CASE REPORT

Subcutaneous granuloma annulare following influenza vaccination in a patient with diabetes mellitus

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Abstract

An influenza vaccination often causes local reactions, such as induration and erythema at the injection site, and occasionally systemic reactions. The association between these reactions and influenza vaccinations has not been fully recognized. By contrast, granuloma annulare (GA) is an idiopathic, palisaded, granulomatous condition, and has some clinical variants, including localized, generalized, perforating, and subcutaneous types. We report a 76-year-old woman, who was suffering from a tender subcutaneous nodule on her left upper arm. One month before, she had just received influenza vaccination on the same area. Histological analysis demonstrated that subcutaneous tissue contained numerous large areas of necrosis, surrounded by palisaded epithelioid histiocytes. We diagnosed our case as a subcutaneous type of GA following influenza vaccination. To our knowledge, this is the first report of GA associated with influenza vaccination.

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Introduction

Influenza vaccination often causes local reactions, such as induration and erythema at the injection site, and occasionally systemic reactions. Despite the high incidence of the skin reactions, the histopathology of the reactions remains not fully characterized.

Granuloma annulare (GA) is an idiopathic, palisaded, granulomatous condition and has several clinical variants, including localized, generalized, perforating, and subcutaneous types. Here, we report a case of subcutaneous GA arising at the site where an influenza vaccination was injected.

Case report

A 76-year-old woman was referred to us for evaluation of a 1-month history of a tender subcutaneous nodule on her left upper arm. One month before, she had received an influenza vaccination on the same site. She had suffered from hypertension and diabetes mellitus. There was no history of egg allergy. On physical examination, a 6 × 6 mm tender, solid subcutaneous nodule was seen on the outer aspect of her left upper arm (Figure 1A). Magnetic resonance imaging showed that a nodule was located in the subcutaneous fat tissue overlying the superficial fascia (Figure 1B).

Histological analysis of the totally excised nodule demonstrated a globular, well-demarcated, cell-infiltrating lesion in the subcutaneous fat (Figure 1C). The nodule contained a central necrotic area with irregular configuration. The abundant epithelioid histiocytes surrounded the foci of necrosis in a palisading manner (Figure 1D). No organisms could be detected by Ziel-Neelsen stain. We diagnosed the lesion as the subcutaneous type of GA following an influenza vaccination.

Discussion

It is well known that GA is occasionally associated with diabetes mellitus. Thus, she had a predisposing factor for GA. In this patient, however, there was no GA lesion before the influenza vaccination, and GA occurred only at the site of vaccination. After the resection of GA, there was no recurrence on either the same site or other sites. Therefore, it is tempting to speculate that diabetes mellitus served as a predisposing factor for GA and vaccination directly triggered GA in our patient. We reviewed the previous reports describing GA following vaccinations; 11 cases have been reported (Table 1). The types of vaccinations included those against hepatitis B virus, Bacillus Calmette-Guerin (BCG), human papilloma virus, diphtheria, and tetanus. To the best of our knowledge, our case is the first report of GA associated with influenza vaccinations. Only three cases, including our case, were the subcutaneous type. In

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the vast majority of cases, the duration between the vaccination and the GA onset was within 2 months. The patients were often treated with topical corticosteroids or excision, or untreated.

Although one reported case suggested the relationship between an adjuvant and development of subcutaneous GA, it remains unknown whether GA was triggered by vaccines per se or by adjuvants. Since the initial use of adjuvants in the 1920s, aluminum salts had been the most common adjuvant for vaccine formulations. However, current influenza vaccinations in Japan do not include the aluminum adjuvants. This raises the possibility that our patient’s GA was caused by a specific vaccine antigen. It is suggested that vaccine antigen may evoke a T cell-mediated, granuloma-inducing immune reaction in predisposed individuals. Given that our patient had diabetes mellitus, a disease potentially promoting granuloma formation, such as necrobiosis lipoidica and GA, she might be susceptible to vaccine-induced GA.

Table 1  GA following vaccinations.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age/sex</th>
<th>Type of vaccinations</th>
<th>Type of GA</th>
<th>Duration of onset following vaccination</th>
<th>Location</th>
<th>Treatment</th>
<th>Authors, year (Reference)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>51 y/F</td>
<td>HBV</td>
<td>Generalized</td>
<td>1 month</td>
<td>Non-injection site</td>
<td>DDD</td>
<td>Wolf F et al, 1998⁴</td>
</tr>
<tr>
<td>2</td>
<td>5 m/M</td>
<td>BCG</td>
<td>Generalized</td>
<td>1 month</td>
<td>Non-injection site</td>
<td>Moisturization</td>
<td>Nagase K et al, 2011⁵</td>
</tr>
<tr>
<td>3</td>
<td>52 y/F</td>
<td>BCG</td>
<td>Localized</td>
<td>30 years</td>
<td>Injection site</td>
<td>INH + PSL</td>
<td>Middelburg TA et al, 2009⁹</td>
</tr>
<tr>
<td>4</td>
<td>26 y/F</td>
<td>HPV (aluminum adjuvants)</td>
<td>Subcutaneous</td>
<td>1 month</td>
<td>Injection site</td>
<td>Excision</td>
<td>Marsee DK et al, 2008⁷</td>
</tr>
<tr>
<td>5</td>
<td>8 y/F</td>
<td>Diphtheria</td>
<td>Generalized</td>
<td>1 week</td>
<td>Injection site</td>
<td>Topical or oral steroid</td>
<td>Criado PR et al, 2004⁹</td>
</tr>
<tr>
<td>6</td>
<td>58 y/F</td>
<td>HBV</td>
<td>Generalized</td>
<td>2 months</td>
<td>Injection site</td>
<td>Corticosteroid ointment</td>
<td>Baykal C et al, 2002¹⁰</td>
</tr>
<tr>
<td>7</td>
<td>6 y/F</td>
<td>Tetanus</td>
<td>Localized</td>
<td>2 months, 3 days</td>
<td>Injection site</td>
<td>Corticosteroid ointment</td>
<td>Kakurai M et al, 2001¹¹</td>
</tr>
<tr>
<td>8</td>
<td>12 y/M</td>
<td>BCG</td>
<td>Generalized</td>
<td>5 days</td>
<td>Non-injection site</td>
<td>Corticosteroid ointment</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>3 y/M</td>
<td>BCG</td>
<td>Generalized</td>
<td>1 month</td>
<td>Injection site</td>
<td>No treatment</td>
<td>Houche-Bruge C et al, 2001¹²</td>
</tr>
<tr>
<td>10</td>
<td>3 y/M</td>
<td>BCG</td>
<td>Generalized</td>
<td>1 month</td>
<td>Injection site?</td>
<td>No treatment</td>
<td>Houche-Bruge C et al, 2001¹²</td>
</tr>
<tr>
<td>11</td>
<td>2 y/F</td>
<td>BCG</td>
<td>Subcutaneous</td>
<td>2 month</td>
<td>Non-injection site</td>
<td>No treatment</td>
<td>Houche-Bruge C et al, 2001¹²</td>
</tr>
<tr>
<td>Our case</td>
<td>76 y/F</td>
<td>Influenza</td>
<td>Subcutaneous</td>
<td>1 month</td>
<td>Injection site</td>
<td>Excision</td>
<td>Present article</td>
</tr>
</tbody>
</table>

GA – granuloma annulare; y – years; m – month; HBV – hepatitis B virus; BCG – Bacillus Calmette-Guerin; HPV – human papilloma virus.

References


