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Case Report

Re-Visiting Immune Thrombocytopenia with Covid-19 Vaccination: A Case Report

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ABSTRACT

The Covid-19 pandemic has seen the emergence of various vaccines being produced at an unprecedented speed. It is not surprising that new adverse events to these vaccines are still being reported and Immune thrombocytopenic Purpura [ITP] happens to be one among them. Moderna and Pfizer vaccine have been linked to it. Association of ITP with SARS-CoV-2 vaccine is poorly understood. We present to you a case of severe symptomatic thrombocytopenia post ChAdOx1 nCoV-19 vaccination which responded to conventional therapies. Aggressive use of immunosuppressive treatment may jeopardize the intended purpose of SARS-CoV-2 vaccine. Also, the schedule and alternative vaccine for the second dose and the role early use of non-immunosuppressive treatment like Thrombopoietin receptor agonist are unclear. While the universal immunization program needs to continue, vigilance to the occurrence of severe thrombocytopenia due to vaccination is needed.

Immune thrombocytopenic purpura [ITP] is a rare autoimmune condition characterized by low platelets in the blood. It has a slight female preponderance with an incidence rate of 1.6 to 3.9 per 100,000 patient-years, increasing with age [1]. The SARS-CoV-2 global pandemic has led to many deaths and vaccination is essential. ITP is a known complication of COVID-19 infection. Thrombocytopenia in COVID-19 infection can be due to decreased production, increased destruction or other possible immune mechanisms [2]. The SARS-CoV-2 vaccine rarely causes ITP similar to that seen with other vaccines. Post-vaccination thrombocytopenia is hypothesized to be immune mediated and B-cell hyper-function [3-4]. With billions of people getting the SARS-CoV-2 vaccination, cases of "thrombocytopenia" have been reported post-vaccination [5]. SARS-CoV-2 vaccine related thrombocytopenia has a varied onset, severity, and duration. It responds well to first-line treatment with corticosteroids and Intravenous immunoglobulin [IVIG] [6]. Here we present a patient diagnosed with severe immune thrombocytopenia after the first dose of ChAdOx1 nCoV-19 vaccine.

Case Report

A 27-year-old female with no previous illness or co morbidities presented with one-day history of gum bleeding, malena and diffuse cutaneous purpura. She did not have any history of fever, cough or breathing difficulty. She had received the ChAdOx1 nCoV-19 vaccine 15 days prior to this presentation and the post vaccination period was uneventful. Prior to vaccination, her platelet count was 243 x 109/L. On presentation, she had a platelet count of 10x 109/L following which she was transfused random donor platelets but the subsequent platelet counts further decreased to 4 x 109/L. All her regular infective workup including for tropical fever was negative. Bone marrow smear showed normal cellular marrow for age and tri-lineage haematopoiesis with increased megakaryocytes. Bone marrow biopsy revealed megakaryocytic hyperplasia. Polymerase chain reaction assay for the SARS-CoV-2 was negative. D dimer and fibrinogen levels were normal and with no clinical evidence of thrombosis ruling out vaccine induced thrombotic thrombocytopenia. Additional tests for Hepatitis B and C viruses, human immunodeficiency

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virus were negative. Vaccination is known to trigger an underlying autoimmune diathesis and in our patient assay for anti-nuclear antibodies was negative. She was given 1 gm/kg of intravenous immunoglobulin, as the response was minimal she was given 2 mg/kg of methylprednisolone followed by oral steroid. Her platelet counts started improving following this. Her platelet count had improved to 110 × 109/L on post- vaccination day 20. Steroids were tapered and she was discharged home.

Discussion

ITP is a rare complication following routine vaccinations against infections like measles, mumps, rubella and pneumococcus. Our patient presented with severe thrombocytopenia 15 days after receiving the ChAdOx1 nCoV-1 vaccine needing steroids, IVIG and platelet transfusions.The pathogenesis of post COVID-19 vaccination thrombocytopenia is not yet clear and seems to be multifactorial. Both the humoral immunity and cell-mediated immunity are involved during the ITP pathogenetic process. Hyperfunction of B cells and altered signaling pathway of CD4 + T cells have been implicated. Glycoprotein (GP) IIb-IIIa and GPIb-IX detected on activated platelets using antigen-specific assays act as autoantigens in ITP for antiplatelet autoantibodies. The ChAdOx1nCoV-1 vaccine is a simian adenovirus vector which is replication-deficient. It has a full length optimized codon with a sequence of SARS-CoV-2 spike protein along with a tissue plasminogen activator leader sequence [7-8]. Adenovirus vector based vaccines have been known to induce thrombocytopenia [9]. Post vaccination immunomodulatory therapies have resulted in attenuation but not abolishment of immune response to the administered vaccine in previous studies [10]. Hence nonimmune suppressive therapies if available needs to be considered in such patients and adequate interval needs to be provided between vaccination and immunomodulatory therapies. A Scotland study reported that individuals with higher age[>65years] and associated chronic health problems were more likely to develop ITP post-vaccination [5]. Our patient was young with no associated comorbidities. A close follow up is warranted to watch for development of other autoimmune manifestations in the future in such patients. Most cases with vaccine associated immune thrombocytopenia have a short limited course requiring steroids for a limited period. Development of chronic ITP requiring second line agent is uncommon. In our patient steroids were completely stopped in two weeks and follow up platelet count was also normal. The risk of developing ITP post-vaccination is lesser than the risk of developing thrombocytopenia due to Covid -19 itself and hence it should not discourage vaccination. Also, the question remains unanswered as to whether the second dose of the same vaccine can be given or a non-adenovirus based vaccine should be considered for such patients.

Conclusion

As different SARS-CoV-2 vaccines are becoming available, it is important to understand their mechanisms of action and adverse effects. ITP though very rare is an important, life threatening adverse event. However, this should not discourage the ongoing robust vaccination program.

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