

Subacute thyroiditis after seasonal influenza vaccination

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Abstract

We report the first patient with subacute thyroiditis after influenza vaccination in Japan. A 49-year-old woman received a seasonal influenza vaccination in October 2009. She also received a seasonal influenza vaccination in 2008. After the vaccination, she experienced spontaneous pain and tenderness in the right lower neck. Together with the results of laboratory examinations and thyroid echography, we established the diagnosis of subacute thyroiditis. The patient had human leukocyte antigens (HLAs) of A2/A11 and B62/B35. HLA-A2-positive is reported at a risk of interferon-alpha-induced autoimmune thyroid disorder, and HLA-B35-positive is reported at a risk of subacute thyroiditis. Since fever and cervical pain are reported as adverse effects of influenza vaccination, subacute thyroiditis after influenza vaccination might have been missed.

Introduction

Influenza vaccination has well-established effects against influenza virus infection.¹ However, various complications have been reported as adverse effects of this vaccination.¹ Here, we report the first patient with subacute thyroiditis after influenza vaccination in Japan, and discuss the possible involvement of the human leukocyte antigen (HLA).

Case Report

A 49-year-old woman with no history of thyroid disease received a seasonal influenza vaccination (influenza hemagglutinin (HA) vaccine; SEIKEN®, Takeda Pharmaceutical Co. Ltd., Tokyo, Japan) in October 2009. She also received a seasonal influenza vaccination in 2008. The patient does not have any drug allergies, including allergies against vaccinations. At the time of vaccination, she did not have a

cold. At 2 days after vaccination, she experienced spontaneous pain and tenderness in the right lower neck, however, she did not feel a fever. After 9 days, the pain worsened, and her body temperature became approximately 37.0°C. She experienced general fatigue and shortness of breath when she walks fast. After 16 days, the pain worsened and radiated to the right ear. After 22 days, the patient visited our hospital. Physical examinations showed no anemia, no lung rale, no cardiac murmur, and no arrhythmia. The thyroid was not enlarged but exhibited tenderness. Laboratory examinations including urinalysis, cell blood count (CBC) and blood biochemical test revealed mild inflammation: white blood cell count (WBC), 7400 cells/ μ L (reference, 2700-10,300); neutrophil, 71.7% (reference, 37.0-80.0); C-reactive protein (CRP), 1.02 mg/dL (reference, <0.30); and erythrocyte sedimentation rate (ESR), 69 mm/hour (reference, 2-10). Parameters describing thyroid function and thyroid antibodies were as follows: thyroid stimulating hormone (TSH), <0.01 μ U/mL (reference, 0.35-4.94); free triiodothyronine (FT3), 6.33 pg/mL (reference, 1.71-3.71); free tetraiodothyronine (FT4), 2.60 ng/dL (reference, 0.70-1.48); thyroglobulin, 603.6 ng/mL (reference, <32.7). Thyroid antibodies were negative. Thyroid ultrasonography with color doppler revealed low bloodstream area throughout the thyroids, and a hypoechogenic area in the right lobe of the thyroid. This hypoechogenic area corresponded to the area of spontaneous pain, and probe touching worsened the pain (Figure 1). The patient tested positive for the following human leukocyte antigens (HLAs) by lymphocyte analysis: A2/A11, B62/B35, DR4/DR14 = DRB1*04 DRB1*14.

On the basis of the history of illness, laboratory results, and the results of thyroid echography, we diagnosed the patient with subacute thyroiditis using the criteria for subacute thyroiditis of the Japan Thyroid Association.² After the administration of prednisolone 10 mg/day, the patient's symptoms improved.

Discussion

According to a standard textbook of Endocrinology, subacute thyroiditis is thought to be caused directly or indirectly by various viral infections, including influenza virus;³ therefore, influenza vaccine may cause subacute thyroiditis. Since the influenza vaccine is an inactive vaccine, direct mechanisms, such as virus proliferation, may not be involved. Instead, indirect mechanisms, such as immune responses, may be involved in the subacute thyroiditis in the present patient.

As reported previously, HLA-A1, A2, B8, and

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Key words: subacute thyroiditis, influenza, vaccination, human leukocyte antigen.

Contributions: FY, patient diagnosis and treatment; KO, TK, clinical suggestion between influenza virus and its complications; MY, patient medical care; HK, manuscript writing, patient medical care.

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B35 enhance influenza A virus-specific cytotoxic T-lymphocyte response, and HLA-A2 has the strongest effect.⁴ In patients with chronic hepatitis C, HLA-A2, B46, and Cw7 were associated with an interferon-alpha-induced autoimmune thyroid disorder; especially, the relative risk of HLA-A2 was 10.2.⁵ Further, subacute thyroiditis was associated with HLA B-35 and B-67; especially, the relative risk of HLA-B35 was 18.02.⁶ Since our patient showed HLA-A2/A11 B62/B35, we suppose that her HLA was related to the subacute thyroiditis after

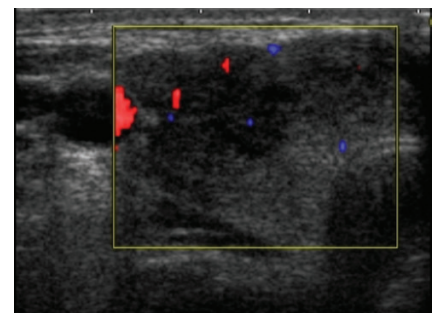


Figure 1. Thyroid ultrasonography (Color Doppler): the low bloodstream area throughout the thyroids, and a hypoechogenic area in the right lobe of the thyroid. The hypoechogenic area corresponded to the area of spontaneous pain, and probe touching worsened the pain.

influenza vaccination. There have been two case reports of subacute thyroiditis after influenza vaccination.^{7,8} However, HLA was not reported in both case reports. Since fever and cervical pain are reported as adverse effects of influenza vaccination,⁹ subacute thyroiditis after influenza vaccination might have been missed. Medical practitioners should be aware of subacute thyroiditis when administering influenza vaccine to patients.

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