Thrombocytopenic Purpura after the Administration of an Influenza Vaccine in a Patient with Autoimmune Liver Disease

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Dear Sir,

Influenza, a contagious viral disease, can usually be prevented by receiving an influenza vaccine. Almost 15 million doses of influenza vaccine were produced in Japan for the 2003–2004 influenza season. Although serious side effects from the influenza vaccine are extremely rare, the influenza vaccine, as all vaccines, may sometimes induce or trigger autoimmune reactions in susceptible individuals (e.g., the development of Guillain-Barré syndrome) [1]. This report describes a patient with autoimmune liver disease (AILD) who developed idiopathic thrombocytopenic purpura (ITP) after receiving an influenza vaccine.

In August 2005, a 75-year-old female living in Tokyo was referred to the Jikei Daisan Hospital because of abnormal liver function test results. She had no history of daily alcohol consumption or obesity. The physical examination was unremarkable. Her laboratory data showed: aspartate aminotransferase (AST), 70 IU/l; alanine aminotransferase (ALT), 40 IU/l; lactate dehydrogenase (LDH), 222 IU/l; alkaline phosphatase (ALP), 266 IU/l; γ -glutamyl triphosphate (γ -GTP), 200 IU/l, and total bilirubin (T-Bil), 1.0 mg/dl (normal ranges: AST, 10–33 IU/l; ALT, 6–35 IU/l; LDH, 130–235 IU/l; ALP, 96–300 IU/l; γ -GTP, 9–27 IU/l; T-Bil, 0.2–1.2 mg/dl). The peripheral blood cell counts were as follows:

RBC, 6,600/ μ l; WBC, 4.15×10^6 /ml; Hb, 13.2 g/dl; Ht, 39.5%; Plt, 164×10^3 /ml (normal ranges: RBC, 4,500–8,500/ μ l; WBC, 3.80 – 4.80×10^6 /ml; Hb, 11.5–14.5 g/dl; Ht, 35.0–42.0%; Plt, 150 – 350×10^3 /ml). The serological findings showed: antinuclear antibody (ANA), titer 1/320 (normal value, $<1/20$); antimitochondrial antibody (AMA), titer 1/160 (normal value, $<1/20$); IgG, 3,180 mg/dl; IgM, 1,231 mg/dl (normal ranges: IgG, 870–1,700 mg/dl; IgM, 35–220 mg/dl). Moreover, anti-hepatitis B surface antibody and anti-hepatitis C antibody were negative. The ultrasound examination findings did not show any evidence of a specific disease causing the abnormal liver function, such as a liver tumor. She was diagnosed as having AILD and was treated with ursodeoxycholic acid (UDCA; 10 mg/kg, daily). Three months later, her liver function returned to almost normal levels (AST, 38 IU/l; ALT, 20 IU/l).

On January 23, 2006, she presented at an outpatient clinic with epistaxis and petechiae on her lower extremities. No evidence of lymphadenopathy or hepatosplenomegaly was noted. She had received an influenza vaccine (Influenza HA Vaccine ‘Kitaken’) 1 week before the onset of her symptoms. Upon admission, her platelet count was 5×10^3 /ml. The remainder of her differential blood counts and a co-

agulation test were normal. An assay for antiplatelet antibodies (IgG and IgM) was positive. An oral corticosteroid treatment (prednisone, 0.5 mg/kg, daily) was initiated. After 2 weeks of treatment, her platelet count increased to 89×10^3 /ml.

On February 8, 2006, after her platelet count had recovered in response to the oral corticosteroid treatment, a liver biopsy was performed to access the severity of the AILD. Marked lymphocyte infiltration and moderate fibrosis were observed in the portal area, but no other signs of an injured septal or interlobular bile duct were seen.

Thrombocytopenia occasionally occurs after routine immunization in children. Although serious autoimmune side effects are rare and most of them are transient, there are arguments against routine vaccination in patients with autoimmune diseases. On the other hand, Arakawa et al. [2] reported that ITP was rarely observed as a disease concomitant with AILD. This is apparently the first case report of a patient with AILD who developed ITP after receiving an influenza vaccine. UDCA was effective for this case. Moreover, primary biliary cirrhosis (PBC) is an AILD characterized by the presence of AMA. The liver damage in this case may have been related to PBC. PBC is known to be associated with several autoimmune

diseases, including Hashimoto's thyroiditis. ITP is another autoimmune condition resulting in increased platelet destruction. Previous reports of patients with ITP developing into PBC have been published [2, 3]. Although some reports have described concomitant ITP in PBC patients not undergoing immunosuppressive therapies [4, 5], the present report describes an el-

derly patient with PBC who developed ITP following an influenza vaccine. The pathogenesis of thrombocytopenia in patients with PBC is usually attributed to the splenic pooling of platelets. In addition, Panzer et al. [6] showed platelet-reactive antibodies to bind to the 70-kDa mitochondrial antigen M2 in a patient with PBC. These findings suggest that immune-mediated

platelet destruction may to some extent play a role in the pathogenesis of thrombocytopenia in PBC. The present report also supports the theory that the influenza vaccine can exacerbate potential immune-mediated platelet destruction in AILD patients, thus leading to severe autoimmune side effects.

References

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