CASE REPORT

Plate-like osteoma cutis: nothing but skin and bone?

Inês Coutinho, V Teixeira, J C Cardoso, J P Reis

Department of Dermatology,
Coimbra University Hospital,
Coimbra, Portugal

Correspondence to

Dr Inês Coutinho,
inesdantascoutinho@gmail.
com

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SUMMARY

Osteoma cutis encompasses a group of cutaneous ossifying disorders, more commonly secondary to trauma, inflammation or neoplasms. Fourteen per cent, however, are primary, and these may be syndromic (associated to Albright's hereditary osteodystrophy) or occur in isolation. We report a case of a 10-year-old girl who presented with a stone-hard plate on the scalp, with no relevant personal or family history, nor changes in calcium-phosphate metabolism, parathyroid hormone or thyroid function. Skin biopsy confirmed osteoma cutis. Plate-like osteoma cutis is rare, and believed to be a non-progressive form of heterotopic ossification, included in the spectrum of progressive osseous heteroplasia and Albright hereditary osteodystrophy, due to GNAS gene mutations. This recently clarified association should remind us of the possible unfavourable evolution of a seemingly innocent clinical picture, emphasising the need for appropriate evaluation, management and follow-up.

BACKGROUND

Heterotopic ossification is nothing other than extraskelatal bone formation and can occur in the skin, hence the name osteoma cutis. Contrary to cutaneous calcification, which can occur in renal disease or inflammatory conditions, ossification can only be stated when there is dermal deposition of calcium and phosphorus in a proteinaceous matrix as hydroxyapatite crystals, sometimes extending to deeper tissues.¹

Osteoma cutis can be classified according to whether it occurs as a primary event or secondary to trauma, inflammation or neoplasm. It may also be divided on the basis of its clinical features, whether it is single, plate-like, widespread or presenting as multiple military osteomas of the face.

Primary osteoma cutis comprises 14%² of all skin ossifications. Given its rarity (only 10 cases found in 20 000 pathology specimens³) many physicians are not aware of the possible association with other syndromes such as Albright's hereditary osteodystrophy (AHO) or progressive osseous heteroplasia (POH), with the added difficulty that in many cases only time will tell the evolution of the disease.

POH and AHO occur with osteoma cutis.⁴ The former is a rare disorder in which progression of ossification affects not only the skin but also deep tissues, including fascia and muscle, leading to severe impairment due to movement restriction. The latter frequently includes osteoma cutis as a part of a syndrome that also encompasses endocrinological abnormalities, round faces, obesity,

mental retardation and short fourth and fifth metacarpals.

Plate-like osteoma cutis, a rare variant of primary cutaneous osteomas, was first described in 1978 and many reports have stated its association to GNAS gene mutations.^{5–8}

The same gene has been implicated in the pathogenesis of POH and AHO,⁴ and may be responsible for adipose tissue-derived mesenchymal cell commitment to osteogenic differentiation, with considerable phenotypic heterogeneity and overlap between the different diseases. Therefore, current knowledge groups primary plate-like osteoma cutis as a limited non-progressive variant of POH, and highlights the complex relationship between these three entities.

CASE PRESENTATION

We report the case of a 10-year-old girl, with normal birth weight, and no relevant personal history, who presented with a stone-hard, round, erythematous, crusted, alopecic plaque that measured 6×7 cm on the right parietal region (figure 1). This lesion was neither painful nor pruritic and was slowly evolving since she was a few months old. She had no other symptoms. Parents were non-consanguineous, family history was unremarkable

Figure 1 Stone-hard erythematous crusted plaque on the right parietal region.

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and physical examination revealed no abnormal features and a normal weight-for-age and length/height-for-age.

INVESTIGATIONS

We performed a 5 mm punch biopsy of the centre of the lesion that showed a dermal well-differentiated ossified plaque with adipocytes and small vessels between bone trabeculae, resembling bone marrow (figures 2 and 3). The overlying epidermis was normal and there was no significant involvement of the subcutis.

Renal function, serum calcium and phosphate values were within normal range. Urinalysis, parathyroid hormone (PTH), thyroid-stimulating hormone, FT3 and FT4 levels were also normal.

DIFFERENTIAL DIAGNOSIS

Metastatic, dystrophic, idiopathic and iatrogenic calcification are all included in the differential diagnosis of stone-hard skin lesions, however, in this case they were ruled out on the basis of actual bone formation in the dermis (as opposed to just calcium deposits) and a negative personal history. Secondary osteomas were also excluded because of no evidence of a predisposing condition.

Among the primary cutaneous osteomas, the conformation and location of the patient's plaque, its congenital presentation and the absence of metabolic abnormalities allowed us to classify it as plate-like osteoma cutis.

Since there were no facial dysmorphisms, orthopaedic anomalies, obesity, mental retardation or a positive family history, AHO was also unlikely.

Finally, only a longer follow-up will show whether this lesion will recur and progress to deeper tissues, allowing us to define it as POH.

TREATMENT, OUTCOME AND FOLLOW-UP

The patient is currently waiting for surgical treatment of the lesion, and maintains follow-up consultations with no extension of the plate.

Figure 2 Biopsy, H&E stain, ×4 augmentation, displaying a trabecular ossified plaque with adipocytes.

Figure 3 Biopsy, H&E stain, ×40 augmentation, showing adipocytes resembling bone-marrow within the bony plate.

DISCUSSION

Plate-like cutaneous osteoma, as it was coined by Burgdorf and Worret in 1978,⁹ is a rare variant of primary osteoma cutis that fulfils the following:

1. A bony plate, present since birth or in the first year of life.
2. No associated metabolic changes.
3. Presence or not of other associated osteomas.
4. No evidence of trauma, infection or other predisposing events.

Most cases are present since childhood, on the scalp and there is a slight female predominance, but there are also reports of acquired primary osteoma cutis, presenting mainly during the second and third decade.

POH is a rare disease, described since 1994,¹⁰ in which there is progressive ossification of the dermis in infancy and subcutaneous and deep connective tissue during childhood. It progresses more slowly in adulthood, but tends to lead to ankylosis of the affected joints and focal growth retardation of the affected limbs. It can be either inherited in an autosomal dominant manner or appear sporadically, and it is not associated with endocrinological abnormalities.⁴

AHO, reported first in 1942 by Albright *et al*¹¹ encompasses heterogeneous clinical features such as obesity, round faces, short stature, short metacarpals and mental retardation with osteoma cutis and endocrinological abnormalities. It classically presents with pseudohypoparathyroidism (elevated PTH, hypocalcaemia and hyperphosphatemia due to renal PTH resistance), but it can also occur without these features in the AHO/pseudopseudohypoparathyroidism with no hormonal resistance.¹²

The link between primary osteoma cutis, including the plate-like variant, and POH/AHO is currently being investigated. Recent publications have shown its clear relation to GNAS1^{5–8} gene mutations, a key regulatory gene also in POH and AHO.^{4 12}

The GNAS1 gene is located on chromosome 20 and encodes a transcript for the α subunit of the G stimulatory protein of adenyl cyclase (Gs α),^{13 14} which is thought to be a negative regulator for osteogenic lineage. It is subject to imprinting in a

tissue-specific manner in which maternal inheritance is responsible for an AHO phenotype and paternal inheritance for POH or AHO with pseudo-pseudohypoparathyroidism.^{13 14}

Inactivating mutations, due mainly to frameshift or nonsense mutations, lead to reduction of protein expression or functional activity by 50%,^{4–8} but the mechanism through which G stimulatory protein regulates osteogenesis, and how exactly the mutated protein allows for de novo bone formation in the skin and underlying tissues is still unknown.

Thus, when faced with a primary osteoma cutis, it seems advisable to perform a thorough clinical history, completed with family history and physical examination (that can reveal dysmorphisms) and search for laboratory signs of pseudohypoparathyroidism such as hypocalcaemia and elevated PTH.¹⁵ Even when the clinical picture is innocent, yearly follow-up to monitor progression of ossification is of interest because a single plate-like osteoma cutis may represent a slowly evolving POH.¹⁶

First treatment option for isolated plate-like cutaneous osteoma is surgery, with good results and low recurrence rate, however, if the lesion is regarded as POH, because of its relentless course, the risk of recurrence will rise.

Learning points

- Osteoma cutis corresponds to de novo bone formation in the dermis.
- Its pathogenesis is linked to GNAS gene mutations.
- It may represent a limited variant of progressive osseous heteroplasia.
- It can be associated to pseudohypoparathyroidism.
- Endocrinological evaluation and yearly follow-up is advisable.

Contributors IC is the corresponding author, she elaborated the manuscript and performed literature search. VT was responsible for literature search, JCC was

fundamental in the evaluation of the patient, histopathological evaluation and manuscript review. JPR was responsible for supervising and reviewing the manuscript.

Competing interests None.

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