CLINICAL IMAGE

Hypercalcemia associated with sodium thiosulfate treatment in a patient with calciphylaxis

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An 18-year-old woman was admitted to our hospital complaining of hardening in her breasts over the previous 2 weeks and dyspnea for 1 week. Chest computed tomography and mammography revealed diffuse calcification patches bilaterally in the lungs and breasts (FIGURE 1A and 1B). Her medical history was remarkable for severe pneumonia 7 months earlier and a weight loss of 12.5 kg during the 4 weeks of illness (body mass index, 13.2 kg/m^2). In addition, 4 months before the presentation, she experienced painful dermal ulcers of unknown origin (FIGURE 1C).

On admission, the serum levels of calcium, phosphorus, parathyroid hormone, creatinine, 25-hydroxy vitamin D, tumor markers, immunoglobulins, type I collagen C-terminal telopeptide (CTX), and bone alkaline phosphatase (BALP) were within the reference ranges. To identify the cause of calcifications, a lung biopsy was performed, which revealed diffuse calcifications in the alveolar septa and arteriolar walls (FIGURE 1D). The patient was subsequently diagnosed with calciphylaxis of nonuremic origin and received intravenous sodium thiosulfate (STS) at a dose of 6 g/d. No side effects were observed. After 2 months of the STS treatment, the lung and breast calcifications were reduced (FIGURE 1E and 1F). However, serum calcium levels increased dramatically to 4.09 mmol/l (reference range, 2.1–2.7 mmol/l), and parathyroid hormone levels were reduced to 0.9 pmol/l (reference range, 1.6–6.9 pmol/l). The therapy was immediately discontinued. The levels of CTX and BALP increased to 9.28 ng/ml (reference range, 0.29–0.57 ng/ml)

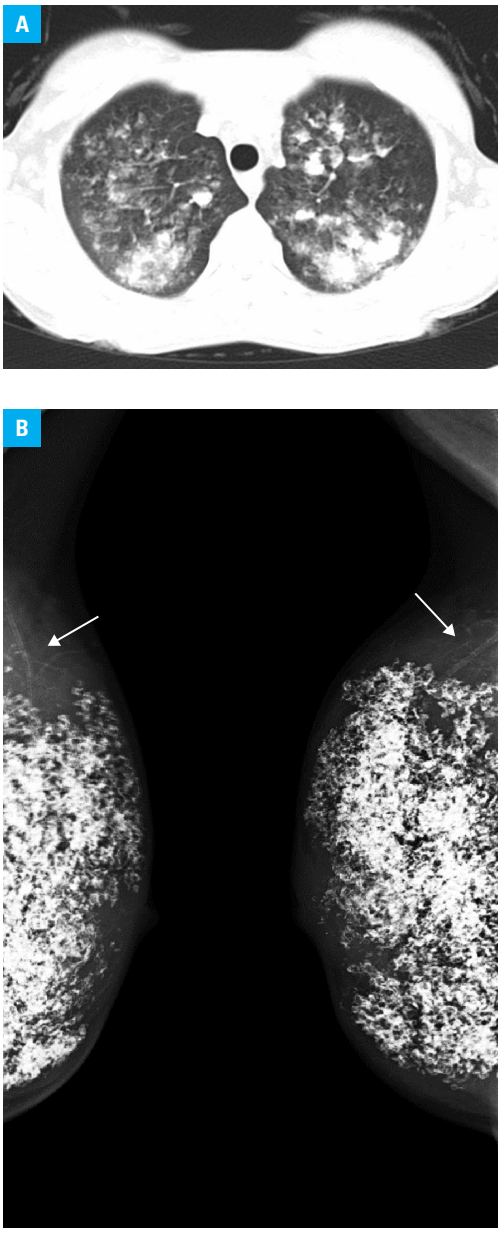

FIGURE 1 A – chest computed tomography showing diffuse calcification patches in bilateral lungs; B – mammography showing diffuse calcifications in bilateral breasts (the arrows indicate calcified vessels)

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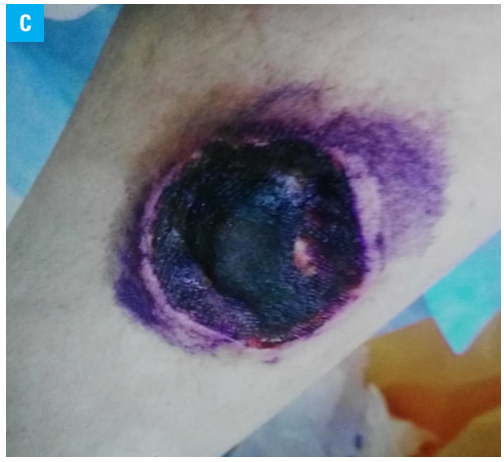

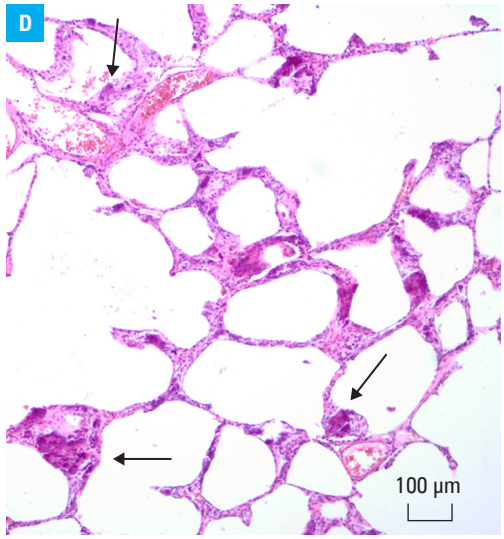

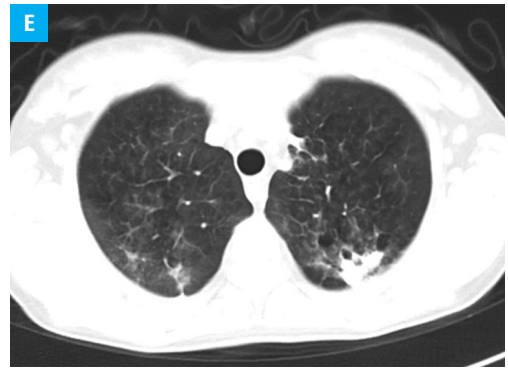

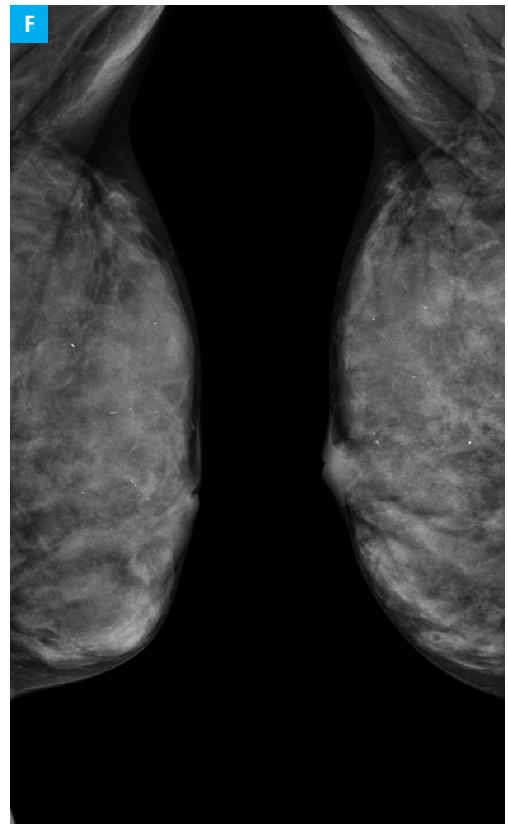

FIGURE 1 **C** – a large deep dermal ulcer (about 4×4 cm in size) on the left thigh (a picture taken by the patient herself after the ulcer was treated with gentian violet); **D** – a histologic examination of lung tissues (hematoxylin and eosin staining, magnification ×100), showing diffuse calcifications of the vascular walls and alveolar septa (arrows); **E** and **F** – reduction in calcifications of the lungs (**E**) and breasts (**F**) after sodium thiosulfate treatment

and 57.2 ug/l (reference range, 11.4–24.6 μg/l), respectively. Therefore, the patient was given a single 4-mg dose of intravenous zoledronate. Serum calcium and CTX concentrations returned to normal on the following day. No recurrence was observed over a 2-year follow-up.

Calciphylaxis is a rare and life-threatening syndrome. It is characterized by small vascular calcifications that cause painful ischemic dermal ulcers or visceral calcifications.[1] In the present case, a history of pneumonia and rapid weight loss might have contributed to calciphylaxis.[1,2] The therapeutic effects of STS in calciphylaxis are mediated by the formation of highly soluble calcium thiosulfate, as well as by vasodilatory and antioxidant properties.[3] To the best of our knowledge, hypercalcemia has not been described so far in patients treated with STS. Interestingly, a previous animal study demonstrated that STS could adversely affect bone integrity.[4] Therefore, we speculated that bone damage resulted in the hyperactivity of osteoblasts and osteoclasts in our patient, which induced hypercalcemia. This was confirmed by the elevation of CTX and BALP levels after STS therapy.

Importantly, in most cases, calciphylaxis causes only vascular calcifications. Severe diffuse calcifications involving multiple organs, as in our patient, are quite rare. Thus, we speculated that the large amounts of soluble calcium thiosulfate, which was produced at a much higher volume than could be excreted by the kidneys, might also have induced hypercalcemia. Therefore, a lower dose of STS should be recommended for patients with calciphylaxis with large-area calcifications who are not on dialysis, or dialysis should be administered intermittently during STS treatment. Finally, our case underlies that it is important to monitor serum calcium levels during STS treatment, while more evidence on the optimal STS dosage for patients with calciphylaxis is still needed.

ARTICLE INFORMATION

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CONFLICT OF INTEREST None declared.

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