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Case Report

Resection of granulomatous tissue resolves silicone induced hypercalcemia

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ABSTRACT

Because of the increasing trend of body contour enhancements with injections, implants, and fillers, clinicians should be on high alert for the possibility of silicone-induced hypercalcemia as one of the differential diagnoses in a patient with history of silicone use. Hypercalcemia as a result of silicone injections has been reported, and there is concern that there will be more cases given the popularity of cosmetic silicone. Cases involved a mother and daughter (70 & 55 years) who presented in 2013 with hypercalcemia after cosmetic silicone injections in 2007. Evaluation showed 1, 25-dihydroxyvitamin D-mediated hypercalcemia and progressive renal dysfunction; lymph node biopsy showed granulomatous silicone lymphadenitis. MRI of the pelvis revealed abnormal signal enhancement within the subcutaneous gluteal adipose tissue and enlarged inguinal lymph nodes. For persistent hypercalcemia and hypercalciuria, surgical resection of silicone material and granulomas is a successful approach to normalize the serum calcium level.

1. Introduction

Hypercalcemia as a result of silicone injections has been reported, and there is concern that there will be more cases as the popularity of cosmetic silicone grows. We report two cases (mother and daughter) of silicone-induced hypercalcemia that resolved after surgical removal of granulomatous tissue.

2. Case 1

A 50-year-old Latina woman was referred to University of Texas MD Anderson Cancer Center for evaluation of hypercalcemia. This patient had received 3 injections of 'silicone'-like material in each gluteal region for cosmetic purposes in 2007 from an unlicensed individual. Between 2010–2013 she developed inguinal lymphadenopathy, induration over the injection area, fatigue, polyuria, intermittent confusion, weight gain, tingling and numbness and hair loss. In 2013 she was found to have a corrected serum calcium of 16.7 mg/dL (8.4–10.2 mg/dL), 1,25-dihydroxyvitamin D of 71 pg/mL (18–78 pg/mL), intact parathyroid hormone level of 5 pg/mL (9–80 pg/mL), an undetectable parathyroid hormone-related protein and angiotensin converting enzyme (ACE) level of 96 U/L (8–53 U/L). She was hospitalized, hydrated, treated with corticosteroids (prednisolone 20 mg) and referred for evaluation.

The patient developed nephrolithiasis in 2007 and had ureteral stent placement in 2012. She had frequent urinary tract infections, migraine headaches, depression, anxiety, arthritis, and hypothyroidism. Physical examination revealed an anxious female; abdominal examination was remarkable for abdominoplasty and firm palpable bilateral inguinal lymph nodes. There was hyperpigmentation and induration over the buttocks consistent with post-inflammatory hyperpigmentation and fibrosis due to silicone injection. Numerous firm nodules were palpated in the gluteal area bilaterally. Laboratory testing revealed serum calcium of 10.24 mg/dL (Table 1) and serum creatinine of 1.7 mg/dL (eGFR 44 mL/min/1.73 m^2) (0.6–1.00 mg/dL; 80–120 mL/min/1.73 m^2). Pelvic MRI revealed abnormal signal enhancement within the subcutaneous adipose tissue over the gluteal region and enlarged lymph nodes. The largest node in the right inguinal region was 1.5 × 1.8 × 2.2 cm; biopsy of a right inguinal lymph node showed granulomatous silicone lymphadenitis. Histologic sections of the lymph node showed diffuse involvement by non-necrotizing granulomatous inflammation with numerous variably sized vacuoles and foreign-body giant cells. In addition to the vacuoles, scattered round, pigmented, foreign material-containing

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Table 1
Laboratory results for case 1 and case 2 with corresponding reference levels.

Test	Case 1		Case 2		References
	Pre-presentation Oct 2013	Post-presentation Oct 2014	Pre-presentation Oct 2013	Post-presentation Oct 2014	
Serum calcium (mg/dL)	17.3	10.2	11.5	9.6	8.4–10.2
Parathyroid hormone (pg/mL)	5	16	<3.0	22	9–80
25-OH vitamin D (ng/mL)	28	39	24	20	30–100
1,25-OH vitamin D (pg/mL)	71	69	89	65	18–78
Serum phosphate (mg/dL)	3.5	3.6	3.5	3.8	2.5–4.5
CTX beta Crosslaps (pg/mL)	244	574	274	865	40–840
Serum creatinine (mg/dL)	1.4	0.66	1.3	0.99	0.6–1.00
Angiotensin converting enzyme (U/L)	96	37	65	26	8–53
Glomerular filtration rate (mL/min)	40	95	40	55	80–120
Luteinizing hormone (mIU/mL)	62.2				1.0–11.4 Postmenopausal 7.7–58.5
Estradiol, S (pg/mL)	<12.0				Postmenopausal <55

central vacuoles were also present. On the initial evaluation at MD Anderson, the patient had Cushingoid features and requested cessation of corticosteroids; she was subsequently treated with pentoxiphylline (400 mg two times a day). Pentoxiphylline is a competitive nonselective phosphodiesterase inhibitor that raises intracellular ATP, activates protein kinase A, and inhibits TNF α and leukotriene synthesis, thereby reducing inflammation. The patient tolerated pentoxiphylline.

Over the next 2 months, she showed signs of persistent hypercalcemia. The patient resumed corticosteroids and pentoxiphylline was increased (400 mg four times a day). Serum calcium level remained in the high normal range (Fig. 1) without improvement of renal function. Suboptimal response to medical therapy resulted in a decision for surgical intervention. She underwent sharp excisional debridement of the granulomatous tissue in her buttocks and 90% of the granulomatous tissue was successfully resected. Serum calcium, 1,25-dihydroxyvitamin D, intact PTH and renal function normalized (Table 1).

3. Case 2

The mother received one 'silicone' injection in each gluteal region in 2007, from the same unlicensed individual. Co-morbidities included nephrolithiasis (2010), diabetes mellitus, Hashimoto's thyroiditis, and GERD. In 2012, the patient presented with fatigue, abdominal bloating, diarrhea, urinary tract infections, cold intolerance, polydipsia, and polyuria. Serum calcium was 13 mg% (8.4–10.2 mg/dL). She received similar treatment with corticosteroids and was subsequently referred to MD Anderson Cancer Center for further management.

She appeared as a well-nourished Latina patient. Induration and hyperpigmentation were noted in the gluteal region with inguinal lymph node enlargement. Serum calcium was 9.74 mg/dL, ACE level of 60 U/L (8–53 U/L) and 1,25-dihydroxyvitamin D level was 106 pg/mL (18–78 pg/mL); intact parathyroid hormone was 23 pg/mL (9–80 pg/mL). Consider factors such as age and potential effect on renal function as well as comorbidity of diabetes mellitus, case 2 was not considered for aggressive medical management that was initially attempted for case 1. After her daughter's successful surgical resection of granulomatous material, the patient underwent sharp excisional debridement of the granulomatous tissue. Delayed healing of surgical incision was evident.

4. Discussion

We report that surgical excision of granulomatous tissue leads to resolution of silicone induced hypercalcemia. A large number of

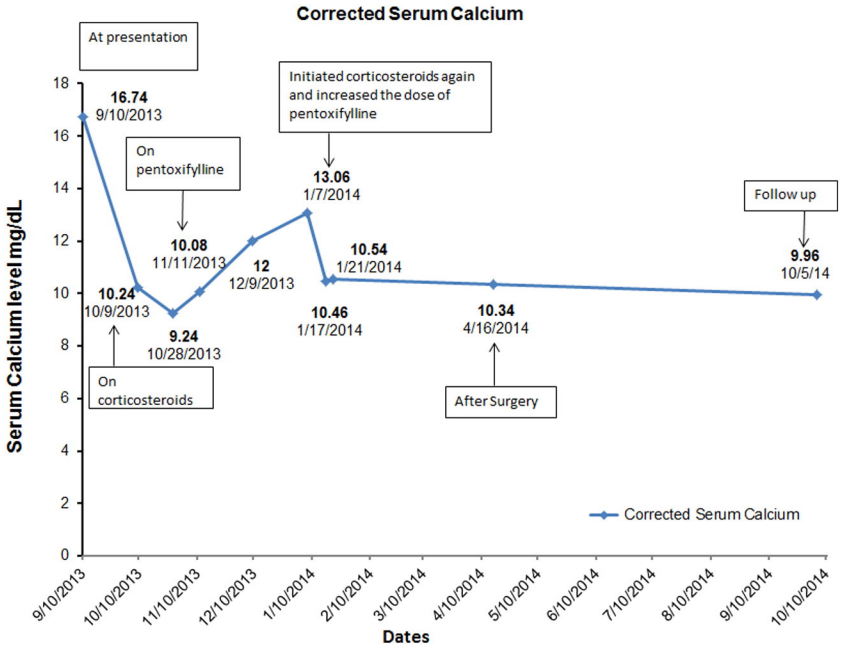

Fig. 1. Serum calcium level and interventions at various time points for Case 1.