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Progressive Osseous Heteroplasia: a Distinct Developmental Disorder of Heterotopic Ossification

TWO NEW CASE REPORTS AND FOLLOW-UP OF THREE PREVIOUSLY REPORTED CASES*

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We report here two new cases of severe progressive osseous heteroplasia, as well as the findings at the most recent follow-up of three patients whose cases were reported previously.

Progressive osseous heteroplasia is clinically distinguishable from Albright hereditary osteodystrophy[1,22,24,31] and fibrodysplasia ossificans progressiva[5-7,16,17,19,20,26,30], two other rare primary developmental disorders of heterotopic ossification in children. We believe that the unique constellation of clinical, pathological, and roentgenographic features that characterizes progressive osseous heteroplasia justifies its consideration as a distinct developmental disorder of heterotopic ossification.

Case Reports

CASE 1. This girl was the product of a full-term, uncomplicated, first pregnancy and vaginal delivery; the mother was seventeen years old. When the child was two weeks old, the mother detected a plaque of skin that resembled grains of rice in the left popliteal fossa and proximal part of the calf. Several additional plaques had appeared and coalesced by the time that the child was eleven months old. Motion of the left knee became severely restricted, and the disease rapidly progressed to involve the left ankle and foot.

The child was seen at Children's Hospital of New Orleans when she was eighteen months old. Numerous maculopapular plaques were noted over the entire left lower limb. Sensation was grossly normal over these plaques and the child had no discomfort. Active and passive motion of the left knee and ankle was severely restricted secondary to progressive heterotopic ossification (Figs. 1-A and 2-A).

By the time that the girl was thirty months old, the left knee and ankle were ankylosed, and there was progressive ossification of deep connective tissues (Figs. 1-B, 2-B, and 3-A). An anteroposterior roentgenogram of the left foot did not show any malformation of the first ray. Despite the presence of severe heterotopic ossification, growth continued at the proximal tibial physis with progressive bowing of the tibia.

By the age of eight years, the markedly shortened, ankylosed left lower limb had become a severe impediment to her ability to carry out the activities of daily living. The child attended a public school and functioned at an appropriate intellectual level for her age. All cognitive and motor milestones had been normal.

The patient's height and weight were in the fortieth percentile. The facies appeared normal. Growth of the tibia had continued with severe anteromedial bowing (Figs. 1-C and 2-C). The posterior muscles of the left leg had been almost completely replaced by heterotopic bone. Despite the presence of distal pulses and intact sensation, the left lower limb was approximately twenty centimeters shorter than the unaffected, right lower limb. The range of motion of the left hip was normal, but a small cutaneous maculopapular plaque was detected along the medial aspect of the left groin. The remainder of the musculoskeletal and neurological examination was normal.

Roentgenograms revealed patchy heterotopic ossification along the medial aspect of the left hip (Fig. 4). Hematological studies; liver-function tests; and levels of serum electrolytes, calcium, phosphorus, alkaline phosphatase, creatinine, and uric acid were normal. A high-resolution karyotype analysis of cultured lymphocytes revealed a normal female (46,XX) pattern.

The shortened, ankylosed left lower limb was disarticulated through the knee. The amputation specimen revealed marked anterior bowing of the distal aspect of the tibia (Fig. 5) and subcutaneous osseous nodules of the left foot. A hallux valgus deformity was noted, but an anteroposterior roentgenogram (Fig. 3-B) did not show the congenital malformation of the great toe that is characteristic of fibrodysplasia ossificans progressiva[7].

The skin was mobile over the subcutaneous connective tissue except in the region of the dermal plaques around the lateral malleolus and the dorsum of the foot (Fig. 5).

Thin longitudinal sections were made of the amputation specimen, and they revealed extensive ossification of the dermis, subcutaneous fat, tendons, and posterior muscles of the leg (Fig. 6-A). The nerves and vessels were grossly normal but were encased in a network

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of bone throughout their course. A lateral roentgenogram of a longitudinal section (Fig. 6-B) revealed extensive mature osseous trabeculae in the superficial and deep connective tissues.

Histological sections showed extensive ossification involving the dermis, subcutaneous adipose tissue, tendons, fascia, and skeletal muscle (Fig. 7). Early lesions consisted of a cluster of thin-walled blood vessels from which new bone arose in the surrounding connective tissue (Figs. 8 and 9). Osteoblastic rimming was prominent and osteoclastic activity was also seen. This active process of new-bone formation and remodeling led to irregular, scattered deposits of lamellar bone of various dimensions and contours (Fig. 10). The complex vascular pattern with its surrounding loose connective tissue represented the only marrow elements identifiable in this process of new-bone formation. Neither hematopoietic nor adipose marrow was present in the early bone or in the mature bone after remodeling. The ossification process appeared to occur *de novo*, without previous formation of cartilage. Immunostaining with S-100, a non-specific but sensitive marker for chondrocytes and their precursors, was negative[17,32]. The articular cartilage and growth plates of the proximal and distal aspects of the tibia and the fibula were normal.

The patient had two younger brothers and three younger sisters, all of whom were normal (Fig. 13, *A*). There was no family history of bunions, digital anomalies, arthritis, heterotopic ossification, immobility, soft-tissue calcification, endocrinopathies, short stature, round facies, mental retardation, miscarriages, or stillbirths.

CASE 2. This girl weighed four pounds and twelve ounces (approximately two kilograms) when she was delivered by cesarean section after an uncomplicated gestation of thirty-seven weeks. Gritty cutaneous and subcutaneous ossification was noted in both shoulders and arms at birth, and it progressed rapidly to involve a wider area of both upper limbs, including the forearms, wrists, and hands, by the age of twelve months. The range of motion of the shoulders and elbows was full at the age of seven months, but it was severely limited bilaterally by the age of nine months.

An extensive metabolic workup was done to exclude disorders of mineral metabolism. There was no evidence of hyperparathyroidism, pseudohypoparathyroidism, or pseudopseudohypoparathyroidism. Laboratory studies revealed normal levels of serum calcium, albumin, phosphorus, alkaline phosphatase, urea nitrogen, creatinine, C-terminal parathyroid hormone, calcitonin, and vitamin-D metabolites. Analysis of a twenty-four-hour collection of urine revealed nor-

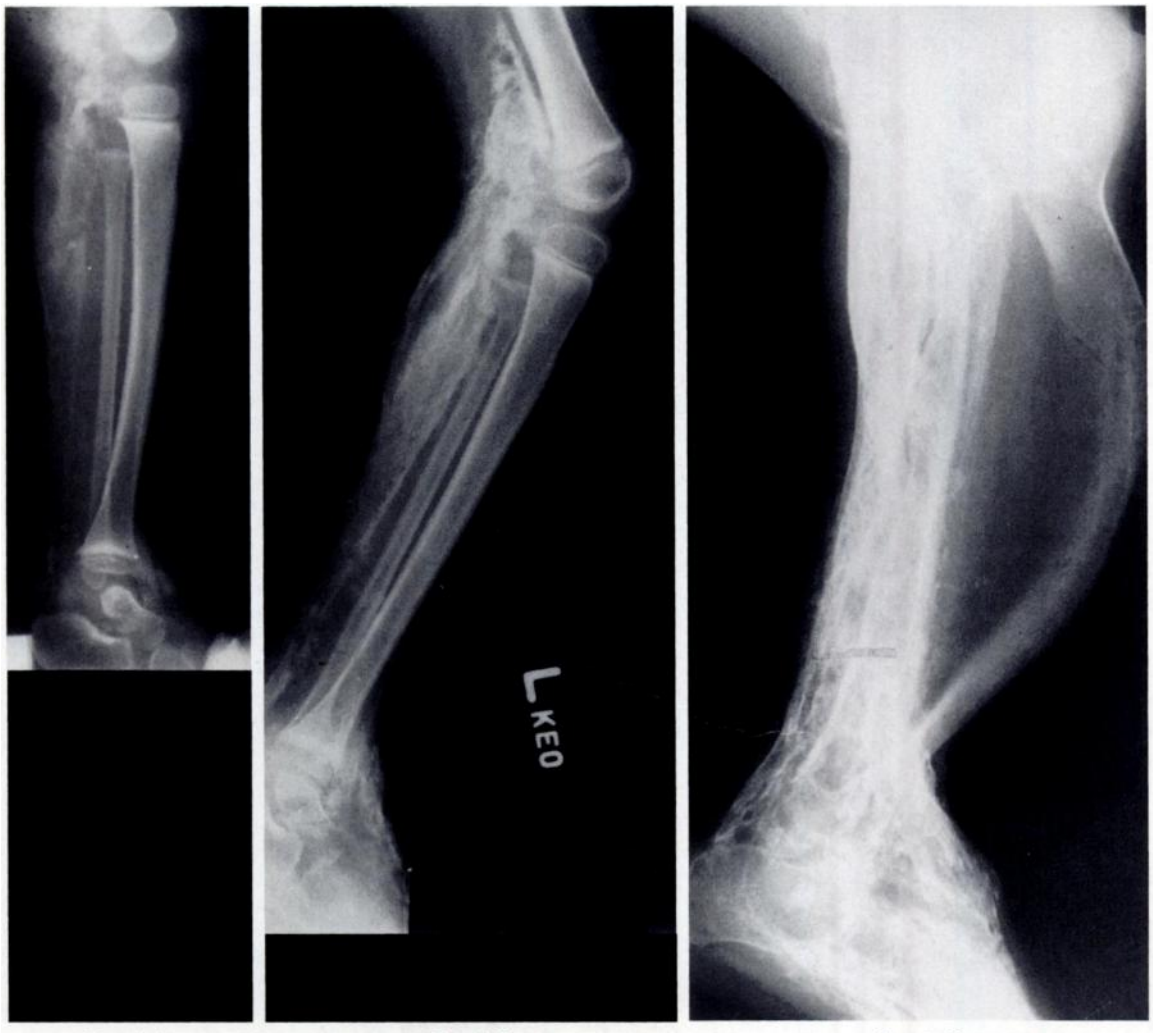

FIG. 1-A FIG. 1-B FIG. 1-C

Figs. 1-A through 10: Case 1.

Figs. 1-A and 1-B: Lateral serial roentgenograms of the left leg, showing progressive heterotopic ossification of the soft tissues when the patient was eighteen months old (Fig. 1-A) and thirty months old (Fig. 1-B).

Fig. 1-C: Lateral roentgenogram of the amputation specimen, showing extensive ossification of the soft tissues of the superficial and deep posterior compartments of the leg. There is severe disuse osteopenia and anterior bowing of the tibia.

mal levels of calcium and phosphorus. A computed tomographic scan revealed extensive ossification of the subcutaneous and periarticular tissues of both shoulders.

Excisional biopsies of lesions of the left arm and forearm were performed when the patient was twenty-three months old. Histopathological evaluation of excised tissue confirmed the presence of focal membranous ossification of the dermis. Intramembranous ossification was predominant in the deep fascia between the biceps and brachioradialis muscles. There was a tiny, isolated focus of endochondral ossification.

Excisional biopsies of lesions of the right upper limb were performed when the patient was twenty-five months old. The histopathological findings were similar to those for the left arm.

By the age of four years, the skin lesions had all recurred and had spread more deeply along the fascial planes of both upper limbs. The active range of flexion of the left elbow was 55 to 100 degrees, and that of the right elbow was 75 to 90 degrees. An attempt was made to excise the deeper lesions of the right elbow completely. Histopathological evaluation of excised tissue revealed immature woven bone with extensive areas of intramembranous and endochondral ossification.

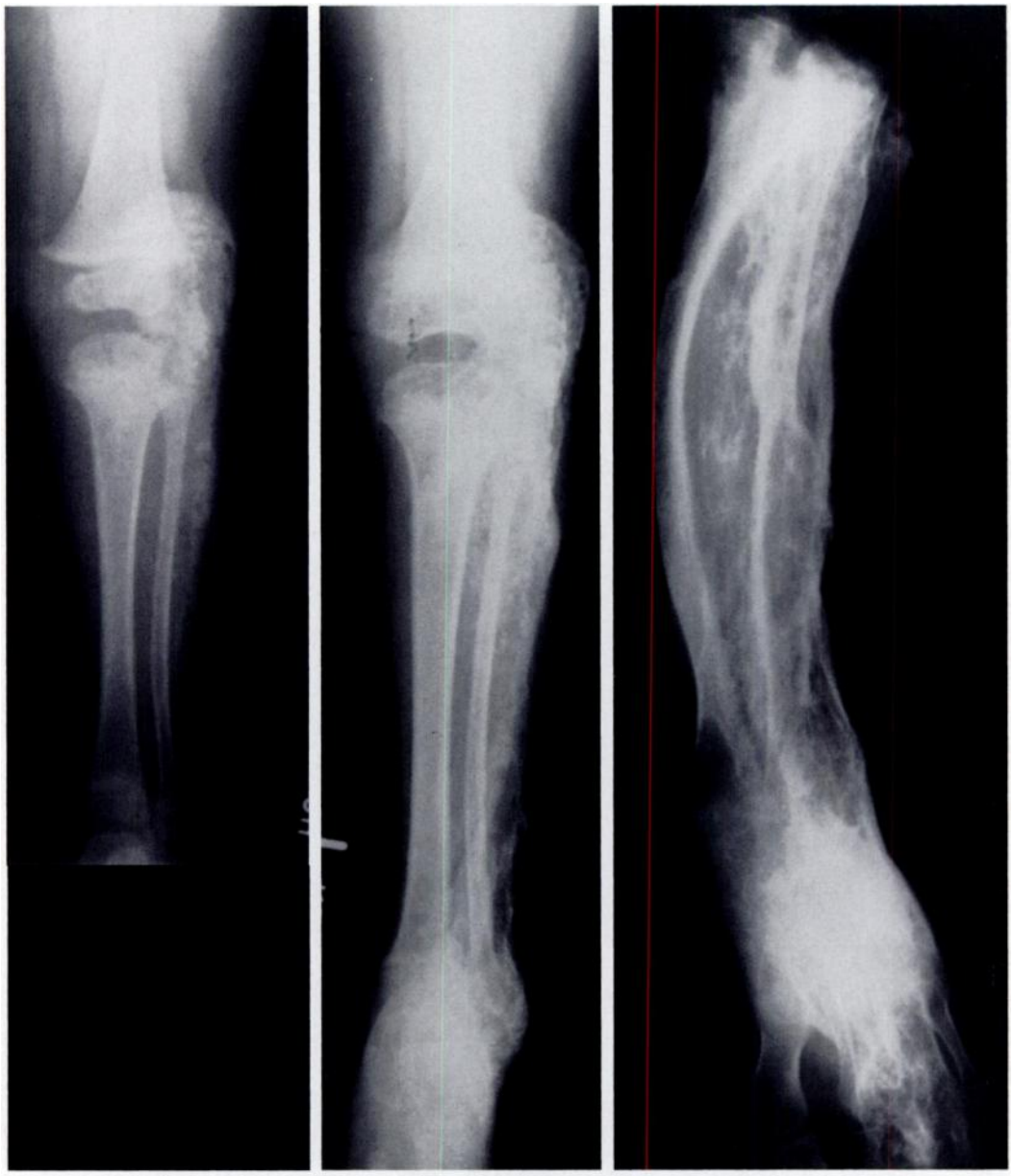

FIG. 2-A FIG. 2-B FIG. 2-C

Figs. 2-A and 2-B: Anteroposterior serial roentgenograms of the left leg, showing progressive ossification of the soft tissues when the patient was eighteen months old (Fig. 2-A) and thirty months old (Fig. 2-B).

Fig. 2-C: Anteroposterior roentgenogram of the amputation specimen.

The lesions promptly recurred; the right elbow became ankylosed at 90 degrees of flexion and the right wrist, at 10 degrees of palmar flexion. By the time that the patient was six years old, the skin lesions had extended into contiguous areas on the posterior aspect of both shoulder girdles, as well as into the right hand.

When the child was examined at the age of seven years, she was attending a public school and functioned at an appropriate intellectual level for her age. All cognitive and motor milestones had been normal. There was no family history of bunions, digital anomalies, arthritis, heterotopic ossification, endocrinopathies, short stature, round facies,

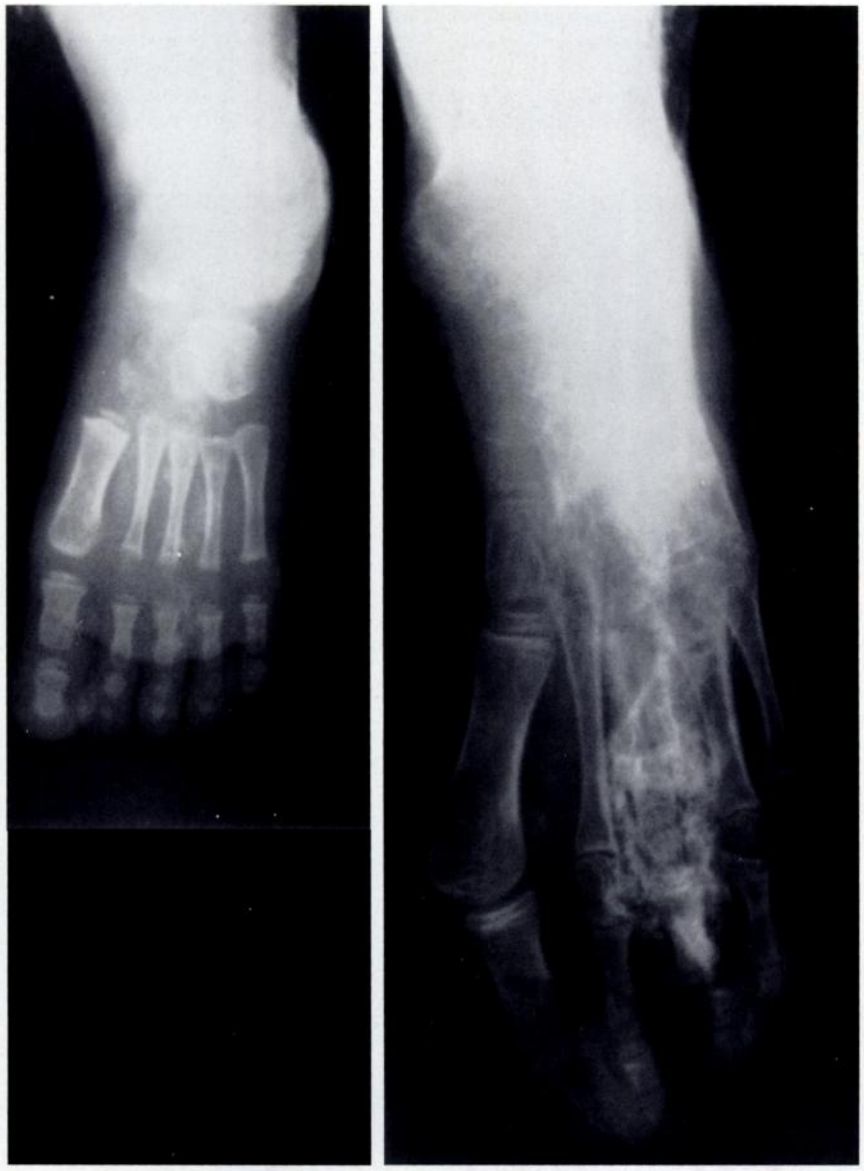

FIG. 3-A FIG. 3-B

Fig. 3-A: Anteroposterior roentgenogram of the left foot, made when the patient was thirty months old. There are no malformations of the toes.

Fig. 3-B: Anteroposterior roentgenogram of the amputation specimen, showing progressive soft-tissue ossification, compared with that seen in Fig. 3-A, and secondary deformity of the great toe.

mental retardation, miscarriages, or stillbirths. A younger brother was normal (Fig. 13, *B*). The facies of the patient appeared normal, and her height and weight were in the twenty-fifth percentile for her age. The abnormal physical findings were limited to both upper limbs; the more severe cutaneous ossification and limited motion were in the left upper limb.

Follow-up of Cases That Were Reported on Previously

CASE 3. This sixteen-year-old girl had originally been seen in infancy and early childhood[10,18] because of extensive areas of a maculopapular rash (Fig. 11) with associated dermal ossification (Fig. 12). During childhood, she had progressive ossification of the deeper tissues underlying areas of earlier involvement of the skin. Progressive ossification involved the entire left upper limb and both lower limbs, with minimum residual motion of associated joints. When she was nine years old, new isolated lesions of intradermal ossification began to appear on the scalp and back and in the right popliteal fossa. Treatment with a brace or an operation was not considered for the scoliosis because of the skin lesions. Menarche occurred when she was twelve, and longitudinal growth ceased soon after.

At the most recent follow-up examination, when she was sixteen years old, the patient was using a motorized scooter to attend classes at a public school. There was no family history of a connective-tissue disorder (Fig. 13, *C*). The patient had diffuse subcutaneous ossification from the pelvis to the feet on both sides, with ankylosis of the hips, knees, and ankles and severe atrophy of both lower limbs. The scoliosis was severe, with a thoracic curve of 77 degrees and a lumbar curve of 90 degrees.

CASE 4. This girl was originally seen at the National Institutes of Health when she was three years old, and her condition at that time was reported[10] (Table I). During the seven subsequent years, the disease slowly progressed. Several new areas of dermal ossification appeared on the left leg, with progressive ossification of deep tissues of the left hip, knee, and ankle.

At the most recent examination, when the patient was ten years

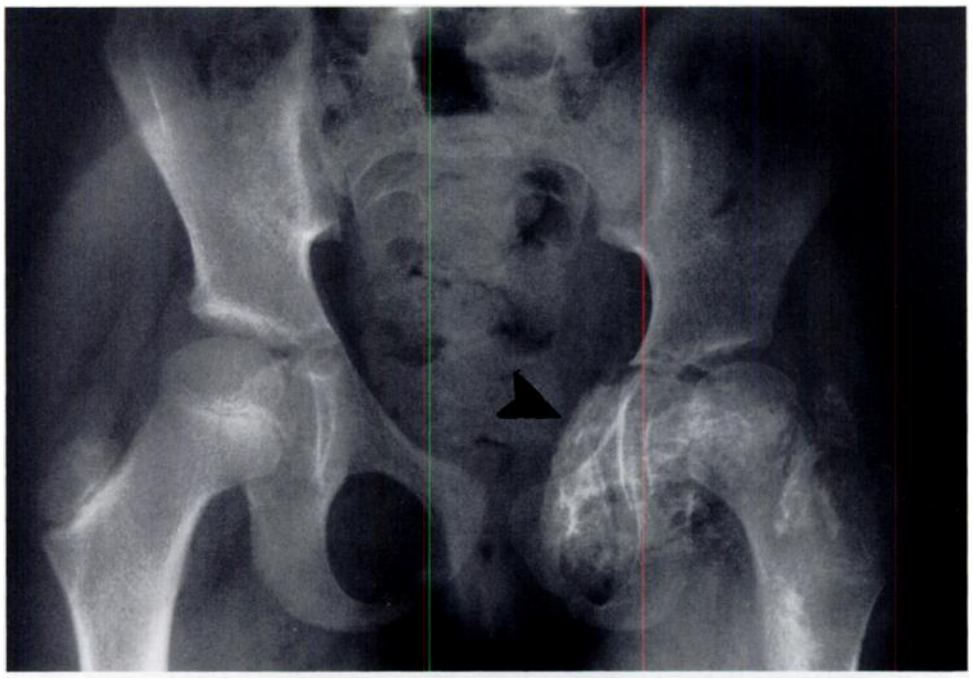

FIG. 4

Anteroposterior roentgenogram of the pelvis, made when the patient was eight years old, revealing heterotopic ossification of the left hip and pubic region (arrowhead).

old, the left knee and ankle were ankylosed, and there was a cavus deformity of the left foot. The range of motion of the left hip had decreased, and the discrepancy between the lengths of the affected left lower limb and the unaffected right limb had increased.

Several plaques of subcutaneous ossification (confirmed by biopsy) over the chest, right shoulder, and right leg developed in an older sister, who had been previously reported to be normal. At the time of the most recent examination of the patient, this sister had no ossification of deep connective tissues or any functional limitation of joint motion. An eleven-year-old sister remained unaffected. There was no parental consanguinity or any family history of a rheumatological or endocrine disorder (Fig. 13, *D*).

CASE 5. One of us (R. J. McK. G.) originally described this patient in 1988[11]. She was a dizygotic female twin and the only patient of the six reported on here who was a member of a large family in which ectopic ossification was inherited as a dominant factor. The severe localized disease prompted the subsequent discovery of minor dermal

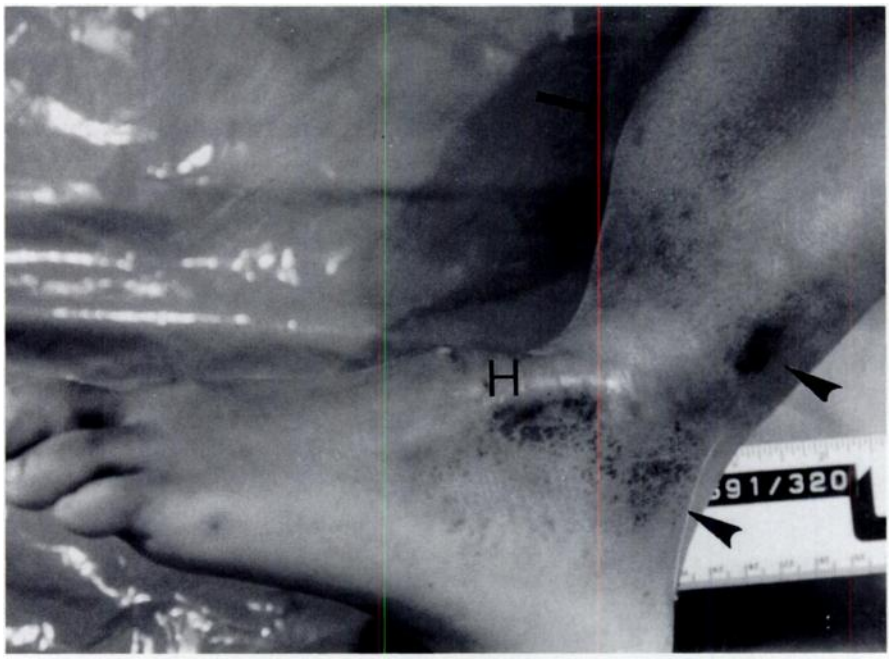

FIG. 5

Photograph of the left leg and foot, made immediately after the amputation. There is anterior bowing of the tibia (arrow), heterotopic bone on the dorsum of the foot (H), and a patchy maculopapular area on the lateral aspect of the foot and leg (arrowheads).

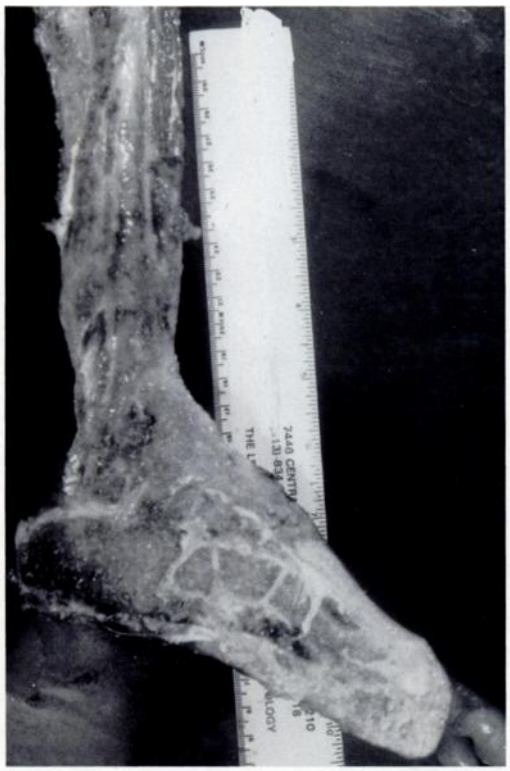

FIG. 6-A

Longitudinal section of the amputated left leg reveals extensive heterotopic ossification of the dermis and deeper connective tissues.

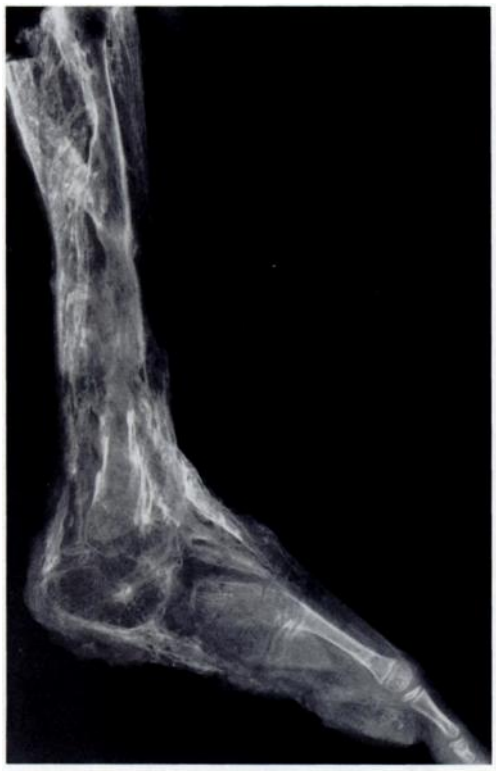

FIG. 6-B

Lateral roentgenogram of the specimen reveals extensive, well developed networks of osseous trabeculae involving the dermis, subcutaneous tissue, tendon, and muscle.

ossification in many members of the family (Fig. 13, *E*). There was no family history of digital anomalies, short stature, round facies, or endocrine disorders.

Characteristic features of progressive osseous heteroplasia in the right lower limb of the patient were first recognized at the age of three weeks. The disease progressed during childhood, with extensive involvement of deep tissues and severe retardation of growth of the right lower limb.

At the most recent examination, the patient was thirty-one years old, was married, and had a daughter who was clinically normal. Since the patient had reached adulthood, the disease had neither progressed nor extended.

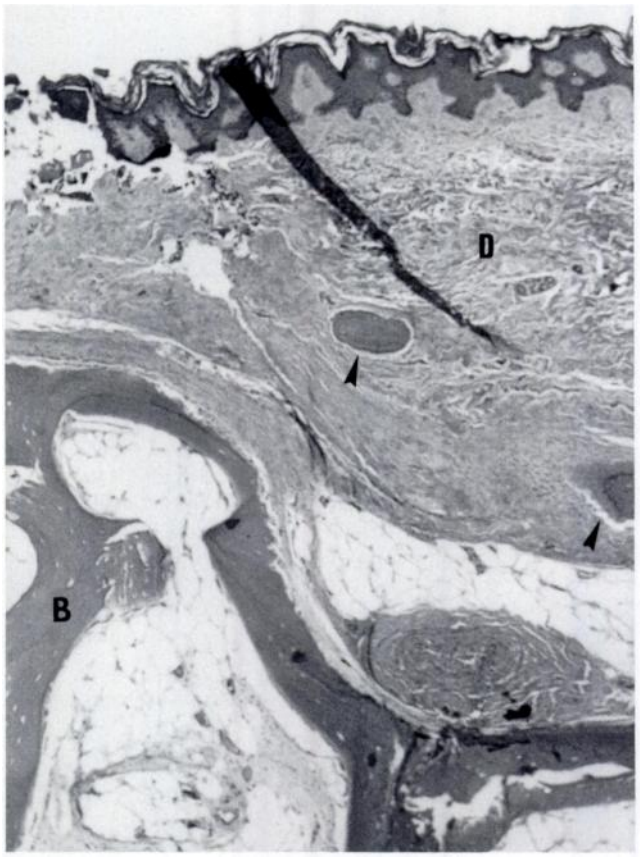

FIG. 7

Low-power photomicrograph of the skin and subcutaneous tissue. Islands of bone (arrowheads) are present in the dermis (D). There are irregular deposits of lamellar bone (B) in the subcutaneous fat (hematoxylin and eosin, original magnification × 50).

Discussion

In a search of the English-language medical literature of the twentieth century, we found reports of only four patients who had primary infantile dermal ossification with progressive ossification of deep connective tissues[8,10,11,18]; three of these patients (Cases 3, 4, and 5) had been described by two of us (R. J. McK. G. and M. A. Z.)[10,11]. Data on Case 6 were available only through a published report[8] (Table I). All five of our patients (Cases 1 through 5) had been seen in childhood. Complete medical histories were obtained from parents and responsible caretakers, and physical examinations

TABLE I

DATA ON THE SIX PATIENTS WHO HAD PROGRESSIVE OSSEOUS HETEROPLASIA

	Case 1	Case 2	Case 3[10,18]	Case 4[10]	Case 5[11]	Case 6[8]
Term used for disorder	Present study	Present study	Dysplastic cutaneous osteomatosis	Limited dermal ossification	Familial ectopic ossification	Osseous heterotopia
Sex	Female	Female	Female	Female	Female	Female
Age when skin involved	2 wks.	Birth	Birth	6 mos.	3 wks.	1 mo.
Description of initial skin involvement	Plaque of skin resembling grains of rice, L leg	Gritty subcut. plaques	Erythematous follicular papular rash, L chest and L upper limb	Gritty papulo-vesicular rash, L leg	Thickened, indurated skin; subcut. tissue, R groin	Hard, enlarging, reddened area, L arm
Cutaneous ossification	Yes	Yes	Yes	Yes	Yes	Yes
Non-inflam. osseous heteroplasia	Yes	Yes	Yes	Yes	Yes	Yes
Marrow elements within sites of ossification	No	No	No	No	No	No
Extensive ossification of muscles, fascia, and deep connect. tissue	L leg	Upper limbs	Lower limbs	L shoulder, both hips, both lower limbs	R hip, knee, ankle	L upper limb
Axial involvement	Yes	No	Yes	No	Yes	Yes
Brachydactyly, digital malform., short stature, or round facies	No	No	No	No	No	No
Laboratory findings	Normal	Normal	Elevated serum alkaline phosphatase level	Elevated serum alkaline phosphatase level	Normal	Normal
Family history	See Fig. 13, *A*	See Fig. 13, *B*	See Fig. 13, *C*	See Fig. 13, *D*	See Fig. 13, *E*	1 sister, normal

were performed periodically. Routine laboratory tests included a complete blood-cell count and determination of the erythrocyte sedimentation rate and the levels of serum calcium, phosphorus, albumin, alkaline phosphatase, urea nitrogen, creatinine, transaminases, vitamin-D metabolites, and parathyroid hormone.

The lesions of the skin were biopsied and serial roentgenograms of the affected limbs were made during the periodic evaluations, and the findings were reviewed for all five of our patients. Routine histopathological studies were performed prospectively in Cases 1 and 2, according to standard protocols[17].

The characteristic features of progressive osseous heteroplasia that were noted in all of the children in the present study included female sex and the presence of non-inflammatory osseous heteroplasia in infancy with progressive ossification of muscles, fascia, and deep connective tissue (Table I).

Primary cutaneous ossification is rarely seen in childhood. Cutaneous ossification occurs more commonly as a secondary manifestation of disorders such as acne, burns, hemorrhage, infection, granulomata, nevi, scars, trauma, tumors, and connective-tissue diseases[1,2,23,25,27]. Many reported cases of primary cutaneous ossification in childhood were actually mild variants of Albright hereditary osteodystrophy[1,9,21,24,29]. We have found that focal cutaneous ossification during infancy with progressive osseous heteroplasia of deep connective tissues is very rare.

Progressive osseous heteroplasia is a disorder of mesenchymal differentiation characterized by infantile dermal ossification with progressive intramembranous ossification of deep connective tissues. The cause and pathogenesis of the disorder are unknown.

In two of the patients (Cases 3 and 6) who were reported on previously and in the present study, the progressive osseous heteroplasia appeared to have been sporadic[8,18], while the other two patients (Cases 4 and 5) had a family history of clinically minor dermal ossification (Fig. 13, *D* and *E*). Clinical observations of the family of Case 5 support the suggestion that there is a dominant mode of inheritance for the trivial osteoma cutis lesions[11]. We postulated that the severe local disease in the proband arose from an early somatic conversion to homozygosity (analogous to retinoblastoma)[11]. Such a conversion would lead predictably to somatic-cell mosa-

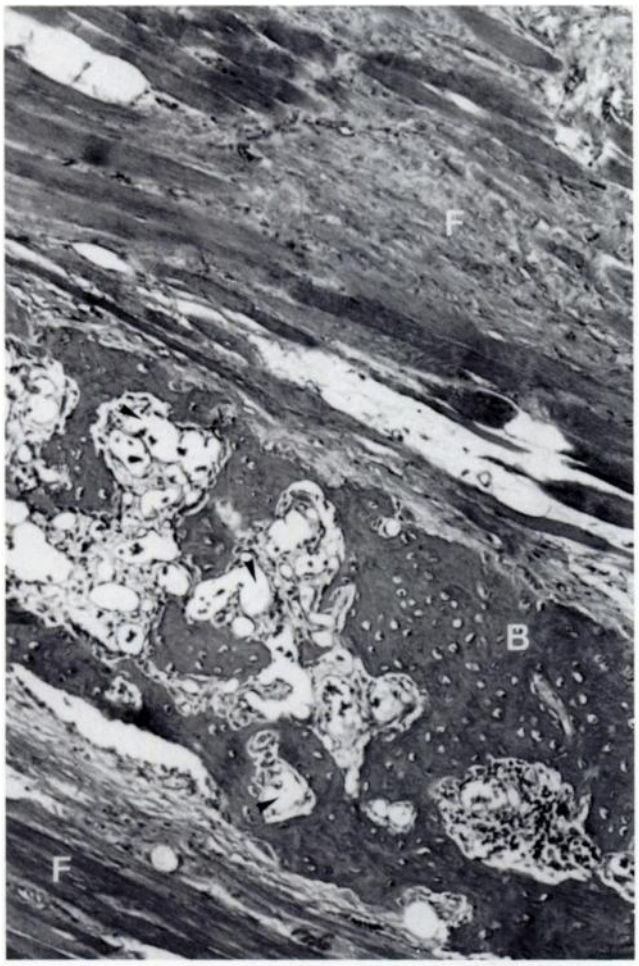

FIG. 8

Medium-power photomicrograph of deeper tissue from the left leg. There is a focus of new woven bone (B) within the fibromuscular tissue (F) and numerous thin-walled blood vessels (arrowheads) (hematoxylin and eosin, original magnification × 125).

icism with severe localized disease in tissues containing the homozygous mutant alleles[13]. Somatic variation for the newly recognized mechanism of allele expansion[28] is another possible explanation for regional anatomical involvement. Several additional families who had primary cutaneous ossification have been reported on, but none had severe disease[9,21,29].

A curious feature of progressive osseous heteroplasia is that only female patients are affected. Although this finding may be a coincidence, because of the small number of patients seen to date, it may prove to be an important clue. The lack of male patients suggests the possibility of male lethality *in utero*, possibly with linkage with the X chromosome. Although most (but not all) X-borne loci are functionally monoallelic after lyonization, we must also consider the possibility that the putative abnormal gene resides on the X chromosome and leads to a mutation associated with a mild gain of function rather than with a loss of function; if this were so, somatic-cell conversion to homozygosity before lyonization might account for a more severe phenotype in female patients. An autosomal location with sex limitation is also possible. Investigation of X linkage, with use of a range of X-chromosome DNA markers, on the family of Case 5 is currently under way in our laboratory.

The anatomical distribution of lesions in progressive osseous heteroplasia suggests that the pathogenesis may involve a mesenchymal stem cell destined for widespread mosaic distribution[3,11]. Although dermal fibroblasts and internal limb structures arise embryonically from limb-bud mesenchyme, the fate map of a mammalian blastoderm embryo suggests that a differentiated cell type, such as muscle or bone, is of polyclonal origin[12,14,18]. Conversely, in a mature organism, a single stem cell of hematopoietic or connective lineage can generate a wide variety of cell types[3,12,14]. At present, little is known about the molecular mechanisms of the signal and response system of mesodermal induction, and the potential clonal nature of lesions in progressive osseous heteroplasia remains a mystery[15].

Although a wide range of endogenous growth factors are known to induce mesoderm[15], we cannot ex-

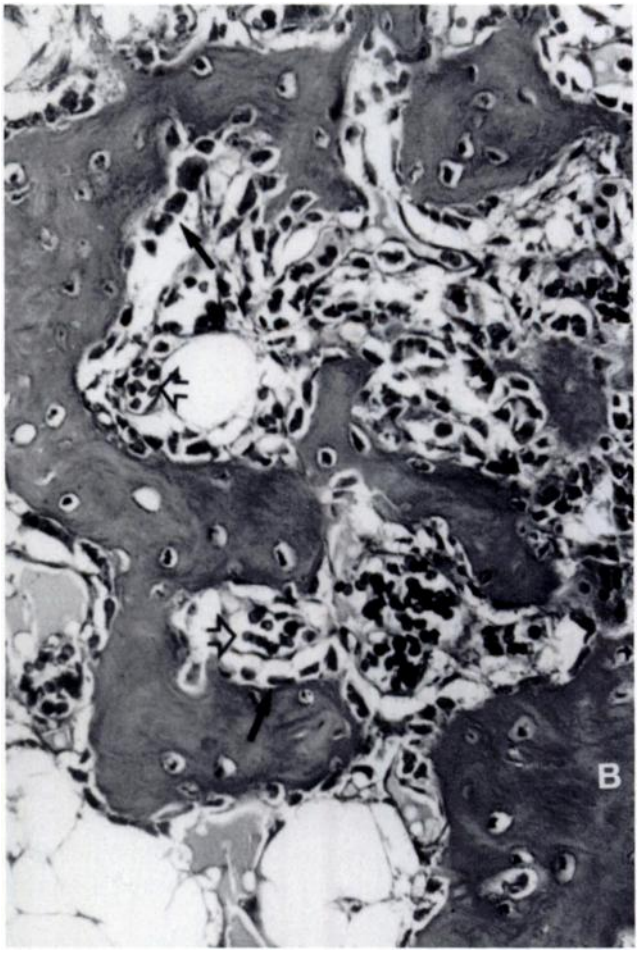

FIG. 9

Higher-power photomicrograph of the highly vascular new-bone deposit (B). There is osteoblastic rimming (solid arrows) and erythrocytes within vascular lumina (open arrows) (hematoxylin and eosin, original magnification × 250).

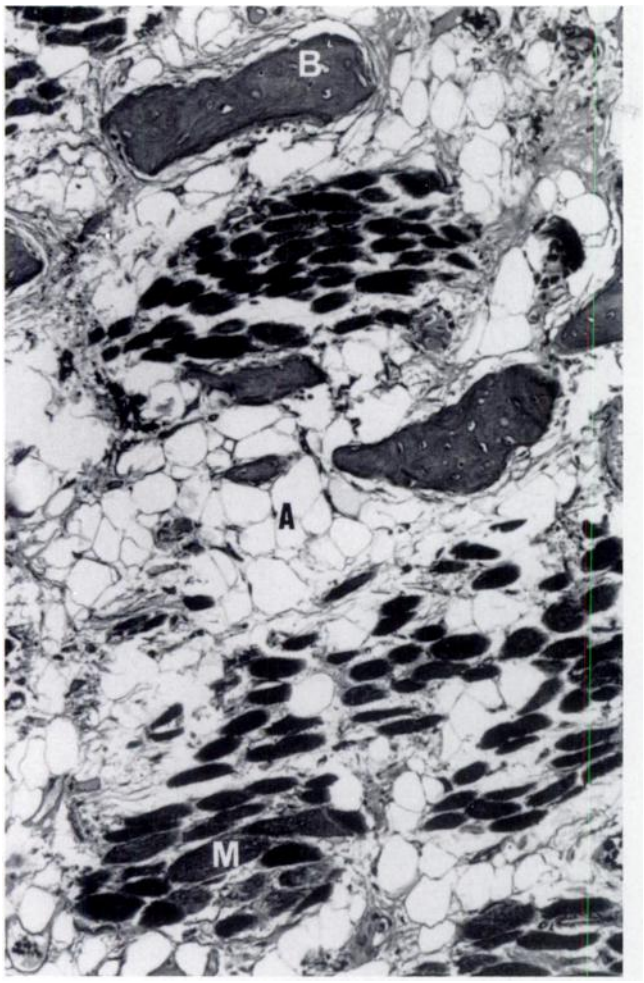

FIG. 10

Photomicrograph revealing irregular islands of bone (B) surrounded by adipose tissue (A), and residual muscle fibers (M) (hematoxylin and eosin, original magnification × 250).

clude the possibility of osteogenic induction by chemical or viral agents in at least one of the patients reported on here. The mother of Case 3 was exposed to the herbicide 2,4-D early in her pregnancy[10]. This agent is not known to be a mutagen in humans, but it has been reported to cause lumbar rib formation in the offspring of rats that were exposed during pregnancy. While neurological or vascular disorders can be associated with heterotopic bone formation[25], there was no evidence of a primary neurological or vascular disorder in any patient who had progressive osseous heteroplasia.

The initial appearance of heterotopic ossification occurred predominantly by an intramembranous pathway in all six patients in the present report. Intramembranous ossification was observed only on the initial biopsy specimen from five of the six patients. A tiny nidus of endochondral ossification was seen amidst the predominant intramembranous ossification in the initial biopsy specimen from Case 2. A more heterogeneous picture of intramembranous and endochondral ossification was seen in that exact region of the right upper limb of this patient two and one-half years after the initial biopsy. While we cannot exclude the possibility of histopathological heterogeneity in the natural history of this disorder, it seems more likely that the previous operative intervention at that site led to these findings.

Although the predominant pathway of intramembranous heterotopic osteogenesis seen in progressive osseous heteroplasia is similar to that observed in Albright hereditary osteodystrophy, the lesions in Albright hereditary osteodystrophy are limited to the skin, while those in progressive osseous heteroplasia also involve the deeper tissues. Furthermore, no patient who had progressive osseous heteroplasia had the morphological or endocrine disturbances characteristically seen with Albright hereditary osteodystrophy. In contrast, fibrodysplasia ossificans progressiva, which also involves ossification of deeper tissues, is characterized by a predominant mechanism of endochondral ossification[17] (Table II).

The anatomical patterns of the disease and its progression differ markedly among the three conditions. In progressive osseous heteroplasia, heterotopic ossification is generally asymmetrical, begins in the dermis, and progresses to involve deeper tissues as well as contigu-

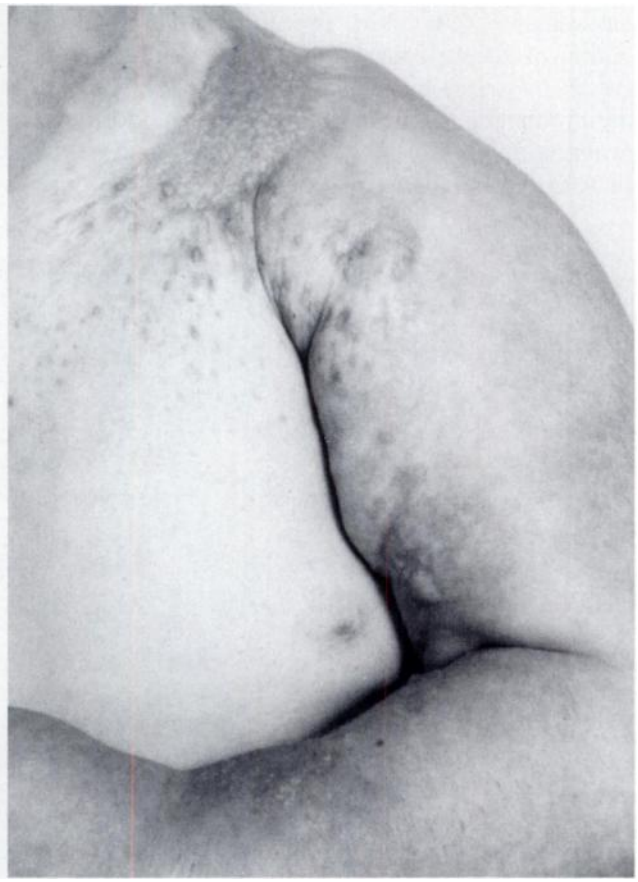

FIG. 11

Figs. 11 and 12: Case 3.

Fig. 11: Photograph of the left axilla and arm of a nine-year-old girl, showing focal maculopapular lesions.

TABLE II
DEVELOPMENTAL DISORDERS OF HETEROTOPIC OSSIFICATION

	Fibrodysplasia Ossificans Progressiva	Albright Hereditary Osteodystrophy	Progressive Osseous Heteroplasia
Sex distribution	Equal	More female than male	Female only
Congenital papular rash	No	No	Yes
Congenital malformation of great toes	Yes	No	No
Brachydactyly, short stature, obesity, round facies, and mental retardation	No	Yes	No
Cutaneous ossification	No	Yes	Yes
Extensive heterotopic ossification of deep connective tissue	Yes	No	Yes
Predominant mechanism of ossification	Endochondral	Non-inflammatory osseous heteroplasia	Non-inflammatory osseous heteroplasia
Presence of hematopoietic marrow in mature heterotopic bone	Yes	No	No
Stringent developmental patterns of progressive ossification	Yes	No	No
Exacerbated by trauma	Yes	No	No
Hypocalcemia, hyperphosphatemia, and urinary cAMP response to parathyroid hormone	No	Pseudohypoparathyroidism; pseudopseudohypo-parathyroidism	No
Serum alkaline phosphatase level	Usually elevated	Usually normal	Variable
Serum parathyroid hormone level	Normal	Elevated	Normal
Pathogenesis	Unknown	Inherited defect in stimulatory G protein of adenylate cyclase	Unknown

ous regions of the skin. The apparent random distribution of severe progressive ossification seen in progressive osseous heteroplasia contrasts markedly with the predictable symmetrical distribution and temporal progression of fibrodysplasia ossificans progressiva[4]. In Albright hereditary osteodystrophy, heterotopic ossification is scattered and apparently random in distribution, as it is in progressive osseous heteroplasia. However, unlike in progressive osseous heteroplasia or fibrodysplasia ossificans progressiva, the heterotopic ossification seen in Albright hereditary osteodystrophy is generally limited to the skin and superficial tissues.

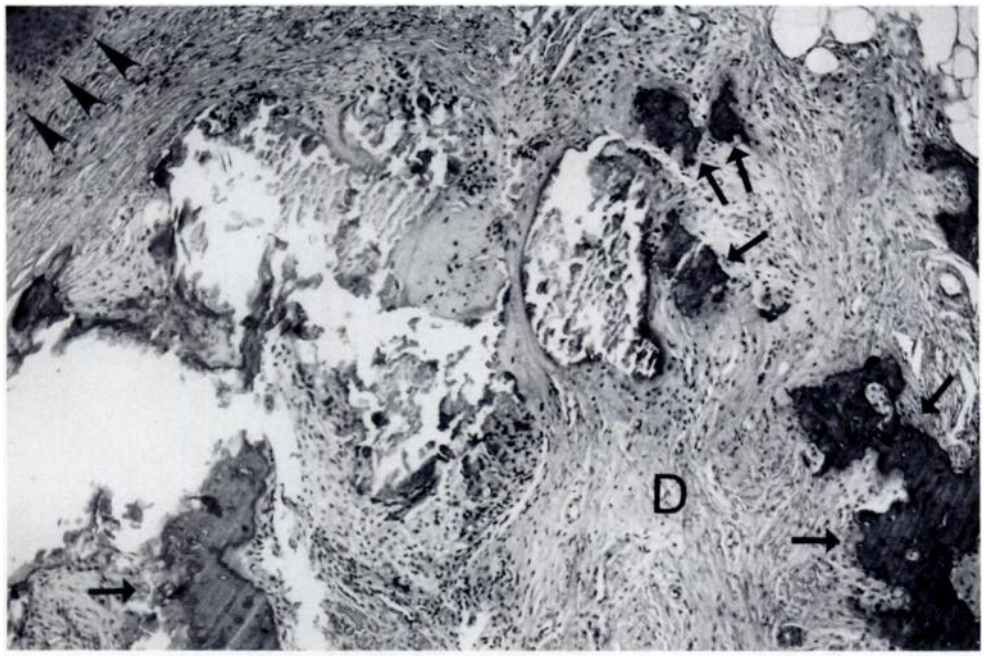

FIG. 12

Photomicrograph of a lesional biopsy specimen, showing islands of heterotopic bone (arrows) in the dermis (D). The arrowheads indicate epidermis (hematoxylin and eosin, original magnification × 50).

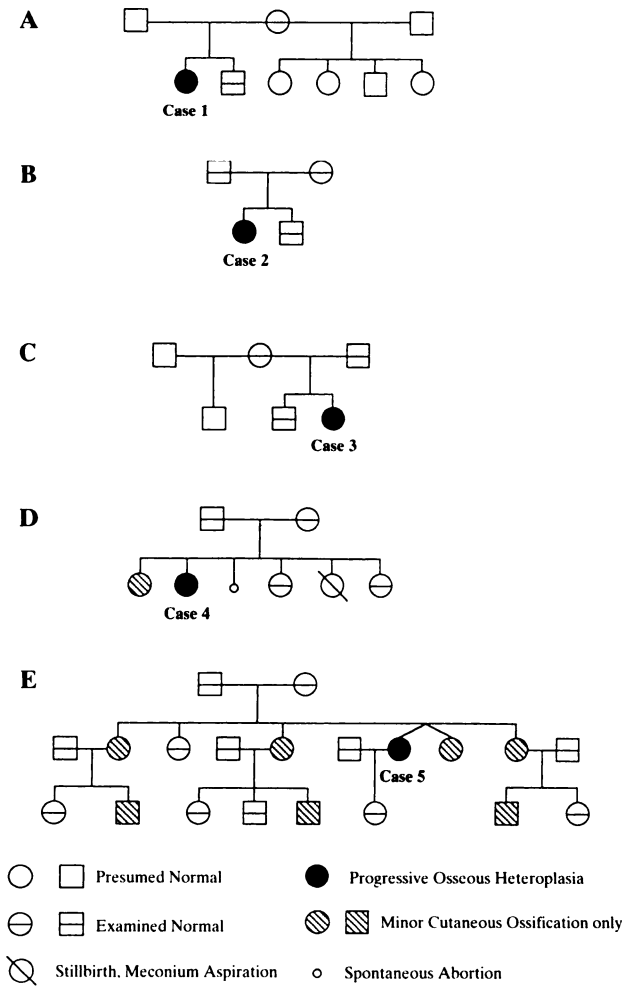

FIG. 13

Pedigrees of five patients who had progressive osseous heteroplasia. *A* = Case 1, *B* = Case 2, *C* = Case 3, *D* = Case 4, and *E* = Case 5.

Digital anomalies are common in all three conditions, but they differ in type and severity. Congenital malformations of the great toes are a characteristic feature of fibrodysplasia ossificans progressiva and have been described extensively by Connor and Evans[7]. The most common malformations encountered are brachydactyly of the great toes, with either monophalangism or delta-shaped phalanges, and malformations of the first metatarsal heads with valgus subluxation at the metatarsophalangeal joints. While malformations of the hands are occasionally seen in fibrodysplasia ossificans progressiva[7], they are more commonly seen in Albright hereditary osteodystrophy and they characteristically involve brachydactyly with symmetrical shortening of the fourth metacarpals[22,24,27]. Although many of the children who had progressive osseous heteroplasia had digital deformities in either the hands or the feet, all deformities developed secondary to progressive ossification of soft tissues and none were noted at birth.

The long-term prognosis for patients who have progressive osseous heteroplasia is uncertain, as only one (Case 5) of the six patients in the present report was followed beyond adolescence[11]. However, there appears to have been an arrest of the progression of the disease since that patient reached adulthood. At present, there is no effective prevention or treatment for progressive osseous heteroplasia. When lesions have been excised in children who have fibrodysplasia ossificans progressiva, heterotopic ossification recurs predictably at the site of the excision[7,19,20,32]. The prognosis after excision is less certain in children who have progressive osseous heteroplasia. The extensive coalescence of ossified skin plaques and the relentless progression of ossification of deep tissues are troubling.

We believe that progressive osseous heteroplasia has characteristic features that clearly distinguish it from fibrodysplasia ossificans progressiva and from Albright hereditary osteodystrophy (Table II). Physicians should be aware of the distinctions between these childhood disorders of heterotopic ossification, as the natural courses of these conditions differ markedly. The unique constellation of clinical, pathological, and roentgenographic features that characterizes progressive osseous heteroplasia justifies its consideration as a distinct developmental disorder of heterotopic ossification.

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