Pulmonary embolism and acute cytomegalovirus infection in an immunocompetent patient

Embolia polmonare e infezione acuta da citomegalovirus in un paziente immunocompetente

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INTRODUCTION

Acute cytomegalovirus (CMV) infection causes a mononucleosis-like syndrome characterized by fever, malaise and muscular-skeletal pain. It is not associated to pneumonia in immunocompetent patients, while the reports of tromboembolic events such as pulmonary embolism (PE) associated to acute CMV infection are increasing [1]. Pitfall in diagnosis of pulmonary embolism is common [2]. The assessment of all pro-coagulant risk factors could be useful to suspect the diagnosis.

Here, we present the case of an immunocompetent patient with acute CMV infection associated with pulmonary embolism (PE).

CASE REPORT

A 37-year-old Caucasian male with 15-day history of fever (max temperature of 38.5 °C) asthenia and cervical lymphadenopathy was admitted to the hospital for cough, chest pain and detection at chest-X-ray of two consolidation areas in left and right lobe. A previous blood-test performed at home, three days before admission, detected IgM anti-CMV antibodies at high titer and mild hypertransaminasemia. Diagnosis of acute CMV infection was made. At the admission physical examination revealed fever, crackles at both lung bases and abdominal pain in the left upper quadrant but there was no lymphadenopathy or hepatosplenomegaly. The heart rate was 92 beats/min, his white blood cells (WBC) and red blood cells (RBC) count were normal, platelets (PLT) were 120,000/mm³, C-reactive-protein was 10.42 mg/liter, eritrocyte sedimentation rate was 37 mm/hr, fibrinogen was 522 mg/liter, D-dimer was 494 mg/liter. IgM and IgG antibodies for CMV were positive; IgM antibodies against viral capsid antigen of Epstein Barr virus were negative (IgG anti-EBNA positive). Chest radiographs continued to show bilateral areas of consolidation. Empirical antibiotic therapy with piperacillin-tazobactam and clarithromycin was started. The fever disappeared after six days and the patient was discharged with oral antibiotic therapy with levofloxacin. Control chest radiograph ten days after the admission showed resolution of parenchimal infiltrates in right lobe and persistence of the consolidation in left lung base with slight pleural effusion.

Four days after discharge, the patient complained new onset fever up to 38°C with right-sided chest pain and dyspnoea and he was readmitted to hospital. Heart rate was 106 beats/min. A chest X-ray revealed the presence of a new opacity in the right lung, not documented in the previous chest X-ray. At second admission WBC were 10500/mmc, C-reactive protein was 15,37 mg/liter; and D-dimers were 422 mg/liter.
A more aggressive diagnostic procedure was performed. The results of serological tests for HIV, toxoplasma, chlamydia IgG and IgM antibodies and blood cultures were negative. Arterial blood analysis showed PaO₂: 68.8 mmHg, PaCO₂: 35.3 mmHg, pH: 7.48, SatO₂: 96.8%. A wide spectrum antibiotic therapy with teicoplanin and meropenem was started.

The waxing-waning picture pointed to the possibility of pulmonary embolism and Geneva score for the evaluation of the risk of PE was calculated with score of 5 points, indicating an intermediate-probability of PE (heart rate > 95 beats/min) [3]. An echocardiogram showed slight mitral and tricuspid insufficiency and a slightly raised pulmonary arterial pressure at 33 mmHg.

A contrast medium enhanced CT-scan documented an intraluminal filling defect that occluded the anterior basal segmental artery of the right lower lobe (Figure 1), suggesting a pulmonary embolism in the right lung. Low-molecular-heparin was administered, subsequently shifted to dicumarol therapy. Chest pain and fever disappeared progressively in following days.

Color Doppler ultrasonography for the detection of deep venous thrombosis was negative. A coagulation screen performed before the introduction of heparin therapy detected heterozygous mutation of Factor V Leiden and abnormal heterozygous form of Factor II. The screening did not reveal abnormalities of prothrombin time ratio, activated partial thromboplastin time, plasma antithrombin III, protein C and S activity, or antiphospholipid antibodies and lupus anticoagulants. Seven days after the second admission, a control CT of the lungs and abdomen showed a slight reduction in the areas of consolidation. In the following months the patient continued anticoagulant therapy. No evidence of other embolism episodes was observed after one year of follow-up.

Several experimental studies suggest that acute CMV infection can infect endothelial cells and cause several manifestations similar to disseminated intravascular coagulation (DIC). Various studies demonstrated that cells infected by CMV can develop a pro-coagulant phenotype [4]. In humans DIC or other thrombotic events associated to CMV infection have been reported in immunocompromised patients (e.g. HIV positive patients or transplant recipients on immunosuppressive treatment), particularly as re-activated infections [5, 6]. On the contrary, few cases have been reported in immunocompetent individuals [7]. These cases are frequently associated with risk factors such as coagulation anomalies (homozygous mutation of Factor V Leiden, Protein C and S deficiency, aPL antibodies, cryoglobulinemia) and involved various vasal districts [8, 9].

In our case a thrombophilic screening revealed a heterozygous mutation of Factor V Leiden and Factor II, representing an important risk factor for thromboembolism, but in other case reports no coagulation anomalies were identified and CMV infection was the only causal factor [10].

Pulmonary embolism is an insidious disease with protean manifestation requiring high index of suspicion especially in young patients. PE can present with cough, fever, C-reactive-protein elevation and pulmonary opacity, so that bacterial pneumonia could represent a confounding diagnosis. Many score systems have been developed for clinical probability assessment of PE [2]. The Geneva Score is an important instrument for both the prediction and evaluation of a patient with suspected pulmonary embolism. Recently a revised version has been published, it is very easy to apply when PE diagnosis is suspected also in the Emergency Department but infections in particular with CMV are not considered in calculation of score [3].

Figure 1 - Thromboembolic occlusion of the anterior basal segmental artery of the right lower lobe during acute CMV infection.
Retrospective application of the Geneva score in first admission show a very low risk (3 points) with slight increase in the second admission (5 points). Awareness of CMV active role in thrombosis is an important point to integrate the score for suspect embolism and to avoid pitfalls in non resolving or relapsing pneumonia. To our knowledge, this is only the eleventh case ever reported of CMV associated PE in an immunocompetent patient [10].

In conclusion acute CMV infection can be the cause or precipitating factor of thromboembolic events in immunosuppressed and immunocompetent patients, with or without risk factors. For this reason we suggest to consider PE as differential diagnosis in patients presenting with acute CMV infection and aspecific clinical signs of pneumonia also in the presence of normal embolic scores.

Key words: cytomegalovirus, pulmonary embolism, Geneva Score

A case of an immunocompetent man with acute CMV infection associated with a pulmonary embolism is described. Acute CMV infection could be a risk factor for developing thromboembolism. Pulmonary embolism should be included in differential diagnosis in patients with acute CMV infections and pulmonary opacities.


