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Case Report

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Varicella Infection May Cause Thrombosis: A Case Report

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Abstract

This case was presented due to development of DVT and pulmonary embolism after VZV infection and determination of Factor V Leiden mutation and activated protein C resistance. A 19-year old male patient presented with fever at the 10th day of varicella zoster virus (VZV) infection, and pruritic vesicopustular skin lesions and increased leukocyte and CRP levels. Acyclovir and ampicillin-sulbactam therapy were started. On the fourth day of hospitalization, left leg DVT and pulmonary embolism developed. Anticoagulant therapy was started. Tests revealed activated protein C resistance and Factor V Leiden mutation. The patient was discharged after the relief of symptoms with anticoagulant therapy. Thrombosis rarely develops in the course of VZV infection. It is essential to investigate the factors contributing to predisposition to thrombosis in patients with thrombosis.

Keywords: Varicella zoster infection, Factor V Leiden mutation, Thrombosis

Introduction

Seropositivity varies depending on age in varicella, and it rises beyond 90% after the age of 16 years [1,2]. Although rare, disease associated complications can be life-threatening. Pneumonia, central nervous system complications (including encephalitis, cerebellitis, central facial palsy), secondary bacterial infections, pyogenic arthritis, osteomyelitis, necrotizing fasciitis, orbital cellulitis, and gastroenteritis are complications that can be seen after varicella infection [3,4].

Deep vein thrombosis is very rare after varicella infection. Factor V Leiden mutation and activated protein C resistance were identified in one case developing deep vein thrombosis and pulmonary embolism after varicella infection. The purpose of this paper is to point out that viral infections such as varicella may predispose to thrombosis and is to emphasize the need for investigatation of genetic factors in patients developing thrombosis as well as the necessity for not neglecting varicella vaccine in patients at risk.

Case Report

A 19-year old male patient applied to our emergency clinic with complaint of fever and rash all over the body. Rashes had started in the trunk 10 days ago, then spread to arms and legs. The patient had asthma history. The mother was being followed-up due to systemic lupus erythematosus (SLE). In physical examination, temperature was 38.4 °C, the pulse was 100, the blood pressure was 130/80 and breathing rate was 16/min. In the trunk and extremities there were vesicopustular skin lesions. Other physical examination findings were normal. WBC: 12 000/ mm^3 (74% neutrophils), Htc: 39%, plt: 277 000/mm^3, sedimentation: 60 mm/h, CRP: 24.3 mg/dL (N value, <0.8), AST: 39 IU/L, and ALT was 95 IU/L. Varicella Zoster, IgM, and IgG were positive. Bacterial infection secondary to varicella infection was considered in this patient. Acyclovir 5x800 mg tb, and ampicillin-sulbactam 4x1.5 g IV were started.

On the 4th day of hospitalization, pain and swelling in the left leg, pain in the right upper quadrant, and respiratory distress developed. Breath sounds diminished in right lower zone. Infiltration in the right lower lobe and diaphragm elevation in the right were detected in the chest x-ray. The values were as follows: WBC: 14 800 /mm^3 (78% neutrophils), CRP: 30.6 mg/dL, CK: 644 IU/L, AST:125 IU/L, ALT: 368 IU/L, LDH: 560 IU/L, D-dimer: 2 797 ng/ml, fibrinogen: 985 mg/dl. Blood gas values were pH: 7.4, pO2: 82.9 mmHg, and pCO2: 37.5 mmHg. Thoracic CT revealed pneumonic infiltration in the right inferior lobe, and nodular infiltration in the neighbourhood (Figure 1). Doppler US revealed findings consistent with deep vein thrombosis in left superficial femoral, popliteal and deep muscular veins of both extremities and lymph edema in the left foot. Thoracic CT angiograph revealed almost complete thrombus in the right main artery starting from first branching area; and 50% narrowing in the upper and middle lobe arteries (Figure 2). Echocardiography was unremarkable. Laboratory tests were asked to determine the cause of thrombosis. Acyclovir 3x10 mg/kg was continued as IV; low molecular weight heparin 2x0.8 cc SC was started.

According to the results of examination of the patient Anti-Nuclear Antibody (ANA), Anti-ds DNA, Anti-cardiolipin IgM, Anti-cardiolipin IgG, Anti-Sm were negative. Protein S activity, .prothrombin and MTHFR gene mutation were normal, Protein C activity: 33% (70-130), Activated protein C resistance: 1.6% (1.2-2.3 heterozygous), factor V Leiden mutation was heterozygous positive. In the patient, 5 mg of warfarin anticoagulant therapy was continued.

The patient responded to anticoagulant therapy and was discharged at the 30th day of hospitalization. Thrombophilia tests were asked from his parents. His mother was heterozygous in terms of Factor V Leiden mutation. Patient had no symptoms in the outpatient follow-up after one year. Thoracic angiography was normal.

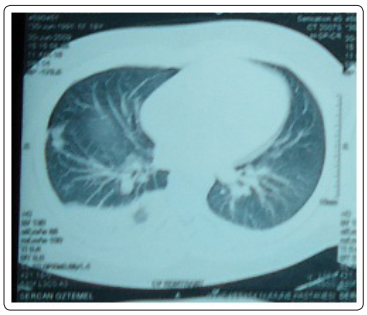

Figure 1: Thoracic tomography: Pneumonic infiltration in the right lower lobe; nodular infiltrations in the neighbourhood

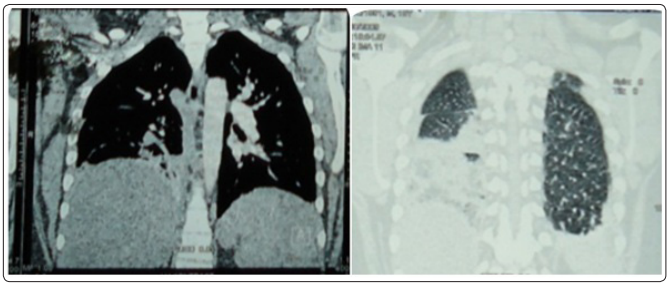

Figure 2: Thoracic angiography: Right main pulmonary artery. Thoracic CT angiograph revealed almost complete thrombus in the righ main artery starting from 1st branching area; and 50% narrowing in the upper and middle lobe arteries.

Discussion

Varicella zoster virus is one of eight herpes viruses known to cause infection in humans. Complications of VZV infection may occur before, during, or after the start of rash [5]. In the treatment of complicated infections of varicella zoster intravenous acyclovir thearpy is advised although it was not shown to reduce the incidence of complications [6].

The treatment with acyclovir and ampicillin-sulbactam was initiated at admission. On the fourth day of admission, deep vein thrombosis and pulmonary embolism were noted. Activated protein C resistance and factor V Leiden mutation were found. It has been reported in the literature that protein S deficiency was identified in two cases with varicella pneumonia and that factor V Leiden mutation was present in another case with venous thrombosis. It has been reported that, in the other case with varicella pneumonia, knee amputation was performed due to thrombosis, and the reason for predisposition to thrombosis could not be detected [1,7,8].

The most common cause of activated protein C resistance is Factor V Leiden mutation. Factor V Leiden mutation is the most common genetic cause of thrombophilia; the prevalence is reported to be 12-40% [9]. As a result of this mutation, the inactivation of Factor Va by APC is prevented. The most common findings of Factor V Leiden mutation are deep vein thrombosis and pulmonary embolism [10]. Factor V Leiden mutation was not known prior to admission in our patient. However, causes of thrombophilia were investigated due to the development of deep vein thrombosis and pulmonary embolism and factor V Leiden mutation was identified in both the patient and the mother.

As a result, thrombosis, albeit rare, may occur following VZV infection. The reason for thrombophilia has to be investigated in patients developing thrombosis, and varicella vaccine is required for people disposed to thrombosis.

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