Pulmonary Embolism in a Young Immunocompetent Adult Infected with Cytomegalovirus: Are Novel Oral Anticoagulants an Efficient Alternative?

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Abstract. Background/Aim: Cytomegalovirus (CMV) infection is a common disease especially in young adults. Thromboembolism-like deep vein thrombosis and pulmonary embolism is increased among patients with CMV infection. Most cases represent immunocompromised patients usually treated with low molecular weight heparin. Case Report: Herein, we describe a 25-year-old immunocompetent male who presented at the emergency department with sudden onset of chest pain. One month prior to admission, he had developed persistent fever and cough and the diagnosis of CMV infection had been established. After extensive workup, the diagnosis of pulmonary embolism after CMV infection was set and he was treated with rivaroxaban. During the next six months the patient continued on the same anticoagulant therapy with no other episode of pulmonary embolism at 1-year follow-up. Conclusion: To our knowledge, this is the first case of CMV-associated pulmonary embolism treated with novel oral anticoagulants (NOACs). NOACs, such as rivaroxaban, seem to be safe and may represent an attractive alternative with promising results in this particular group of patients. Studies incorporating a greater cohort of patients are needed in order to draw safe conclusions regarding the relationship between NOACs and CMV infection.

Cytomegalovirus (CMV) infection is usually asymptomatic or resembles infectious mononucleosis syndrome, which is characterized by fever, malaise, muscular-skeletal pain, lymphadenopathy and atypical lymphocytosis. Of note, the reports of thromboembolic events such as pulmonary embolism (PE) associated to acute CMV infection are increasing (1). Venous thromboembolism has been reported in association with CMV infection both in immunocompromised and immunocompetent patients. In the latter population, it is yet not determined whether CMV alone provokes venous thromboembolism (VTE) or other predisposing conditions are involved (2, 3). The correct assessment of the patient’s clinical status, in association with the procoagulant risk factors could be useful to reach the diagnosis of PE. We present and analyze the first –to our knowledge– case of CMV related PE in an immunocompetent young patient, treated with novel oral anticoagulants (NOACs).

Case Report

A 25-year-old male presented to the emergency room with sudden onset of chest pain. One month prior to the admission, he had developed persistent fever and cough, and following detailed assessment, diagnosis of CMV infection was established. There was no history of smoking, alcohol intake or other comorbidities. His temperature was 36.9°C, blood pressure was 125/55, heart rate 125/min, respiratory rate 22/min with oxygen saturation 100% at 2lt of oxygen.
Blood gas test revealed normal values whereas heart auscultation revealed a normal rhythm with no murmurs.

Laboratory data on admission revealed a WBC count of 7,200 cell/ml with 60% atypical lymphocytes. Platelet count was 186,000 cells/ml, aspartate aminotransferase (AST) was 60 U/l, alanine aminotransferase (ALT) 175 U/l, alkaline phosphatase (ALP) 98 U/l and D-Dimers 4.5 mg/dl. A CT of the lungs with intravenous contrast (Figure 1), showed a filling defect in the right pulmonary artery. Moreover, color Doppler of the lower limb veins revealed a fresh thrombus in the posterior tibial vein of the right foot (Figure 2). A hypercoagulability workup performed before the introduction of heparin therapy detected normal plasma antithrombin III, Protein C and S activity. There was no V Leiden factor or prothrombin mutation. Homocysteine levels were 11.35 mg/dl.

Treatment with new oral anticoagulants (rivaroxaban) was immediately initiated with 15 mg twice a day for 21 days and thereafter 20 mg once a day. Nine days after the admission, a control CT of the lungs and abdomen showed a slight reduction in the areas of consolidation. During the next six months the patient continued on anticoagulant therapy with no other episode of pulmonary embolism at 1-year follow-up.

Discussion

The association of CMV infection with vascular thrombosis was first described in immunocompromised patients. However, CMV-associated thrombosis has been reported in immunocompetent patients as well (4-7). Certain theories suggest that CMV triggers thrombosis by infecting endothelial cells and enhancing platelet adhesion to the infected cells, by activating factor X and increasing circulatory levels of factor VIII (8) as well as through the gene IE84 (9). However, the most accepted theory supported by several in vitro studies suggests that CMV transiently induces production of anti-phospholipid antibodies (10). Recently, various studies (2, 3, 11-13) evaluated the incidence of CMV associated thrombosis. These studies revealed that acute CMV infection may increase the likelihood of thrombosis only during active infection. In the
literature, administration of intravenous heparin, low-molecular weight heparin and warfarin were selected as a treatment of choice in treating PE. A large retrospective study of 1007 VTE patients demonstrated an incidence of 0.1% synchronous acute CMV infection. These patients with coexistent VTE and acute CMV infection were typically younger and exhibited a female predominance (3). Hereditary thrombophilia was identified in 90% of these patients. Oral contraceptives and pregnancy were not additive risk factors (3).

The most recent update of the American College of Chest Physicians (ACCP) Guidelines on Antithrombotic Therapy from 2012 (14) recommends rivaroxaban as an alternative option for PE treatment to warfarin. Rivaroxaban was shown to be non-inferior to warfarin in both the DVT and PE studies (15, 16), whereas the risk of major bleeding was statistically lower only in the PE study (16). Based on these findings and according to the younger age of the patient, NOACs were selected as a treatment of choice for 6 months. This is the unique case in which the patient was immunocompetent without thrombosis risk factors and the use of NOACs was effective in the progress of the disease. Due to the mild symptoms of primary infection, it was decided that the patient should not receive any antiviral drugs. This approach was confirmed by a recent review suggesting that antiviral therapy should be considered for patients presenting with severe VTE, VTE with a negative outcome despite anticoagulation, severe organ involvement, or for patients managed in the intensive care unit (17).

Conclusion

Our case highlights that physicians should be alert for symptoms and signs of thrombosis in patients with acute CMV infection and vice versa. NOACs, such as rivaroxaban, seem to be safe and may represent an attractive alternative with promising results in this particular group of patients. Studies incorporating a greater cohort of patients are needed in order to draw safe conclusions regarding the relationship between NOACs and CMV infection.

Conflicts of Interest

None.

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None.

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