CASE REPORT

Calcitriol mediated hypercalcaemia with silicone granulomas due to cosmetic injection

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SUMMARY

We present a case of a 41-year-old woman with medical history significant for urolithiasis presenting to our hospital for psychiatric evaluation due to worsening depression and suicidal ideations for the past 2 weeks. Initial laboratory results show hypercalcaemia of 13.5 mg/dL that led to consulting internal medicine. On further questioning, the patient admitted to cosmetic silicone injections in her buttocks which were causing calcium deposition under her skin, leading to disfigurement of the sacrum and lumbar regions. She underwent further evaluation with CT and laboratory testing, which effectively ruled out malignancy and primary hyperparathyroidism. The hypercalcaemia was diagnosed as non-PTH-dependent with high levels of 1,25-dihydroxyvitamin D and low PTH. She eventually underwent tissue biopsy confirming the presence of silicone granulomas responsible for the calcitriol-mediated hypercalcaemia. This case reminds one to keep a broad differential especially in patients with hypercalcaemia in which malignancy and primary hyperparathyroidism have been ruled out.

BACKGROUND

Silicone has been used for soft tissue augmentation in cosmetic purposes for many years. It is inexpensive but with previous reported side effects that include cellulitis, abscess and the formation of granulomas.¹ Silicone granulomas form as a reaction to the foreign material. As with other granulomas, such as those found in sarcoid, leprosy or tuberculosis, they have the ability to cause hypercalcaemia via elevation of calcitriol. Calcitriol-mediated hypercalcaemia secondary to silicone granulomas is extremely rare as there have only been a handful of prior reported cases.²

In the patient with hypercalcaemia, it is of utmost importance to perform a thorough history which includes history of prior cosmetic procedures after ruling out the more common causes of elevated calcium such as hyperparathyroidism, malignancy and sarcoidosis.

CASE PRESENTATION

A 41-year-old woman with a medical history of hypertension and urolithiasis presented to the hospital for psychiatric evaluation due to worsening depression and suicidal ideation over the past 2 weeks.

The patient had no other significant past medical, social or family history. Review of systems was negative. Relevant home medications include buspirone, escitalopram, lisinopril, hydrochlorothiazide,

risperidone and trazodone with questionable compliance. In addition, the patient denies any accessory supplementation of vitamins or minerals. The vital signs on admission were within normal limits with the exception of blood pressure of 191/113 mm Hg. Physical examination was only remarkable for multiple hard, non-mobile, nodular deformities of varying sizes along the lumbar spine and superior sacrum.

When further questioned about the deformity found on physical examination, she admitted to cosmetic liquid silicone injection 15 years ago.

INVESTIGATIONS

The relevant initial laboratory results revealed a basic metabolic panel (sodium, potassium, chloride, bicarbonate, blood urea nitrogen, creatinine and glucose) that was within normal limits and elevated calcium of 13.5 mg/dL (8.6–10.3 mg/dL). Owing to the incidental finding of hypercalcaemia, internal medicine was consulted and further laboratory testing was performed. Further workup on the second day of hospitalisation returned with low phosphorus 2.2 mg/dL (2.5–5.0 mg/dL), low PTH 7 pg/mL (15–88 pg/mL), low 25-hydroxyvitamin D 9 ng/mL (25–80 ng/mL), high 1,25-dihydroxyvitamin D 84 pg/mL (18–78 pg/mL) and normal PTH-related peptide 0.4 pmol/L (<2.0 pmol/L).

The above laboratories are consistent with calcitriol-mediated hypercalcaemia. Thiazide-induced hypercalcaemia was unlikely given the low 25-hydroxyvitamin D and the high 1,25-dihydroxyvitamin D levels.

Figure 1 Abdominal/pelvis CT with contrast showing innumerable infiltrative nodular densities throughout the subcutaneous tissues of the pelvis, primarily posteriorly and overlying the gluteal musculature. Numerous infiltrative nodular densities extend into and involve the gluteal musculature bilaterally.

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Figure 2 Excisional biopsy of pelvic nodule showing agglomeration of fibrosis, histiocytes and foreign body-type giant cells containing vacuoles filled with weakly birefringent material mingled among larger free pools of a similar substance consistent with silicone.

Primary hyperparathyroidism was ruled out as the PTH level was low. Since the PTH level was not elevated, urinary calcium was not performed. In patients with hypercalcaemia, it is important to rule out malignancy. To accomplish this, a CT scan of the chest, abdomen and pelvis was ordered looking for potential malignancy. This showed a normal chest, bilateral hydronephrosis due to obstructing bilateral calculi and subcutaneous intramuscular nodules throughout the lower pelvis, gluteal area and lower abdominal wall, which explained the deformities found on physical examination (figure 1).

The patient did not have any risk factors, chronic clinical symptoms or physical findings compatible with other granulomatous diseases such as sarcoidosis or tuberculosis, so no further workup was ordered.

On day 3 of hospitalisation, a pelvic nodule excisional biopsy was completed showing fibrosis, histiocytes and foreign body cells consistent with silicone, confirming the diagnosis of silicone granuloma (figure 2).

TREATMENT

Treatment was initiated with intravenous normal saline and pamidronate shortly after the results returned indicating hypercalcaemia on day 1 of hospitalisation. The serum calcium decreased from 13.5 to 9.2 mg/dL within 3 days, and no further intervention was necessary.

OUTCOME AND FOLLOW-UP

The patient is currently on no treatment at time of follow-up with endocrinology 1 year later. Her most recent calcium level was 9.2 mg/dL. She is to undergo routine laboratory testing with a short course of corticosteroids if the serum calcium begins to rise.

Unfortunately on discharge, the patient has not been compliant with follow-up and her psychiatry manifestations apparently remained constant despite adequate control of serum calcium.

DISCUSSION

Calcium is a crucial mineral that is tightly regulated in the body and can affect almost any organ system. Symptoms of hypercalcaemia vary greatly and include difficulty concentrating, depression, confusion, renal calculi, hypertension, shortened QT intervals, constipation, nausea, musculoskeletal weakness and

pain. Our patient presented to the hospital with worsening depression, hypertension and renal calculi.³

The most common cause of hypercalcaemia is primary hyperparathyroidism and malignancy, which make up ~90% of the cases. A much less common aetiology is hypercalcaemia secondary to granulomatous disease, as seen in our patient. The pathophysiology for this process is thought to be secondary to activated macrophages located within the granulomas. These macrophages contain 1- α hydroxylase that is the same enzyme found in the kidney that converts 25-hydroxyvitamin D into 1,25-hydroxyvitamin D. These elevated calcitriol levels increase intestinal absorption of calcium along with increasing bone resorption, therefore elevating serum calcium.⁴

Hypercalcaemia mediated by calcitriol is a relatively uncommon condition that can be caused by many different disease processes. A retrospective case series found that of 101 patients with hypercalcaemia and elevated or inappropriate normal calcitriol, sarcoidosis was the most common aetiology (49%). Haematological malignancy was second at 17%, with infections at 8%.⁵ A much less common aetiology of hypercalcaemia is from silicone injections. According to Agrawal's case report, as of 2013, there were only three prior cases of hypercalcaemia secondary to silicone injection,² the first reported in 1964.⁶

Silicone has been used for cosmetic augmentation for many years as this material is fairly inexpensive, chemically inert and has low surface tension with a high resistance to heat.⁶ However, there are numerous reported side effects of introducing this foreign element into the body, including cellulitis, abscess and the formation of granulomas. Granuloma formation has been reported to occur anytime from 3 weeks to up to 20 years postinjection,⁷ with an incidence rate up to 20%.⁸

Treatment typically involves surgery to remove the granulomas; however, less invasive options exist.⁹ This includes actions to limit intestinal calcium absorption, such as eliminating vitamin D supplementation and decreasing sun exposure. First-line medical therapy typically consists of corticosteroids, especially in cases such as sarcoidosis and lymphoma.⁴

Antimalarial medications (chloroquine and hydroxychloroquine) can also be used to decrease calcitriol and in turn serum calcium. These medications are typically reserved for second-line treatment as these medications typically have a higher side effect profile.⁴

In summary, hypercalcaemia is a fairly common condition that can be caused by relatively rare diseases. Therefore, it is imperative to complete a thorough history, including prior cosmetic procedures, in the patient with elevated calcium of unknown origin after malignancy, hyperparathyroidism and sarcoid have been ruled out.

Learning points

- ▶ Patients with hypercalcaemia must first be ruled out for the common diseases such as malignancy and primary hyperparathyroidism.
- ▶ In the patient suffering from elevated calcium, it is important to complete a thorough history, including cosmetic procedures.
- ▶ Silicone injections can cause a wide variety of side effects, including granulomas and more uncommonly hypercalcaemia.

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