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CORRESPONDENCE

Calcinosis cutis following seasonal influenza vaccination

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Calcinosis cutis results from deposits of calcium and phosphorus in the skin. We report here for the first time two cases of calcinosis cutis following the local injection of influenza vaccine.

A 51-year-old woman presented to our clinic with a 1-year history of an asymptomatic subcutaneous mass over the left deltoid area, which developed 6 months after an intramuscular administration of the seasonal influenza vaccine. No systemic symptoms such as fever, malaise, myalgia, or loss of appetite were noted. On physical examination there was a subcutaneous induration at the injection site (Fig. 1A). The histopathological examination showed basophilic deposits of calcium material in the subcutis (Fig. 1B). The laboratory examination was normal, including serum calcium, phosphate, parathyroid hormone level, and autoimmune blood tests.

A 56-year-old man presented with a painless, coin-sized indurated plaque in the left deltoid region. This patient had also received an intramuscular injection of seasonal influenza vaccine 6 months earlier. Ultrasonography showed echogenic foci with an acoustic shadow, which is the diagnostic feature of calcification that differentiates it from local inflammation (Fig. 1C). A biopsy sample of the mass also indicated calcinosis cutis in the subcutaneous layer. This patient did not have hypercalcemia,

hyperphosphatemia, hyperparathyroidism, or an autoimmune disease.

Influenza remains an important cause of morbidity and mortality worldwide and therefore seasonal vaccination of at-risk groups of patients is recommended each year by health authorities in many countries. The most common side effects of vaccination include soreness, erythema, tenderness, or swelling at the injection site, headache, fatigue, muscle ache, and malaise. Rare cutaneous adverse reactions including exanthem, urticaria, vasculitis, erythema multiforme, lichen planus, Sweet's syndrome, bullous fixed drug eruption, and linear immunoglobulin A dermatosis have been documented to probably be induced by influenza vaccination.^{1–4}

Calcinosis cutis is classified into four major categories according to different etiologies: dystrophic, metastatic, iatrogenic, and idiopathic. Based on the localized lesions without spreading and the normal laboratory data in these two patients, we propose two possible mechanisms for the development of calcinosis cutis following the administration of the seasonal influenza vaccine. Firstly, the calcinosis cutis may be secondary to local trauma by an inappropriate injection technique or an incorrect injection route, such as dermal or subcutaneous. Secondly, the calcification could have been iatrogenically induced by the calcium-containing additives of the influenza vaccine. Calcium chloride is a common approved additive in seasonal influenza vaccines and has been reported to induce iatrogenic calcinosis cutis by extravasation. In addition, calcium phosphate adjuvants have been introduced to influenza vaccines for the induction of potent immunogenic responses.⁵ Thus we speculated that calcium-containing influenza vaccines may have a higher risk of inducing calcinosis cutis at the injection site

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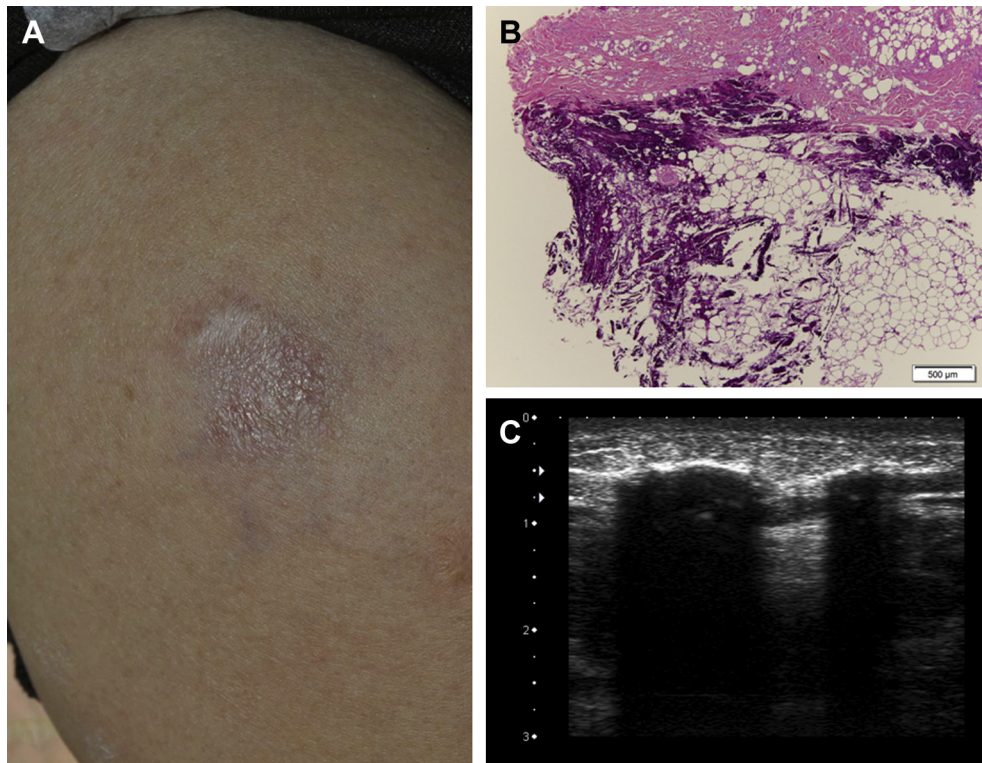


Figure 1 (A) A subcutaneous induration is found at the injection site of the seasonal influenza vaccine on the left deltoid area of a 51-year-old woman. (B) Histopathological examination shows basophilic deposits of calcium material in the subcutis (hematoxylin and eosin stain, $\times 40$). (C) Soft tissue sonography reveals features of calcification: echogenic foci with an acoustic shadow on the left deltoid region of a 56-year-old man.

than calcium-free vaccines. Further clinical observations and research are required to confirm this hypothesis.

In conclusion, we have described two cases of calcinosis cutis at the deltoid injection site following the administration of a seasonal influenza vaccine. Similar cases have not been reported previously and may be underdiagnosed because of the insidious onset. Medical ultrasonography is a useful diagnostic tool to distinguish calcinosis cutis from local inflammation before doctors take a skin biopsy sample to confirm the diagnosis.

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