Primary Active Epstein-Barr Virus Infection Coexisting with Immune Thrombocytopenia in Children-A Rare Trigger Factor of Immune Thrombocytopenia

Çocuklarda İmmün Trombositopeni ile Birlikte Görülen Primer Aktif Epstein-Barr Virüs Enfeksiyonu - İmmün rombositopeninin Nadir Bir Tetikleyici Faktörü

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İmmün trombositopeni (ITP), çocuk çağında izole trombositopeni ile karakterize bir trombositopeni nedenidir. Epstein barr virüs enfeksiyonu (EBV) ITP için tetikleyici bir faktör olabilecek hafif ve komplikasyonsuz bir hastalıktır. Burada, Epstein barr virüs enfeksiyonuna ikincil ITP gelişen iki olgu tartışılmıştır.

Anahtar kelimeler: İmmün trombositopeni, Epstein-Barr virüs, çocuk
Abstract

Immune thrombocytopenia (ITP) is a reason of thrombocytopenia that is characterized by isolated thrombocytopenia in childhood. Epstein-Barr virus infection (EBV) is a mildly and uncomplicated ailment that might be a trigger factor for ITP. Here, we discuss two cases with ITP secondary Epstein-Barr virus infection.

Keywords: Immune thrombocytopenia; Epstein-Barr virus; children

Introduction

Immune thrombocytopenia (ITP), formerly recognized as idiopathic thrombocytopenic purpura or immune thrombocytopenic purpura, is a circumstance with reduced platelet values due to extermination in peripheral circulation. The immunological reaction characterized by an isolated thrombocytopenia is defined as platelet count < 100,000/microliter (mL). Viral infections might be a trigger factor for ITP among children and the adults. Interestingly, patients may have a few or no evidence of purpura or bleeding though severe thrombocytopenia that could be explained as an immune-mediated mechanism (1). Epstein-Barr virus is a member of the gamma herpesvirus family that replicate in lymphoid cells. EBV-infected B cells are in charge of the dissemination of infection and lytic damage in epithelial cells and fibroblasts. Actually, EBV infections are typically occur as an asymptomatic infection in all population groups and 90–95 % of the population have serological evidence of previous infection (2). However, primary EBV infection may be supposed to be a the triggers of onset or aggravation of several entities. Epstein-Barr virus is the primary agent of infectious mononucleosis (IM) presented with pharyngitis, adenopathy, fever, malaise, and atypical lymphocytosis. The other clinical manifestations of EBV consist of cerebellitis, hepatitis, peripheral neuritis, interstitial nephritis, myocarditis, Gullian-Barré syndrome, myocardiitis, and neutropenia-associated sepsis. Hematological effects including neutropenia, haemolytic anaemia and thrombocytopenia are rare involvements (3). EBV infection-induced ITP with severe thrombocytopenia has been infrequently shown in literature search. This report represents two cases of primary EBV infection leads to secondary ITP that present with infectious mononucleosis.

Case Presentations

A previously healthy 8-year-old boy was referred to our ward with a two-day history of diffuse petechial rash and ecchymosis on bilateral lower extremities, and epistaxis. Six days before admission, he had developed fever, malaise, throat ache, rhinorrhea, nasal congestion, and cough. There was no family history or past history of chronic disorders. On admission, her temperature was 37.6 °C, heart rate 110 per minute, respiratory rate 20 per minute, and blood pressure was 106/76 mmHg. His height was 135 cm and he weighed 30 kg (75-90 and 90-97 percentiles, respectively). There were 5-10 ecchymoses and diffuse petechiae on lower extremities, and oral mucosal hemorrhages, and grade 3-4 hypertrophic exudative tonsillitis on his physical examination. The lymph node enlargement examination show size: on right submandibular area measured as 1.5x1.5 cm, on left axillary area measured as 1x1 cm and multiple minimal reagent lymphadenopathies over the bilateral sternocleidomastoid muscles. On Traube’s area percussion there was submatite sound. White blood cell count (WBC) 11.100/mm³ with 66% reactive lymphocyte and 20% monocytes, 14% atypical lymphocytes; hemoglobin 11.5g/ dl, platelet count 6000/mm³ on laboratory investigations at admission and his peripheral blood smear noticeably showed a decreased number of platelets, and there were no atypical cells or blast cells; reactive/ atypical lymphocytosis (Downey cells) and obvious thrombocytopenia were identified. Biochemical studies revealed aspartate amino transferase 72 IU/L, alanine aminotransferase 81 IU/L, and gamma-glutamyltransferase 10 IU/L, C-reactive protein 4.9mg/dL, blood coagulation tests, renal function and urinary analysis were normal. The EBV serology tests demonstrated Anti-EBV VCA IgG/EA positive, Anti VCA IgM positive with no positive signs of other virological and bacterial investigations. Infectious mononucleosis (IM) acknowledged as acute clinical manifestation of EBV was diagnosed because of the child’s signs of tonsillitis, malaise, continuing fever, cervical lymph node enlargement, and mild splenomegaly. In light of these findings, the patient was diagnosed with ITP which was triggered by primary active acute EBV/IM and immunglobuline (1 gr for kg, per day, 2 days) treatment was given. A 3 days later of discharging, his follow-up examination the blood work results was WBC count 102000/mm³, hemoglobin 11.6 g/dL, platelet count 102000/mm³.

A 4.5-year-old girl, who was previously healthy, presented with intraoral hemorrhagic lesions and common petechial rashes and ecchymosis throughout the lower extremities. There was no family or past history of chronic sicknesses. On admission, her temperature was 37 °C, heart rate 134 per minute, respiratory rate 26 per minute, and blood pressure was 118/75 mmHg and her weight 16 kg (10 P), height 105 cm (10 P). Physical examination was significant for oral hemorrhages on the palate and diffuse petechiae over lower extremities, and grade 2 hypertrophic exudative tonsillitis. The lymph node enlargement examination shows size: on the left submandibular area measured as 2x1.5 cm. On Traube’s area percussion there was a tympanic sound. Laboratory research at the time of
application included WBC count 12,720/mm³ with 70% lymphocytes and 10% monocytes, hemoglobin 13 g/dl, platelet count 2,000 mm³; peripheral blood smear showed normal neutrophil and erythrocytes signs without blastic cells. However platelets was never seen, also there were atypical lymphocytes as Downey cells. Biochemical studies revealed C-reactive protein 0.9mg/dL, albumin of 4.3 g/dl, aspartate aminotransferase 102 IU/L, alanine aminotransferase 94 IU/L, and gamma-glutamyltranspeptidase 11 IU/L. Renal function and urinary analysis were normal. The EBV serology tests showed Anti-EBV VCA IgG/EA positive, Anti-VCA IgM positive with no positive signs of other virological and bacterial investigations. In light of these findings, the patient was diagnosed with ITP which was triggered by primary active acute EBV/IM, and immunoglobulin (1 gr for kg, per day, 2 days) treatment was given. Diagnosis of secondary ITP likely due to acute EBV infection/mononucleosis was made for the two patients.

Discussion
We herein report two cases of ITP diagnosed with primary EBV infection. Immune thrombocytopenia (with normal parameters of hemogram) is an entity presented with low platelet value due to the platelet destruction caused by an immune-mediated reaction. It is one of the most common causes of symptomatic thrombocytopenia in children. Terminologically, the primary ITP announces as lack of other causes or disorders that may be associated with the thrombocytopenia, and secondary ITP might be described as immune-mediated thrombocytopenia with an underlying cause (drug-induced or associated with systemic illness such as infections, systemic lupus erythematosus (SLE), immune deficiency and other causes) (1). The peak incidence predominance of boys to girls is between two and five years and a smaller peak in adolescence with an annual incidence of 4.8 per 100,000 children younger than 15 years of age in ITP. However, there is a contrast in epidemiological distributions with the tendency of girls in adolescent ages (4). Seasonal fluctuations, temperate climates, allergic rhinitis, and atopic dermatitis have also been reported as a relation with ITP occurrence (5). Although the pathogenesis of ITP is clearly not understood; it is known that an autoimmune disorder is defined as the early usage of platelets by the reticuloendothelial system due to sensitization of antiplatelet glycoprotein autoantibodies. Additionally, there has been reported that the mechanism of the illness could be inadequate thrombopoiesis, complement-mediated lysis, or a viruses documented as 13.3% in childhood. Thrombocytopenia associated with viral diseases might be defined as a degradation of the immune system that may be caused by immune complexes, antiplatelet antibodies or inappropriate platelet generation, or an altered reticuloendothelial performance during the diseases (6). Some studies have stated that ITP is related to infections like Epstein-Barr virus (EBV), varicella, hepatitis A/B, helicobacter pylon, streptococcus, measles, mycoplasma, tuberculosis, vaccines, some medications, and foods (7).

Epstein-Barr virus infection with ITP is uncommonly and triggering of the autoimmune system with EBV is also seldom seen and implies a variety of syndromes entity in childhood. It is put forwarded that EBV might be a factor that triggers autoimmunity due to the association with many autoimmune diseases of EBV infection. Epstein-Barr virus can also result in several haematological abnormalities, including atypical lymphocytosis and cytopenias. The mechanism thrombocytopenia during the EBV-associated infectious mononucleosis appears to be multifactorial and might be defined as unclear (8). To our knowledge, Epstein-Barr virus infection has been recorded in a limited pediatric patients with ITP in the literature. First line treatment of thrombocytopenia associated with viral diseases has been specified by The National Institute for Health and Care Excellence as corticosteroids and intravenous immune globulin (IVIG). Immune globulin has several potential antiinflammatory and immunomodulatory effects that may prevent reticuloendothelial uptake of autoantibody-coated platelets. Suppression of inflammatory / autoimmune processes performed as interaction / blocking of the Fe receptor on phagocytic cells in the spleen and liver, such as spleen macrophages, constitutes the main mechanism of IVIG treatment (9).

In conclusion, the cases highlights the point of acute primary EBV infection that might rarely be an among the factors for trigger the onset or exacerbation of Immune thrombocytopenia. We suggest that the serologic examinations may help to specify the possible etiology and/or warning factors of ITP during the disease episode.
Ethics
Informed Consent: Informed consent was taken prior to writing this case report from the patient’s parents.

Peer-review: Externally peer-reviewed.


Conflict of Interest: The authors declared that there were no conflicts of interest.

References