A rare granulomatous reaction to Q fever vaccination following influenza vaccination

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To the Editor: We report the case of a 19-year-old female veterinary student who presented with a 2-week history of a rapidly growing mass on the lateral side of the deltoid area of her left arm. On examination, the mass was soft, freely movable, slightly warm and non-tender. There was no regional lymphadenopathy. The patient was afebrile, with no signs of systemic illness. Ultrasound showed a 3.2 × 2.3 × 1 cm, low-echogenic, lobulated lesion in the subcutaneous fat, with surrounding increased echogenicity suggestive of inflammation. Magnetic resonance imaging showed a poorly defined lesion throughout the deep and superficial fascia, with infiltration into the underlying deltoid muscle (Box 1). A provisional diagnosis of sarcoma was made, but an ultrasound-guided core biopsy sample showed non-necrotising epithelioid granulomas (Box 2).

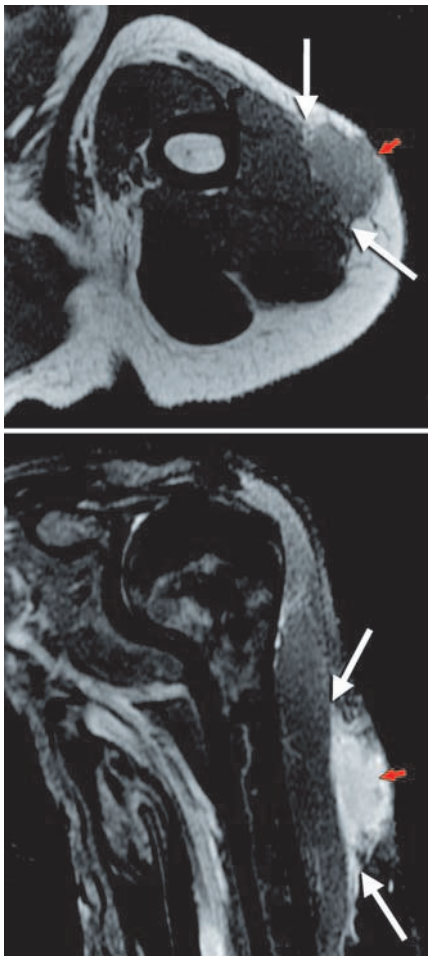
Two weeks after presentation, the patient noticed a smaller raised lump, about 1 cm in diameter, on the volar aspect of her left forearm. Four months before presentation, following negative results of both Q fever serological testing and a Q fever skin test administered on the volar aspect of her left forearm (at the site of the smaller lump), the patient had received a Q-VAX (CSL, Melbourne, Vic) vaccination in the left deltoid (at the site corresponding to the larger mass). Three months after this, and about 3 weeks before the deltoid mass first appeared, the patient received a Fluvax (CSL, Melbourne, Vic) influenza vaccination at the same left-deltoid site as the Q fever vaccination. This raises the possibility that the influenza vaccination may have been associated with the subsequent Q fever granuloma reaction.

Q fever, a disease caused by the zoonotic rickettsial organism *Coxiella burnetii*, is an occupational hazard for many Australians in animal-related professions. The disease is characterised by an acute, self-limiting febrile illness, with pneumonia and hepatitis being infrequent complications. In 2001, an Australian national Q fever vaccination program was initiated, which led to a 50% decline in the incidence of Q fever.[1] Side effects are normally rare and minor; during 2001–2004, only 86 adverse reactions were reported from about 49 000 vaccinations.[2]

Development of non-necrotising granulomas following Q fever vaccination is uncommon, with only six cases previously described.[3-5] To explore the possibility of a causal association between influenza vaccination, Q fever vaccination, and development of a granuloma, we traced four of these six patients with Q fever granuloma by contacting the authors of the previous reports. One patient had been vaccinated against influenza 2 months before the time of Q fever vaccination, and another had influenza vaccination afterwards (as in our case). Of the five cases (including our case) for which clinical history was available, three had a temporal association between influenza vaccination and Q fever vaccination, followed by the development of the non-necrotising granuloma. The indurated lesion at the separate Q fever skin-test site on the volar forearm, found in two other patients[5] as well as ours, supports the notion of a systemic immune reaction rather than simply a local reaction at the vaccination site. The Naranjo score in this case was 7, indicating a "probable" adverse drug reaction.

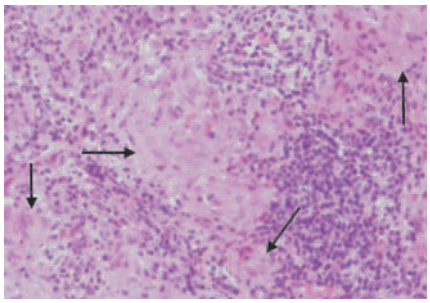
Although the granuloma was self-limited in all known cases, this case shows that there is significant risk of misdiagnosis on clinical grounds. It seems prudent to be aware of the possible association between these two vaccinations.

1 Magnetic resonance images of lesion



Axial (top) and coronal T1-weighted fat-saturated post-contrast (bottom) images demonstrate a poorly defined enhancing lesion (red arrows) in the subcutaneous fat, which superficially infiltrates and extends in a plaque-like manner in relation to the underlying deltoid muscle (white arrows). ◆

2 Ultrasound-guided core biopsy sample of lesion



The core biopsy of fibroadipose tissue shows numerous well formed non-necrotising epithelioid granulomas (arrows). The granulomas are composed of epithelioid histiocytes and a few multinucleated giant cells, surrounded by numerous lymphocytes (a mixture of B and T cells, with a greater proportion of T cells).

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