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Immune-Mediated Thrombotic Thrombocytopenic Purpura after BNT162b2 Vaccine

BNT162b2 Aşısı Sonrası Gelişen İmmün Aracılı Trombotik Trombositopenik Purpura

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To the Editor,

Immune-mediated thrombotic thrombocytopenic purpura (iTTP) is a rare but life-threatening condition characterized by microvascular thrombosis [1]. The roles of several vaccines have been described in its etiology [2,3]. With the coronavirus disease-19 (COVID-19) pandemic, various vaccines have been developed. As a result of vaccine studies, the BNT162b2 (BioNTech) vaccine was approved by the US Food and Drug Administration in August 2021. The first case of iTTP following administration of BNT162b2 was reported around the same time [4].

A 48-year-old female patient was admitted to the hematology outpatient clinic on June 26 with complaints of weakness, nausea, dizziness, and bruising. There was no positive finding in her history, except that she had received the first dose of the BNT162b2 vaccine on June 14, 2021. She was taking no medications. She stated that ecchymoses had developed from the third day after vaccination. On admission, hemoglobin was 10.7 g/dL, platelet count was $88x10^9$/L, creatinine level was 0.5 mg/dL, lactate dehydrogenase (LDH) level was 515 U/L, reticulocyte count was $231x10^9$/L, Coombs tests were negative, and a peripheral smear showed polychromasia and normoblasts with schistocytes. Prothrombin and activated partial thromboplastin times were normal, the PLASMIC score was 6 with a high risk for ADAMTS13 (a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13) deficiency, and a polymerase chain reaction testing for SARS-CoV-2 was negative. ADAMTS13 enzyme activity was dramatically reduced to <0.2% with a high antibody titer level of >90 U/mL. Antiplatelet factor 4 testing cannot be performed in our center. As the patient was diagnosed with iTTP, methylprednisolone treatment at 1 mg/kg/day with one daily volume of therapeutic plasma exchange (TPE) was started. After 10 sessions of TPE, the patient had not responded (platelets $80x10^9$/L, LDH 368 U/L), and rituximab was added at 375 mg/m^2 once a week. After a total of 4 doses of rituximab, hemoglobin was 11.1 g/dL, thrombocyte count was $323x10^9$/L, and LDH was 472 U/L. ADAMTS13 activity was 0.2% with a persistently high antibody level of 50 U/mL one month after the last dose of rituximab. Additional immunosuppressive treatment was planned. Although COVID-19 vaccines have been in use for a limited period of time and there are still unknowns in the score calculation, the Naranjo Adverse Drug Reaction Probability Score was calculated as 6, meaning that the reaction was a probable adverse reaction.

In early-phase studies, heparin-induced thrombocytopenia with thrombosis, thrombosis in unusual locations, and thrombotic microangiopathy cases were reported after administration of viral vector-based COVID-19 vaccines such as ChAdOx1 nCoV-19 and Ad26.COV2.S [5,6]. Antibodies against platelet factor 4 have also been clearly defined [7]. However, the pathogenesis of COVID-19 vaccine-associated iTTP is currently unclear. Despite its rarity, disease activation was reported in patients with a previous history of iTTP in early-phase studies with the BNT162b2 mRNA vaccine [8,9,10]. Like in our case, the median time to disease diagnosis after vaccination was found to be 14 days on average in most of those cases. Responses were achieved with TPE, corticosteroids, rituximab, and caplacizumab. Unfortunately, since we do not have access to caplacizumab in our country, we could not use caplacizumab for our patient. So far, few cases of iTTP have been reported after mRNA-mediated vaccination. As a result, we wanted to draw attention to this rare and potentially fatal condition that can be encountered after mRNA-based vaccination against COVID-19. It is generally difficult to control such cases solely with TPE, and one or more lines of immunosuppressive therapy with or without caplacizumab are required in some cases.

Keywords: COVID-19 vaccine, Thrombotic thrombocytopenic purpura, BNT162b2

Anahtar Sözcükler: COVİD-19 aşı, Trombotik trombositopenik purpura, BNT162b2

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Authorship Contributions

Concept: T.G., F.C., S.A., Ö.S.K., İ.D.; Design: T.G., F.C., S.A., Ö.S.K., İ.D.; Data Collection or Processing: T.G., F.C., S.A., Ö.S.K., İ.D.; Analysis or Interpretation: T.G., F.C., S.A., Ö.S.K., İ.D.; Literature Search: T.G., F.C., S.A., Ö.S.K., İ.D.; Writing: T.G., F.C., S.A., Ö.S.K., İ.D.

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