Cutaneous ossification is a marker of Albright hereditary osteodystrophy

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Abstract

Cutaneous ossification is a rare group of disorders seen in paediatric population. Initial presentation is with asymptomatic hard lesion in skin. It may manifest at birth or shortly thereafter. In addition to cutaneous manifestation child may have dysmorphic features or stigmata of end organ resistance to hormones. Here we report a case of Albright hereditary osteodystrophy in a four years and seven months old girl for its rarity.

Introduction

Cutaneous ossification is classified in to primary form the osteoma cutis and secondary form the metaplastic ossification. In primary form there is an absence of a preexisting lesion or associated lesion and there are several distinct clinical variants. In secondary type ossification develop in association with or secondary to wide range of inflammatory, traumatic or neoplastic processes[5,6].

Case history

A four years and seven months old girl was referred by a paediatrician for evaluation of skin plaques. She was born to non-consanguineous healthy parents following an uneventful antenatal period by an emergency cesarean section due to foetal distress. Her birth weight was 2.5 kg. Her postnatal period was uneventful. Her younger brother who is 2 years old was healthy. Child was clinically normal up to 2 months of age.

Since 2 months of age child had excessive weight gain and evaluated in paediatric clinic since 5 months of age. At 5 months her weight was more than 4SD, height was between median and 1SD, weight for height was more than 5SD. This was attributed to over feeding. Her blood glucose, serum cholesterol, liver function and serum cortisol were normal. Her bone age was age appropriate. Her USS of abdomen showed mild hepatomegaly and no suprarenal masses. USS brain was normal.

At 6 months of age mother noticed a brownish rash on the skin and hard lesions beneath the affected skin. These lesions were seen in left lower abdomen, right thigh and right ankle. The lesions were asymptomatic and increased in size with the age. No new lesions appeared. At the 4 years and seven months of age child was referred by a pediatrician to dermatology clinic for evaluation of skin plaques.

On examination her weight was 19.2kg (1SD-median), height was 0.99m (-1SD – -2SD) and BMI was 19.5kg/m^2 (more than 98th centile) indicating obesity. She had a round face with short stocky built and short fingers (brachydactily). There were no other dysmorphic features (Figure 1 & 2).

Figure 1. *Round face with short stocky built.*

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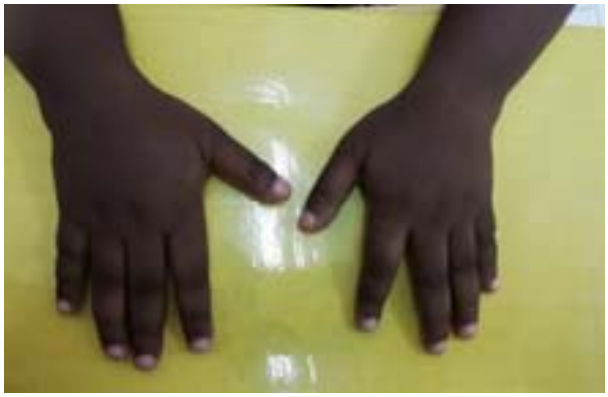

Figure 2. *Brachydactyly.*

Cutaneous examination revealed brownish ill defined plaques over lower abdomen, right thigh and right ankle (Figure 3, 4 & 5). On palpation they were hard and non tender. Her system examination was normal.

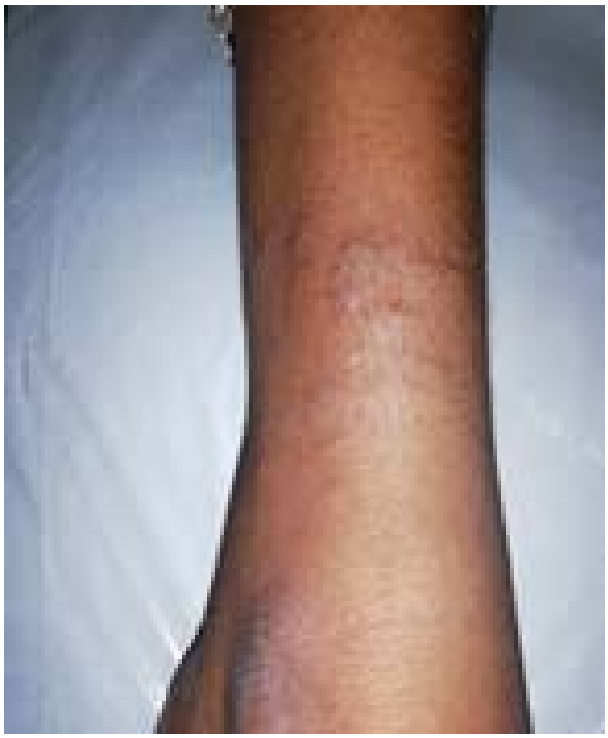

Figure 3. *Lesion on ankle.*

The differential diagnosis of cutaneous calcification and cutaneous ossification were made. The skin biopsy from the left lower abdominal lesion was done under local anaesthesia. Histology showed unremarkable epidermis. Within the dermis there were segments of bone focally rimmed by osteoblasts. There was no evidence of calcification, inflammation or neoplastic cells (Figure 6 & 7). These features were compatible with osteoma cutis (primary cutaneous ossification).

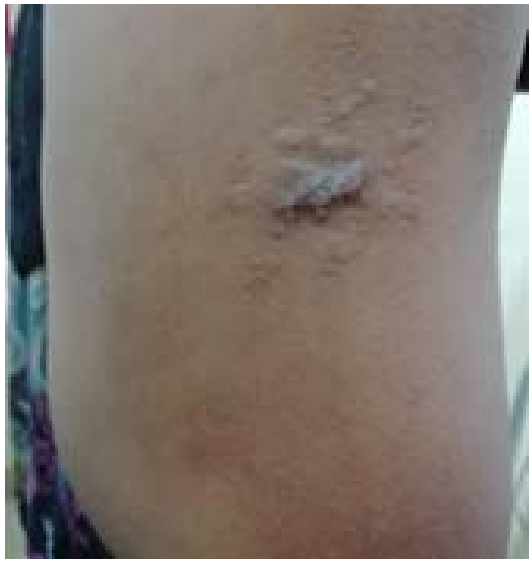

Figure 4. *Hard plaques.*

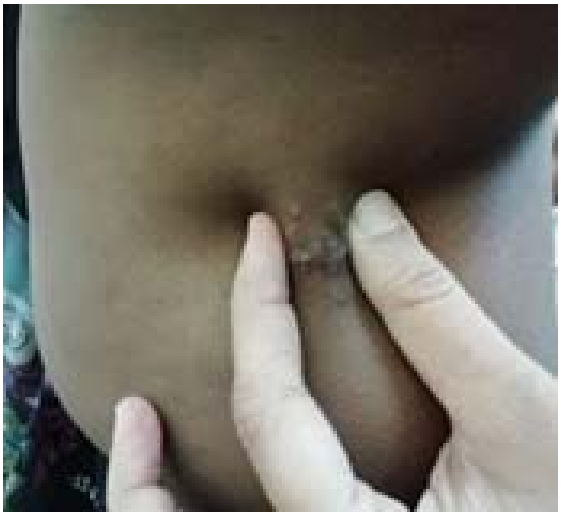

Figure 5. *Abdominal lesion.*

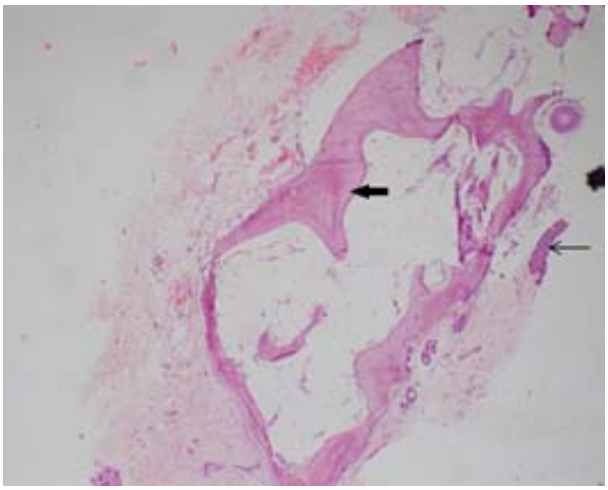

Figure 6. *×20 Thin arrow show epidermis. Thick arrow show bone (H&E).*

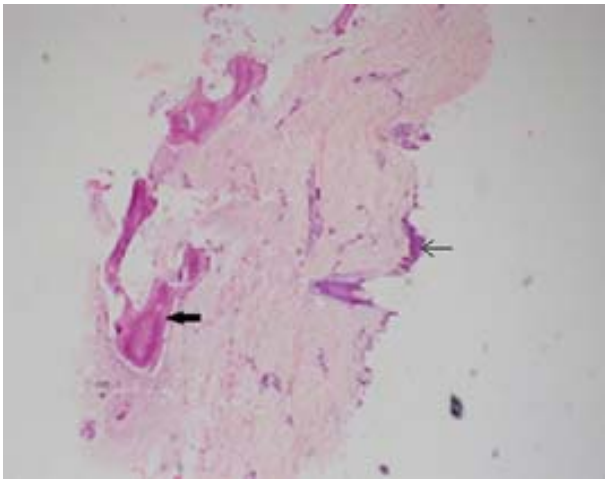

Figure 7. ×*20 Thin arrow show epidermis. Thick arrow show bone (H&E).*

Her serum calcium level was normal, serum phosphate and alkaline phosphatase (ALP) levels were high, parathyroid hormone level was markedly high and TSH level was within normal range. The radiological imaging didn't show underlying fascia or muscle involvement.

Considering the clinical presentation and investigations diagnosis of Albright hereditary osteodystrophy with the association of pseudo hypoparathyroidism type 1a or type 1c was made. The child was referred to the paediatric endocrinologist for further management of pseudo hypoparathyroidism and to the paediatric surgeon for surgical excision of the plaques.

Discussion

Primary cutaneous or subcutaneous ossification can be divided in to four main sub types. They are progressive osseous heteroplasia (POH), Albright hereditary osteodystrophy (AHO), fibrodysplasia ossificans progressiva (FOP) and plate like osteoma cutis (POC). POH, AHO and POC are spectrum of diseases associated with heterozygous inactivating mutations of GNAS, the gene encoding the alfa subunit of the stimulatory guanine nucleotide binding protein (Gsα). This coupling factor enhance binding of hormones like PTH to cell surface and stimulate cyclic adenosine monophosphate (cAMP) production[1,2].

There have been two mechanisms which explain the heterotrophic bone formation in skin. The first mechanism is persistence of primitive mesenchymal cells in skin differentiating into osteoblasts which lead to bone formation known as hamartomas. The second mechanism is transformation of extra skeletal mesenchymal cells into bone forming cells known as metaplasia[1].

Albright hereditary osteodystrophy is associated with ossification limited to skin and subcutaneous tissue. There are characteristic features of AHO. They include round face with short stocky built, obesity, shortening and widening of long bones in hand and foot (brachydactyly) specially shortening of 4th and 5th fingers, dimpling over dorsal surface of metacarpophalangeal joints, abnormal dentition and neurobehavioral problems. AHO is usually associated with end organ resistance to parathyroid hormone (pseudo hypoparathyroidism) or other hormones like thyroid stimulating hormone (TSH), gonadotropins and glucagon[1,2,3,4].

The child presented to us had similar AHO features of round face with short stocky built, brachydactyly, obesity, cutaneous ossification and biochemical evidence of PHP type la or type lc. Facilities to measure Gsα level was not available in our laboratory setup limited the accurate sub typing of PHP in index case.

When consider the other types of primary cutaneous ossification, in progressive osseous heteroplasia the lesions present at birth or shortly thereafter. During infancy ossification limit to superficial dermis but during childhood it progresses to deep connective tissue and skeletal muscle. There will be elevated ALP level due to active ossification and elevated muscle enzymes secondary to muscle invasion. Some patients may present with resistance to PTH or TSH[1].

Fibrodysplasia ossificans progressiva is extremely rare disease. In here fibrous tissue including muscle, tendon and ligament are ossified spontaneously or following damage. Usually first ossification present before 10 years of life and ossification progresses from top of the body to downwards. The ALP and bone specific ALP is high[8].

Plate like osteoma cutis is characterized by presence of at least one bony plate with or without other osteomas present at birth or first year of life. There are no features of abnormal calcium and phosphate metabolism and not associated with trauma or other predisposing event[1].

The treatment for AHO is vitamin D active metabolites and calcium supplements to maintain serum calcium and phosphate levels. It is recommended to give alfacalcidol and calcitriol 20-50 mg/kg/day in two divided doses. For the osteomas surgical excision is the only way of treatment[1,7].

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