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Silicone injection-induced granuloma formation, hypercalcemia and nephrolithiasis: a case report

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ABSTRACT

Hypercalcemia and nephrolithiasis have been associated with various etiologies, including dysregulation of the parathyroid glands, malignancies, or sarcoidosis. Other causes of hypercalcemia, such as granulomatous disease resulting from silicone-based cosmetic injections, have been reported but without specific emphasis on nephrolithiasis. Herein, we report an unusual case of simultaneous bilateral obstructing ureteral calculi (SBUC) triggered by recalcitrant hypercalcemia and granulomatous disease due to silicone-based cosmetic injections. A careful surgical history, physical exam, and imaging identified the underlying etiology, which was confirmed by final histopathology. Using a multidisciplinary approach, the patient's condition was successfully managed with endoscopic procedures and concurrent corticosteroid therapy.

Introduction

Several case reports have described the development of noncaseating granulomas and resultant hypercalcemia following cosmetic silicone injection. While its mechanism remains poorly understood, T-cell mediated activation can trigger formation and activation of granulomas, resulting in hypercalcemia. Oftentimes, gastrointestinal calcium absorption also outpaces parathyroid hormone (PTH) suppression, thereby leading to hypercalcemia – a well-documented abnormality among granulomatous diseases regardless of etiology. Herein, we report a case of simultaneous obstructing bilateral ureteral calculi (SBUC) resulting from hypercalcemia and silicone-associated granulomatous disease. Furthermore, we describe a case of rapid ureteral stent encrustation in this setting.

Case report

A 35-year-old healthy, Caucasian female presented to the Emergency Department (ED) with subjective fevers, flank pain, and nausea. Her past surgical history was notable for breast and gluteal augmentation, the latter via autologous fat and silicone injections. On initial presentation, she was afebrile and hemodynamically stable. The physical exam revealed mild left costovertebral angle tenderness and suprapubic tenderness. Laboratory tests revealed a normal serum creatinine of 0.98 mg/dL, mild leukocytosis to $10.9x10^3\mu L$, and hypercalcemia with a serum calcium of 11.6 mg/dL. Urinalysis with microscopy was nitrite negative but demonstrated pyuria (25 WBC per high power field). Non-contrast computed tomography of the abdomen and pelvis (CTAP) revealed mild bilateral hydroureteronephrosis from SBUC (7mm left distal ureter, 5mm right ureterovesical junction) and non-obstructing renal stones bilaterally (largest of 6mm) (Fig. 1A). Bilateral breast implants and soft tissue calcifications in the buttocks were also seen.

Given the concern for a possible super-imposed urinary tract infection, definitive stone treatment was deferred in lieu of bilateral ureteral stent placement for decompression. The patient later underwent an uncomplicated bilateral ureteroscopic laser lithotripsy, right stent exchange, and left stent removal prior to discharge. Stone analysis demonstrated 90% calcium oxalate dihydrate and 10% calcium oxalate monohydrate. Office stent removal and metabolic workup were scheduled; however, the patient was lost to follow-up.

She re-presented to the ED four months later with malaise, nausea, vomiting, and right flank pain. Labs demonstrated an acute kidney injury with serum creatinine of 2.02 mg/dL and calcium of 15.1 mg/dL. CTAP revealed a retained right stent with marked encrustation of both

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the proximal and distal curls and severe right hydronephrosis. Several non-obstructing right lower pole stones were also noted (Fig. 1B). Endocrinology was consulted, and a detailed hypercalcemia workup demonstrated: high ionized serum calcium of 1.71 mmol/L (reference range: 4.4–5.4 mg/dL), low albumin of 3.3 (3.9–5.2 g/dL), low PTH of 10.7 pg/mol (15–65 pg/mL), low 25-OH vitamin-D of 9.9 ng/mL (20–50 ng/mL), high 1,25-OH vitamin-D of 89.8 ng/mL (19.9–79.3 pg/mL), and high Angiotensin Converting Enzyme (ACE) of 124 (9–67 U/L). Additional evaluation of malignant, infectious and other endocrine etiologies was all negative with a normal UPEP/SPEP, negative QuantiFERON-TB, negative HIV test, and normal TSH, respectively. Ultrasound-guided biopsy of gluteal calcifications demonstrated cicatricial fibrosis and CD163 positive histiocytic reactions, suggestive of granulomas (Fig. 2). Taken together, these findings suggested that hypercalcemia and subsequent nephrolithiasis likely resulted from silicone-induced granulomas.

During this admission, she underwent a successful bilateral ureteroscopic laser lithotripsy and exchange of the encrusted stent. She was monitored on telemetry, and her hypercalcemia was treated with intravenous fluids and prednisone. She was also evaluated by Plastic Surgery for surgical excision of granulomas but was deemed ineligible given their significant gluteal involvement. Her serum calcium stabilized to 11.5 mg/dL, creatinine to 1.60 mg/dL and eGFR to 36–44 mL/min prior to discharge for close multidisciplinary outpatient follow up.

Discussion

In contrast to other reports of hypercalcemia in the setting of silicone-based granulomatous disease, this is the first case report highlighting its association with nephrolithiasis. Because routine radiographic studies cannot definitively diagnose this condition, dermatologic heterogeneities and patient history are important features in raising clinical suspicion. In our case, silicone-induced gluteal calcifications on CT, thorough laboratory evaluation, and histologic confirmation of CD163 – a marker for cells of the monocyte/macrophage lineage that is upregulated in inflammatory diseases – were paramount to the diagnosis and management.

Silicone-mediated granuloma formation has been reported up to 20% among those receiving injections, with variable onset from three weeks to 20 years after injection. As instances in which silicone-mediated granulomas trigger hypercalcemia have been extremely rare, its mechanism remains poorly understood. At the same time, immunohistochemical studies have demonstrated activated 1-α hydroxylase in macrophages of sarcoid and foreign-body granulomas, suggesting that silicone-induced hypercalcemia may in part be regulated by calcitriol.[1] Moreover, it is hypothesized that a T-cell mediated reaction triggered by silicone, adulterants, infection, or even trauma may activate macrophages and trigger release of cytokines such as TNF-α, IL-1, and IL-6.[1,2] In our patient, delayed follow-up revealed worsening hypercalcemia, hypoparathyroidism, depressed plasma calcidiol, and relatively increased plasma calcitriol, consistent with those seen in granulomatous diseases with preserved renal function.[3,4]

Treatment of this condition focuses on addressing granuloma activity and mitigating symptoms of hypercalcemia. Edwards et al. demonstrated that complete surgical excision may attenuate hypercalcemia by reducing calcitriol formation.[5] The extent of gluteal involvement in our patient, however, made complete surgical excision fraught with risk. Moreover, while corticosteroids are commonly used to mitigate symptoms, granulomas frequently recur after their discontinuation. Long-term use is also associated with Cushingoid symptoms and other steroid-related complications. Alternative medications such as isotretinoin, minocycline, and ketoconazole have been efficacious, albeit in small retrospective series.[3] Given this condition's overall rarity, however, no definitive guidelines are available to guide long-term management.

Although ureteral stent encrustation is a common complication of prolonged indwelling time, her event has been attributed to granuloma-induced hypercalcemia with rapid stone development. Regardless of etiology, patient education and multidisciplinary care are essential for the successful management of such complex stone patients. While a comprehensive metabolic workup was unable to be collected, this evaluation is nonetheless encouraged to rule out other etiologies of stone formation, as well as optimize prevention, particularly for patients deemed ineligible for implant excision.

Conclusion

We describe the first known case of bilateral obstructing

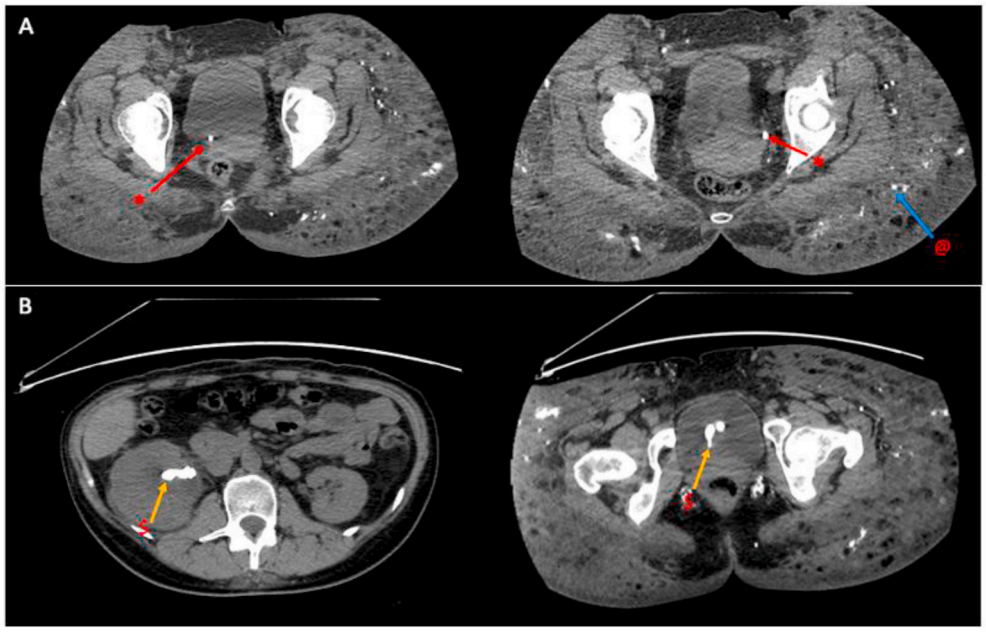

Fig. 1. A. Initial CTAP showed simultaneous obstructing bilateral ureteral stones* (7mm left distal ureter, 5mm right ureterovesical junction) and calcifications due to silicone gluteal injections. @. B. Follow-up CTAP revealed rapid encrustation of right ureteral stent on both proximal and distal curls.$.

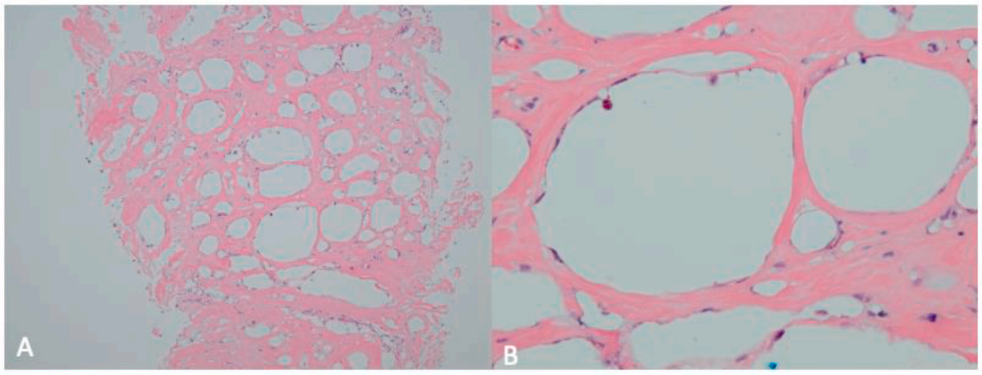

Fig. 2. Histopathology of buttocks calcifications demonstrate fat necrosis with extensive cicatricial fibrosis and histiocytic reaction (CD163+). Fig. 2A and B at 100x and 400x magnification, respectively.

nephrolithiasis secondary to silicone-induced granulomatous disease. A high degree of clinical suspicion and multi-disciplinary, coordinated clinical care were paramount to timely diagnosis and management.

Informed consent

Yes.

Financial conflict of interest

None.

Declaration of competing interest

None.

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