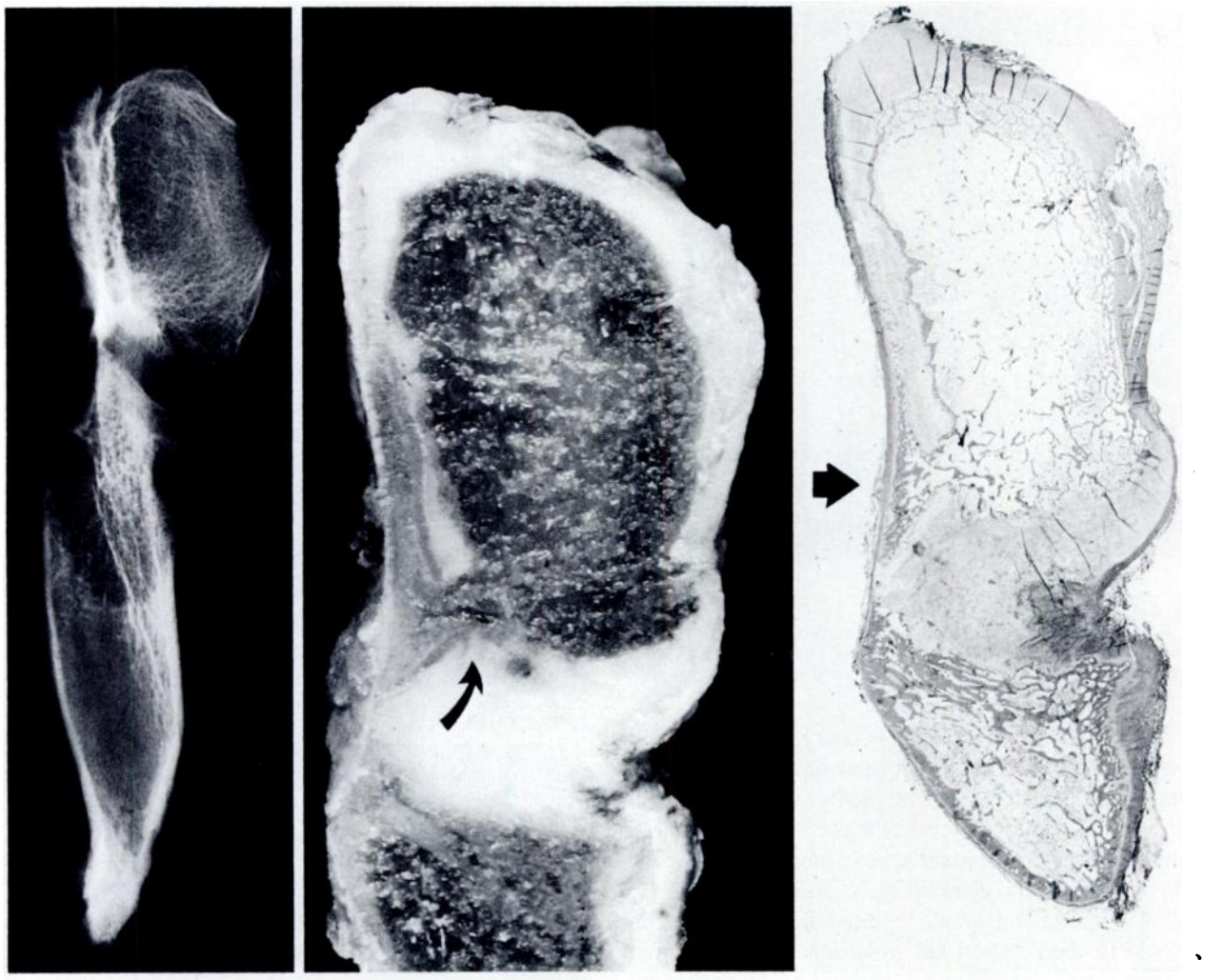

FIG. 5-A FIG. 5-B FIG. 5-C

Figs. 5-A, 5-B, and 5-C: Case 1.
Fig. 5-A: Lateral radiograph of the proximal aspect of the same tibial specimen as in Figs. 3-A, 3-B, and 3-C, showing sclerotic anterior growth arrest. The proximal tibial ossification center has rotated 90 degrees in the lateral plane, with the articular surface now facing directly forward.
Fig. 5-B: Slab section in the lateral plane, showing the fibrinous and fibrocartilaginous nature of the articular surface, a bone bridge (arrow), and blending of the peripheral cartilage into the underlying metaphysis.
Fig. 5-C: Section showing formation of a bone bridge and continuation of the secondary ossification center along the posterior margin (arrow).

the tibia (Case 1) demonstrated growth arrest of the anterior portion of the proximal tibial physis. The entire epiphysis and physis had turned 90 degrees, with the articular surface facing anteriorly. The radiolucent gap was filled with cartilage and fibrous tissue (Figs. 5-A and 5-B). Histologically, most of the proximal tibial physis was situated behind the epiphysis, superior to the bone bridge of the growth arrest. The epiphysis was oriented at a right angle to the longitudinal axis of the tibia (Fig. 5-C); however, the cartilage cells that were not directly adjacent to the bone bridge were active, with limited formation of columns of cells. The articular surface was covered with a densely adherent fibrous pannus. This pattern of loss of articular cartilage was evident in all of the tibial specimens that were obtained by disarticulation at the knee.

A change in the contour of the growth plate was noted in three specimens from the proximal part of the tibia (Fig. 6-A). The physis was severely undulated, in contrast to the normally relatively flat appearance. A linear sclerotic region (Case 5) proved to be a linear extension of this undulating physis, comparable to an enchondroma (Fig. 6-B). The area of the physis that was associated with this change was devoid of cartilage canals. This infarcted region of the physis had, in effect, been left behind as the remainder of the physis grew away from it.

Another specimen from the proximal part of the tibia (Fig. 7) showed early central growth arrest and a 90-degree turn of the physis medially. Under high-power magnification, an osseous core with a thrombosed vessel was seen in the area of growth arrest. The physis had lost all of its cell-column formation, in contrast to the contiguous areas.

Discussion

Meningococcemia is a devastating illness that primarily affects children. Although the rate of survival has dramatically increased due to improved acute medical manage-

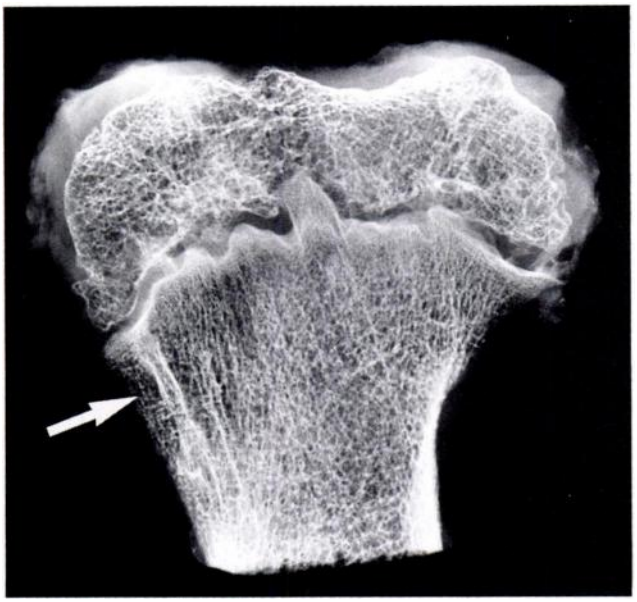

FIG. 6-A

Figs. 6-A, 6-B, and 7: Case 5.
Fig. 6-A: Radiograph of the slab section of the proximal end of the tibia, showing the irregular undulation of the proximal physeal growth plate and a longitudinal linear density (arrow) on the lateral side.

ment[7,24], the victims of the disease continue to have major long-term sequelae. Previous reports described presumed ischemic complications in the acute stage of meningococcemia[1-8,16,18,20,23]. Several of these authors postulated that the subsequent abnormalities of growth were probably due to microvascular disruptions, especially in the physis[1,8,16,18,23]. Trueta and Amato reported that physeal disruption could be the result of selective ischemia. The current study documents these acute and chronic ischemic changes, which were previously only conjecture based on radiographic appearances.

Neisseria meningitidis contains a lipopolysaccharide in its cell wall that acts as an endotoxin to elicit an acute inflammatory response[7,24]. This endotoxemia may initiate diffuse vasculitis and disseminated intravascular coagulation. Hemorrhage and necrosis in all of the organs have been described, with leukocyte-rich fibrin thrombi and vasculitis involving the small vessels[7]. *Neisseria meningitidis* has often been seen in the endothelial cells and in the neutrophils surrounding damaged vessels[24]. Only recently, however, have the clinical effects on the skeletal system of surviving children been well appreciated.

In the acute phase of meningococcemia, two pathophysiological processes interact. First, there is a vascular occlusive process that renders bone and cartilage variably ischemic. All areas of the developing skeleton — the diaphysis, metaphysis, physis, and epiphysis — are involved, but variably, suggesting multiple foci, much like the equally spotty pattern of damage to the skin, subcutaneous tissue, musculature, and internal organs that is seen in these patients.

The most striking finding is the consistent involvement of the small blood vessels in the bone and cartilage of the metaphysis, the physis, and the epiphysis. These blood vessels become thrombosed with fibrinous material that most commonly obliterates the lumen of the vessel entirely. The walls of the vessel are thickened and edematous. Small areas of necrotic bone are associated with these vessels, especially when there has been time for the changes to become recognizable. Vacuolization in the bone, particularly on the metaphyseal side of the epiphyseal plate, is often observed.

Second, and more importantly, a discrete inflammatory response is evident in the trabecular bone of the marrow space and in the subperiosteal space. Abscesses form in the metaphyseal loop area, similar to the lesions that are seen in acute hematogenous osteomyelitis in the neonatal stage[13].

Both acute and chronic orthopaedic problems can be anticipated in children who have this disease. The hemorrhagic lesions, which result in major areas of necrosis and loss of skin, are the most common manifestations related to the extremity. Gangrene of a portion of the extremity necessitates surgical débridement or amputation, or both. The lower extremities are more often involved with the disease than are the upper extremities.

Seven of our nine patients lost at least some portion

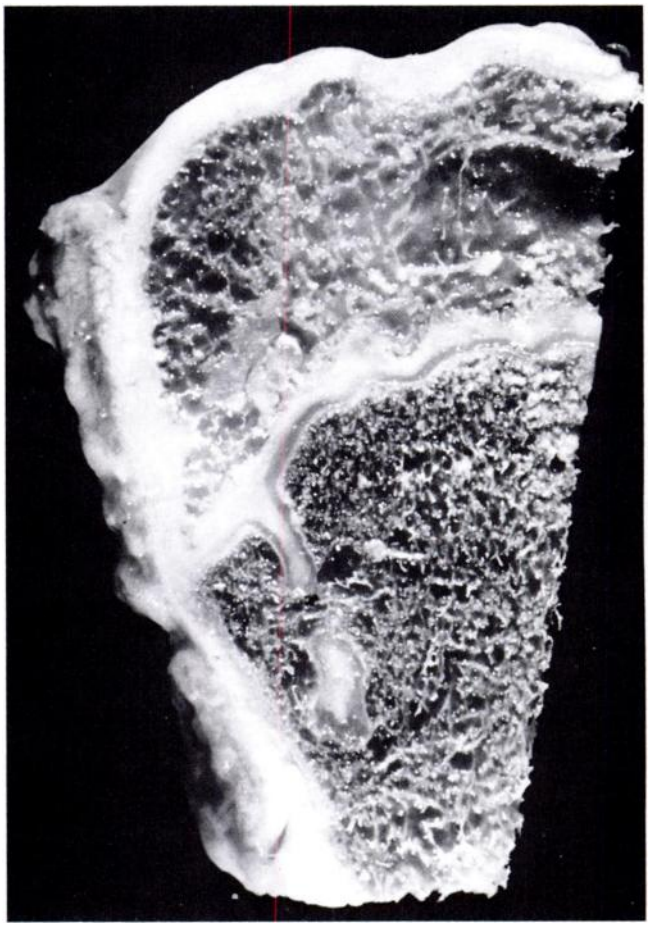

FIG. 6-B

Slab section of the region of lateral density, showing an enchondroma-like structure extending from the physis; it was left behind as the remainder of the physis grew away from it.

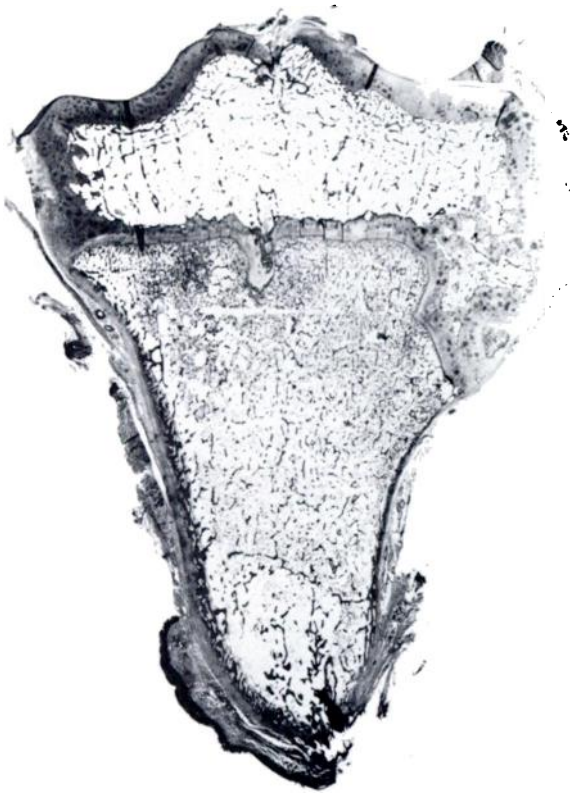

FIG. 7

Anteroposterior section of the proximal end of the tibia. The small area of growth arrest centrally and the large area medially resulted in this section of the physis turning at a right angle. This is associated with irregular ossification and is similar to some of the tissue changes that are associated with Blount disease. A central bone bridge in an early stage of formation is visible (arrow).

of an extremity, ranging from a single fingertip to major loss of all four extremities. Very often, multiple débridements and amputations at progressive levels are needed. Certainly, allowing the level of amputation to become demarcated before amputation is prudent, but the decision as to level must take into consideration the requirements for soft-tissue coverage of the injured limb, the natural history of amputation at any of several levels in the pediatric (skeletally immature) population, and the degree of involvement in the other extremities and the organ systems. We agree with Canale and Ikard that the amputation should be left open and delayed closure performed, and that the digits should be allowed to autoamputate. The level of amputation that resulted at the end of the acute disease was not the subsequent level in seven limbs in our series. Limbs that had below-the-knee amputation, in particular, did not do well. Because of continued problems with overgrowth of bone and with soft-tissue coverage (such as deficient or scarred skin, or loss of muscle coverage), or because split-thickness skin grafts did not ultimately stand up to wear of the prosthesis, three extremities had conversion to a disarticulation at the knee, and conversion was planned for one to three more knees. Above-the-knee amputations were less common in our patients, but in one patient a revision was needed at this level for reasons that were already mentioned. Revision of the below-the-elbow stump was done in two patients.

Diaphyseal and metaphyseal amputations present problems in children, particularly those who have the added problem of soft-tissue involvement in the ischemic process. In the current series, difficulty often was encountered acutely, relative to the requirements of skin coverage, and chronically, with fitting of the prosthesis. Although we would not advocate a higher level than is absolutely necessary for the initial amputation, so as to handle less involved tissues, it should be kept in mind that reamputation may be needed. This possibility is important, particularly when the parents are instructed regarding future treatment.

Damage to the growth plate may become evident in several ways[13]. Irregularities of the physis may be seen radiographically shortly after the illness. These may persist as radiographic abnormalities representing focal areas of ischemia at the growth plate, due to thrombosis of small vessels; or, if large enough, they may represent major physeal damage capable of leading to further physeal and metaphyseal abnormalities and, usually, to growth arrest. A survey of the appearance and activity of the growth plates, either radiographically or by bone-scanning, within several months after the child's recovery, will provide a baseline that can be used to help predict areas of concern before a major clinical deformity develops. Skeletal surveys or bone scans should be made annually, or more frequently, as needed, to monitor any important changes. Areas that appear minimally involved or functionally normal may worsen during the growth spurt of adolescence. Five of our patients had not yet reached adolescence. In the one (Case 3) who had, however, a valgus deformity developed rapidly in a knee that had shown little previous evidence of damage radiographically. Anticipating problems and treating them early may lessen the extent of deformity. The deformities that developed in our patients who had serial radiographic evaluations were often less dramatic and more easily treated than those that were neglected.

One type of disturbance of the growth plate in our patients was comparable with that produced experimentally by Trueta and Amato[15,22]. Premature closure of the physis due to a presumed vascular injury to a portion of the plate was observed radiographically in thirty-two bones. Focal injury to the growth plate often led to the development of an osseous physeal bridge. Treatment of such a bridge must be based on its size, its effect on growth, and the appearance of the remainder of the growth plate[14]. In our patients, several bridges were in a physis that appeared radiographically to be diffusely injured by the acute disease; these bridges, therefore, would probably be less likely to respond to resection. This more diffuse physeal damage and delayed physeal bridging is not uncommon when osteomyelitis occurs in a young child[13]. Seven physeal bars appeared amenable to surgical intervention, according to previously established criteria[14], and they were resected. Four resections were considered successful, with documented growth from the remaining healthy growth plate. Excessive undu-

lation of a physis in which there is a small bar may indicate that the physis is less likely to resume normal growth than is one that has a more normal contour. Concomitant corrective osteotomy is usually necessary to correct the angular deformity.

One growth plate in which there was frequent and severe involvement was the apophysis of the tibial tubercle. This involvement was seen in four of our patients, with dramatic effect in one (Case 1) (Figs. 1-A and 1-B). The reason for the selective tendency for severe involvement is not obvious. It may have to do with the particular vascular supply to this portion of the proximal tibial growth plate[15], or, more likely, it may be secondary to the severe ischemic involvement of the soft tissues that overlie this very superficial growth plate. Certainly, functional considerations, such as the patient's ability to walk with the knee flexed when wearing a prosthesis, may have an additive effect, but this alone does not explain the histological findings.

All nine children remained under our observation and care at the time of writing. Only one child had reached skeletal maturity. The remaining skeletal growth in the other children will probably present additional problems that may necessitate further surgical treatment.

In conclusion, meningococcemia that is associated with disseminated intravascular coagulation may have a profound effect on the skeletal system of the growing child. Although the mortality rate from this disease is much lower than it was, there is severe morbidity. Initial medical management must be aggressive and must include coverage with antibiotics, management of fluid and electrolytes, and pulmonary support[7,24].

Children who survive are at high risk for permanent effects on the musculoskeletal system, a fact that has only recently been appreciated. The degree of injury to the immature chondro-osseous tissues does not appear to be a function of the timing or specific components of the initial medical treatment. These effects are of a vascular nature, secondary to the sequence of events initiated by the microorganism, its endotoxin, and the resulting coagulopathy. When the small vessels supplying the growing ends of the long bones are affected, permanent and often progressive cellular damage may be initiated that may not produce clinical changes until long after the acute disease has been treated. Orthopaedists should be aware of the pathogenesis of this disease and of its possible effects on the developing chondro-osseous structures, in order to search actively for early signs of such damage. This will allow treatment to be initiated early, with the best chance of success.

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