Progressive Osseous Heteroplasia: A Rare Case Report

Abstract

Progressive osseous heteroplasia (POH) is a rare genetic condition of progressive extraskeletal bone formation. POH is clinically suspected by cutaneous ossification, usually presenting in early life, that involves subcutaneous and then subsequently deep connective tissues, including muscle and fascia. We report a case of POH in a 3-year-old child with multiple nontender subcutaneous nodules which, on radiology and histopathology, showed intracutaneous bone formation. Although there is no specific and effective treatment, knowledge about this entity is necessary for early detection and genetic counseling of parents.

Keywords: *Extraskeletal bone formation, intramembranous ossification, osteoma cutis*

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Introduction

Progressive osseous heteroplasia (POH) is a rare genetic condition of progressive extraskeletal bone formation.[1] The presenting features of this condition include early-onset cutaneous ossification, sometimes involving subcutaneous and even deep connective tissues like muscles and fascia. Because of its rarity, most of the physicians are unaware of the condition. Here, we report a case of a 3-year-old child who presented with bone formation on cutaneous and subcutaneous planes. The diagnosis of progressive osseous heteroplasia was proven by plain radiography and histopathology. We report this case because of its rarity and to create awareness among physicians.[2]

Case Report

A 3-year-old male child, born out of nonconsanguinous marriage, presented with three slow-growing painless hard masses over the outer aspect of right leg since the age of 2 months. The child had been delivered at full term without any congenital malformation. He developed multiple asymptomatic solid elevated skin-colored lesions which in course of time coalesced to form large hard masses. There was history of low birth weight and delay in gross-motor type of developmental milestones, but there was no mental retardation or gait abnormality. There was no history of trauma, prior inflammation, or similar lesions in the family members. On examination, there was a single large non-tender subcutaneous hard mass of size 4 cm × 5 cm over anterolateral aspect of right thigh without any surface change [Figure 1]. Skin could be pinched over the lesion. There were two similar smaller lesions of size 2 cm × 3 cm and 2 cm × 2 cm with surface showing atrophy and scaling over the outer aspect of right lower leg [Figure 2]. There was no other skeletal deformity. Plain radiograph of lower limbs in anteroposterior and lateral views showed calcified areas in subcutaneous plane corresponding to the areas of the skin lesions [Figure 3]. The serum levels of calcium, parathyroid hormone, creatinine phosphokinase, alkaline phosphatase, and lactate dehydrogenase were normal. Serum phosphate level was slightly raised (5.5 mg/dL). Histopathological examination showed irregular woven bone spicules in the deep dermis [Figures 4 and 5]. Genetic study was not available in our setup. On the basis of clinical, histopathological, and radiographic features, a final diagnosis of progressive osseous heteroplasia was made. The parents were counseled about the prognosis of the condition, and that no active intervention was helpful. The patient was referred to the physiotherapy department.

Discussion

Disorders of extraskeletal bone formation are classified as nonhereditary and hereditary conditions. Nonhereditary forms usually present at a later age or with prior history

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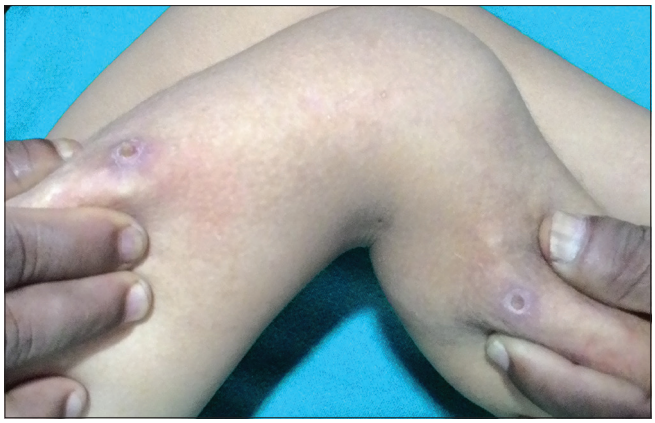

Figure 1: Skin colored to slightly erythematous hard plaques and nodules on the anterolateral aspect of right thigh and lateral aspect of right lower leg. Biopsy scars are visible

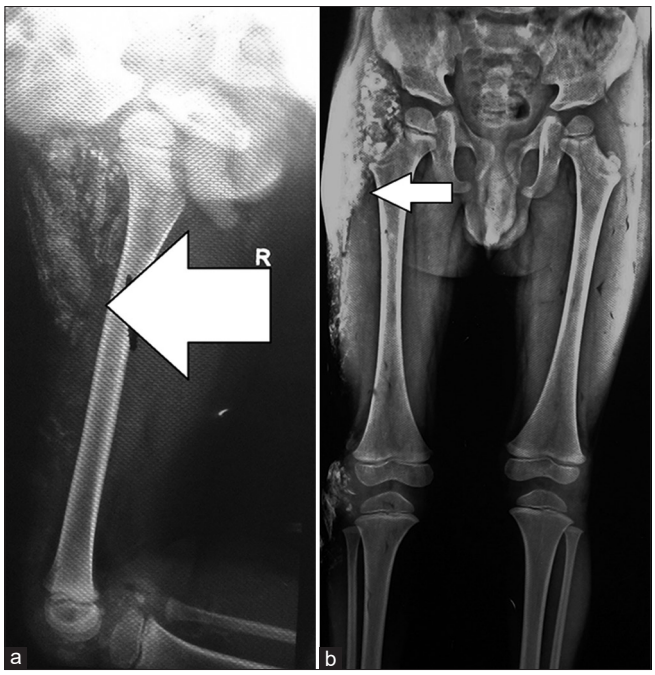

Figure 3: (a): X-ray of right lower limb (lateral view) showing reticular pattern of ectopic bone formation in dermis and subcutis. (b): X-ray both lower limbs (anteroposterior view) showing ectopic bone formation in dermis and subcutis in lateral part of right thigh

of trauma, surgery or arthropathy. Hereditary forms include fibrodysplasia ossificans progressiva, Albright hereditary osteodystrophy, pseudohypoparathyroidism, plate-like osteoma cutis, and progressive osseous heteroplasia.[3,4]

Clinically progressive osseous heteroplasia appears as hard maculopapular lesions which over time coalesce to form plaques and spread into deeper connective tissues including fascia, skeletal muscle, tendon, and ligament. Small spicules of dermal bone may occasionally extrude through the epidermis although bone formation does not originate in the epidermis. Extensive ossification of the deep connective tissues can result in ankylosis of affected joints and growth retardation of involved limbs.[1] Hormonal abnormalities

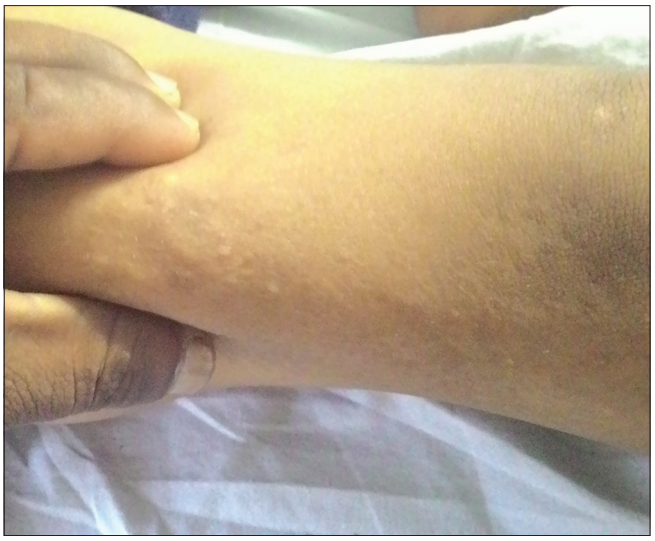

Figure 2: Skin-colored nodule over lateral aspect of right thigh

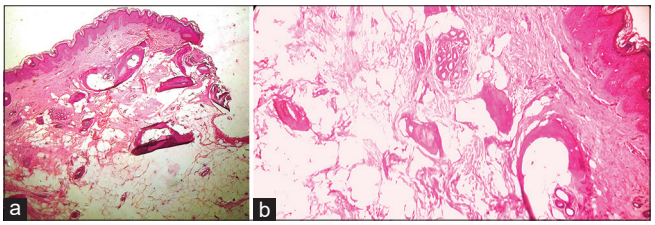

Figure 4: (a): Scanner view showing unremarkable epidermis with intramembraneous ossification and bony spicules in dermis (H and E ×40). (b): Low power view showing intramembraneous ossification and bony spicules in dermis (H and E ×100)

are rarely associated with POH, but parathyroid hormone resistance is never seen.[4] POH is caused by heterozygous inactivating mutations of GNAS, the gene encoding the alpha subunit of the G-stimulatory protein of adenylyl cyclase.[5]

These patients have an average age of onset earlier than 1 year and usually have low birth weight.[6] There is also a striking lateralization of lesions in a dermato-myotomal distribution.[7]

Radiographic appearance of POH shows a distinctive reticular pattern of web-like ectopic bone involving soft connective tissues from the dermis down to skeletal muscle. Lesional biopsy shows mostly intramembraneous ossification, with 20% showing endochondral ossification and 30% both types.[8]

POH is diagnosed on the basis of three major criteria: superficial heterotopic ossification that progresses to deep connective tissue; two or fewer Albright hereditary osteodystrophy features, excluding heterotopic ossification; and no parathyroid hormone resistance [Table 1]. In addition to these key diagnostic criteria, there are several clinical findings that support the diagnosis of progressive osseous heteroplasia [Table 1].[4]

Fibrodysplasia ossificans progressiva differs from progressive osseous heteroplasia in having characteristic malformed

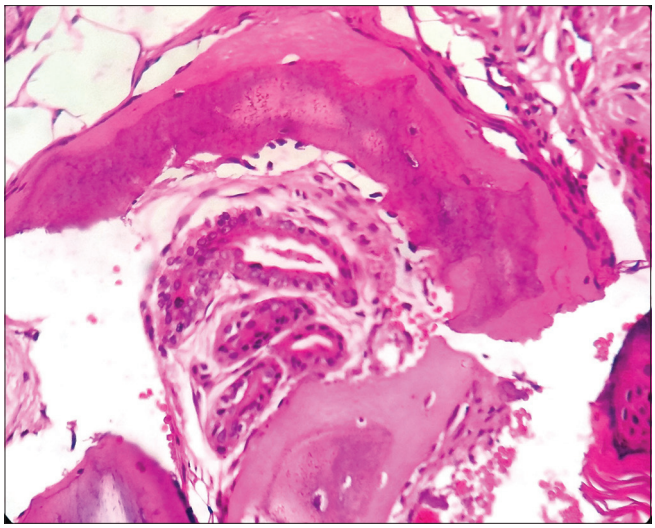

Figure 5: Highpower view showing osteoblasts with eccentrically placed nuclei embedded in eosinophilic matrix (H and E ×400)

Table 1: Diagnostic criteria for progressive osseous heteroplasia

Criteria	Features
Major criteria	Superficial and deep heterotopic ossification
	Two or fewer features of Albright hereditary dystrophy, not including heterotopic ossification
	No parathyroid hormone resistance
Supporting clinical findings	GNAS mutation
	Evidence for paternal inheritance
	Radiographic evidence for reticular pattern of ossification
	Exclusive intramembranous ossification or both intramembraneous and endochondral ossification
	Lateralization in a dermatomyotomal pattern
	History of intrauterine growth retardation
	Leanness
	Age of onset younger than 1 year

monophalangic valgoid short big toes, short thumbs, fifth finger clinodactyly, malformed cervical vertebrae, short broad femoral necks, deafness, scalp baldness, mental retardation, and physical handicap due to progressive ectopic ossification.[2] Similarly, Albright hereditary osteodystrophy is typically associated with dysmorphic "moon" facies, obesity, short stature, brachydactyly, and end-organ resistance to parathyroid hormone. Pseudohypoparathyroidism differs from progressive osseous heteroplasia in having abnormal endocrine function, and associated Albright hereditary osteodystrophy features.[2] In osteoma cutis, true bone is formed in the skin.

Surgical removal does not cure the condition as there is recurrence in most patients. Physiotherapy helps by preserving movement and prevention of skin breakdown. The parents need to be counseled to continue education as the child is mentally normal and disease does not seem to progress rapidly in adults.[2]

Our patient was having features of both superficial and deep heterotopic ossification, with normal serum levels of parathyroid hormone and calcium. There were also other supporting clinical findings of onset younger than one year, leanness, lateralization in a dermo-myotomal pattern, radiological evidence of reticular pattern of bone formation, and histopathological evidence of intramembranous ossification. We report this case because of its rarity, and to create awareness among the dermatologist and pediatricians regarding the benign nature of this condition, which may be confused with other serious hereditary forms of extraskeletal bone formation. As this condition might create apprehension among family members, early diagnosis and proper counseling play a vital role in restoring the child's normal physical and mental health.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to b`e reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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