CASE REPORT

Thrombosis associated with varicella zoster in an adult

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Introduction

Varicella zoster, whilst primarily a disease of children, increasingly presents in adults.1,2 The incidence in young adults is 90/100 000, and falls steadily with age.2 The most common serious complication is pneumonia or pneumonitis.

The varicella-zoster virus (VZV) is a double-stranded DNA virus of the Herpesviridae 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, and the hematological complications of both thrombocytopenia and purpura fulminans. Myocarditis, pericarditis, pancreatitis, and orchitis have all been reported.3

Thrombotic complications of varicella zoster are rare, with only three reported cases in adults.4,5 In two of these patients, thrombosis was associated with free protein S deficiency, and of these, one had antiphospholipid antibodies and the other the lupus anticoagulant.4

Case report

A previously well 38-year-old man presented with a florid, intensely pruritic vesicular rash of two days duration, and increasing dyspnea. He had had contact with his son two weeks earlier, who was suffering from chickenpox. He had no prior history of chickenpox. He was pyrexial 39.4 °C, myalgic, and had a non-productive cough as well as dyspnea at rest. He also complained of loss of sensation in his left foot.

KEYWORDS
Varicella zoster; Thrombosis; Pneumonitis

Summary

The incidence of varicella zoster in adults is increasing, and may be associated with a number of significant complications. An adult male presented with varicella zoster complicated by pneumonitis and thrombosis, leading to a below-knee amputation. Thrombosis with varicella zoster has been associated with vasculitis and free protein S deficiency. Other microthrombotic complications, such as purpura fulminans, are more common in children. Current treatment recommendations include acetaminophen (paracetamol) and lotions for symptomatic treatment. Intravenous acyclovir is recommended in the treatment of complicated varicella zoster, although it has not been shown to reduce the incidence of complications.

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On examination, he was tachypneic and hypoxic on room air, with fine inspiratory crackles throughout all lung fields. He was in type 1 respiratory failure, with a PO2 of 10.1 kPa on 98% O2 via humidified venturi, giving a PaO2:FiO2 ratio of 10.3 kPa. His PaCO2 was 4.4 kPa. A chest X-ray demonstrated symmetrical pulmonary infiltrates in all lung fields, but with good expansion and no evidence of consolidation.

A poplar and vesicular rash was present in all areas, concentrated more centrally, with crusting. The femoral and popliteal pulses were present. Throughout the first four days of his admission, there were also striking evanescent vascular changes in the right foot and right hand, thought to be due to vasospasm.

The patient was commenced on acyclovir (800 mg, three times daily), and systemic heparinization with intravenous unfractionated heparin was commenced, titrated to an activated partial thromboplastin time (APTT) ratio of 1.8–2.2.

The diagnosis of varicella pneumonitis was suspected and intensive chest physiotherapy was commenced, with humidified oxygen therapy titrated to PaO2 > 9 kPa. Intubation and mechanical ventilation was not required, and the oxygen therapy was weaned to 60% within four days.

Cardiovascular stability and renal and hepatic function were maintained throughout without supportive therapy. The patient developed confusion on the third day, raising concerns of incipient varicella encephalitis, but the confusion was self-limiting and resolved within 36 hours.

Definitive amputation of the affected foot was delayed in order to allow delineation of the vascular margin. The patient began to suffer pain from the left leg, and was commenced on acetaminophen (paracetamol), breakthrough opioids, and incrementally increasing gabapentin. He underwent an uneventful below-knee amputation 12 days after onset of the disease.

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 s and APTT of 25 s, and platelets were in the normal range throughout his stay. IgA, IgG, and IgM levels were within normal ranges and there were normal levels of protein C, activated protein C, protein S, and antithrombin III. He did not have factor V Leiden. Autoantibody screening for mitochondrial, smooth muscle, gastric, and liver/kidney microsomal (LKM) antibodies were all negative, as were antinuclear antibodies (ANA) and anti-neutrophil cytoplasmic antibodies (ANCA) screens. No biochemical, immunological, or hematological cause was found to account for the thrombosis.

**Discussion**

Chickenpox is extremely common, with 90% of the population seropositive by age 15. Secondary bacterial infection of vesicles is common, and pneumonitis occurs in 6% of infected adults. Treatment options include symptomatic treatment of itch with lotions plus antipyrptic treatment with acetaminophen, with immunoglobulin and acyclovir 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 well children and adolescents. Treatment with acyclovir does not significantly reduce complications associated with VZV infection. Intravenous acyclovir is recommended in adults presenting with signs of complicated chickenpox.

Microthrombotic complications of varicella zoster are not unusual in children. Purpura fulminans is a syndrome of microvascular thrombosis in association with disseminated intravascular coagulation, resulting in hemorrhagic gangrene in the affected periphery. Classical purpuric lesions develop in association with the features of ischemia. There was no evidence of purpura in this patient.

Three reports of thrombosis have been reported in adults without purpura fulminans. The first patient was immunocompromised, being on cyclosporine. Immunofluorescence performed on vessel biopsy showed C3 deposits, from which the authors concluded that thrombosis was due to vasculitis secondary to VZV infection. Vasculitis also has been reported causing glomerulonephritis, orbital vasculitis, and stroke in children. The remaining two reported cases of thrombosis were deficient in free protein S, a vitamin K-dependent cofactor to protein C, which, in its activated form, inactivates activated factor V and VIII. One patient was also found to have lupus anticoagulant and the other to have antiphospholipid antibodies. The reduction in free protein S in children with a similar picture of thrombosis has been attributed to an antibody to protein S, which has been isolated in affected children.

Here we have presented a case of a male presenting with varicella pneumonitis and thrombosis leading to amputation of his lower limb below the knee. In contrast to previously reported cases, we could not demonstrate an increased susceptibility to coagulation, either innate or secondary to VZV infection. Acyclovir was used from presentation in accordance with current recommendations for the treatment of complicated varicella zoster, and there was a sustained improvement from the second day onwards. He was discharged 14 days after admission.

**Conflict of interest:** No conflict of interest to declare.

**References**

