



Vigilance regarding immune thrombocytopenic purpura after COVID-19 vaccine

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Abstract

Introduction: Based on the severity of thrombocytopenia, patients with immune thrombocytopenic purpura (ITP) are at an increased risk of mucocutaneous or major bleeding.

Discussion: There has been an increased risk of ITP after administration of various vaccines like influenza, measles-mumps-rubella, hepatitis B, and diphtheria-tetanus-pertussis. The pathogenesis of vaccine-related thrombocytopenia is not completely clear and is probably caused by molecular mimicry. Till date, there have been few reported cases of thrombocytopenia in the pharmacovigilance databases after patients received the Pfizer and Moderna coronavirus disease-19 (COVID-19) vaccines.

Conclusion: Emergency physicians should be aware of the occurrence of vaccine-induced ITP in patients who present with bleeding manifestations, especially after the current boost in COVID-19 vaccination drive worldwide.

Keywords COVID-19 · Emergency medicine · Immune thrombocytopenic purpura · Thrombocytopenia · Vaccine

Immune thrombocytopenic purpura (ITP), also known as idiopathic thrombocytopenic purpura or immune thrombocytopenia, is an immune-mediated disease characterized by a decrease in platelet count, secondary to impaired platelet production as well as destruction of circulating ones. Based on the severity of thrombocytopenia, patients are at an increased risk of bleeding, either mucocutaneous bleeding, manifested as skin bruise, petechiae, bleeding gums, or life-threatening bleeding.

Many patients presenting with symptoms of acute ITP are idiopathic, but may usually have a history of preceding infection about 7–10 days before the onset of symptoms. Common infections include Epstein–Barr virus, Varicella zoster virus, rubella, and influenza virus. There is also an increased risk of ITP after administration of vaccines like influenza, measles-mumps-rubella (MMR), hepatitis B, human papilloma virus, varicella, and diphtheria-tetanus-pertussis (DPT) vaccines in children and adolescents [1–3].

The pathogenesis of vaccine-related thrombocytopenia is not completely clear, but it is probably caused by molecular mimicry. The peptide hemagglutinin in the influenza vaccine manifests structural similarity to antigens on the platelets.

Thus, activation of antibodies and T cells responsible for the clearance of virus antigens may cross-react with antigens present on platelet membrane [3]. The antibody-coated platelets are cleared by tissue macrophages, resulting in a shortened half-life of platelets. In addition, these antibodies also inhibit platelet production [2]. Alternately, ITP can also be induced by other constituents of the vaccine like yeast proteins, adjuvants, and preservative diluents [4]. Adjuvants, like aluminium hydroxide and phosphate, are chemicals which are incorporated into the vaccine to enhance its immunogenicity. They have been implicated in the autoimmune/inflammatory syndrome induced by adjuvants (ASIA) [5].

ITP after influenza vaccine is often found in elderly patients because the vaccine is recommended for elderly, and they easily exhibit bleeding manifestations [6]. The onset of post-influenza vaccine ITP has a strict temporal relationship, and usually develops between 4 and 35 days after administration of the influenza vaccination [5]. This range in the duration of symptom onset depends on the patient's influenza antibody levels. Some patients who took influenza vaccine in the past may have preexisting antibodies, while others may mount an anamnestic (memory) response, leading to rapid production of antibodies due to prior exposure to the antigen. Other patients who did not have any prior exposure to the antigen may be undergoing primary alloimmunization. An anamnestic response occurs in about 3–10 days, while primary alloimmunization requires at least 2–3

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weeks. Thus, post-influenza vaccination ITP in the elderly can either occur within few days, or up to 2–3 weeks after vaccination [7].

Till the end of January 2021, 36 cases of ITP have been reported to the Vaccine Adverse Event Reporting System after receiving the Pfizer/BioNTech and Moderna coronavirus disease-19 (COVID-19) vaccines [8]. Also, a recent report in *BMJ* states that there have been about 150 reported cases of thrombocytopenia post-COVID-19 vaccination recorded in the pharmacovigilance databases [9]. It is still unclear whether this relationship between COVID-19 vaccination and thrombocytopenia is coincidental or causal. US Food and Drug Administration and Centers for Disease Control and Prevention have said that the incidence of ITP post-COVID-19 vaccination was not higher than that of the general population. Favorable response was noted in most of these patients treated with corticosteroids and intravenous immunoglobulin (IVIG) [10]. Hence, taking into consideration the increased risk of ITP after administration of various vaccines as well as patient response to standard ITP therapy, there is a possibility that there may be an association between ITP and COVID-19 vaccine.

As influenza vaccines, and currently the COVID-19 vaccines, are routinely used in the elderly for prevention of these infections, it is important to inquire about recent infections, medications, and vaccinations when assessing a patient presenting with symptoms suggestive of ITP. Emergency physicians should be aware of the occurrence of vaccine-induced ITP in patients who present with bleeding manifestations, especially after the current boost in COVID-19 vaccination drive worldwide.

Author contribution SP and SG conceived the idea for the manuscript. VS and PS reviewed the literature and contributed to initial draft of the manuscript. SP and SG reviewed and edited the final draft of the manuscript.

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