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CASE REPORT

Autoimmune/Inflammatory Syndrome Induced by Adjuvants (ASIA) following Influenza Vaccination

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ABSTRACT

BACKGROUND

To describe two patients who developed autoimmune/inflammatory syndrome induced by adjuvants (ASIA) following influenza vaccination.

METHODS

Case report.

CASE REPORT

Case 1: A 65-years-old female patient who presented symptoms in the day that she received the influenza vaccination, entailing fever, myalgia, arthralgia in her shoulders, and arthritis of the wrists bilaterally, and morning stiffness. Laboratory tests revealed an erythrocyte sedimentation rate (ESR) of 89 mm/1st hour and C-reactive protein (CRP) of 9.25 mg/L and positive HLA-B27. Bone scintigraphy showed increased uptake of the shoulders, right knee, and wrists. An ultrasound confirmed the involvement of wrists, shoulder, and both knees, without erosions. A diagnosis of rheumatoid arthritis was determined. Methotrexate was started at a dosage of 15 mg/week and one single dose of betamethasone depot. She had a marked clinical and laboratory improvement, normalization of CRP and ESR, but she continues using methotrexate eight years later. Case 2: A 54-years-old female in 2013 received an H1N1-adjuvanted vaccine and, after 15 days, starting with complaints of diffuse myalgia, more critical in her thighs, without muscle weakness and severe fatigue. Her past medical history was positive for undetermined leprosy adequately treated and considered healed ten years ago. Laboratory tests revealed a creatine kinase of 174 U/L (NR: 26-140 U/L), lactate dehydrogenase (LDH) 533 U/L (NR: 120-246U/L), and 25-OH-vitamin D of 19 ng/mL. Antinuclear antibodies were positive in a titer of 1:80 with a speckled pattern. Electromyography and a thigh magnetic resonance imaging were interpreted as normal. She received vitamin D supplementation of 600,000 IU in a single dose and remained on clinical and laboratory

observation. After three months, she was asymptomatic, and the levels of creatine kinase, LDH, and vitamin D were within the normal range.

CONCLUSION

This article illustrates two patients who developed ASIA syndrome after the influenza vaccine. Therefore, the influenza vaccination policy requires considering adverse events, including the development of autoimmune disorders.

KEYWORDS

Vaccine; Vaccination; Arthritis; Autoimmunity; Adjuvants; Autoimmune/inflammatory syndrome induced by adjuvants

INTRODUCTION

Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) or the Shoenfeld's syndrome is a recently described autoimmune disorder, characterized by autoimmune manifestations or disease development after adjuvants exposure. An extensive description of 500 subjects with ASIA was recently published and showed a female predominance, and most cases were well-defined as immune diseases and were linked mainly to exposure to hepatitis B and influenza vaccinations [1].

An extensive description of 500 subjects about ASIA was published, showing a female predominance, and most cases were well-defined as immune diseases and were linked to exposure to the hepatitis B and influenza vaccinations [1].

After the influenza vaccine, there are several ASIA cases represented by systemic vasculitis, Crohn disease, spondyloarthritis, mixed connective tissue disease, Sjögren syndrome, systemic lupus erythematosus, undifferentiated connective disease, Guillain-Barre syndrome, autoimmune liver diseases, inflammatory polyradiculopathy, fibromyalgia, and chronic fatigue syndromes. In the description mentioned above, 11.2% of all cases developed an autoimmune disease after influenza vaccination [1].

This article has the objective to report two new cases of ASIA after influenza vaccination.

CASE RREPORT

Case 1

A 65-years-old female patient with a past medical history of systemic arterial hypertension, pre-diabetes, dyslipidemia, and pulmonary thromboembolism 36 years ago in her puerperium, using telmisartan 40mg/day and simvastatin 10 mg/day. She had a history initiated in May 2012 in the day she received influenza vaccination started with fever, myalgia, arthralgia in her shoulders and hand with edema on her wrists associated with morning stiffness that lasts 1 hour. She used celecoxib with low improvement. Her physical examination demonstrated arthritis of wrists bilaterally and Heberden and Bouchard nodules, compatible with osteoarthritis [2]. Laboratory tests revealed blood cell count normal, glucose 119 mg/dL, erythrocyte sedimentation rate (ESR) of 89 mm/1st hour, and C-reactive protein (CRP) 9.25 mg/L and the presence of HLA-B27. Antinuclear antibodies, anti-dsDNA, anti-RNP, anti-Ro/SS-B, anti-La/SS-B, IgG, and IgM anticardiolipin, rheumatoid factor was all negative.

Tuberculin test was absent; serology for hepatitis B and C, HIV 1 and 2, and HTLV I and II were negative. IgG for Epstein-Barr, human cytomegalovirus, toxoplasmosis, and rubella was positive with negative IgM. Levels of creatine kinase were 41 U/L (normal range: 26 U/L - 140 U/L). Bone scintigraphy showed increased uptake of the shoulders, right knee, and wrists. An ultrasound confirmed the involvement of the wrists, shoulder, and both knees, without erosions. X-rays of these joints showed only edema, and no erosion was observed. A diagnosis of rheumatoid arthritis was determined since she had arthritis of wrists, shoulders, and knee for more than six weeks, associated with increased ESR and CRP levels [3]. Methotrexate was started at a dosage of 15 mg per week, associated with folic acid 5 mg per week, and one single dose of betamethasone depot was administered. She evolved with marked clinical and laboratory improvement, normalization of CRP and ESR, but continues under methotrexate treatment eight years later.

Case 2

A 54-years-old female in 2013 received an H1N1-adjuvanted vaccine and, after 15 days, started diffusing myalgia, more critical in her thighs, without muscle weakness and severe fatigue. In the day after the vaccine, she felt fever and needed antipyretics. Her past medical history was positive for undermined leprosy adequately treated and considered healed ten years ago. Laboratory tests revealed creatine kinase of 174 U/L (NR: 26 U/L - 140 U/L), lactate dehydrogenase 533 U/L (nr: 120 U/L - 246 U/L), erythrocyte sedimentation rate of 11mm/1st hour, and C-reactive protein of 0.1 mg/L. 25-OH-vitamin d of 19 ng/mL. Antinuclear antibodies were positive in a titer of 1:80, speckled pattern. Anti-dsDNA, anti-RNP, anti-Sm, anti-Ro/SS-B, anti-La/SS-B, IgG, and IgM anticardiolipin, anti-Jo-1, and rheumatoid factor were all negative, and complement levels were within the normal range. Tuberculin test was absent; serology for hepatitis B and C, HIV 1 and 2, and HTLV I and II were negative. IgG for Epstein-Barr, human cytomegalovirus, toxoplasmosis, and rubella was positive with IgM negative. Electromyography and a thigh magnetic resonance imaging were interpreted as normal. She had a mild myositis clinical picture. She received a single dose of vitamin D supplementation (600,000 IU) and stayed on clinical and laboratory observation. After three months, she was asymptomatic, and vitamin D, creatine kinase, and LDH were within the normal range.

DISCUSSION

The present article case report adds two new ASIA cases to the literature, one of them evolved with rheumatoid arthritis and the other with a transient myopathy disorder.

Our patient developed myalgia, fever, and arthritis in the same day of her influenza vaccination. Furthermore, she developed the clinical picture of rheumatoid arthritis, fulfilling the diagnosis criteria for RA [3]; however, the patient did not present erosion on x-rays or positivity to rheumatoid factor or anti-CCP antibodies.

A clear relationship between the influenza vaccine and the RA development was observed, considering that the patient started clinical manifestation in the same day of her vaccination. In most cases published, an interval until in general 30 days is observed between vaccine administration and the onset of autoimmune disease [4].

These articles bring an example of the "mosaic of autoimmunity," i.e., the interconnected relationship among genetic, environmental factors, hormones, vitamin D, and smoking are key factors that increase autoimmune disease risk susceptible people [5].

In the extensive description of 500 cases of ASIA patients, 10 fulfilled RA criteria [1]. Furthermore, previous studies have demonstrated that vaccinations are a risk factor for developing connective tissue diseases, including rheumatoid arthritis with a relative risk of 1.32 (95%CI 1.09-1.60, P = 0.004) [6].

Interesting, one of our patients was positive for HLA-B27 and did not present spondyloarthritis features. However, there are descriptions of reactive arthritis and several autoimmune conditions after influenza vaccination [4].

Myopathy after vaccination is not a novelty. Myalgia has been described in 16.2% % of influenza vaccinated subjects [5]. Induction of myositis after vaccination is reported [4,6]. Although, our patient had an increase of creatine kinase levels and also marked augmentation of LDH and positive ANA in low titers.

The first inactivated influenza vaccine was established in the 1940s in the United States. Vaccines are considered a safe and effective tool, by the medical community, for the general population, and patients with autoimmune rheumatic diseases. Although there are several case reports showing an association between the influenza vaccine and diverse autoimmune diseases such as lupus, antiphospholipid syndrome, giant cell arteritis, and polymyalgia rheumatic, childhood narcolepsy, myositis, and several types of systemic vasculitis [7-11].

In conclusion, this article describes two additional cases of ASIA induced by the influenza vaccine. Therefore, the cost-effectiveness of influenza vaccination policy requires considering all adverse events, including the appearance of autoimmune disorders. In this line, technology improvement with peptide selection is desired in the field of vaccination.

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CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.

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