

Influenza H1N1 infection in a patient with psoriatic arthritis in treatment with Adalimumab: a case report

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Abstract In March 2009 was the beginning of an epidemic flue caused by avian influenza A virus H1N1. The disease varies from mild to serious and fatal cases. There are many hypotheses explaining why this virus infection would be fatal. One of these is the impaired immune response of the infected patient. The use of tumor necrosis factor-alpha inhibitors may cause decreased immune response and greater susceptibility to infections. We presented a case of a patient using adalimumab that have developed H1N1 without complications. This is the first case of H1N1 in a patient using adalimumab reported in Brazil. We discuss the possibility that anti-TNF may not predisposes to a serious form of the disease or fatal complications.

Keywords Adalimumab · H1N1 infection · Influenza · Psoriathic arthritis

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Introduction

Influenza A H1N1 also known as swine flu is a respiratory illness that emerged in pigs caused by an influenza virus type A which attacks poultry, pigs, and humans. Swine flu is a variant of the H1N1 virus whose transmission can occur through human contact with animals or contaminated objects and from man to man. This virus was originally called “swine flu” because laboratory tests showed that several of its genes were very similar to the influenza virus that usually affects pigs in North America. Further studies showed that many genes of this new virus were quite different from those that normally circulate in pigs from North America. H1N1 has two genes of influenza viruses circulating in pigs in Europe and Asia and also genes of avian and human influenza. Scientists call it “the quadruple recombinant virus.”

The outbreak of swine flu, which started in Mexico in April 2009, spread around the world infecting millions of people in all countries [1]. Because of this, on 11 June 2009, the World Health Organization declared a State Pandemic Phase 6 for the influenza A H1N1, which means that the influenza has affected much of the global population spreading easily throughout the world and infecting thousands of people. Cases of novel influenza A (H1N1) virus infection have included rapidly progressive lower respiratory tract disease resulting in respiratory failure, development of acute respiratory distress syndrome (ARDS), and prolonged intensive care unit admission [2].

In the infection by influenza H1N1, the risk group consists of elderly, children under 2 years old, pregnant

women, people with diabetes, heart disease, lung or kidney disease, immune deficiency (such as cancer patients undergoing treatment for AIDS), people with morbid obesity and also diseases caused by changes in hemoglobin, such as sickle-cell anemia. In the same way, it is believed that people with rheumatic diseases using immunobiologic agents could be included in the risk group. TNF-alpha inhibitors are indicated to psoriatic arthritis (PsA) patients who do not respond or cannot tolerate common DMARDs, methotrexate or leflunomide. The three currently available TNF- α inhibitors in Brazil are etanercept, infliximab, and adalimumab. Until this case, we have not reported any case of patients using anti-TNF that have developed H1N1 infection in Brazil.

Case report

PCLR is a 24-year-old woman who has PsA since 1994. The disease began with skin lesions compatible with psoriasis. Since 2003, the patient has multiple episodes of arthritis, and in 2007, the diagnosis of PsA was done. She was treated with methotrexate 12.5 mg per week and prednisone 5 mg per day. Because of failure to response, her treatment was replaced by adalimumab 40 mg every other week, methotrexate 15 mg per week, and prednisone 5 mg per day and a complete remission of the cutaneous and articular disease was obtained.

However, some time later, she developed repeated infections of the upper airways. In end of July 2007, the patient started with fever, malaise, sore throat, joint pain, headache, and runny nose. Due to the epidemiological risk and immunosuppression, nasopharyngeal aspiration was collected to research H1N1, and empirical treatment with oseltamivir two times a day for 5 days was started. After 4 days, there was complete remission of respiratory symptoms. Later the diagnosis of influenza A was confirmed by RT-PCR in real time by the kit SuperScript III Platinum One-Step Quantitative RT-PCR System.

Discussion

We presented a case of a PsA patient using adalimumab that have developed H1N1 without complications. This is the first case reported in Brazil of H1N1 occurring in a patient using adalimumab. The pandemic H1N1 infection was considered widespread in Brazil on 16 July 2009. Since then, more than 50,000 cases of acute respiratory syndrome have been reported in our country [3]. It is believed that the H1N1 virus spreads in the same way that the common influenza virus does. The case of our patient occurred during the pandemic infection in the south of

Brazil and was considered a typical infection by influenza virus that spreads commonly from person to person through coughing or sneezing and contact with respiratory secretions of infected people.

The use of inhibitors of TNF-alpha is recommended in cases of PsA patients who do not respond or can tolerate methotrexate [4]. Our patient was treated with adalimumab which is an inhibitor of TNF-alpha and is very effective in the treatment of PsA [5, 6].

The immunologic response to influenza virus infection, like many other viruses, is characterized by robust production of proinflammatory cytokines. The H5N1/97 and H5N1/04 subtype influenza A viruses are more potent inducers of proinflammatory cytokines and chemokines in primary human respiratory epithelial cells than subtype H1N1 virus. Some authors even suggest that the hyper-induction of cytokines may be relevant to the pathogenesis of human H5N1 disease but not for H1N1 [7]. In comparison with human seasonal influenza (H1N1) viruses, clade 1, 2.1, and 2.2 H5N1 viruses induced higher levels of tumor necrosis factor-alpha in primary human macrophages, and some viral genetic determinants of H5N1 influenza viruses may contribute to cytokine dysregulation [8].

Anyway, the cytokine dysregulation is thought to contribute to the pathogenesis of the influenza virus infection, but it remains a challenge understanding the complex interactions of cytokines and H1N1 infection. In a recent study, the autopsy findings of 21 Brazilian patients with confirmed S-OIV infection showed evidence of pulmonary aberrant immune response. There was marked expression of TLR-3 and IFN-gamma and a large number of CD8+ T cells and granzyme B+ cells within the lung tissue confirming this immune dysregulation [9].

It will be very important to our community to know more cases of psoriatic arthritis patients or other rheumatic patients using anti-TNF alpha who has developed H1N1. The effect of the timing of vaccination in relation to administration of infliximab on the efficacy and safety of influenza vaccine in patients with rheumatoid arthritis and ankylosing spondylitis treated with this anti-TNF was assessed in a study. Influenza virus vaccine generated a good humoral response in these patients [10].

Wang and others have demonstrated that both human H1N1 and avian H5N1 influenza viruses can infect mouse microglia and astrocytes and induce apoptosis, cytopathy, and proinflammatory cytokine production in them in vitro. Expression of IL-1beta, IL-6, and TNF-alpha mRNA examined at 6 and 24 h p.i. was upregulated, and their expression levels were considered by the authors more particularly in the H5N1 infection [11].

Oseltamivir is used for the treatment of uncomplicated acute illness due to influenza infection, and the early

initiation of treatment with the drug provides greater clinical benefits. Although most of the influenza virus strains are sensitive to oseltamivir, development of drug resistance may limit the clinical utility of the drug in the future. Although in this case we believe that the early use of oseltamivir was partially responsible for the better prognosis of the patient, we question whether the control of the production of TNF and other cytokines may contribute to a less aggressive organic response to the virus [12].

Disclosures None.

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