Short Communication

Cytomegalovirus Pneumonitis in a Patient with Homozygous β-Thalassemia and Splenectomy

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SUMMARY: Cytomegalovirus (CMV) rarely causes disease in immunocompetent individuals but may cause severe disease in immunocompromised patients. We report the case of a young woman who had undergone multiple transfusions and splenectomy for homozygous β-thalassemia. She presented with prolonged fever and respiratory distress. Although broad-spectrum antibiotic therapy had initially been administered, the patient had clinically deteriorated. Serology and molecular blood testing established CMV infection and viremia. Computed tomography of the chest demonstrated pneumonitis and she was successfully treated with a 3-week administration of ganciclovir. In β-thalassemia patients who undergo splenectomy necessitating multiple blood transfusions, CMV infection should be considered as a differential diagnosis.

β-Thalassemia major is a hereditary disorder characterized by genetic deficiency in the synthesis of β-globulin chains that may lead to transfusion-dependent anemia. Splenectomy is usually performed to reduce excessive blood consumption and consequent severe iron overload. Although a patient with thalassemia major should not be considered as immunocompromised per se, infection is a common cause of death in thalassemia major patients. Cytomegalovirus (CMV) is a member of the Herpesviridae family that is transmitted between humans through sexual intercourse, the placenta, breastfeeding, saliva, blood transfusion, and transplantation of solid organs or hematopoietic stem cells (1). In healthy individuals, primary CMV infection is presented as an asymptomatic or self-limiting mononucleosis-like febrile illness. However, severe life-threatening disease has been described in immunocompromised patients (2).

A 36-year-old woman was generally well until 1 week before admission to another hospital, when she developed fever with a temperature up to 38°C, chills, and fatigue. A chest radiograph and urine and blood cultures yielded negative results at that time. Amoxicillin-clavulanate was commenced with no clinical improvement, and she was transferred to the University Hospital of Heraklion 5 days later for further evaluation. The patient had a history of homozygous β-thalassemia necessitating multiple transfusions with packed red blood cells every 10 days, asplenia due to the splenectomy, secondary liver hemosiderosis along with hepatomegaly, secondary thrombocytosis, and hypothyroidism. Her medications included deferiprone, levothyroxine, and folic acid. Pneumococcal and meningococcal vaccinations had been administered before splenectomy. No allergies, smoking, alcohol drinking, or use of illicit drugs were reported.

Upon admission, her temperature was 38°C, blood pressure was 110/60 mmHg, pulse was 100 beats per minute, respiratory rate was 20 breaths per minute, and oxygen saturation was 88% while she was breathing ambient air. Physical examination revealed decreased breath sounds at the bases of the lungs, palpable axillary lymph nodes, and tender hepatomegaly. The rest of the clinical examination was unremarkable. Chest radiography revealed diffuse consolidation in both pulmonary bases with coexisting pleural effusions (Fig. 1). Arterial blood gas values were pH 7.425, PaCO2 43.5 mmHg, PaO2 51.8 mmHg, and HCO3 29.9 mmol/L while the patient breathed room air. Her white-cell count was 25,700/mm3, with 36.9% polymorphonuclear cells, 53% lymphocytes, 6.9% monocytes, and 3% eosinophils. The hemoglobin level was 11.5 g/dL, and the platelet count was 981,000/mm3. The aspartate aminotransferase

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Fig. 1. Chest X-ray revealed diffuse consolidation in both pulmonary bases with co-existing pleural effusions.
level was 34 (normal range, 8 to 40) U/L, the alanine aminotransferase level was 55 (normal range, 8 to 40) U/L, gamma-glutamyl-transferase was 117 (normal range, 8 to 40) U/L. The erythrocyte sedimentation rate was 53 mm/hour, and the C-reactive protein level was 4.2 (normal range, 0.08 to 0.8) mg/dL. Intravenous ceftriaxone had been commenced initially, but because of her rapid clinical deterioration with a high fever (temperature up to 40°C) and dyspnea, the antimicrobial therapy was changed to meropenem (1 g three times daily), moxifloxacin (400 mg once daily), and vancomycin (1 g twice daily). High-resolution computed tomography of the chest demonstrated diffuse consolidation and atelectasis of both lower pulmonary fields and pleural effusions as well as a micronodular interstitial pattern of both lungs (Fig. 2). Blood and urine cultures were sterile. Transthoracic echocardiography was normal with no valvular vegetations. Tests for antibodies against human immunodeficiency virus, hepatitis B and C virus, and CMV upon admission as well as urine antigens for Legionella pneumophila and Streptococcus pneumoniae yielded negative results. Subsequent serological tests for CMV (ARCHITECT CMV IgM assay [chemiluminescent microparticle immunoassay; Abbott, Chicago, IL, USA] and enzyme-linked immunosorbent assays [ELISAs] for the detection of IgG and IgM antibodies to CMV in human serum [SERION ELISA classic CMV IgG and IgM tests; Virion/Serion, Würzburg, Germany]) showed increased levels of IgM antibodies (0.91 arbitrary units [AU]/mL; positive, > 0.8 AU/mL) and low IgG antibodies (2 AU/mL; negative, < 15 AU/mL) that increased again after 5 days (IgM, 3.16 AU/mL; IgG, 15 AU/mL), consistent with acute CMV infection. Quantitative polymerase chain reaction for CMV (artus® CMV QS-RGQ Kit; QIAGEN, Hilden, Germany) in plasma was also positive (10⁸ copies/mL). Bronchoscopy was normal and bronchoalveolar lavage showed lymphocytosis with a CD4 to CD8 ratio of 0.3. Ganciclovir (5 mg/kg/12 h) was commenced and the patient became afebrile on day 5 of ganciclovir treatment. She received intravenous ganciclovir for 2 weeks and was continued on oral valganciclovir 900 mg per day at home for 1 more week. One month later she was in good condition without any evidence of infection.

Severe CMV infections have been described in patients having undergone splenectomy after major surgery or severe trauma (3–5). Five cases of severe pneumonitis have been reported in patients with post-traumatic splenectomy and multiple transfusions (5). All of these patients had a long period of high fever, severe interstitial pneumonitis with hypoxemia, and marked lymphocytosis with numerous atypical lymphocytes as in our case. While this case report was being written, another group published a similar case (6), making these the first 2 cases of CMV pneumonitis in patients with β-thalassemia major and splenectomy.

It is widely known that splenectomy reduces the humoral response and is a risk factor for invasive infection by encapsulated bacteria. However, changes in cellular immunity have been reported after splenectomy, such as decreased natural killer activity and a weakened IgM memory B cell response (7–8). Therefore, an impaired immune response may be associated with the increased severity and uncommon manifestations of CMV infection in patients having undergone splenectomy.

Furthermore, individuals with thalassemia who had undergone splenectomy should be considered at high risk for CMV infection owing to the high prevalence of transfusion-transmitted disease (9). In recent decades, serological testing and blood-component leukoreduction have been used to reduce the risk of CMV transmission in patients necessitating transfusions (2). Therefore, serological and molecular screening should be suggested for high-risk patients.

CMV pneumonitis is a life-threatening disease in immunocompromised patients and is diagnosed by the detection of CMV in bronchoalveolar lavage fluid or lung tissue samples (10). In our case, an increased lymphocyte differential count and low CD4 to CD8 ratio in the bronchoalveolar lavage as well as the micronodular interstitial pattern of the lung in the context of CMV viremia and the rapid clinical response to ganciclovir.

Fig. 2. High resolution computed tomography of the chest demonstrated diffuse consolidation and atelectasis of both lower pulmonary lobes and pleural effusions (A). Intrapulmonary, an homogeneous air pattern was seen, especially in the right middle lobe. Multiple pulmonary micro-nodules were revealed in both upper lobes, the right middle lobe and both apical segments of the lower lobes (B). Enlarged lymph nodes were found in both lung hilums, as well as thickening of the anterior pericardium.
supported the diagnosis of CMV pneumonitis.

In conclusion, although CMV pneumonitis is an extremely rare clinical manifestation among immunocompetent patients, in thalassemia patients with pneumonitis who have undergone splenectomy, CMV infection should be included in the differential diagnosis.

Conflict of interest None to declare.

REFERENCES