

Sclerosing lipogranulomatosis-induced chronic hypercalcemia and acute pancreatitis



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INTRODUCTION

In pursuit of cosmetic augmentation, various US Food and Drug Administration–approved and unapproved injectable agents are used, often by unlicensed individuals. In such circumstances, foreign modeling agent reactions (FMAR) may evolve and go untreated for some time. This report presents a reaction to synthol injection causing FMAR in the form of paraffinoma (sclerosing lipogranulomatosis) in the gluteal and thigh region.

CASE REPORT

A 61-year-old Asian-American woman was referred to the dermatology department for a 7-year history of progressively enlarging rash on her buttocks and lateral thighs. She reported receiving cosmetic injections of synthol oil by an unlicensed individual 10 years earlier. She reported leakage of an oil-like substance from the injection sites that ceased a short time after the injections. She noted intermittent pain requiring ice packs in the evening but denied pruritus or difficulty with sitting or movement. Her medical history was significant for cardiomegaly, gastric ulcer, hypercalcemia, and pancreatitis. She did not report any current medications. Family history was noncontributory.

Approximately 1 year before presentation, the patient was hospitalized for acute pancreatitis likely caused by hypercalcemia, measured at 15.4 mg/dL (8.4–10.5 mg/dL). Angiotensin-converting enzyme was reported high but value unknown, and 1,25 dihydroxyvitamin D at 103 pg/mL (21–65 pg/mL) was elevated. Upon resolution of her pancreatitis, evaluation of her hypercalcemia was initiated by the endocrinology department. A follow-up noncontrast

Abbreviation used:

FMAR: foreign modeling agent reactions

computed tomography scan of the abdomen and pelvis was significant for normal configuration of the pancreas, suggesting resolution of pancreatitis. Noncompartmentalized high-density heterogeneous material with intervening low-density foci throughout the gluteal subcutaneous space bilaterally and extending to the proximal thigh regions posterolaterally was also noted. Bilaterally enlarged internal and external iliac nodes were reported as reactive. The following workup of hypercalcemia sources was negative: hyperparathyroidism, malignancy, immobilization, vitamin D toxicity, multiple myeloma, thyrotoxicosis, pulmonary processes, sarcoidosis, tuberculosis, and coccidioidomycosis. The patient was treated with 20 mg of prednisone for 2 months for likely granulomatous hypercalcemia, decreasing her calcium to 10.4 mg/dL. Prednisone was then tapered to 5 mg for 2 weeks with an increase in calcium to 12.6 mg/dL. An additional course of prednisone of 30 mg daily was tapered at an unknown rate over 5 months to 10 mg daily, which was then continued for 5 months. Because of iatrogenic Cushing disease, the patient declined further prednisone, and it was tapered off with serum calcium at 10.2 mg/dL at that time. The effect on serum calcium after prednisone cessation is unknown because of lack of follow-up. Her hypercalcemia was attributed to a granulomatous process from synthol injections, and she was referred to the dermatology department for definitive diagnosis.

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Fig 1. Indurated tan-pink to violaceous plaques on bilateral buttocks.



Fig 2. Well-demarcated indurated, tan-pink to violaceous plaques on lateral right thigh.

At the time of dermatology evaluation, the physical examination found multiple hyperpigmented tan-pink to violaceous indurated plaques covering the bilateral gluteal region (Fig 1), with bilateral extension to the lateral thighs in (Fig 2). The lesions were nontender without any associated masses or lymphadenopathy. No other lesions were noted on full-body skin examination. Review of systems was otherwise unremarkable.

Two punch biopsies were performed at the borders of the left superior buttock and the right lateral proximal leg. Histopathology found (Fig 3 and 4) diffuse sclerosis with numerous cystic spaces and minimal fat necrosis, favoring paraffinoma.

Based on the history and workup, paraffinoma was diagnosed. The patient declined surgical evaluation; therefore, the goal was symptomatic

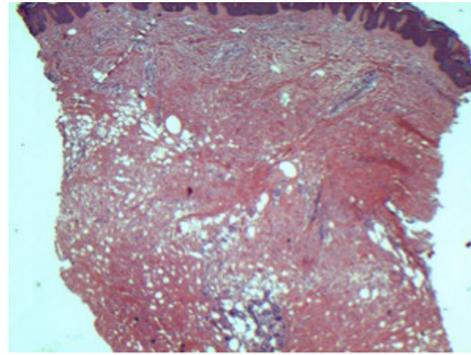


Fig 3. Extensive fibrosis and sclerosis with cystic cavities throughout the dermis. (Hematoxylin-eosin stain; original magnification: $\times 2$.)

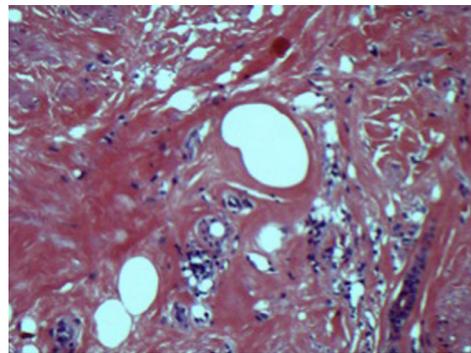


Fig 4. Reactive fibrous tissue surrounding mineral oil droplets with disperse macrophages, histiocytes, and lymphocytes. (Hematoxylin-eosin stain; original magnification: $\times 10$.)

management. The patient was started on continuous doxycycline, 100 mg twice a day, hydroxyzine, 25 mg daily, and prophylactic topical triamcinolone ointment 0.1% as needed for pruritus. Patient response to therapy is unknown because of loss to follow-up.

DISCUSSION

This patient presented with severe paraffinoma of the buttocks with contiguous extension to the lateral thighs and granulomatous-induced metabolic involvement that is typically not seen in dermatology. Disease latency of her skin examination findings was approximately 3 years. This patient's condition is characterized by pain and induration, resulting in significant disruption of sleep and daily tasks.

Histologic analysis supports FMAR, specifically paraffinoma. Paraffinomas are typically described as inflammatory “granulomatous foreign body reactions, resulting from interstitial application of oily substances” with round cavities from residual

oil.¹ Adverse effects of cosmetic augmentation with injectable agents usually result in confinement of inflammatory reaction to injection sites with possible extension via lymphatic or hematogenous spread, likely seen in our patient per her computed tomography results.¹ Treatment of paraffinomas include anti-inflammatory drugs, such as tetracyclines, systemic and intralesional corticosteroids, and/or surgical excision. Surgery may pose a challenge given lymphatic or hematogenous dissemination of oil throughout tissues. Therapies for paraffinomas often focus on symptom management and inflammation reduction. Other innovative therapies have been described, including radiofrequency therapy² and dermabrasion.³ However, the feasibility of these treatments is highly reliant on the ability to cover the cost of procedures, availability of technology and expertise, location of substance in the tissue (ie, superficiality), and safety and efficacy concerns.

A less frequently encountered complication of FMARs includes hypercalcemia. Complications of hypercalcemia are treated with glucocorticoids, ketoconazole, or hydroxychloroquine.^{4,5} Although steroid treatment is typically used for granulomatous hypercalcemia, side effects can be a limiting factor. A mechanism for hypercalcemia associated with skin lesions from injectable filler is discussed by Moraitis et al.⁵ Briefly, the inflammatory cell infiltrate induces CYP27b1 in a fashion unregulated by usual feedback mechanisms. Increased extrarenal production of 1,25 hydroxyvitamin D results in hypercalcemia. The severity of hypercalcemia may be related to the extent of granulomatous involvement. It is

feasible that the discontinuous medical care this patient received and chronicity of hypercalcemia are contributors to the severity of associated symptoms, including acute pancreatitis.

When evaluating a chronic condition with granulomatous pathology findings, the possibility of hypercalcemia must be considered for workup. Associated symptoms of hypercalcemia can include nausea, vomiting, constipation, pancreatitis, headache, confusion, depression, muscle weakness, and shortened QT interval. Based on extent of tissue involvement, symptomatology, and physician discretion, we recommend baseline serum calcium with possible serial monitoring, 1,25 dihydroxyvitamin D, and parathyroid hormone values. In addition, a referral to the endocrinology department for further work up of hypercalcemia may be needed.

REFERENCES

1. Friedrich RE, Zustin J. Paraffinoma of lips and oral mucosa: case report and brief review of the literature. *GMS Interdiscip Plast Reconstr Surg DGPW*. 2014;3. Doc05. Retrieved from <https://doi.org/10.3205/iprs000046>.
2. Kim HK, Kim BJ, Kim MN, et al. Facial paraffinoma treated with a bipolar radiofrequency device. *Int J Dermatol*. 2015; 54(1):89-91.
3. Zarei M, Levy D, Kerdel FA, Salgado CJ, Romanelli P. Dermabrasion: a novel treatment for diffuse silicone granuloma. *J Clin Aesthet Dermatol*. 2015;8(5):47-49.
4. El Muayed M, Costas AA, Pick AJ. 1,25-Dihydroxyvitamin D-mediated hypercalcemia in oleogranulomatous mastitis (paraffinoma), ameliorated by glucocorticoid administration. *Endocr Pract*. 2010;16(1):102-106.
5. Moraitis AG, Hewison M, Collins M, Anaya C, Holick MF. Hypercalcemia associated with mineral oil-induced sclerosing paraffinomas. *Endocr Pract*. 2013;19(2):e50-e56.