

Wells syndrome (eosinophilic cellulitis) following vaccination: Two pediatric cases with positive patch test to aluminium salts

Cynthia Fournier  | Isabelle Auger | Marie-Claude Houle

Division of dermatology, CHU de Québec, Laval University, Québec, Canada

Correspondence

Dr Cynthia Fournier, Division of dermatology, CHU de Québec, Laval University, Hôtel-Dieu de Québec, 11 Côte du Palais, Québec, QC G1R 2J6, Canada.
Email: cynthia.fournier.2@ulaval.ca

KEYWORDS: aluminium salts, eosinophilic cellulitis, patch test, vaccine reaction, Wells cellulitis, Wells syndrome

CASE REPORT

Case 1. A 10-year-old boy with a past history of atopic dermatitis and allergic rhinitis presented with pruriginous erythematous annular plaques with vesicles on the dorsum of his right foot (Figure 1A). The eruption appeared 12 days after he had received hepatitis B and human papillomavirus vaccines (Recombivax HB, Cervarix). Laboratory tests revealed eosinophilia of $1.000 \times 10^9/L$ (normal range $< 0.600 \times 10^9/L$). Cutaneous biopsy showed dermal and

subcutaneous lympho-eosinophilic infiltrate with rare flame figures (Figure 1B), suggesting the diagnosis of Wells syndrome. He was successfully treated with prednisone 0.5 mg/kg daily tapered over 6 weeks.

Case 2. A 12-year-old girl with a past history of atopic dermatitis presented with pruriginous violaceous annular plaques on both legs (Figure 2A). The eruption appeared 14 days after she had received her second injection of human papillomavirus vaccine (Gardasil 9).

FIGURE 1 (A) Erythematous annular plaques with vesicles on the dorsum of the right foot. (B) Dermal and subcutaneous interstitial and perivascular lymphoeosinophilic infiltrate with rare flame figures (hematoxylin and eosin)

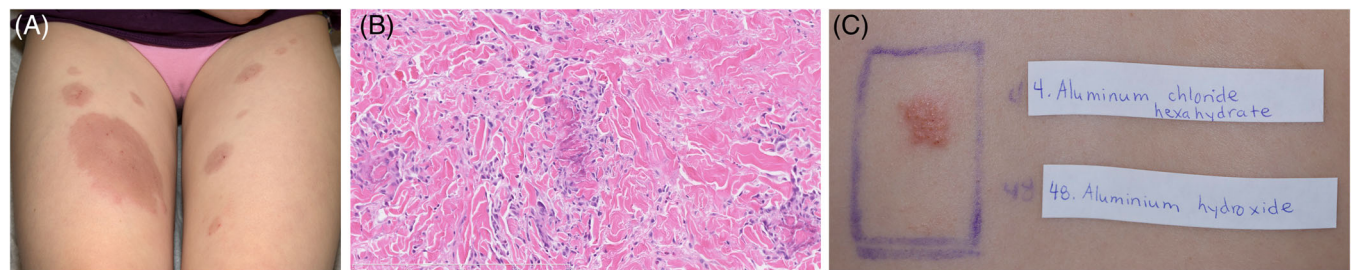
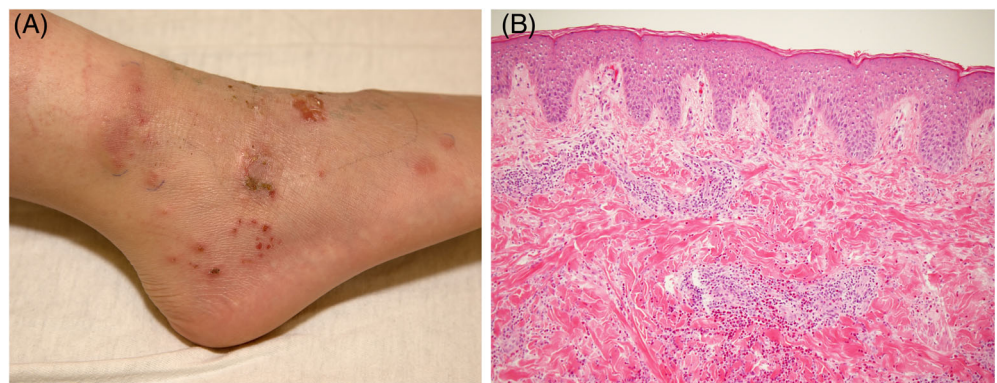


FIGURE 2 (A) Violaceous edematous annular plaques on both legs. (B) High power view of flame figures (hematoxylin and eosin). (C) Positive patch test to aluminium chloride hexahydrate

TABLE 1 Vaccine additives

Recombivax HB	Cervarix	Gardasil 9
Aluminum hydroxy phosphate, Sodium borate, Formaldehyde, Sodium chloride	Aluminum hydroxide, Sodium chloride, Sodium dihydrogen phosphate	Aluminum hydroxyphosphate sulfate, Polysorbate 80, Sodium borate, Sodium chloride, L-histidine

Interestingly, 2 weeks after receiving her first injection, she had developed the same cutaneous eruption that persisted for 2 months, but she did not seek medical care at that time. No laboratory tests were done. A cutaneous biopsy showed an interstitial dermal infiltrate composed of lymphocytes, histiocytes, and eosinophils with numerous flame figures (Figure 2B), also consistent with a diagnosis of Wells cellulitis. She also was successfully treated with prednisolone 0.5 mg/kg daily tapered over 2 weeks.

Both patients were patch tested with possible allergens contained in their respective vaccines (Table 1). Patient 1 was patch tested to aluminum chloride hexahydrate, aluminum hydroxide, and formaldehyde. He was found to have a ++ reaction to aluminum hydroxide at day (D) 4. Patient 2 was patch tested to polysorbate 80, aluminum chloride hexahydrate, and aluminum hydroxide. Reading at D4 revealed a ++ reaction to aluminum chloride hexahydrate (Figure 2C). No other patch test series were performed. Patient 1 had already received vaccines containing aluminium salts (Twinrix and Gardasil 9) without any cutaneous adverse reactions. Before the occurrence of Wells cellulitis, following both injections of Gardasil 9 vaccine, patient 2 had already received a vaccine containing aluminium hydroxide and aluminium phosphate (Twinrix) without any cutaneous reaction.

DISCUSSION

Wells syndrome is a rare cutaneous reaction of unknown aetiology. It typically presents with erythematous oedematous plaques mimicking bacterial cellulitis.¹ Laboratory investigation reveals eosinophilia in approximately 50% of patients.¹ Histopathology is characterized by a dermal infiltrate of histiocytes and eosinophils, with eosinophil granules surrounding collagen fibers (flame figure).¹

Six cases of vaccine-induced Wells syndrome have been reported,^{2–7} half of these proven by patch testing. Culprit allergens in those cases were neomycin and aluminum hydroxide,² as well as thimerosal.^{4,6} Other drugs can trigger Wells syndrome, including antibiotics, anticholinergic agents, anaesthetics, non-steroidal anti-inflammatory agents, thyroid medications, chemotherapeutic agents, and anti-TNF agents.⁸

We present two cases of Wells syndrome following vaccination with test-proven sensitivity to aluminum salts, an additive commonly used in vaccines to enhance a specific and longer-lasting immune response.⁹ The onset of cutaneous manifestations after vaccination was 12 days and 14 days in cases 1 and 2, respectively.

Given that one of our patients had a positive reaction to aluminium hydroxide while the other reacted to aluminum chloride hexahydrate, we suggest testing with different aluminum salts when investigating possible allergy to vaccines. Further studies are necessary to validate which aluminum salt would be the best screening agent in those cases.

CONFLICT OF INTERESTS

The authors declare no conflicts of interest.

ORCID

Cynthia Fournier  <https://orcid.org/0000-0003-3806-1098>

REFERENCES

1. Caputo R, Marzano AV, Vezzoli P, Lunardon L. Wells syndrome in adults and children: a report of 19 cases. *Arch Dermatol*. 2006;142(9):1157–1161.
2. Yu AM, Ito S, Leibson T, et al. Pediatric Wells syndrome (eosinophilic cellulitis) after vaccination: a case report and review of the literature. *Pediatr Dermatol*. 2018;35(5):e262–e264.
3. Simpson JK, Patalay R, Francis N, Roberts N. Influenza vaccination as a novel trigger of Wells Syndrome in a child. *Pediatr Dermatol*. 2015;32(4):e171–e172.
4. Koh KJ, Warren L, Moore L, James C, Thompson GN. Wells' syndrome following thiomersal-containing vaccinations. *Australas J Dermatol*. 2003;44(3):199–202.
5. Moreno M, Luelmo J, Monteagudo M, Bella R, Casanovas A. Wells' syndrome related to tetanus vaccine. *Int J Dermatol*. 1997;36(7):524–525.
6. Safran T, Masckauchan M, Maj J, Green L. Wells syndrome secondary to influenza vaccination: a case report and review of the literature. *Hum Vaccin Immunother*. 2018;14(4):958–960.
7. Calvert J, Shors AR, Hornung RL, Poorsattar SP, Sidbury R. Relapse of Wells' syndrome in a child after tetanus-diphtheria immunization. *J Am Acad Dermatol*. 2006;54(5 Suppl):S232–S233.
8. Heelan K, Ryan JF, Shear NH, Egan CA. Wells Syndrome (eosinophilic cellulitis): proposed diagnostic criteria and a literature review of the drug-induced variant. *J Dermatol Case Rep*. 2013;7(4):113–120.
9. Reed SG, Orr MT, Fox CB. Key roles of adjuvants in modern vaccines. *Nat Med*. 2013;19(12):1597–1608.

How to cite this article: Fournier C, Auger I, Houle M-C. Wells syndrome (eosinophilic cellulitis) following vaccination: Two pediatric cases with positive patch test to aluminium salts. *Contact Dermatitis*. 2020;1–2. <https://doi.org/10.1111/cod.13485>