Wells Syndrome Secondary to Influenza Vaccination: A Case Report and Review of the Literature

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Wells Syndrome Secondary to Influenza Vaccination: A Case Report and Review of the Literature

Running Head: Wells Syndrome Influenza Vaccine

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Key Words: Wells Syndrome, Eosinophilic cellulitis, Vaccination, Influenza

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ABSTRACT:
Vaccinations have been shown repeatedly to be extremely safe with low incidence of complications. Given the rarity, these adverse events, they must be reported and examined cautiously. This case report illustrates the first case of an adult presenting with Wells syndrome...
that developed soon after vaccination with the thiomersal, a common preservative, containing influenza vaccine. Wells syndrome, also known as eosinophilic cellulitis, is an uncommon dermatologic condition of unknown etiology. Lesions in patients with Wells syndrome (eosinophilic cellulitis) progress over a few days to become large indurated plaques with associated edema and erythema. Although the etiology of Wells syndrome remains unknown, certain precipitants have been described in the literature, including but not limited to parasitic infections, contact dermatitis, Churg-Strauss disease and various medications. This article describes a possible sensitivity to thiomersal, as well as describes other cases that have reported a similar sensitivity secondary to receiving thiomersal-containing vaccines.

Key Words: Wells Syndrome, Eosinophilic cellulitis, Vaccination, Influenza
INTRODUCTION:

Vaccinations have been shown repeatedly to be extremely safe with low incidence of complications. One study performed by Weisser et al. highlight vaccination trials boasting an adverse event ratio frequency of 1:1,000 to 1:10,000 individuals\(^1\). Given the rarity, these adverse events, they must be reported and examined cautiously. One of the possible manifestations is skin disease, such as reported secondary to the influenza vaccination as seen this case report. Additionally as rare is Wells syndrome, also known as eosinophilic cellulitis. Wells syndrome is an uncommon dermatologic condition of unknown etiology. Lesions in patients with Wells syndrome (eosinophilic cellulitis) progress over a few days to become large indurated plaques with associated edema and erythema. Some pustular and nodular lesions may also be present, with or without accompanying vesiculo-bullae on their surface. Other symptoms previously described include itching and burning. This eruption usually fades away within four to eight weeks in the absence of any treatment. The diagnosis of Wells syndrome is made on the basis of clinical examination findings and biopsy confirmation, demonstrating the presence of eosinophilic infiltrates. As well, the biopsy can include characteristic ‘flame figures.’ In terms of systemic findings, serum eosinophil levels are often elevated in this condition. Although the etiology of Wells syndrome remains unknown, certain precipitants have been described in the literature, including but not limited to parasitic infections, contact dermatitis, Churg-Strauss disease and various medications\(^2\). In rare instances, it has been described to be caused by certain vaccinations\(^2\). This case report illustrates the first case of an adult presenting with Wells syndrome that developed soon after vaccination with the influenza vaccine.

CASE:
An 86-year-old male known for hypertension, insulin dependent type 2 diabetes and chronic kidney disease presented to his dermatologist with a pruritic rash that started on his right flank and subsequently progressed to most of his body. He was immediately sent to the local emergency room. The patient denied any new medications, allergies, travel history, sick contacts or previous history of rash, but admits to having received a thiomersal-containing influenza vaccination 13 days prior. He also denied fever, weight loss or any other systemic symptoms. On admission to the medical ward, the patient had a polymorphic rash with targeted eruptions, blisters, bullae, and deep seeded nodular lesions (Figure 1-4). These lesions extended to his entire body, palms and soles but spared the scalp and oral mucosa. Initial workup demonstrated an elevated white blood cell count (24.6 WBCs x 10^9/L) with neutrophilia (18.6 x 10^9/L) and eosinophilia (3.6 x 10^9/L), as well as elevated inflammatory markers (CRP of 60.86 mg/L and ESR of 33 mm/hr). The only systemic finding was elevated creatinine (130 µmol/L), for which nephrology was consulted. Urine microscopy was negative for glomerular disease and renal function improved with intravenous fluids. Dermatology was also consulted and their differential diagnosis included Wells syndrome, Sweet’s syndrome and bullous pemphigoid. Skin biopsies demonstrated urticarial eruption with prominent papillary dermal edema, mild acute epidermal spongiosis, and numerous eosinophils, without evidence of flame figures. The patient was diagnosed with Wells syndrome that developed soon after vaccination with the influenza vaccine based on the clinical picture, histology and the absence of other potential etiologies. The patient was subsequently started on 60 mg of prednisone daily for seven days, with a dramatic improvement in his rash and was discharged with follow-up
with dermatology. He then was then started on a taper of prednisone eliminating 5 mg per 3 days. Patient will participate in further allergy testing, via skin test, which will confirm the sensitivity to thiomersal.

**DISCUSSION:**

Wells syndrome is a rare condition, only being first described in 1971. The treatment of choice for this disease has been shown to be oral steroids (1-2 mg/kg), with antihistamines and topical steroids for symptom control. Wells syndrome has often been considered a histological diagnosis by many. The typical pathohistological feature of Wells syndrome has been eosinophilia with characteristic “flame figures.” However, a case series by Caputo et al. shows that only 50% of patients with clinical Wells syndrome show evidence of flame figures. This finding was then supported by a literature review looking at all the idiopathic cases of Wells. In order to facilitate the diagnosis, Heelan et al. propose a set of diagnostic criteria, which they tested on a series of drug-induced Wells syndrome patients. There are four major and four minor criteria. A diagnosis of Wells syndrome can be made when at least two major and one minor criteria are present. (Table 1). The current case presented fits the proposed diagnostic criteria and achieved full resolution after a course of oral steroids. The current case was diagnosed given the major criteria: (1) not caused by systemic disease (2) the histiology of eosinophilic infiltrates (3) the papulonodular type dermatologic manifestation. Additionally, the minor criteria being that developed soon after a drug, in this case the influenza vaccination.

Although this is the first case described of an adult presenting with Wells syndrome after receiving the influenza vaccination, there have been two cases of children being diagnosed with Wells syndrome post-influenza vaccination and one case of an adult being diagnosed after
receiving the tetanus vaccination\textsuperscript{5-7}. Indeed, all the vaccinations described in the literature along with the influenza vaccination received in this case include thiomersal, a common preservative. In the case of the patient with Wells syndrome post-tetanus vaccination, a skin test with thiomersal was found to be positive, demonstrating the possibility that part of the pathophysiology of Wells is related to hypersensitivity reactions.\textsuperscript{6} The patient in this study did opt for a skin test that will allow confirmation of the thiomersal hypersensitivity.

This case illustrates the first patient who presented with clinical Wells syndrome after receiving the thiomersal-containing influenza vaccination. This stresses the importance for clinicians to obtain a complete drug history (including vaccination) when a patient presents with a rash of unknown etiology. Additionally, clinicians must be aware of the possible sensitivity to thiomersal when a patient presents with a possibly unknown drug reaction.

REFERENCES:


FIGURE LEGENDS:

Fig 1: Lower abdomen and lower extremity
Fig 2: Lower Extremity
Fig 3: Palmar Distribution
Fig 4: Abdomen and Thorax
Table 1: Diagnostic Criteria for Wells Syndrome

<table>
<thead>
<tr>
<th>Major Diagnostic Criteria Wells⁵</th>
<th>1) Diverse Clinical Picture to include any of the previous reported variants:</th>
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<tbody>
<tr>
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<td>• Plaque-type</td>
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<td></td>
<td>• Annular-Granuloma-Like</td>
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<td></td>
<td>• Urticaria-like</td>
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<tr>
<td></td>
<td>• Papulovesicular</td>
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<td>• Bullous</td>
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<tr>
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<td>• Papulonodular</td>
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<td>• Fixed-Drug Eruption-like</td>
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<tr>
<td></td>
<td>2) Relapsing, Remitting course</td>
</tr>
<tr>
<td></td>
<td>3) No Evidence of Systemic disease</td>
</tr>
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<td></td>
<td>4) Histology: Eosinophilic infiltrates, with no vasculitis</td>
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<tr>
<th>Minor Diagnostic Criteria Wells⁵</th>
<th>1) Flame Figures</th>
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<tr>
<td></td>
<td>2) Histology: Granulomatous Change</td>
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<td></td>
<td>3) Peripheral Eosinophilia not persistent and not greater than</td>
</tr>
<tr>
<td></td>
<td>&gt;1500/ul</td>
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<td></td>
<td>4) Triggering Factor (Drug)</td>
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Table 1: Diagnostic Criteria for Wells Syndrome⁵