

Scrotal calcinosis in a patient treated with isotretinoin: a rare entity

Mohamad Abou Chakra¹✉, Mouatasem Jida², Elie Hanna¹, Michael Peyromaure¹, Nicolas Barry Delongchamps¹, Sabine Roux¹, Igor Duquesne¹

¹Department of Urology, Cochin Hospital, Assistance Publique-Hôpitaux de Paris, Paris Descartes University, Paris, France. ²Skin and Laser Center, Scin Center Cassel, Kassel, Germany.

Abstract

Scrotal calcinosis is a rare disorder characterized by multiple papules or nodules of calcification in the scrotal skin. The pathogenesis of this disease is poorly understood. The condition presents as several brown to yellowish asymptomatic nodules on the scrotum. Excision followed by scrotal reconstruction is the treatment of choice. It leaves a good cosmetic result with low chances of recurrence. Newer treatments, such as ablative lasers, have been proposed with very good results. We describe the case of a 28-year-old patient with a history of severe acne treated with oral isotretinoin that presented for scrotal nodules. On laboratory examination, hypercalcemia was found with normal phosphorus, parathyroid hormone, and vitamin D hormone levels. Hypercalcemia was linked to his isotretinoin therapy. Serum calcium concentrations normalized after cessation of isotretinoin and hydration. Because the patient refused surgery, a biopsy of the lesion confirmed the diagnosis of scrotal calcinosis. Then the patient was referred to a cosmetic laser center to treat his condition.

Keywords: scrotal, calcinosis, isotretinoin, hypercalcemia

Received: 23 April 2022 | Returned for modification: 20 July 2022 | Accepted: 2 August 2022

Introduction

Scrotal calcinosis is a rare benign local process characterized by multiple, painless, hard scrotal nodules in the absence of any systemic metabolic disorder (1). The exact etiology of this condition is not known. However, there is an intense ongoing discussion about the idiopathic nature of the disease (2). We report an unusual case of a 28-year-old patient with a history of severe acne treated with isotretinoin that presented at our urology clinic with a complaint of multiple scrotal nodules. The diagnosis of scrotal calcinosis was confirmed based on clinical features and biopsy results.

Case report

A 28-year-old male presented to the urology clinic complaining of asymptomatic scrotal nodules that had gradually increased in size and number. He stated that the first lesion had appeared 3 months previously. Fever, chills, dysuria, and urethral discharge were absent. He had no recent trauma of any kind to the scrotum. The patient had no significant past medical or surgical history except for severe acne treated with isotretinoin 40 mg b.i.d. for 4 months. A physical exam revealed brown nodules ranging in size from 0.5 to 1 cm involving the ventral surface of the scrotum and sparing other parts of the genitalia and the body (Fig. 1). A testicular exam revealed no swelling or pain on palpation.

Laboratory examinations found the following to be within normal limits: complete blood count, serum creatinine level, albumin, liver enzymes, TSH, electrolytes, and lipid profile. Serum calcium was 12.6 mg/dl (normal range: 8.6–10.3 mg/dl), phosphorus 3.5 mg/l (normal range: 2.5–4.5 mg/dl), parathyroid hormone (PTH) 41 pg/ml (normal range: 10–65 pg/ml), and PTH-related protein (PTHrP) < 0.3 (normal range < 0.3). Vitamin D level was within the normal range. At this point, isotretinoin therapy was discontinued, and the patient was treated with hydration. Serum

calcium concentrations normalized within 48 hours to 9.6 mg/dl (normal range: 8.6–10.3 mg/dl). His clinical findings were consistent with the working diagnosis of scrotal calcinosis. The patient refused surgical excision of the lesions, and so a biopsy confirmation was suggested. It demonstrated amorphous calcified areas in the dermis with no surrounding epithelial lining. The patient was referred to a cosmetic laser center to treat his condition.



Figure 1 | Multiple scrotal nodules.

Discussion

Scrotal calcinosis is a rare benign local process characterized by multiple, painless, hard scrotal nodules in the absence of any systemic metabolic disorder. Idiopathic scrotal calcinosis (ISC) was first described in 1883 by Lewinski (3). Its pathogenesis remains unknown. There is an ongoing discussion about the idiopathic nature of the disease. The difficulty in finding a preexisting lesion in most cases has led to the conclusion that scrotal calcinosis is idiopathic. One theory suggests that minor trauma plays an important role as the starting point of dystrophic calcification. Another theory mentions that epithelial inclusion cysts constitute the basic abnormality, and that scrotal calcinosis is not idiopathic (4).

✉ Corresponding author: mohamedabouchakra@hotmail.com

Recently it was reported that degeneration and necrosis of the dartos muscle are the initial events in the pathogenesis of the disease, followed by necrotic masses that eventually form dystrophic calcifications (5). There are some differential diagnoses to idiopathic scrotal calcinosis such as multiple epidermal cysts of the scrotum, sebaceous cysts, and steatocystoma multiplex (6).

Because the condition is benign and mostly asymptomatic, treatment is for aesthetic purposes. Excision followed by scrotal reconstruction is the treatment of choice, with good cosmetic results (2). Newer therapeutic approaches have been proposed using laser therapy. This is considered a procedure with much less invasive action and less tissue loss. Meissner et al. used an erbium:yttrium-aluminum-garnet (Er:YAG) laser to treat a patient with scrotal calcinosis. They performed the procedure under local anesthesia, whereby the epidermis over the cyst was removed with the laser until the cyst wall lay open and a chalky material was extravasated from the cyst. The long-term outcome was excellent, and there were only discrete hypopigmentations after 2 years and no sign of recurrence (7). Cannarozzo et al. reported their experience in the treatment of scrotal calcinosis with a CO₂ laser. Five patients affected by the disease were enrolled for CO₂ laser treatment. All patients had excellent healing. Four patients reported minimal scarring. No bleeding was reported after the procedure. Two patients reported itching and were treated with oral antibiotics and antihistamine drugs (8). Najar Seyf reported two cases of scrotal calcinosis treated with a CO₂ laser. The cosmetic results were excellent, with minimal or no scarring, the patients reported a high level of satisfaction, and no recurrence was observed at the follow-up visits (9).

If the scrotal calcinosis is truly idiopathic, the laboratory investigations need to be within the normal limits. However, in our patient, hypercalcemia was detected. His normal PTH level ruled out secondary hyperparathyroidism as the cause for his hypercalcemia. The normal vitamin D, PTHrP, and TSH levels narrow the differential diagnosis of non-PTH-related hypercalcemia to

hypervitaminosis A. The reversibility of hypercalcemia after cessation of therapy with isotretinoin and the patient's previous laboratory tests (calcium and phosphorus were normal before isotretinoin) favor the hypothesis that the isotretinoin was responsible for hypercalcemia. Although uncommon, hypercalcemia caused by chronic hypervitaminosis A has been reported (10, 11). Isotretinoin is a derivative of vitamin A and, as such, can cause the side effects associated with chronic hypervitaminosis A. There is only one case in the literature that associates hypercalcemia with isotretinoin treatment (12). Valentic et al. reported an occurrence of hypercalcemia after 2 months of therapy with oral isotretinoin in a 19-year-old patient with severe cystic acne. The dosage of isotretinoin was 60 mg every morning and 50 mg orally each evening at bedtime (1.6 mg/kg/day) in the 2nd month of therapy. Calcium concentration was 11.5 mg/dL, and it normalized within 36 hours of isotretinoin discontinuation (12). It is important to note that metastatic calcification cannot be the etiology of calcinosis in our case because metastatic calcification accompanies abnormal metabolism of calcium and phosphate, resulting in secondary hyperparathyroidism, hyperphosphatemia, and an elevated calcium-phosphate product. There are several types of calcification in calcinosis, including dystrophic, idiopathic, metastatic, and iatrogenic. The question about etiopathogenesis in scrotal calcinosis is not resolved. The definition of idiopathic scrotal calcinosis is consistent with the absence of any metabolic disorder. The isolated hypercalcemia entity found in our case may contribute to the pathophysiology of calcinosis or could be a coincidence.

Conclusions

Scrotal calcinosis is a benign condition that presents as slowly growing yellowish nodules consisting of calcification. The treatment of choice is surgical excision, which has good cosmetic results.

References

- Dubey S, Sharma R, Maheshwari V. Scrotal calcinosis: idiopathic or dystrophic? *Dermatol Online J.* 2010;16:5.
- Syed MMA, Rajbhandari A, Paudel U. Idiopathic calcinosis cutis of the scrotum: a case report and review of the literature. *J Med Case Rep.* 2018;12:366.
- Pompeo A, Molina WR, Pohlman GD, Sehr D, Kim FJ. Idiopathic scrotal calcinosis: a rare entity and a review of the literature. *Can Urol Assoc J.* 2013;7:E439-41.
- Saad AG, Zaatari GS. Scrotal calcinosis: is it idiopathic? *Urology.* 2001;57:365.
- Pabuçuoğlu U, Canda MS, Güray M, Kefi A, Canda E. The possible role of dartos muscle degeneration in the pathogenesis of idiopathic scrotal calcinosis. *Br J Dermatol.* 2003;148:827-9.
- Wollina U, Schönlebe J, França K, Tchernev G, Lotti T. Idiopathic scrotal calcinosis—a case report. *Open Access Maced J Med Sci.* 2018;6:108-9.
- Meissner M, Kleemann J, Kaufmann R, Ochsendorf F. The erbium:YAG laser: a new technique for the treatment of scrotal calcinosis. *J Eur Acad Dermatol Venereol.* 2017;31:e207-9.
- Cannarozzo G, Bennardo L, Negosanti F, Nisticò SP. CO₂ laser treatment in idiopathic scrotal calcinosis: a case series. *J Lasers Med Sci.* 2020;11:500-1.
- Najar Seyf A, Alenmyr L. Scrotal calcinosis treated with carbon dioxide laser: two cases and a short literature review. *Acta Derm Venereol.* 2021;101:adv00444.
- Safi KH, Filbrun AG, Nasr SZ. Hypervitaminosis A causing hypercalcemia in cystic fibrosis. Case report and focused review. *Ann Am Thorac Soc.* 2014;11:1244-7.
- Bhalla K, Ennis DM, Ennis ED. Hypercalcemia caused by iatrogenic hypervitaminosis A. *J Am Diet Assoc.* 2005;105:119-21.
- Valentic JP, Elias AN, Weinstein GD. Hypercalcemia associated with oral isotretinoin in the treatment of severe acne. *JAMA.* 1983;250:1899-900.