A case of polymyalgia rheumatica following influenza B infection

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Abstract: Polymyalgia rheumatica (PMR) is relatively common among the elderly, and is characterized by multiple body aches with an elevated erythrocyte sedimentation rate. Even though the etiology of PMR remains unknown, a number of infectious agents have been suggested to cause PMR. Also, there are reports of PMR after influenza vaccination. The exact role of influenza vaccination on the development of PMR remains unknown, but may be associated with specific human leukocyte antigens (HLAs), such as HLA-DRB1 and HLA-DQB1. Whether postvaccination PMR is caused by influenza virus antigen or adjuvants in the vaccine is another unanswered question. We herein report a case of an 85-year-old woman who developed PMR shortly after contracting influenza virus B. Even though infections are hypothesized to be one of the causes of PMR, this is the first-ever case of PMR following influenza virus infection. Further studies may elucidate the exact role of influenza virus infection on the etiology and pathogenesis of PMR.

Keywords: polymyalgia rheumatica, influenza, etiology

Introduction

Polymyalgia rheumatica (PMR) is relatively common among people who are over 50 years of age. The combination of persistent pain over multiple joints and muscles of the body, morning stiffness, and elevated erythrocyte sedimentation rate (ESR) are characteristics of this condition.¹ Multiple genetic and environmental factors are considered to influence susceptibility to this illness, but the exact etiology and pathogenesis of PMR remains unknown. Although there are reports on the occurrence of PMR after influenza vaccination, we here report the first case in which PMR occurred after influenza infection.

Case report

Institutional Review Board approval was not sought, as this is a case report that does not require IRB approval as per our IRB protocol. An 85-year-old woman with a medical history of diabetes mellitus and dyslipidemia presented in March 2015 to an internal medicine outpatient clinic with myalgia, morning stiffness, and difficulty in standing up from a chair lasting for several weeks. She also complained of pain in the shoulders bilaterally, particularly on the right, and in the proximal arms bilaterally. She also complained of back pain. Symptomatic treatment of unknown detail did not improve her symptoms, and she presented to our clinic.

Prior to the onset of her symptoms in February 2015, she had developed high fever, was diagnosed with influenza B by one of the rapid influenza diagnostic tests at a clinic

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nearby, and was provided with intravenous peramivir. Her fever declined in a few days, and the symptoms of influenza subsided. However, she started to develop myalgia and the other symptoms described on the day of defervescence. Medications given by her internist at presentation included insulin, glibenclamide, voglibose, rosuvastatin, neurotrophin, and acetaminophen.

On physical examination, she appeared generally well. She was alert and oriented, with blood pressure of 142/85 mmHg, pulse rate of 66/minute, respiratory rate of 13/minute, and body temperature of 36.6°C. There was tenderness over the trapezius muscles, elbow joints bilaterally, both thighs, particularly on the lateral side, and both calves. There were no thickened temporal arteries and there was no tenderness on palpation. No lymphadenopathy, rash, or arthritis was found on physical examination.

She was able to stand up from a chair without using her arms, but she found it somewhat difficult and had to do it slowly, although she was able to walk in the examining room without difficulty. The rest of her physical examinations, including neurological, were unremarkable. Laboratory tests revealed white blood cell counts of $10.3 \times 10^9/L$ with 73% neutrophils, hemoglobin of 10.5 g/dL with mean corpuscular volume of 86.2%, C-reactive protein (CRP) of 4.79 mg/dL, and ESR 56 of mm/hour. Serum creatinine kinase (CK) level was 32 IU/L, and rheumatoid factor (RF) and anticyclic citrullinated peptide antibody (anti-CCP) levels were within normal limits. Based on the presence of myalgia, morning stiffness, physical findings suggestive of bursitis in the shoulders and glenohumeral areas, absence of RF and anti-CCP, absence of CK elevation, and elevated CRP and ESR, she was diagnosed with PMR. Oral corticosteroid (prednisolone 15 mg/day) was initiated. Her symptoms improved gradually, and she continues to receive a lowered dose of prednisolone as of this writing. Workup of malignancies was declined by the patient.

Discussion

Even though the etiology of PMR remains unknown, a number of infectious agents have been suggested to cause PMR. These include *Mycoplasma pneumoniae*, *Chlamydia* (*Chlamydophila*) *pneumoniae*, and parvovirus B19.² In addition, there are reports of PMR after influenza vaccination.^{3–8} The exact role of influenza vaccination on the development of PMR remains unknown, but may be associated with specific human leukocyte antigens (HLAs), such as HLA-DRB1 and HLA-DQB1.³ Whether postvaccination PMR is caused by influenza virus antigen or adjuvants in the vaccine is another unanswered question.

The incidence of PMR in Japan appears to be correlated with the influenza season.⁹ However, there has been no single case report of PMR after influenza virus infection from Japan or otherwise. This report is therefore the first, as far as we know of, case report of post-influenza virus infection PMR. Although we could not demonstrate influenza virus directly from the patient, rapid influenza diagnostic tests are highly specific,¹⁰ and her history of influenza, together with her medical history, was fairly plausible, even though the lack of a standard confirmatory test, such as reverse-transcription polymerase-chain reaction, for the diagnosis of influenza infection somewhat lessens the scientific validity of our hypothesis.

A wide variety of conditions may mimic PMR. Rheumatoid arthritis can occur in the elderly, and can be difficult to distinguish from PMR clinically. However, both RF and anti-CCP antibody were negative in this case, making this diagnosis less likely. Giant-cell arteritis and remitting seronegative symmetric synovitis with pitting edema (RS3PE) are considered to be associated with PMR, and they can be very similar to PMR, but the lack of such symptoms as fever, headache, and pitting edema made both diagnoses less likely. Diseases with myositis, including those caused by statins and influenza itself, are less likely, since there was no elevation of CK, another characteristic of PMR. Influenza per se can cause myalgia, myositis, or even rhabdomyolysis, but these tend to occur in children and the onset is during not after influenza illness,^{11–13} unlike such infections as chikungunya.¹⁴ Our case met diagnostic criteria by Hunter, Healey, Jones, Hazelman, and Bird, with typical age, symptoms, elevated ESR, and good response to low-dose corticosteroid,¹⁵ and the case also met the provisional classification without ultrasound of the European League Against Rheumatism/American College of Rheumatology collaborative initiative,¹⁶ making the diagnosis of PMR most likely.

The incidence of PMR is common in the US,¹ but had been thought to be less common in Japan. However, a recent report suggests PMR may be more common in Japan, with possible misdiagnosis or underdiagnosis.⁹ If one suspects PMR more avidly and looks into the preceding episodes of viral infections, such as influenza, we might be able to see more association between such viral infections as influenza and PMR.

This single case report like ours merely suggests but does not prove the causality of influenza infection as a cause of PMR, even though chronological immediacy strongly suggests its contributory role in the pathogenesis of PMR.

In conclusion, we report a case of PMR following influenza virus B infection. Further studies may reveal the true incidence of PMR in Japan, its triggering factors, including influenza virus infection, and its etiology and pathogenesis.

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Disclosure

The authors report no conflicts of interest in this work.

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