OBSERVATIONS: CASE REPORTS

Transient Thrombocytopenia With Glycoprotein-Specific Platelet Autoantibodies After Ad26.COV2.S Vaccination: A Case Report

Background: Immunohematologic complications, including thrombosis and thrombocytopenia syndrome (TTS) (1), immune thrombocytopenia (2), and autoimmune hemolytic anemia (3), have been reported after vaccination against COVID-19. Thrombocytopenia after COVID-19 adenoviral vector vaccination is of particular concern due to the potential for TTS, but other causes of vaccine-related thrombocytopenia must be investigated and characterized.

Objective: To illustrate an alternative cause of thrombocytopenia, transient glycoprotein-specific platelet autoantibodies, after receipt of a COVID-19 adenoviral vector vaccine (Ad26.COV2.S; Johnson & Johnson).

Case Report: We evaluated a 71-year-old woman with a history of polymyalgia rheumatica who presented with acute thrombocytopenia after receipt of the Ad26.COV2.S vaccine. The patient had been diagnosed with polymyalgia rheumatica 6 years prior, which remitted on completion of a 3-month course of low-dose prednisone and did not recur. Before vaccination, the patient was in good health; 3 weeks prior, a routine examination showed an unremarkable complete blood count and a platelet count of 429×10^9 cells/L. However, 35 days after vaccination, she developed headaches in the left temporal region, prompting evaluation by her rheumatologist for possible giant cell arteritis given her history of polymyalgia rheumatica. She did not report recurrence of polymyalgia rheumatica symptoms, and giant cell arteritis was believed to be unlikely after laboratory evaluation showed an erythrocyte sedimentation rate of 8 mm/h (reference, 0 to 20 mm/h) and a C-reactive protein level of 1.0 mg/L (reference, <8.0 mg/L). However, this same evaluation did show isolated thrombocytopenia (platelet count, 115×10^9 cells/L) with no other complete blood count abnormalities. The patient did not have a preexisting immune thrombocytopenia diagnosis but had experienced brief mild thrombocytopenia (platelet count, 55 to 110×10^9 cells/L) in the setting of an acute right ear infection in the previous year. Given ongoing headaches and recent receipt of an adenoviral vector SARS-CoV-2 vaccine, the patient was further evaluated using magnetic resonance angiography of the brain and a heparin–platelet factor 4 antibody enzyme-linked immunosorbent assay, both of which had unremarkable findings (the assay optical density was 0.057; reference, <0.400). The patient's headaches were ultimately attributed to referred dental pain due to occlusal trauma from a temporary dental bridge, and they resolved after dental intervention.

The patient's platelet count further declined to 96×10^9 cells/L on postvaccination day 38 and then to 59×10^9 cells/L on postvaccination day 42. At this time, platelet autoantibodies were assessed using a direct, solid-phase, enzyme-linked immunosorbent assay measuring antibodies against glycoproteins IIb/IIIa, Ib/IX, and Ia/IIa eluted from the platelet surface (Versiti). Testing was done following expert recommendations (4), and the results were positive for platelet autoantibodies directed against all 3 glycoproteins at optical densities of 0.119 for anti–glycoprotein IIb/IIIa (threshold, ≥0.090), 0.180 for anti–glycoprotein Ib/IX (threshold, ≥0.094), and 0.267 for anti–glycoprotein Ia/IIa (threshold, ≥0.108). The optical density positivity thresholds for each glycoprotein in this assay are set to twice the normal calibrator values (which are averaged from antibody-negative plasma samples from healthy donors).

The patient's platelet count was monitored closely and showed stability and rapid recovery without intervention as follows: at 43 days, 56×10^9 cells/L; at 44 days, 67×10^9 cells/L; at 45 days, 76×10^9 cells/L; at 48 days, 143×10^9 cells/L; and at 51 days, 248×10^9 cells/L. Platelet autoantibody testing was repeated 3 weeks after platelet count normalization; results for all 3 platelet glycoproteins were negative.

Discussion: Platelet autoantibody testing is not routinely recommended in patients with suspected immune thrombocytopenia because of its modest sensitivity (about 50%) (5). However, when glycoprotein-specific antibody testing is done in adherence with expert guidelines, specificity is 90% to 95% (4,5). Although many vaccines are associated with thrombocytopenia, the occurrence of potentially fatal TTS may be uniquely associated with adenoviral vector vaccines against SARS-CoV-2. Therefore, characterizing the natural history of alternative causes of new-onset acute thrombocytopenia in recipients of these vaccines is of paramount importance. In this case, the patient had an initial presentation that was concerning for possible TTS, but on further evaluation, she was found to have transient immunologic thrombocytopenia with detected (and similarly transient) direct glycoprotein-specific platelet autoantibodies, suggesting that vaccination with Ad26.COV2.S may provoke transient production of antibodies targeted against, or capable of cross-reactivity with, platelet glycoproteins in certain individuals. If antiviral spike protein antibodies cross-reactive with platelet glycoproteins resulted in this clinical presentation, thrombocytopenia due to this mechanism could occur with other SARS-CoV-2 vaccines. The potential development of platelet autoantibodies or antiviral antibodies capable of cross-reactivity with platelet glycoproteins after vaccination against SARS-CoV-2 is a phenomenon worthy of further study.

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