Osteoperiostitis in Early Yaws: Case Series and Literature Review

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We describe the clinical and radiological manifestations and outcome after treatment of 7 children who received a diagnosis of early yaws osteoperiostitis. Osteoperiostitis occurred some weeks after the primary infection, and the most common finding was hypertrophic periostitis of long bones. All treated patients had excellent responses to benzylpenicillin therapy.

Yaws is a contagious, nonvenereal, treponemal infection that mainly occurs in children <15 years of age. The disease is caused by infection with *Treponema pallidum pertenue* and occurs primarily in warm, humid, tropical regions among poor rural populations [1, 2]. Although a mass eradication campaign in the 1950s greatly reduced the incidence of yaws, a resurgence of the disease has recently occurred in West and Central Africa, Southeast Asia, and the Pacific Islands [3,4]. The most recent World Health Organization estimate (1997) suggested that the prevalence of yaws at that time was 3 million cases [5].

Direct personal skin-to-skin contact is the major route of transmission in yaws. The most common clinical manifestations in early yaws are the single papillomatous reddish primary lesion and multiple hyperkeratotic papules in the secondary stage [1]. Bone and joint involvement, including periostitis and osteitis, have been reported in the early stages and may result in severe bone pain and swelling [6–8]. Moreover, if untreated, the chronic osteoperiostitis may result in destructive lesions during the late yaws period [9–12].

In this series, we describe children treated at our institution who received a diagnosis of early yaws osteoperiostitis and review other cases of early yaws osteoperiostitis reported in the English-language literature.

PATIENTS AND METHODS

We evaluated all cases of yaws from January through December 2009 at Lihir Medical Center (Lihir Island; Papua New Guinea).

The diagnosis of yaws was based on clinical suspicion and serologic parameters. Patients <15 years of age whose mothers had negative treponemal test results at antenatal screening, with clinical evidence of early yaws (primary or secondary stage) and scoring positive in both the nontreponemal test (Venereal Disease Research Laboratory [VDRL]) and the Treponema pallidum hemagglutination test were eligible. A diagnosis of primary yaws was established by clinicians on the basis of chronic (>2 weeks), painless, atraumatic ulcers with raised margins and a soft, red, moist bed. Criteria for the diagnosis of secondary yaws included one of the following signs or symptoms: (1) multiple hyperkeratotic papules or (2) bone pain and swelling affecting the fingers or toes (dactylitis), forearm, tibia, or fibula.

Four experienced clinicians were responsible for screening the patients and ordering radiological studies based on the following criteria: visible bone changes or palpable thickening of the bone or surrounding soft tissue swelling or marked pain in the long bones of extremities. Arthralgias are well-recognized symptoms of secondary-stage yaws and usually affect the knees, ankles, elbows, and wrists. They do not in themselves constitute an indication for a radiological study. Radiological diagnostic criteria of early yaws osteoperiostitis were periosteal reaction or osteolysis affecting the fingers or toes, forearm, tibia, or fibula.

Patients were re-examined clinically and serologically 6 months and 9 months after treatment. A 4-fold decrease in VDRL titer after 9 months was considered to be necessary to demonstrate cure.

RESULTS

During the 12-month period, 222 patients received a diagnosis of yaws on the basis of epidemiological, clinical, and serological criteria. Of 194 patients for whom clinical data were available, 104 (53.6%) presented with skin lesions, 64 (33.0%) with joint or bone pain, and 26 (13.4%) with both. Radiological studies were performed at the time of diagnosis in 28 (43.7%) of 64 patients with bone and joint pain.

Seven children had cases that met the radiological diagnostic criteria of early yaws osteoperiostitis. Six patients underwent follow-up clinical, radiological, and laboratory evaluation at 6

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Table 1. Epidemiology and Clinical Presentation for Children with Early Yaws Osteoperiostitis

				Signs and symptoms						
Patient	Age	Sex	Village	Join Pain	Bone afection	Soft tissueswelling	PrimarySkin lesion status	Primary skin lesion localization	Duration, [a]weeks	Secondary skin lesions
1	6	M	Komat	Present	Monodactilitis	Present	Active	lower limb	6	Absent
2	8	M	Komat	Present	Periostitis	Present	DR	DR	DR	Absent
3	4	F	Kunaye1	Present	Poli-periosteitis	Present	Healed	lower limb	8	Present [b]
4	5	F	Kul	Present	Periostitis	Absent	Healed	lower limb	8	Present [b]
5	6	M	Latahul	Present	Periostitis	Present	Healed	lower limb	3	Absent
6	5	M	Latahul	Present	Periostitis	Present	Active	upper limb	4	Absent
7	9	M	Kul	Present	Poli-periosteitis	Present	Healed	lower limb	12	Absent

NOTE. DR, do not remember.

[a] Time since appearance of primary lesion.

[b] Skin biopsy specimen was taken.

and 9 months after diagnosis. One patient was evaluated at the time of infection and was subsequently lost to follow-up. Including the 7 cases that are described here for the first time, there are, to our knowledge, 25 cases documented in the literature of bone involvement in yaws and only 18 during the early period (primary or secondary stage) [7, 8, 10, 11]. The demographic characteristics, clinical presentation, diagnostic test results, radiological findings, treatment, and outcome for the 7 cases from Lihiri Medical Center are shown in tables 1 and 2.

The cases were all diagnosed 3 weeks to 3 months after the primary lesion appeared. Patients presented with bone pain (7 [100%] of 7), soft tissue swelling (6 [85.7%] of 7), multiple bones involved (3 [42.9%] of 7), hand lesions (3 [42.9%] of 7), and elevated alkaline phosphatase level (4 [100%] of 4 for whom data were available). Radial involvement was most common (5 cases [71.4%] of 7), followed in frequency by ulnar and phalanges, metacarpals, or metatarsals.

Spindle-shaped soft-tissue swelling was visible around the phalanges in the patients with dactylitis (Figure 1). The bony changes consisted of increased density and sclerosis involving the shaft of the phalanx (Figures 1 and 2). When long bone involvement was noted, the presence of a periosteal reaction was the predominant bone lesion (Figure 1). In 2 patients, there was also a loss of clarity of the cortex of the distal radius diaphysis, corresponding to areas of osteolysis (Figure 2).

Six patients (85.7%) recalled having recently had a large, single papule on the lower limbs; this papule had resolved spontaneously in 4 of these patients, leaving a tissue paper scar. The other 2 patients (28.7%) still presented with the active primary skin lesion, and another 2 presented with multiple hyperkeratotic skin papules at the time of diagnosis. The main findings on skin biopsy for these 2 cases were parakeratosis with prominent epidermal hyperplasia and intraepidermal microabcesses. The result of an immunoperoxidase stain for spirochaetes was negative, and *T. pallidum* DNA (NAA) was not detected in either of the 2 cases.

After the diagnosis was serologically confirmed, all treated patients had excellent responses to antibiotic therapy with 3 doses of intramuscular benzyl-penicillin. The mean duration of follow-up was 9 months to date and showed that the bone

Table 2. Laboratory and Radiological Findings for Children with Early Yaws Osteoperiostitis

Patient	Initial VDRL titer	VDRL titer at 9 months after treatment	TPHA	AlkPh level,[a] U/L	Type of bone affection	Number of bones affected	Hands or feet affected	Radius or ulna involvement	Tibia or Peronne involvement
1	1:16	Negative	Positive	Not available	Monodactilitis	1	Unilateral	Absent	Absent
2	1:64	1:8	Positive	201	Poli-periostitis	5	Absent	Bilateral	Unilateral
3	1:32	Negative	Positive	188	Poli-osteoperiostitis	7	Bilateral	Bilateral	Absent
4	1:32	1:2	Positive	Not available	Mono-periostitis	1	Absent	Absent	Unilateral
5	1:32	1:32	Positive	149	Poli-osteoperiostitis	2	Absent	Unilateral	Unilateral
6	1:32	Lost of follow up	Positive	Not available	Poli-osteoperiostitis	2	Absent	Unilateral	Unilateral
7	1:32	Negative	Positive	240	Poli-periosteitis	5	Bilateral	Bilateral	Absent

NOTE. AlkPh, alkaline phosphatase; TPHA, treponema pallidum hemagglutination; VDRL, Venereal Disease Research Laboratory test.

[a] Reference range in our laboratory is 36–126 U/L

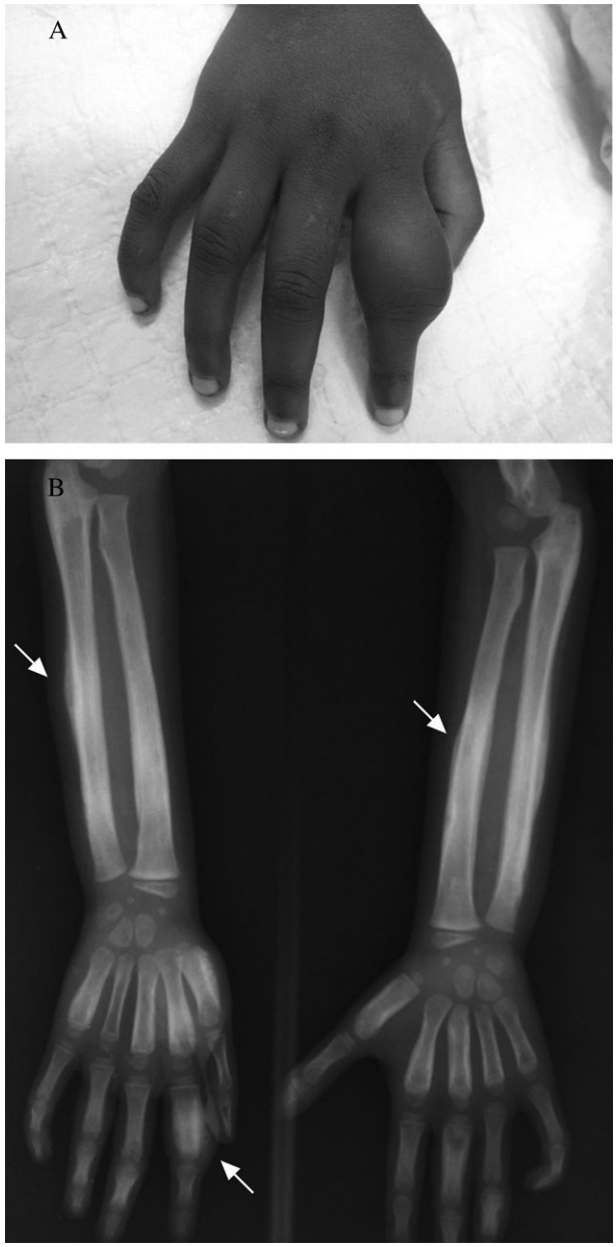

Figure 1. Fusiform swelling of the second digit in patient 3 *(A)* and radiograph of her forearms and hands *(B)*. Arrows show dactilitis with organized periosteal reaction, some thickening of the cortex, and increase in width of the phalanx and bilateral periosteal reaction of the ulna and radius with widespread "onion layering" deposition of periosteal bone.

lesions had resolved in all patients, complete healing of all cutaneous lesions occurred in most instances, and VDRL had decreased by >2 dilutions in 5 of 6 patients. No long-term sequelae were observed.

DISCUSSION

Yaws is an increasing public health concern in Papua New Guinea. The disease occurs primarily in populations living in

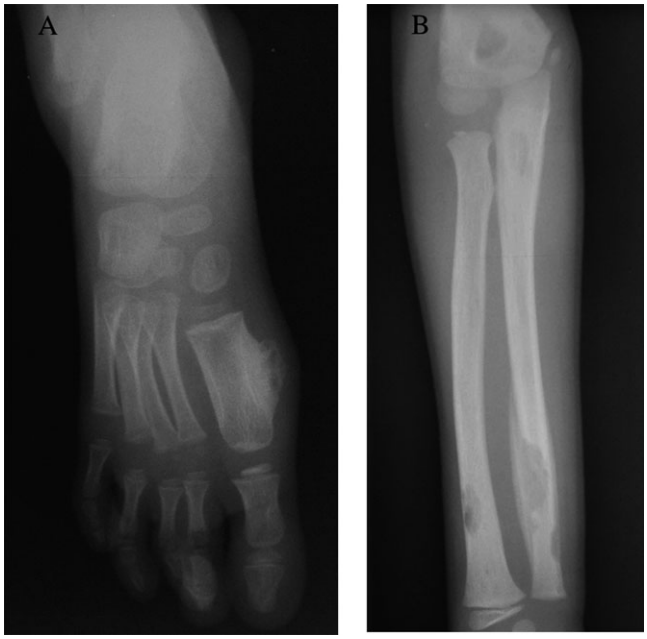

Figure 2. Radiograph of the right foot of patient 7, showing dactilitis of the proximal phalanx of the first digit *(A)* and radiograph of his arm with a loss of clarity of the cortex of the distal radius and ulna *(B)*.

rural areas where lack of sanitation and hygiene prevails and varies in severity from a self-limiting illness to irreversible, incapacitating bone lesions.

After the World Health Organization–sponsored mass eradication campaign in the 1950s, clinical and radiographical descriptions of bone abnormalities in yaws have rarely been published. Archaeological-based research has been the only source of information that has increased the understanding of osteoperiostitis in yaws. Examination of skeletons from populations with clinically diagnosed yaws revealed pathological changes distinctive to that disease, clearly separating it from changes caused by other bone diseases (eg, infantile cortical hyperostosis and hypertrophic osteoarthropathy) or from other treponemal infections, such as syphilis [13].

Yaws, as one form of pathologic treponematosis, alters the appearance of bones in a highly specific manner. According to our observations, yaws is a polyostotic disorder. The mean number of affected bones was 3.3 (range, 1–7), similar to that noted by Lin et al [7]. The radius, ulna, and phalanges were the bones most frequently implicated, and involvement was often bilateral. This contrasts with the pauciostotic presentation and rare involvement of hands and feet found in syphilis. An archaeological study in which skeletons from a 500-year-old site were examined found yaws-related periostitis in 19% of skeletons. Invariably, polyostotic involvement was present, and hand and foot lesions were frequent [14].

The radiological abnormalities demonstrated in early yaws consisted of dactylitis and osteoperiostitis. We did not observe any

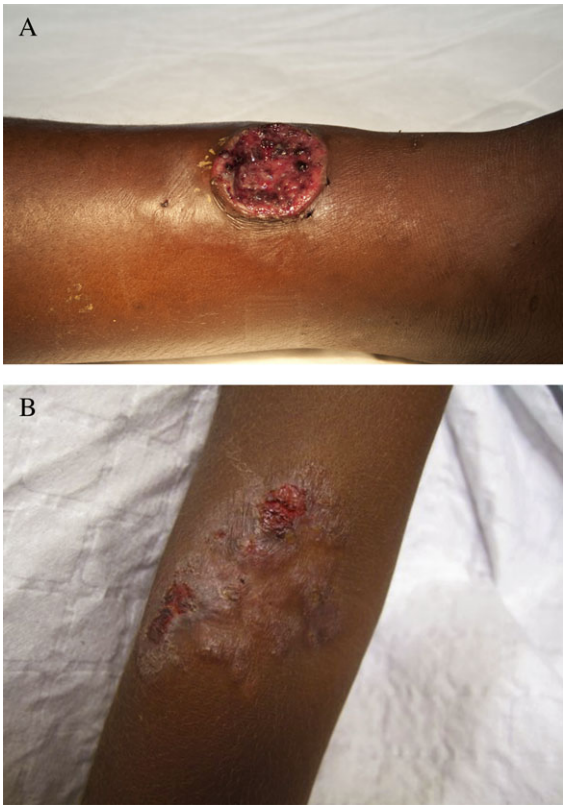

Figure 3. Primary yaws skin lesion (ulcer with raised edges) on the leg of patient 1 *(A)* and secondary skin lesion (crustopapillomatous) on the left arm of patient 4 *(B)*.

characteristic late-stage lesions, such as juxtaarticular nodules (gummas), bowing of the tibia (saber shins), nasal cartilage destruction (gangosa), or exostosis of the paranasal maxilla (gondou). In contrast with secondary yaws, tertiary yaws is a devastating and deforming process that occurs 5–10 years after inoculation. This article describes the findings of 3 cases of dactylitis that are very similar to those documented previously in 2 cases reported from Indonesia [6]. Of note, mild hyperphosphatasemia was found, probably resulting from elevations in the bone isoform of alkaline phosphatise caused by an accelerated skeletal turnover.

In our study, secondary skin lesions appeared somewhat less frequently (28.5%) than in a recent Chinese study of 9 patients with early yaws osteoperiostitis in which most of the patients were noted to present with them [7].

On the basis of the limited number of cases reported to date, early yaws osteoperiostitis appears to be a relatively mild disease if it is diagnosed and treated in a timely manner. The diagnosis should be considered in young children who present with bone pain in regions where yaws is endemic. In patients in whom the illness is suspected, attempts should be made to confirm the diagnosis serologically. Diagnosis of the specific treponema causing bone disease, however, is necessarily on the basis of epidemiological data (children without history of sexual relations and a VDRL-negative mother), because no histological, biochemical, immunologic, or microbiologic techniques are available for distinguishing between them. This series of cases suggests that the presence of supportive clinical and radiological findings may be useful in the clinical diagnosis.

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Potential conflicts of interest. All authors: no conflicts.

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