

Deep vein thrombosis: A rare complication of varicella zoster infection.

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Introduction

Chickenpox (varicella) is a benign illness caused by varicella zoster virus which occurs predominantly in childhood. The incidence in young adults is 90/100,000 population and falls steadily with age. The varicella-Zoster virus is a double-stranded DNA virus of the Herpes viridae family. It affects only humans and the primary route of spread is via the respiratory tract. The incubation period from contact to appearance of the rash is 10-20 days. Complications include pneumonitis, encephalitis, rare neurological sequelae including optic neuritis and transverse myelitis. Hematological complications of thrombocytopenia and purpura fulminans myocarditis, pericarditis, pancreatitis and orchitis have all been reported.

There are few case reports of hypercoagulable state leading to deep vein thrombosis and other thromboembolic sequelae following varicella induced auto antibodies to natural anticoagulants in children. But such a clinical entity is rarely seen in adults. In two of these paediatric patients thrombosis was associated with free protein S deficiency and of these one had antiphospholipid antibodies and the other lupus anticoagulant. Vasculitic arterial infarction is known while deep vein thrombosis has rarely been reported with varicella zoster virus infection. We report a young man with varicella infection who developed deep vein thrombosis.

Case Report

A previously well immune competent 22 year old student presented with a florid, intensely pruritic vesicular rash of two week duration and pain along with swelling of right lower limb of one week duration. He had contact with his friend who was suffering with chicken pox.

On examination he was conscious, alert, and afebrile. There was no pallor, icterus, cyanosis, clubbing, pedal oedema or lymphadenopathy. Pulse was 80/min, regular, good volume, bilaterally symmetrical. All peripheral pulses were well felt. Blood pressure was 120/80 mm of mercury in right arm supine position. Detailed systemic examination revealed no abnormality. Pleomorphic rashes were present all over the body which was centrifugal in distribution. Right lower limb was swollen up to knee joint. It was tender, erythematous with local rise in temperature. Humans sign was positive. We have done Wells Clinical Prediction guide for DVT clinical parameter score. In our patient the score was 4 which is a high probability score.

Routine investigations including complete haemogram, serum biochemistry were normal. Serology for Human

Immunodeficiency Virus (HIV), hepatitis B surface antigen (HBsAg) and HCV was negative. ANA was negative. ECG showed normal sinus rhythm. Chest X-Ray was also normal. Vascular Doppler was done which revealed features of acute deep vein thrombosis in common and superficial femoral vein extending to popliteal vein, right external, common Iliac veins and profunda femoris. Thrombus was visualized directly with loss of compressibility and no obvious flow. There was reactive soft tissue oedema in leg and foot. No augmentation was seen on muscle squeezing. 2D echocardiography was done showing normal ejection fraction. There was no regional wall motion abnormality, valves were normal.

A diagnosis of DVT was made. The patient was treated with systemic heparinization with unfractionated heparin 1000 units per hour for seven days. Oral anticoagulants were added on fifth day. The dose was titrated to maintain an effective heparinization. Monitoring was done with APTT values and platelet count as heparin is known to cause thrombocytopenia. Antivirals in the form of tablet Acyclovir was added in the dose of 800 mg five times a day for seven days. Supportive care was given in the form of calamine lotion and antipruritic agents to take care of pruritus. Antibiotics were added to prevent secondary infection. After three to four days patient improved. Pain and swelling reduced.

The patient was investigated for associated vasculitis and prothrombotic tendency. The clotting screen was normal prior to heparinization, with a Prothrombin Time (PT) of 14 seconds and INR of 1.6 and APTT of 25 seconds and platelets were in the normal range. Patient improved. Pain was relieved. Leg swelling decreased. A repeat Doppler done after seven days revealed echogenic thrombus with absent colour flow in common and superficial femoral vein. However Popliteal vein and distal end of external Iliac vein showed partial thrombus with partial filling and augmentation on distal compression.

His thrombophilia profile revealed reduction of Protein S to 38.5%. Protein C was normal. Factor V Leiden mutation, prothrombin gene mutation and MTHFR gene mutation was not detected. D-dimer was raised to 11.35 mg/l. ASO titre was also raised to 583 IU/ml showing co-infection with Streptococcus bacteria. Antiphospholipid panel revealed a rise in IgM antibody 16.36 MPL-U/ml.

The patient was under close follow up. A repeat vascular doppler was done after six months which revealed complete resolution of deep vein thrombus. Thrombophilia profile done later also revealed normal Protein S value. D-dimer and ASO titre was also touched normal value.

Discussion

Chicken pox commonly occurs in children. It is rare in adults. 90% of population is seropositive by the age of fifteen. In adults secondary infection of vesicles are common. Pneumonitis occurs in 6% of infected adults. Treatment options include symptomatic treatment of itch with lotions plus antipruritic treatment with immunoglobulin and antivirals reserved for serious disease. Acyclovir a DNA polymerase inhibitor, has been shown to shorten the disease course, reducing the number of days with fever and the number of days with lesions in otherwise immune competent adolescents. Treatment with acyclovir does not significantly reduce complications associated with it [1]. Intravenous acyclovir is recommended in adults presenting with signs of complicated chickenpox [2]. Thrombotic complications are extremely rare in varicella zoster infection. Few case of varicella complicated with thrombotic complications namely purpura fulminans, necrotic vasculitis, stroke and deep vein thrombosis has been reported but deep vein thrombosis in adult is scarce in world literature. Varicella associated purpura fulminans and DVT-a pediatric case report published in a French journal [3]. This case report illustrates the pathophysiology of DVT occurring in a patient of chicken pox disease to be acquired protein C and S deficiencies and emphasizes the importance of thrombophilia testing. During recovery from varicella D Angelo et al first reported the occurrence of thrombosis with a transient deficiency of Protein S ascribed to the presence of a circulating auto antibody to the protein [4]. Since then a few reports have confirmed the presence the presence of anti-PS antibodies after varicella associated with severe thrombotic complications [5].

There are still many unresolved issues concerning the dramatic thromboembolic complications after varicella. The first one deals with the origin of such autoantibodies. It is possible that there is epitope mimicry between the infecting virus and Protein S. Many authors have found that the severity of clinical manifestations correlated with the concentrations of anti-PS antibodies and the severity of PS deficiency [6]. In our patient PS was 38.5%. It is also possible that co-infection with another infectious agent plays a role; i.e., co-infection with streptococcus is frequently reported as is there in our case. Another explanation could be, as in our patient and in other reports, the simultaneous presence of antiphospholipid antibodies (aPL) [7]. This raises the hypothesis of a very robust but transient and nonspecific immunologic response following varicella. Minick et al. first noted that viruses may induce atherosclerosis and a relationship was proposed between viruses, vasculitis and possibly thrombosis [8]. Ali et al. described a case of iliofemoral vein

thrombosis in a patient with chicken pox and considered this a direct result of VZV infection [9]. VZV infection has been found to induce endothelial damage in blood vessels. Virus in the vessel wall may induce a noncytolytic infection of smooth muscle cells in the media and functional damage to the vascular endothelium. This may result in thrombosis.

Conclusion

Our case demonstrates that deep vein thrombosis can occur in varicella zoster virus infection. A rapid diagnosis is essential for the proper management of the patient. The exact pathophysiology is not known. Probably a transient deficiency of protein C, protein S, coinfection with other viral infection, direct invasion of virus in venous endothelial wall with damage to endothelium leading to thrombosis could be the cause.

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