Mucha-Habermann Disease-like Eruption Following Pandemic Influenza H1N1 Vaccination: Coincidence or Causal Relationship?

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Abstract
Since its emergence reported in April 2009, pandemic influenza H1N1 rapidly spreads among humans all over the world. Although seasonal influenza vaccination has been implicated to occasionally induce skin diseases, extremely rare cases of skin eruption following pandemic influenza H1N1 vaccination have been reported. We here present a case of Mucha-Habermann disease-like eruption following pandemic influenza H1N1 vaccination. With a global H1N1 vaccination program against the pandemic H1N1 influenza, physicians and patients should be appraised of such rare skin reactions that may be induced by pandemic influenza H1N1 vaccination.

Case Presentation
A 51-year-old woman presented in October 2009 with a 19-day history of slightly itchy multiple erythematous papules on her face, trunk, and extremities. She had first noted these lesions two days after pandemic influenza H1N1 vaccination. Dermatological examination found multiple, disseminated, erythematous papules on the face, trunk, and extremities, some with central vesication, erosion, or hemorrhagic centers (Figures 1a-1c). The patient’s general health was good. She denied fever, malaise, mucosal change or arthralgia. She had no history of drug exposure, egg allergy, or side effects of seasonal influenza vaccine. Skin biopsy demonstrated focal parakeratosis in the stratum corneum, and satellite cell necrosis in the epidermis. The dermoeipidermal junction was obscured due to lymphocytic infiltration. The dermis showed superficial perivascular infiltrates of lymphocytes and extravasation of erythrocytes (Figures 2a and 2b). These findings were consistent with Mucha-Habermann disease (MHD), though clinical manifestation is not typical. Routine laboratory tests including complete blood count and biochemical analysis were normal. She quickly responded to oral corticosteroid therapy and had no recurrence.

Discussion
Human infections with pandemic influenza H1N1 virus were first identified in April 2009, and have been reported worldwide. Therefore, health authorities in many countries of the world recommend vaccination against pandemic influenza H1N1 virus, as well as seasonal viruses. Although seasonal influenza vaccination has been implicated to occasionally induce skin diseases, extremely rare cases of skin eruption following pandemic influenza H1N1 vaccination have been reported [1]. In our case, the skin lesions developed only two days after vaccination, and arose on the trunk and extremities as well as the face, which is an uncommon location for MHD. Quick response to systemic corticosteroid application was observed. The patient had no recent history of drug use or infection before the vaccination. This may suggest a causal relationship between the MHD-like eruption and vaccination, although we cannot completely exclude other causes.

MHD, also known as Pityriasis lichenoides et varioliformis acuta (PLEVA), is an uncommon inflammatory skin disease of unknown etiology characterized by a generalized eruption of acute onset, consisting of papular lesions that develop central necrosis and lead to scarring. They are distributed mainly on the trunk and flexural aspects.

Figure 1: Clinical appearance of multiple disseminated erythematous papules. (a) Multiple erythematous papules on the face, (b) neck, and back. (c) Erythematous papules with erosion or hemorrhagic centers on the neck.

Figure 2: Histopathological findings. (a) A lesion with lymphocytic infiltration extending into the papillae and into the epidermis. (b) Higher magnification showing satellite cell necrosis in the epidermis and lymphocytic infiltration. Hematoxylin and eosin, original magnifications (a) x100; (b) x400.
of the extremities. MHD is speculated to be an inflammatory reaction triggered by certain infectious agents, an inflammatory response secondary to T-cell dyscrasia, or an immune complex-mediated hypersensitivity [2]. Various pathogens have been proposed to cause MHD, such as Epstein-Barr virus, Toxoplasma gondii, adenovirus, Parvovirus B19, Staphylococcus aureus and Streptococcus pyogenes. Substances, such as tegafur, astemizole and radiocontrast iodide, have also been implicated in the occurrence of MHD. To our knowledge, only one case of MHD developed after viral vaccination, which was against measles, has been described [3]. We hypothesize that a hypersensitivity reaction to the vaccine components caused the skin eruption in our case, even though pandemic influenza H1N1 vaccine is an inactivated vaccine that does not induce infection.

Due to the worldwide campaign against the pandemic influenza, many more physicians may be involved in the vaccination program. During a pandemic, physicians and patients should be aware of rare skin reactions that may be induced by pandemic influenza H1N1 vaccination.

References