CASE REPORT

Total Ankylosis of the Upper Left Limb: A Case of Progressive Osseous Heteroplasia

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Abstract

Progressive osseous heteroplasia is a rare inherited disease that begins with skin ossification and proceeds into the deeper connective tissues. The disease should be distinguished from other genetic disorders of heterotopic ossification including fibrodysplasia ossificans progressiva (FOP) and Albright hereditary osteodystrophy (AHO). We report a case of progressive osseous heteroplasia in a twenty four years old male with a complaint of ankylosis of the entire upper left limb and digital cutaneous lesions and sparing of the other limbs and the axial skeleton. Absence of great toe malformation, presence of cutaneous ossification, dermal bone spicules extruding in fingers, and involvement of just left upper limb were unique findings in contrast with FOP diagnosis in this case. There is no effective treatment or prevention for POH. Awareness of diagnostic features is necessary in early diagnosis of POH.

Keywords: Congenital abnormalities, Heterotopic ossification, Progressive osseous heteroplasia

Introduction

Progressive osseous heteroplasia (POH) is a rare genetic disorder of heterotopic ossification. First described in 1994 by Kaplan et al. it is characterized by cutaneous ossifications that proceed to involve subcutaneous and deep connective tissues including muscles, tendons and ligaments (1). Extensive ossification of deep tissues can lead to ankylosis of the affected joints and cause severe disability (2). Most cases are sporadic but some cases of familial transmission have been reported suggesting an autosomal dominant mode of inheritance with variable expressivity and somatic mosaicism.

Most cases of POH are caused by heterozygous inactivating mutations of GNAS, the gene encoding the alpha subunit of the G-stimulatory protein of adenylyl cyclase (Gsα). This mutation is also seen in other related genetic disorders with the feature of superficial ossification including Albright hereditary dystrophy (AHO), pseudohypoparathyroidism (PHP), and primary osteoma cutis (OC).

POH should be distinguished from two other distinct genetic disorders of abnormal bone formation: Fibrodysplasia Ossificans progressiva (FOP) and Albright Hereditary Osteodystrophy (AHO) (3, 4).

Presenting Concerns

A twenty four-years-old man presented to us with chief complaint of upper limb deformity. He was born through a normal delivery after a full term uncomplicated gestation. His parents were cousins and all of his five siblings (two brothers and 3 sisters) were healthy.

His mother had found a hardened cutaneous nodule on his medial proximal left arm for the first time when he was 1.5 years old. The pathology report for the excisional biopsy had been as myositis ossificans. By the time he was 5, several nodules developed on his left arm and forearm. Excision of all the nodules was done again as there was no clear diagnosis for his problem. Later, limitation of motion of the shoulder and elbow were gradually developed and heterotopic ossifications forming bony bridges around the shoulder and elbow joints appeared in radiography. Heterotopic ossification proceeded to involve his forearm and wrist when he was 12. Ossification of the index and middle fingers occurred a year later after a blunt trauma to the fingers. The disease progressed insidiously during years until he was 22, when painful ulcers developed on
dorsal, volar and radial sides of the third finger of the left hand.

**Clinical Findings**

The entire left upper limb was involved when we visited the patient. Shoulder range of motion was restricted to 50 degrees forward flexion and 25 degrees abduction through scapulothoracic joint while the elbow and wrist were ankylosed in flexion. Cutaneous ossified lesions with small spicules of dermal bone extruded through the skin were found on the second and third fingers that were deformed and ankylosed [Figure 1; 2].

Radiographic study showed extensive heterotopic ossification from shoulder to middle finger of left upper limb that formed bony bridge through shoulder to the hand [Figure 3; 4; 5].

Serum and urine levels of calcium, phosphorus, vitamin-D, and parathyroid hormone were normal. Creatine kinase, aldolase and liver function tests were also in the normal range.

There were no great toe malformation, no hearing loss and no other limb and axial skeleton involvement [Figure 6].

**Therapeutic Focus and Assessment**

There is no effective treatment or prevention for POH
Physiotherapy of affected limbs may be useful to preserve movement. Although trauma does not seem to precipitate or exacerbate POH lesions, surgical removal of the lesions often lead to recurrence such as the case we reported and is not recommended. Amputations are sometimes needed due to severe growth arrest and functional ankylosis (2, 6, 7).

**Discussion**

Progressive osseous heteroplasia is a very rare genetic disorder of abnormal bone formation. The disease first appears as a patchy bone formation in the skin during early childhood and then progressed to involve deep connective tissues (8-10). Heterotopic ossification can lead to ankylosis of affected joints and lead to severe disability of the patients (6).

In our patient, absence of great toe malformation as a unique feature of FOP, presence of cutaneous ossification, and especially bone spicules that extrude through the skin of the fingers as well as involvement of just left upper limb are in contrast to the diagnosis of FOP (11).

**Table 1. Case reports of progressive osseous heteroplasia (since 2002)**

<table>
<thead>
<tr>
<th>Author (Year, Ref No)</th>
<th>Age at diagnosis</th>
<th>Sex</th>
<th>Area of Calcification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 2: 3</td>
<td></td>
<td>Male</td>
<td>left lower extremity</td>
</tr>
<tr>
<td>Case 3: 9</td>
<td></td>
<td>Male</td>
<td>back and upper/lower extremity</td>
</tr>
<tr>
<td>Schrander DE, et al. (2014, 13) 7</td>
<td>Female</td>
<td>left foot, lumbar spine, and left scapulae</td>
<td></td>
</tr>
<tr>
<td>Goto M, et al. (2010, 14) 6</td>
<td>Male</td>
<td>right heel and right elbow</td>
<td></td>
</tr>
<tr>
<td>Schimmel RJ, et al. (2010,15) 8</td>
<td>Female</td>
<td>left upper limb</td>
<td></td>
</tr>
<tr>
<td>Santiago E, et al. (2009, 8) 50</td>
<td>Male</td>
<td>trunk and the left limbs</td>
<td></td>
</tr>
<tr>
<td>Kumagai K, et al. (2008, 16) 10</td>
<td>Male</td>
<td>Cervical spine, right scapular region, sacro-iliac joint and right ear helix</td>
<td></td>
</tr>
<tr>
<td>Seror R, et al. (2007, 3) 7</td>
<td>Female</td>
<td>lumbar spine and left scapulae</td>
<td></td>
</tr>
<tr>
<td>Hou JW. (2006, 17) 5.5</td>
<td>Female</td>
<td>Scalp, left shoulder and back</td>
<td></td>
</tr>
<tr>
<td>Chan I, et al. (2004, 18) 9</td>
<td>Female</td>
<td>trunk and legs</td>
<td></td>
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</tbody>
</table>

Normal endocrine function of the patient, absence of moon facies, obesity and short stature and progression of heterotopic ossification from skin to the muscles ruled out Albright hereditary osteodystrophy (AHO) and also primary osteoma cutis (6, 12).

Since 2002 nine case report articles including 11 POH patients have been published in English literature. Their characteristics were summarized in Table 1.

Our case is a POH patient with involvement of just one limb and he had not been diagnosed until he was twenty four years old. It is important for pediatricians, dermatologists and orthopedic surgeons to be aware of clinical and radiological features of POH so early diagnosis and proper counseling can be offered.

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References


