

Immune Thrombocytopenic Purpura Following Influenza Vaccination

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Vaccination is clearly one of the greatest achievements and a cornerstone in modern medicine, having reduced morbidity and mortality from many diseases by close to 100%. However, in the last 15 years there have been several reports of adverse autoimmune phenomena following various vaccinations [1]. Although most reports are case reports, there have been some case series as well as epidemiologic surveys attempting to solve the enigma of the relation between vaccination and autoimmune phenomena and diseases. Influenza vaccination has been postulated as the cause of Guillain-Barre syndrome by several large-scale studies [2], while other studies have shown that such an association does not exist [3]. The association between influenza vaccination and thrombocytopenia is very rare and we could not find any similar case reports in the English literature.

We report the development of severe thrombocytopenia with gastrointestinal bleeding in a 68 year old man 14 days after he received an influenza vaccination. The relevant literature is reviewed and the possible mechanisms of such an association are discussed.

Patient Description

A 68 year old man presented with a widespread rash and melena. His past history revealed only hypertension, which was well controlled with calcium channel blockers and diuretics. There had been no recent change of medications and the patient denied taking any new medications in the past few weeks or having any recent infections. Two weeks before admission the patient was vaccinated against influenza with a commercial vaccine (Vaxigrip™, Institute Pasteur, France) as part of a routine vaccination program before winter.

On admission he looked pale, his blood pressure was 120/80 mmHg, pulse 110/minute, and body temperature was normal. A purpuric rash covered large areas of his body, spreading to the legs, hands and trunk. The rest of the physical examination was normal. Rectal examination disclosed signs of dark soft stool. Laboratory tests revealed hemoglobin 10.1 g/dl, white blood cell count 6,700/mm³, and platelet count 3,000/mm³. The blood smear was normal as were routine biochemical and serologic tests. Abdominal ultrasound examination was normal and an urgent gastroscopy revealed signs of erosive gastritis without a visible source of active bleeding. Treatment was started with high dose intravenous gamma globulins, corticosteroids, packed red blood

cells and proton pump inhibitors. A bone marrow biopsy done on the second day of admission revealed hypercellularity with many megakaryocytes and no infiltration of foreign cells.

After 48 hours of treatment the platelet count rose to 20,000 and by the fifth day of hospitalization it reached normal levels. The patient was discharged on the seventh hospital day and was followed at the outpatient clinic. Steroid therapy was tapered slowly and was discontinued by the fifth month. Follow-up examination after 12 months did not show any abnormality on physical examination or in the biochemical and complete blood count tests.

Comment

Vaccination is undoubtedly one of the greatest achievements of modern medicine, significantly reducing mortality and morbidity. Although the purpose of vaccination is to induce immunization, during the last decade reports have accumulated on various side effects of vaccines that had not been observed previously, or were not acknowledged. These include a wide range of autoimmune phenomena as well as full-blown autoimmune diseases [1]. The association between vaccination and autoimmunity has led to a public debate as to whether such diseases could be triggered by vaccines [2,3]. Autoimmune disease can be triggered by infection through two mechanisms: antigen-specific or antigen non-specific, that can operate either alone or together. The most popular hypothetical mechanism for the triggering of autoimmunity by an infectious agent is that of molecular mimicry [4]. According to this hypothesis, antigenic determinants of the microorganisms are recognized by the host's immune system as being similar to its own antigenic determinants, thus causing antibodies and T cells to destroy their own tissues. This theory is well represented by the Guillain-Barre syndrome in which about one-third of cases are preceded by *Campylobacter jejuni* infection. This bacterium expresses a lipopolysaccharide molecule that mimics various gangliosides presented in high concentrations in peripheral nerves. The second way by which a microorganism might induce an autoimmune disease involves bystander activation in an antigen non-specific mechanism. In this case, microbial infection causes tissue damage that leads to the release of self-antigens or stimulates the innate immune response, thus activating the self-antigen-expressing antigen-presenting cells.

Influenza vaccine is probably the most common vaccine used

worldwide, and every year millions of people are vaccinated around the world. Influenza vaccination has been associated with an increased risk of Guillain-Barre syndrome. Since the first report that followed the mass inoculation of “swine-flu” virus vaccine in the United States in 1977, there have been many reports supporting or denying this phenomenon. Nevertheless, despite its wide use, only sparse information has been published concerning the hematologic effects of influenza vaccination. Review of the literature revealed only isolated reports linking influenza vaccine with thrombocytopenia. We could not find any report in the English-language medical literature associating influenza vaccination and immune thrombocytopenia. Casoli and Tumiati [5] published a similar case of acute immune thrombocytopenic purpura following influenza vaccination in 1989 in an Italian journal. We are aware of only two other reports in the English literature reporting other types of thrombocytopenia following influenza vaccination. One of them described a case of thrombotic thrombocytopenic purpura following influenza vaccination, while the other described a relapse of immune thrombocytopenia in a patient suffering already from this disorder after receiving influenza vaccination.

Our case, which is unique in view of the wide use of the influenza vaccine, most probably represents the antigen non-specific mechanism. The influenza vaccine, which does not contain live virus, produces maximal antibody response between days 14 and

28. This non-specific response of the immune system was probably the cause of the anti-platelets antibodies that appeared in our patient on the 14th day following influenza vaccination, thus causing clinical manifestations of thrombocytopenia. Although the immune thrombocytopenia in our case was severe and caused gastrointestinal bleeding, the rarity of such events following mass vaccination of large populations supports the safety of using these vaccines.

References

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