Perforating osteoma cutis: case report and literature review of patients with a solitary perforating osteoma cutis lesion

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Abstract

Osteoma cutis, the development of bone in the dermis and/or subcutaneous fat, can occur as either a primary or secondary condition. Perforating osteoma cutis is rare. A man with a solitary lesion of perforating osteoma cutis is described and the features of individuals with a single perforating osteoma cutis skin lesion are reviewed. A solitary lesion of either primary or secondary perforating osteoma cutis has only been observed in two men and one woman; the lesions had been present from less than one month to 19 or 20 years prior to establishing the diagnosis. The lesion was either located on the forehead (two men) or the breast (one woman). The erythematous (two lesions) or flesh-colored nodules ranged in size from 8×8 millimeters to 1.5×0.5 centimeters. Each had epidermal perforation by bone through a central area that was either crateriform or crusted or keratotic. The clinical differential diagnosis included keratoacanthoma, phlebolith, pilomatricoma, pilomatrical carcinoma, and squamous cell carcinoma. The perforating osteoma cutis lesion was successfully treated with either excision or shave biopsy without recurrence at either 10 or 12-months follow-up.

Keywords: acquired, bone, congenital, cutis, osteoma, perforating, primary, secondary, solitary

Introduction

Osteoma cutis is characterized by the development of bone in the dermis and/or subcutaneous fat, but perforating osteoma cutis is rare. A man with a solitary lesion of perforating osteoma cutis is described and the features of individuals with a single perforating osteoma cutis skin lesion are reviewed [1, 2].

Case Synopsis

A 91-year-old man presented for evaluation of an asymptomatic rapidly growing umbilicated nodule of less than one-month duration on his scalp. He previously had a basal cell carcinoma on his nose that was excised using the Mohs micrographic controlled surgical technique six months earlier with a full-thickness skin graft and subsequent dermabrasion of the wound site; there has been no recurrence. He also has a history of actinic keratoses on his face and scalp that have been treated with liquid nitrogen cryotherapy. His dermatologic history is also significant for rosacea (that is controlled with metronidazole 0.75 percent gel each morning and azelaic acid 15 percent gel each evening), seborrheic dermatitis of the eyebrow and nasal bridge areas (that is controlled with moisturizing cream), and dermatitis of his legs (that is controlled with daily ammonium lactate 12 percent lotion or moisturizing cream).

His medical history was significant for several conditions including benign prostatic hypertrophy, coronary artery disease (with six prior angioplasties, three stents and a pacemaker), gastroesophageal reflux disease, hyperlipidemia, hypertension, hypogonadism (primary) with erectile dysfunction, hypothyroidism, insomnia, lactose intolerance,

osteopenia, and tactile (vibratory) sensory deficit in his feet. His medications include aspirin, clopidogrel, ezetimibe-simvastatin, finasteride, fluticasone propionate nasal spray, hydrochlorothiazide, levothyroxine, omega-3 fatty acids, ranitidine, tamsulosin, travoprost ophthalmic solution, vardenafil, and vitamins (B complex, biotin and cholecalciferol).

Cutaneous examination of his face showed a flesh-colored 8 x 8 mm nodule with extrusion of firm material from a central crateriform depression on his central forehead (**Figure 1**). The clinical differential diagnosis included a keratoacanthoma, squamous cell carcinoma, pilomatricoma, and pilomatrical carcinoma. A shave biopsy was performed.

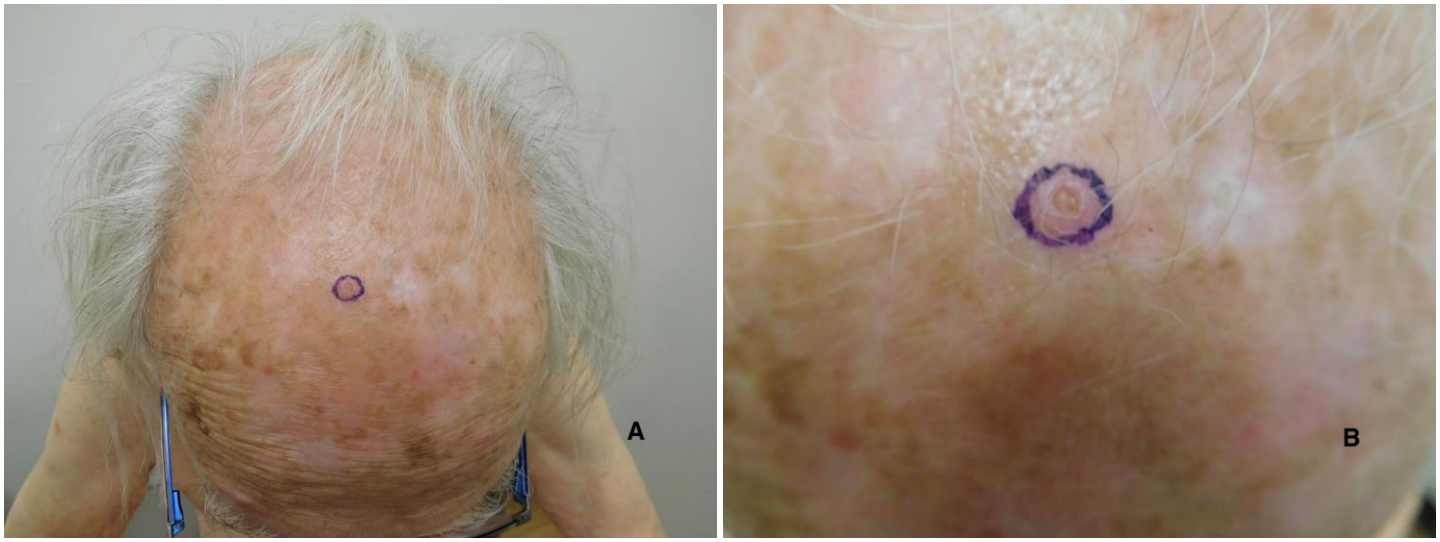

Figure 1. *Distant A) and closer B) views of the clinical features of a solitary perforating osteoma cutis lesion (which is circled in purple ink) that presented as a rapidly growing 8×8 mm nodule with extrusion of osseous material from a central crateriform depression on the central forehead of a 91-year-old man.*

Microscopic examination of hematoxylin and eosin stained sections showed a crateriform lesion with a raised epithelial edge and a central invagination. The invagination is filled with bone centrally and keratin at the lateral edges. At one side of the crater, there is perforation of the epidermis with extrusion of basophilic osseous and partially calcified homogenous material from the dermis through the epidermal channel. There is also inflammation and a proliferation of vessels surrounding the bone in the dermis (**Figure 2**).

An immunoperoxidase study was also performed. Beta-catenin, a 92-kilodalton protein, plays a role in the development of hair follicle-related tumors. In pilomatricomas, the nucleus and membrane of all the basaloid cells shows strong beta-catenin expression whereas the transitional cells and shadow cells show negative immunoreactivity [3]. Beta-catenin staining was negative in the dermal lesion, excluding the possibility of pilomatricoma.

Correlation of the clinical presentation, hematoxylin and eosin stained sections, and the immunoperoxidase studies established the diagnosis of a solitary perforating osteoma cutis. The biopsy site healed within four weeks. There has been no recurrence at one-year follow-up.

Case Discussion

Osteoma cutis is primary in about 15 percent of patients and is secondary in approximately 85 percent of individuals [2, 4, 5]. There are two categories of primary osteoma cutis. The first category is secondary to Albright hereditary osteodystrophy (that may be associated with either pseudohypoparathyroidism or pseudopseudohypo-parathyroidism), progressive osseous heteroplasia, and progressive ossifying fibrodysplasia [4-6]. The other category of primary osteoma cutis has four subtypes: isolated osteoma [5], disseminated osteoma [7], multiple miliary osteo-ma of the face [8, 9], and plate-like osteoma [6, 10, 11].

Secondary osteoma cutis is also ref erred to as acquired osteoma cutis. It occurs at sites of prior chronic venous insufficiency or inflammatory conditions (such as acne vulgaris, dermatomyositis, development: primitive mesenchymal cells (that would have normally differentiated toward osteoclasts and suffered a failure during their migration) now become ossified [13].

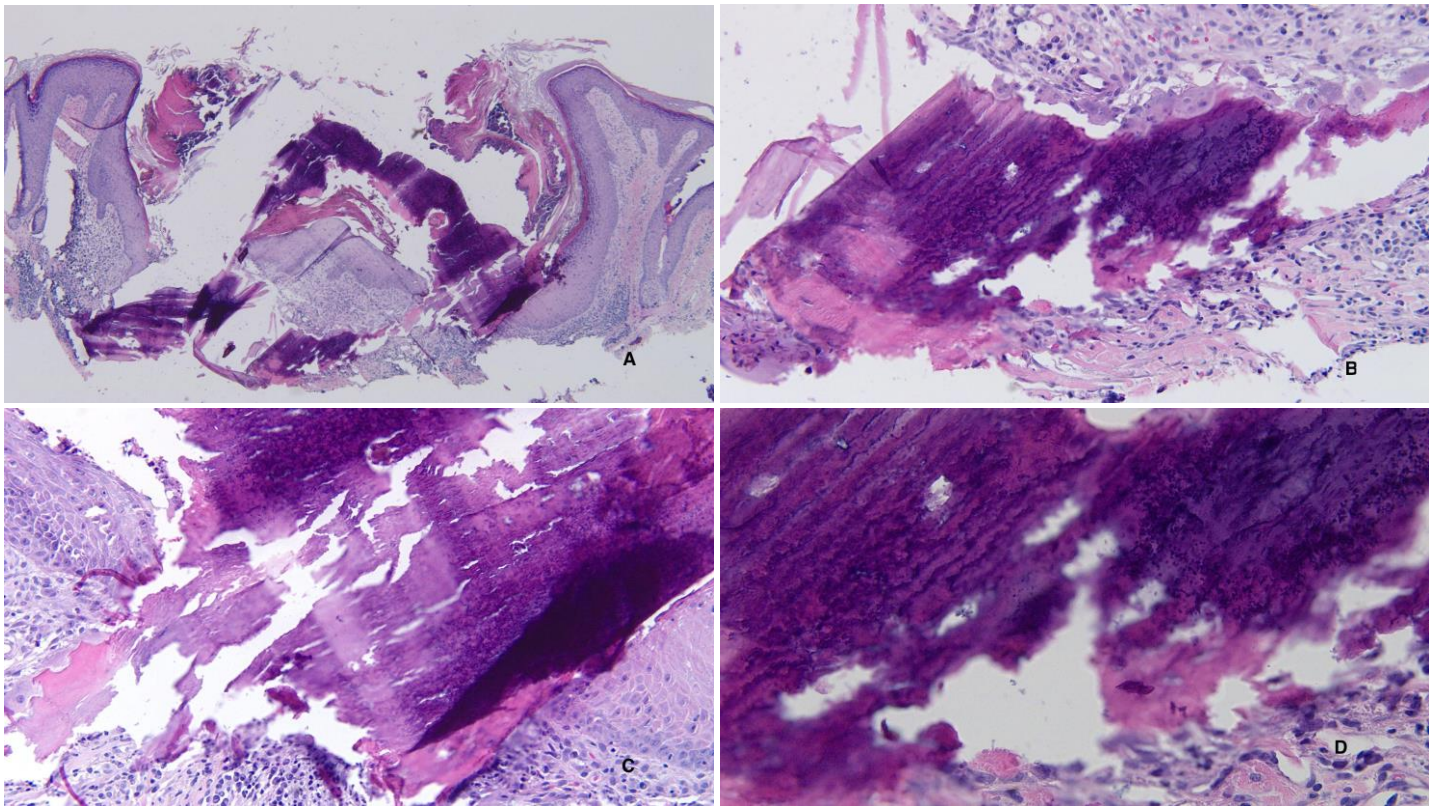

Figure 2. *Pathology features of acquired perforating osteoma cutis. Distant (A and B) and closer (C and D) view of hematoxylin and eosin stained sections of a solitary perforating osteoma cutis lesion from the central forehead of a 91-year-old man. The crateriform lesion has a raised peripheral epithelial border and a central invagination which is filled with bone centrally and keratin at the lateral edges, A). Bone is present with surrounding inflammation and vessels in the dermis, B); protruding through the perforated epidermis, C); and at the base of the central invagination, D). A) 2×; B) 2×; C) 10×; D) 20×.*

and scleroderma). It also can occur in association with benign and malignant cutaneous tumors (such as basal cell carcinoma, chondroid syringoma, hemangioma, nevus, and pilomatricoma) or trauma (such as the site of an accident, chronic irritation, injection or surgery within the scar), [2, 5, 6, 12].

The pathogenesis of osteoma cutis remains to be definitively established [2, 5, 11, 13, 14]. In primary osteoma cutis, intramembraneous ossification — beginning in the dermis — may result in the formation of bone [5]. Some investigators propose that multiple stimuli are capable of causing metaplasia of dermal fibroblasts and the subsequent development of osteoblasts [2, 13]. Alternatively, other researchers suggested bone formation occurs secondary to an alteration of embryonic

A *GNAS1* gene mutation has been identified in a child with severe congenital plate-like osteoma cutis [14]; it has also been found in patients with Albright's hereditary osteodystrophy and progressive osseous heteroplasia [13]. The gene *GNAS1* encodes for the alpha-subunit of the stimulatory G protein; this protein regulates adenyl cyclase activity. Reduced levels of downstream proteins result from inactivating mutations of the *GNAS1* gene. These proteins normally inhibit the cellular induction of osteoblast differentiation in ectopic sites. Therefore, lower levels of these proteins are insufficient to maintain their inhibitory control of ectopic bone formation. However, to date, a mutation in the gene *GNAS1* has not been identified in patients with acquired plate-like osteoma cutis [11, 13].

Perforating dermatoses have been observed in patients with collagenosis, elastosis, folliculitis, granuloma annulare, Kyrle disease, and renal disease. Perforating osteoma cutis is rare. Including the patient in this report, perforating osteoma cutis of a solitary lesion has been described in three individuals (**Table 1**), [1, 2].

A solitary lesion of perforating osteoma cutis has been observed in two men and one woman. The patients range in age at diagnosis from 24 years-old [1] to 91 years-old (current report); the third patient was 40 years-old [2]. Prior to evaluation, the osteoma cutis lesion had been present from less than one month (current report) to as long as 19 [1] or 20 [2] years. The woman who had diabetes mellitus and a lesion on her left breast noticed that the site had thickened and oozed fluid for the final two years prior to diagnosis [2].

The solitary osteoma cutis lesion was located on the forehead in both men. The younger man's lesion was found at his hairline [1]. The lesion was located in a similar area on the older man's forehead. However, he had androgenic alopecia of his scalp without any hair around the osteoma cutis lesion (current report). The woman's lesion was located on the proximal superior region of her left breast [2].

The lesions ranged in size from 8×8 mm (current report) to 1.5×0.5 cm [1]; the third lesion was 1.0×0.5 cm [2]. Two of the lesions were erythematous nodules [1, 2]; the third lesion was flesh-colored (current report). Perforation of bone through the epidermis was described for each lesion. One lesion

Table 1. *Clinical features of patients with a solitary lesion of perforating osteoma cutis.*

C	DA (y) Sex	Dur (y)	Location	Size (mm)	Appear Morph	OC	Etio	DDx	Lab	Tx	FU	Ref
1	24 M	19	Forehead at hairline	15x5	Red Hard nodule with central crust	1°	None -Tma -PSD	NR	[a]	Ex	10	1
2	40 W	20 [b]	Left breast	10x5	Red Nodule with central keratotic crater	2°	Chron irrit	Phl	[c]	Ex	NR	2
3	91 M	0.8	Central forehead	8x8	Flesh-colored Nodule with crater; material extrudes from center	2°	LN2 cryo	KA PCA Pilo SCC	[d]	Bx	12	CR

Abbreviations: Appear, appearance; Bx, biopsy (shave); C, case; Chron irrit, chronic irritation; CR, case report; DA, diagnosis age; DDx, differential diagnosis; Dur, duration of lesion prior to diagnosis; Etio, etiology; Ex, excision; FU, follow up (number of months after excision or biopsy without recurrence); KA, keratoacanthoma; LN2 cryo; liquid nitrogen cryotherapy; M, man; mm, millimeters; Morph, morphology; NR, not reported; OC, osteoma cutis; PCA, pilomatrical carcinoma; Phl, phlebolith (mammography showed solitary calcification at the site); Pilo, pilomatricoma; PSD, prior skin disease; Ref, reference; SCC, squamous cell carcinoma; Tma, trauma; Tx, treatment; W, woman; y, years. 1°, primary; 2°, secondary (or acquired); -, no
[a]Calcium, phosphorus, alkaline phosphatase, and parathyroid hormone were within normal limits.
[b]The lesion thickened and oozed fluid for the two years prior to diagnosis.
[c]The thyroid and parathyroid hormone levels were within normal limits.
[d]Thyroid function tests and calcium and phosphorus were within normal limits.

was a hard nodule with a central crust [1], whereas another lesion had a central keratotic crater [2]. The third lesion was a nodule with extrusion of material from the crateriform depression in its center (current report).

All of the lesions showed similar pathologic changes. Bony nodules were present in the dermis. Some lesions also demonstrated areas of calcium deposits. There was a central channel in the epidermis through which the bone perforated from the underlying dermis. An inflammatory infiltrate was frequently present in the dermis surrounding the perforating bone [1, 2].

The young man's solitary lesion of osteoma cutis was considered to be primary in etiology. It had been present since five years of age and there had been no trauma or prior skin disease at the location [1]. In contrast, the osteoma cutis lesions in the woman and the older man were favored to be acquired or secondary. The investigators speculated that the differentiation cells on the woman's left breast into osteoblasts resulted from superficial inflammation that was induced by persistent and chronic irritation by her brassieres [2]. In the current report, the elderly man's scalp lesion appeared recently and the area had likely been previously treated with cryotherapy using liquid nitrogen.

The clinical differential diagnosis was described for two of the patients. The woman had a mammography of the site on her left breast; the results were interpreted as a phlebolith [2]. The pathology requisition listed the following diagnoses, in order of likelihood, for the older man's lesion: keratoacanthoma, squamous cell carcinoma, pilomatricoma, and pilomatrical carcinoma.

A personal or family history of pseudohypopara-thyroidism or pseudopseudohypo-parathyroidism was not reported for any of the patients with a solitary osteoma cutis lesion. All of the patients had several of the following laboratory studies performed: alkaline phosphatase, calcium, parathyroid hormone, phosphorus, thyroid function tests, and "thyroid hormone." In all cases, the results were within normal limits [1, 2, current report].

The treatment of the solitary osteoma cutis lesion was surgical removal. After an initial 3-millimeter punch biopsy to establish the diagnosis, the residual osteoma cutis from the young man's forehead was excised [1]. Similarly, an excisional biopsy was performed for diagnosis and removal of the lesion on the woman's left breast. The osteoma cutis on the older man's forehead was evaluated with a shave biopsy that removed the epithelial portion of the lesion and extended into the reticular dermis.

Follow up was provided for both men. There was no recurrence for ten months after the excision of the osteoma cutis on the young man's forehead [1]. Similarly, there was complete healing of the biopsy site without clinical evidence of residual osteoma cutis on the forehead of the elderly man at a subsequent skin check one year later.

Perforating osteoma cutis has also been observed as either multiple individual lesions of osteoma cutis with only one that is perforating [15], or a single larger osteoma cutis lesion with multiple sites of perforation [4, 13, 16]. Delacretaz and Koenig described a 44-year-old woman in whom three osteoma cutis lesions had spontaneously appeared on the lateral side of her arm [15]. One of the three lesions had a slight central depression and perforation of bone was demonstrated on microscopic examination.

A 58-year-old man, without any history of prior trauma or skin disorder, developed a pruritic, shiny, erythematous and mottled, hyperpigmented, hard, 6×3 cm, subcutaneous plaque on his upper back of one year duration. The following laboratory studies were within normal range or negative: complete blood cell counts and platelets, serum chemistries (including blood urea nitrogen, creatinine, calcium, phosphorus and liver function tests), antinuclear antibody, urinalysis, chest roentgenogram, and electrocardiogram. The clinical differential diagnosis included osteoma cutis, sclerosing basal cell carcinoma, and morphea profunda. The plaque was excised; microscopic examination showed a plate-like osteoma cutis and transepidermal elimination of bony material from multiple sites of a solitary lesion of morphea profunda [16].

Primary idiopathic plaque-like osteoma cutis, with multiple sites of transepidermal elimination of bone spicules, has also been described in two men [4, 8]. A 35-year-old man had a 10×6 cm lesion involving the left side of his scalp and forehead and a 6×4 cm lesion on his left preauricular cheek of 14-years' duration. The following laboratory studies were normal: complete blood counts, liver and renal function tests, serum calcium and phosphorus, and parathyroid and thyroid stimulating hormones. The mostly asymptomatic lesions (except occasional painful episodes when there was spontaneous ulceration and discharge) were biopsied and subsequently completely excised. Both showed osteoma cutis with several superficial areas demonstrating fragments of bone within breaks in the epidermis [13].

A 50-year-old man with a 20×3 cm rapidly growing asymptomatic mobile linear plaque — with extrusion of yellowish hard material through surface ulceration in some places — extending from his right forehead to occiput, just lateral to the midline, of one-year duration was also described. He had no history of prior trauma or inflammatory process at the site. However, he noticed spontaneous ulceration with chalky white discharge in some areas of the lesion. A skull roentgenogram showed faint radiodense lesions in the soft tissue. His general, neurologic, and ophthalmologic examinations were normal. Laboratory studies (liver function tests, renal function tests, complete blood counts, serum calcium and phosphorus, parathyroid hormone, and thyroid stimulating hormone) were also normal and there was no history of pseudohypoparathyroidism. Biopsy of the lesion showed epidermal ulceration and foci of mature bone formation surrounding the appendages in the dermis. Correlation of the clinical morphology and pathology established a diagnosis of primary plate-like perforating osteoma cutis [4].

Conclusion

Osteoma cutis can occur as either a primary or secondary condition. Perforating osteoma cutis is rare. It has been described in individuals who have a single larger lesion with multiple sites of perforation and in patients with multiple individual lesions with only one that is perforating. To date, solitary lesions of either primary or secondary perforating osteoma cutis have been observed in two men (ages 24 and 91 years) and one woman (age 40 years). Prior to diagnosis, the lesions had been present from less than one month to 19 or 20 years. The solitary perforating osteoma cutis lesion was either located on the forehead (both men) or the breast (the woman). The nodules were erythematous (two lesions) or flesh-colored and ranged in size from 8×8 millimeters to 1.5×0.5 centimeters. Each lesion had a perforation of the epidermis by bone through a central area that was either crateriform or crusted, or keratotic. The clinical differential diagnosis included keratoacanthoma, phlebolith, pilomatricoma, pilomatrical carcinoma, and squamous cell carcinoma. The perforating osteoma cutis lesion was successfully treated with either excision or shave biopsy without recurrence at either 10 or 12-months follow-up.

References

1. Hong SH, Kang HY. Case of perforating osteoma cutis. *Ann Dermatol* 2003;15(4):153-155. doi: 10.5021/ad.2003.15.4.153.
2. Kim BK, Ahn SK. Acquired perforating osteoma cutis. *Ann Dermatol* 2015;27(4):452-453. [PMID: 26273166].
3. Kim YS, Shin DH, Choi JS, Kim KH. The immunohistochemical patterns of the B-catenin expression in pilomatricoma. *Ann Dermatol* 2010;22(3):284-289. [PMID: 20711264].
4. Grandhe N, Dogra S, Saikia U, Handa S. Acquired perforating primary osteoma cutis. *Acta Derm Venereol* 2004;84(6):489-490. [PMID: 15844650].
5. Moreira Amorim G, Mastrangelo Marinho Falcao EMMF, Carvalho Quintella D, Cuzzi T, Canedo de Magalhaes T, Raso Bastos P. Primary isolated osteoma cutis of the face. *Dermatol Online J* 2017;23(4). pii: 13030/qt4zz8d3tm. [PMID: 28541879].
6. Sanmartin O, Alegre V, Marinez-Aparicio A, Botella-Estrada R, Aliaga A. Congenital platelike osteoma cutis: case report and review of the literature. *Pediatr Dermatol* 1993;10(2):182-186. [PMID: 8346117].
7. Oikarinen A, Tuomi ML, Kallionen M, Sandberg M, Vaananen K. A study of bone formation in osteoma cutis employing biochemical, histochemical and in situ hybridization techniques. *Acta Derm Venereol 1992*;72(3):172-174. [PMID: 1357850].

8. Riahi RR, Cohen PR. Multiple military osteoma cutis of the face after initiation of alendronate therapy for osteoporosis. *Skinmed* 2011;9(4):258-259. [PMID: 21980713].

9. Chabra IS, Obagi S. Evaluation and management of multiple military osteoma cutis: case series of 11 patients and literature review. *Dermatol Surg* 2014;40(1):66-68. [PMID: 24320145].

10. Cohen PR, Tschen JA, Schulze KE, Martinelli PT, Nelson BR. Dermal plaques of the face and scalp. Platelike osteoma cutis. *Arch Dermatol* 2007;143(1):109-114. [PMID: 17224551].

11. Vashi N, Chu J, Patel R. Acquired plate-like osteoma cutis. *Dermatol Online J* 2011;17(10):1. [PMID: 22031627].

12. Fazeli P, Harvell J, Jacobs MB. Osteoma cutis (cutaneous ossification). *West J Med* 1999;171(4):243-245. [PMID: 10578679].

13. Haro R, Revelles JM, Angulo J, Farina Mdel C, Martin L, Requena L. Plaque-like osteoma cutis with transepidermal elimination. *J Cutan Pathol* 2009;36(5):591-593. [PMID: 19476531].

14. Yeh GL, Mathur S, Wivel A, Li M, Gannon FH, Ulied A, Audi L, Olmstead EA, Kaplan FS, Shore EM. GNAS1 mutation and Cbfa1 misexpression in a child with severe congenital platelike osteoma cutis. *J Bone Min Res* 2000;15(11):2063-2073. [PMID: 11092389].

15. Delacretaz J, Koenig R. Perforating osteoma-regional acquired osteomatosis. *Dermatologica* 1978;156(4):251-254. [PMID: 624435].

16. Ahn SK, Won JH, Choi EH, Kim SC, Lee SH. Perforating plate-like osteoma cutis in a man with solitary morphoea profunda. *Br J Dermatol* 1996;134(5):949-952. [PMID: 8736344].