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Painful subcutaneous nodules on the thigh

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Abstract

Osteoma cutis is the presence of bone within the dermis or subcutaneous tissue. This condition may occur sporadically or secondary to other dermatologic or genetic conditions. We present a 12-year-old girl with pseudohypoparathyroidism type-1a who developed osteoma cutis on the right thigh.

Keywords: osteoma cutis, ectopic bone, pseudohypoparathyroidism type-1a, PHP1A, Albright hereditary osteodystrophy, AHO

Case Synopsis

A 12-year-old girl with pseudohypoparathyroidism type-1a (PHP1A, OMIM#103580) presented with 2 hard, painful subcutaneous nodules on her right thigh. The nodules appeared 2 years earlier and were growing larger and more tender. She denied a history of trauma to the region. On examination, the patient showed the assemblage of clinical features termed Albright hereditary osteodystrophy (AHO), [1]: short stature (141cm), obesity (32kg/m²), round facies, mild cognitive delay, and brachydactyly related to short metacarpals. On her right thigh, there was a 6cm by 4cm firm, irregular-shaped plaque containing two discrete hard, angular, blue-hued nodules, each 5mm in size (**Figure 1**). The patient also had several dozen depressed, soft, easily dimpled macules scattered on the thighs and abdomen.

The 2 nodules were removed with 5mm punch biopsies. Histopathologic examination showed ectopic bone within the dermis and subcutis

(osteoma cutis), (**Figure 2**). The depressed lesions were clinically consistent with anetoderma but were not biopsied, as the findings would not change clinical management.

Case Discussion

Osteoma cutis is the presence of true bone (deposition of both phosphorus and calcium within proteinaceous matrix as hydroxyapatite) within the dermis or subcutaneous tissue. This condition can develop as an isolated skin disease, secondary to another dermatologic condition such as acne, or in association with genetic syndromes including AHO [2]. Osteomas can be very painful and often surgical excision is necessary to treat this condition.

Albright hereditary osteodystrophy is a rare genetic disorder with a classic phenotype of short stature, obesity, round facies, mental retardation, and brachydactyly related to shortened metacarpals, as seen in this patient (**Figure 3**). X-ray of the hands showing shortening of the 4th metacarpal in particular may be helpful in diagnosing this condition [3].

The AHO phenotype results from autosomal dominant inheritance of a loss-of-function mutation in the Gs-alpha subunit of the *GNAS1* gene (20q13.3), regardless of the parent of origin [4]. Owing to genetic imprinting at this locus, the maternal *GNAS1* allele is more heavily expressed than the paternal allele in several tissues, specifically the proximal renal tubules, thyroid, ovaries, and pituitary [4]. Therefore, inheriting a mutant maternal allele causes widespread endocrine dysfunction and end-organ



Figure 1. Photograph of anterior right thigh showing an irregularly-shaped plaque with two central blue-hued nodules as well as several depressed, easily dimpled macules inferior to plaque.

resistance to parathyroid hormone [5], as seen in our patient. In contrast, those who inherit a mutant paternal allele, have normal endocrine and renal function because they inherit normal maternal Gs-alpha expression. The AHO phenotype in the absence of renal or endocrine gland resistance is called pseudopseudohypoparathyroidism (PPHP, OMIM#612463). Osteoma cutis may develop in both PHP1A and PPHP and, therefore, does not appear to be related to abnormalities in calcium and phosphorus homeostasis [6]. Although the mechanism is not well understood, some suggest that it may result from alterations in the genes that control bone formation [2]. Decreased Gs-alpha activity secondary to mutations in the *GNAS1* gene may lead to the osteogenic differentiation of mesenchymal cells,

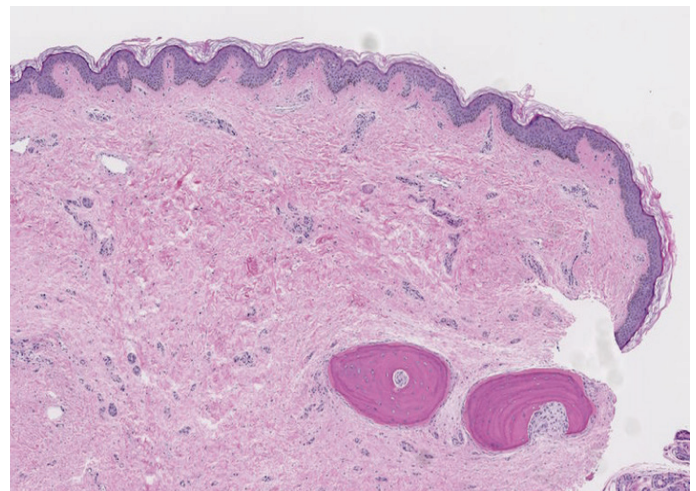


Figure 2. Histopathology of biopsy specimen demonstrating bone within the dermis, (H&E, 10x).

potentially resulting in the development of osteoma cutis in PHP1A and PPHP [7].

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Figure 3. X-ray of left hand showing brachydactyly and short metacarpals with 4th digit most markedly affected.