

Spontaneous Subdural Hematoma Secondary to Influenza Vaccine-Induced Immune Thrombocytopenia

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Abstract

Influenza vaccine-induced immune thrombocytopenia (ITP), though rare, can present with a wide spectrum of clinical manifestations, ranging from mild asymptomatic thrombocytopenia to life-threatening complications, such as gastrointestinal (GI) bleeding, diffuse alveolar hemorrhage (DAH), or intracranial hemorrhage (ICH), particularly when platelet count drops below a critical level of less than 5,000/ μ L. We report a rare case of spontaneous subdural hematoma (SDH) due to severe ITP following the influenza vaccine that showed a dramatic response to high-dose methylprednisolone and intravenous immunoglobulin (IVIG), with platelet count returning to normal and complete resolution of symptoms by the third day of therapy initiation.

Keywords: Subdural hematoma; Influenza vaccine; Immune thrombocytopenia; Methylprednisolone; IVIG

Introduction

Influenza vaccination has been reported in previous studies to cause vaccination-induced adverse reactions, including Guil-

lain-Barre syndrome, convulsions, Bell's palsy, and thrombocytopenia [1-3]. On the other hand, immune thrombocytopenia (ITP) has been associated with vaccinations such as measles-mumps-rubella (MMR), hepatitis A, hepatitis B, diphtheria-tetanus-acellular pertussis (DTaP), and varicella [4]. Although ITP induced by influenza vaccination is uncommon, eight cases of influenza vaccine-induced thrombocytopenia have been described in the French Pharmacovigilance database as well as three in Seichokai Fuchu Hospital, Japan. Due to its rarity, the pathogenesis of vaccine-related thrombocytopenia is unclear with no apparent risk factors, but some cases have been linked to secondary ITP [3, 5-7].

Mild thrombocytopenia is almost always asymptomatic, while severe thrombocytopenia can cause varying degrees of bleeding, such as skin petechiae, hematomas, and bloody stool. Persistent severe thrombocytopenia can lead to very low platelet counts resulting in potentially fatal complications, including subarachnoid hemorrhage, intracerebral bleeding, or diffuse alveolar hemorrhage (DAH) [7, 8]. It has been observed that the onset of these symptoms ranges from mild to severe and follows a strict time-dependent relationship, developing within 4 - 35 days after vaccination [7, 9]. While patients with primary ITP often require long-term therapy due to the chronic progression of their symptoms [10], patients with vaccine-induced ITP usually respond dramatically to glucocorticoids within a few days [9, 11, 12].

Case Report

Investigations

A 70-year-old male presented to the hospital with left-sided weakness, numbness, and generalized, scattered bruising with no history of trauma. His past medical history included hypertension, hyperlipidemia, coronary artery disease, type II diabetes mellitus (DM), chronic kidney disease (CKD), and atrial fibrillation. He was not on direct anticoagulation; however, he was taking 81 mg of aspirin daily. Four weeks prior to admission, the patient was in his usual state of health and received an influenza vaccine. One to two days later, he noticed bruising and swelling around the immunization site on his right upper extremity. Over the subsequent 2 weeks, he developed scattered bruising across his body. On the advice of his primary care physician, he discon-

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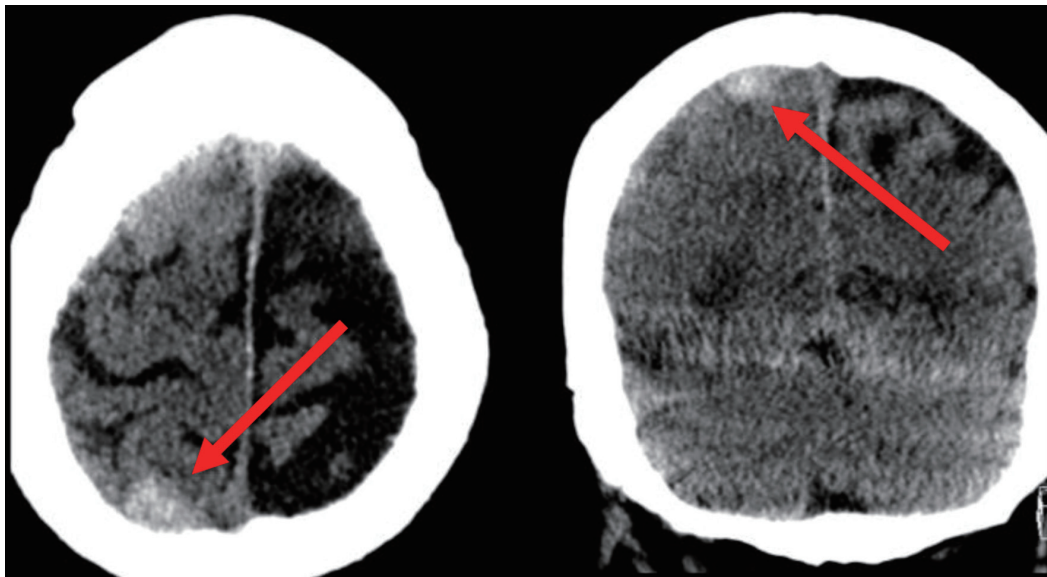


Figure 1. Non-contrast head CT in the axial and coronal planes revealing a right posterior convexity subdural hemorrhage (arrows). CT: computed tomography.

tinued aspirin, but his symptoms persisted.

Seven to ten days prior to admission, he developed sensory and motor deficits, including dysphagia, sialorrhea, and a progressively worsening headache accompanied by extremity weakness. Upon admission, a non-contrast computed tomography (CT) of the head was obtained, revealing an acute right-sided subdural hematoma (SDH) with mild parafalcine herniation and brain compression (Figs. 1 and 2). Surgical intervention was not indicated at this time.

Diagnosis

Laboratory tests revealed a platelet count of 5,000/ μ L, which improved only slightly to 18,000/ μ L after transfusion of two units of platelets before it dropped back to 5,000/ μ L on repeating laboratory tests 12 h later. This necessitated transfusion of another two units of platelets with improvement of platelet count to 22,000/ μ L before it dropped again to 9,000/ μ L on repeated laboratory tests 12 h later. A review of previous laboratory results from months prior showed a normal platelet profile, and the patient's history was negative for alcohol use, liver disease, or splenomegaly, which was confirmed by an abdominal ultrasound.

Treatment

Suspecting ITP, intravenous high-dose methylprednisolone (30 mg/kg/day for 3 days) was delivered. Over the next 3 days, repeat laboratory tests showed a progressive increase in platelet counts to 35,000, 98,000, and 198,000/ μ L, respectively. A non-contrast CT of the head showed stable SDH, and the patient's neuro-examination significantly improved. The influenza vaccine-induced ITP diagnosis was confirmed. The patient was discharged home on oral methylprednisolone (20 mg/kg/day for 4 days).

Follow-up and outcomes

On subsequent outpatient follow-up visit 2 weeks later, platelet count was 227,000/ μ L and the patient's neuro-examination returned back to his normal baseline.

Discussion

Although not a very common adverse reaction to influenza vaccine, ITP has been recorded with varying degrees of throm-

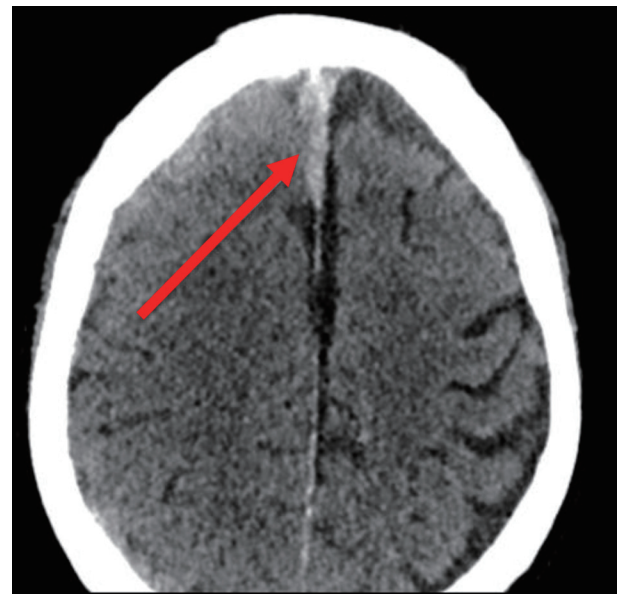


Figure 2. Non-contrast axial CT showing right parafalcine subdural hemorrhage (arrow). CT: computed tomography.

bocytopenia ranging from mildly asymptomatic to severe with serious fatal bleeding when platelet count drops to $< 5,000/\mu\text{L}$. Here, we present a case of spontaneous SDH in a 70-year-old male secondary to severe ITP 4 weeks after receiving an influenza vaccine. This case is unique because of the patient's delayed neurological presentation, their baseline CKD that may be a confounder for low platelet count and dysfunction, the patient's age, and lastly, a negative history of adverse reactions from influenza vaccines in the past.

The progressive course of the disease started as localized bruising and swelling around the injection site 24 h after injection, followed by diffuse skin rash and ecchymosis over the following 2 weeks. Subsequently, the onset of neurological symptoms and spontaneous SDH occurred after 4 weeks. This correlates with the temporal drop in the platelet count over this period, with the lowest count of $< 5,000/\mu\text{L}$ at admission. Immediate correction with two units of platelets showed an insignificant rise in the platelet count from $< 5,000$ to $< 18,000/\mu\text{L}$ before it dropped back to $5,000/\mu\text{L}$ on repeating laboratory tests 12 h later. Another transfusion of two units of platelets was only able to improve platelet count to $22,000/\mu\text{L}$ before it dropped again to $9,000/\mu\text{L}$ on repeated laboratory tests 12 h later. Abdominal ultrasound showed the absence of splenomegaly; this ruled out a primary ITP process. Following treatment with intravenous high-dose methylprednisolone, the platelet count increased dramatically. These clinical events together confirmed the diagnosis of influenza vaccine-induced ITP.

While this case of vaccine-induced ITP resolved by day 3 of intravenous high-dose methylprednisolone initiation, additional therapy is warranted when symptoms are severe or persistent. Current standard of care for primary and secondary ITP includes high-dose corticosteroids with intravenous immunoglobulin (IVIG) therapy, although platelet transfusions are required in instances with active bleeding, and plasmapheresis may be indicated in fulminant cases [13, 14]. While rare, several instances of severe manifestations of ITP following influenza vaccinations have been reported, with symptoms ranging from gross hematuria to DAH leading to acute respiratory failure. In such cases, patients have been shown to respond dramatically to a combination of high-dose steroids, IVIG, and platelet transfusion, with complete resolution of symptoms and normalized platelet counts without necessitation of invasive interventions [8, 12, 13]. However, both primary and post-vaccine ITP processes can become chronic, requiring extended therapy and possible splenectomy [15]. While antineoplastics such as rituximab have been used in intractable cases, studies have demonstrated limited efficacy with slow onset of action and notable adverse side effects [16].

Our case highlights the potentially catastrophic outcomes that can come from undiagnosed ITP, and underscores the critical need for early detection and treatment. Early monitoring of platelet counts post-vaccination may be warranted in individuals with a prior history of autoimmune diseases or previous episodes of thrombocytopenia. Establishing protocols for early intervention upon the first signs of thrombocytopenia, as well as patient education to recognize the symptoms of severe thrombocytopenia following vaccination, can enhance

early detection and prompt medical attention before significant complications arise.

Learning points

Influenza vaccine-induced ITP should be suspected once a patient presents with progressive symptoms such as diffuse erythema, swelling, and ecchymoses in the setting of low platelet count non-responsive to platelet transfusion following influenza vaccine. Early treatment with intravenous high-dose methylprednisolone is required to prevent the development of delayed fatal complications when platelet count drops below a critical level. This treatment is also sufficient to resolve the condition without the need for additional therapy.

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Conflict of Interest

The authors declare that they have no conflict of interest to disclose.

Informed Consent

Informed consent was obtained from this patient.

Author Contributions

Hesham Kelani: conceptualization, study design, drafting, and revisions. Izabella Beniaminova: data collection, critical analysis and drafting. Emina Dzafic: critical analysis, drafting, and manuscript revision. Priya Srivastava: data collection and critical analysis. Noor El-Deen Farghaly: data collection and critical analysis. Saranjeet Kaur: data collection and critical analysis. Lauren Hatcher: data collection, critical analysis, and drafting. Mohammad Jadidi: data collection, critical analysis, and drafting. Marie Mikhail: data collection and critical analysis. Diana Greene-Chandos: supervision, critical revisions, and final approval. Lisa R. Merlina: supervision, critical revisions, and final approval.

Data Availability

The data for this report were obtained through the Brookdale Institutional Review Board (IRB). The IRB committee classified this study as exempt from approval. The data are not publicly available, but further details and contributions for access can be obtained by contacting the corresponding author.

Abbreviations

CKD: chronic kidney disease; DAH: diffuse alveolar hemorrhage; DTaP: diphtheria-tetanus-acellular pertussis; GI: gastrointestinal; ICH: intracranial hemorrhage; ITP: immune thrombocytopenia; IVIG: intravenous immunoglobulin; MMR: measles-mumps-rubella; SDH: subdural hematoma

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