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Mirror, mirror on the wall: Hypercalcemia as a consequence of modern cosmetic treatment with liquid silicone

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Summary

Background:

Hypercalcemia is a common problem in clinical practice and can be related to endocrine disorders or malignant disease, especially in elderly patients. Although rare, other causes can also be responsible.

Case Report:

Granulomatous inflammation of the skin and lymph nodes induced by intravenous or injectable silicone is a rare condition of hypercalcemia that is usually not within the scope of differential diagnosis. Here, we report a 72-year-old woman with symptomatic hypercalcemia related to cosmetic treatment of the neck. Topical applied liquid silicone by means of a focal ultrasound device induced extensive granulomatous inflammation of the skin and local lymph nodes, being the underlying cause for hypercalcemia in this case.

Conclusions:

In rare cases, symptomatic hypercalcemia can be caused by silicone due to a severe granulomatous tissue reaction. This is the first time that a transdermal silicone treatment has been reported to cause severe granulomatous tissue inflammation.

key words:

hypercalcemia • granulomatous inflammation • silicone • ultrasound treatment

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BACKGROUND

Hypercalcemia is a quite common problem in clinical practice and includes endocrine disorders and malignant diseases, especially in older patients [1]. There have been reports that, dermal injections for cosmetic treatment and intravenous silicone derived from dialysis tubes have been reported to cause hypercalcemia due to local or systemic granulomatous inflammatory processes [2,3]. However, this pathomechanism seems to be rare and therefore is usually not considered by physicians treating hypercalcemia. Diagnosis is further complicated due to the fact that most patients are hesitant to report that they have had rejuvenation therapy.

CASE REPORT

A 72-year-old woman was referred to our hospital with progressive fatigue, loss of appetite and weight loss of 16 kg within the last 2 months. However, fever or night sweats were denied. Medical history was remarkable for long-standing type 2 diabetes and osteoporosis with old spinal fractures. Her medication included amlodipine, acetylsalicylic acid, atorvastatin, metformin, insulin glargine and insulin aspart as required. Treatment of osteoporosis included zoledronic acid 5mg intravenously once annually. Two months before presentation at our hospital a DPP-4-inhibitor, sitagliptin, was added to the therapy in order to improve glycemic control. However, this treatment was discontinued before presentation due to an evolving edema and erythema of the face and neck. At physical examination, edema and erythema of the face including the lips and neck with a Quinke-like appearance were still present. Further, submandibular lymph nodes were swollen. The remainder of the physical examination was unremarkable.

The laboratory results on admission revealed hypercalcemia (3.03 mmol/L, normal 2.1–2.65 mmol/L) and normal levels for parathyroid hormone, phosphate, albumin, creatinine, 25-OH-vitamin D and 1,25-OH vitamin D. However, angiotensin converting enzyme (95 U/L, normal <65.7 U/L) and urine calcium (10.9 mmol/24 h, normal 2.5–7.0 mmol/24 h) were elevated (Table 1). The patient had started cosmetic treatment for age-related wrinkles of face and neck several months ago, which she did not initially mention to clinicians.

In order to exclude a malignant process, scintigraphy of the bone, whole body computed tomography and a comprehensive endoscopic evaluation were performed. All examinations revealed normal results. Subsequently, biopsies of the facial skin and a submandibular lymph node were taken. Histological analysis showed a dense granulomatous inflammation with polynuclear giant cells and histiocytes. Strikingly, there were empty vacuoles within the cytoplasm of many giant cells, resembling silicone granuloma (Figure 1). When the patient was asked about silicone “exposure”, she finally confessed to having had cosmetic treatment months ago. In this procedure, a topical silicone-lipid formulation was applied to her face and neck with a transdermal ultrasound device (as far as we could determine, ultrasound frequency was 1 MHz, intensity 0.5–1 W/cm²). This was done to reduce wrinkles of face and neck as a “gentle rejuvenation” of the 72-year-old woman. However, the use of injectable silicone was denied.

Table 1. Patient laboratory results with corresponding reference intervals.

		Reference interval
Calcium (mmol/L)	3.03	2.1–2.65
Phosphate (mmol/L)	0.89	0.8–1.5
Sodium (mmol/L)	131	135–145
Potassium (mmol/L)	4.45	3.5–4.5
Albumin (g/L)	36.1	30–50
Creatinine (mg/dL)	0.59	0.1–1.3
Parathyroid hormone (pmol/L)	2.2	1.3–7.6
25-OH vitamin D (ng/mL)	39.4	6.3–46.4
1,25-OH vitamin D (ng/L)	39.0	25–60
ACE (U/L)	95	<65.7
Urine calcium (mmol/24 h)	10.9	2.5–7.0
Urine volume (ml/24 h)	3500	

ACE – angiotensin converting enzyme.

Figure 1. Granulomatous inflammation of the dermis with multinucleated giant cells, histiocytes and lymphocytes and striking vacuolar formation (appearing as empty holes – silicone is resolved during the tissue fixation process in formalin and alcohol).

Based on these results, the patient was diagnosed with symptomatic hypercalcemia resulting from a granulomatous inflammation. Treatment with 30 mg oral prednisolone once daily was initiated and this treatment improved the facial edema. The erythema and palpable infiltration of the skin still remained within the skin wrinkles. In a final follow-up after 8 weeks of treatment, after oral prednisolone was tapered, calcium levels (2.45 mmol/L, normal: 2.1–2.65 mmol/L) and calciuria (6.8 mmol/24 h; normal: 2.5–7.0 mmol/24 h) were completely normalized and the patient was in good health.

DISCUSSION

Here we report a patient with symptomatic hypercalcemia related to a cosmetic treatment with liquid silicone applied

topically with a focal ultrasound device. Differential diagnosis of non-PTH-related hypercalcemia in older patients includes, in particular, malignant conditions. When malignancy has been excluded, hypercalcemia due to granulomatous diseases needs to be considered. Among them, sarcoidosis and tuberculosis are the most common ones, with inappropriate endogenous overproduction of 1,25-OH vitamin D by activated granulomatous tissue responsible for hypercalcemia [1,4]. However, it is well known that silicone can cause granulomatous inflammation as well [5]. Silicone may disseminate in lymph vessels and organs after ruptured breast implants or injections [2,6]. For many years silicone formulations have been used in aesthetic care settings as so-called injectable “fillers” despite its unpredictable risks [5]. The pathomechanism of silicone-induced hypercalcemia is not entirely understood and seems to be somehow different from the mechanism of other granulomatous disease such as sarcoidosis. Some reports have suggested a vitamin D dependency [2,6,7], while others have not found this dependency, as in our case [2,3,5]. In these cases hypercalcemia might be related to some altered unspecified prostaglandin metabolism [5,6], but this remains speculative. The rarity of silicone-induced hypercalcemia makes further study of underlying mechanisms difficult. However, since removal of disseminated silicone seems to be impossible, cortisone treatment is a suitable therapy, as reported in all cases [2–4,6,7].

CONCLUSIONS

The diagnosis of a granulomatous reaction to filler material in an aesthetic care setting may cause serious medical complications mimicking systemic diseases, and is challenging, especially since patients often deny having had rejuvenation therapy. It is further complicated by the bewildering variety of new and unproven commercial treatments, but it seems that transdermal ultrasound combined with topical silicone-lipid gel can be harmful by inducing severe tissue inflammation and subsequent hypercalcemia. Whether such complications are frequent is not known due to the fact that controlled studies are lacking.

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