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Extended Abstract

Shingles, an unusual cause of stroke

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INTRODUCTION

Varicella zoster virus (VZV) is a neurotropic alphaherpesvirus. As cell-mediated immunity to VZV declines with advancing age and immunosuppression, VZV reactivates to produce herpes zoster (shingles), frequently complicated by postherpetic neuralgia (radicular pain that persists long after the disappearance of rash). Zoster is also complicated by meningoencephalitis, myelitis, multiple serious ocular disorders and VZV vasculopathy. Importantly, all of the neurological and ocular complications of zoster may develop in the absence of rash. Diagnosis is confirmed either by the presence of VZV DNA or anti-VZV antibodies in CSF. Rapid virological verification and prompt treatment with antiviral agents can lead to complete recovery, even in patients with protracted disease.

VZV vasculopathy occurs in adults and children. Patients present with both transient ischemic attacks (TIAs) and stroke. Less often, patients present with subarachnoid or intracerebral hemorrhage secondary to ruptured aneurysm. Disease is often waxing and waning. Multiple cases of protracted disease that lasted for more than one year have been described. Both large and small arteries are affected. The characteristic pathology of VZV vasculopathy matches that of granulomatous arteritis. Virological analysis of intracerebral arteries of patients who died of VZV vasculopathy reveals Cowdry A inclusion bodies, multinucleated giant cells, herpes virions, VZV DNA and VZV antigen, indicating productive arterial infection by VZV. Interestingly, VZV is the only human virus that has been shown to replicate in cerebral arteries and produce disease.

ABSTRACT

VZV (Varicella Zoster Virus) infection in humans is a well-documented entity that is linked to numerous neurological complications, including intraceberal vasculitis. This can lead to ischaemic or haemorrhagic stroke and is a major cause of morbidity and mortality. This complication is more common in immunocompromised or elderly individuals. We present a case of haemorrhagic stroke presenting in an individual with recent onset VZV reactivation. An 83-year-old woman, who was previously living independently, presented to hospital with an acute onset of delirium and expressive dysphasia. This presentation was on the background of a 3 weeks history of an evolving vesicular rash in the dermatomal distribution of the ophthalmic branch of trigeminal nerve, characteristic of herpes zoster opthalmicus. The patient was started on oral acyclovir 3 days prior to admission and initial diagnosis of delirium secondary to herpes zoster infection was made. On admission, she scored 4 /10 on the abbreviated mental test score (AMTS), had a positive Hutchinson's sign and an unremarkable neurological examination. Laboratory testing showed raised inflammatory markers. Subsequent CT and MR brain imaging revealed a right temporal lobe haemorrhage with interventricular extension. Further imaging of the CT angiogram showed widespread vessel narrowing, consistent with vasculitis or a differential diagnosis of widespread atheromatous disease. Cerebral spinal fluid (CSF) polymerase chain reaction (PCR) was positive for VZV and further vasculitic screening including ANA and ANCA was negative. A diagnosis of haemorrhagic stroke secondary to varicella zoster vasculitis was made and the patient was treated with high dose intravenous methylprednisolone and acyclovir. It is important to consider viral induced cerebral vasculitis in susceptible patient groups as a cause of stroke. Correctly identifying patients presenting with this complication allows treatment with steroids and anti-viral agents that have been found to increase chances of a better prognosis.

Stroke after Zoster

In the past few years, multiple epidemiological studies from Taiwan, Europe, the U.K. and the U.S. have shown that the incidence of stroke after zoster is greater than in age-matched control patients. Analysis of Taiwanese National Health Research Institute records revealed a 30% increased risk within 1 year after zoster (2), increasing 4.5-fold with ophthalmic-distribution zoster (3). Similar analysis of the Danish National Registry revealed a 126% increased risk of stroke within 2 weeks after zoster, a 17% increased risk from 2 weeks to 1 year after zoster, and a 5% increased risk of stroke after the first year (4). Studies from the U.K. Health Improvement Network general practice database showed that not only was the risk of TIAs increased 1.15-fold, but also that myocardial infarctions (MIs) were increased 1.10-fold after zoster; and in zoster patients under 40 years of age, the risk for stroke, TIAs and MIs was significantly higher (1.74-, 2.42- and 1.49-fold, respectively) (5). A study from the U.K. Clinical Practice Research Datalink showed that the risk of stroke after zoster decreased over time in all dermatomes, with a statistically significant age-adjusted incidence of 1.63 at 1–4 weeks, 1.42 at 5–12 weeks, and 1.23 at 13–26 weeks after zoster, but no decrease at later times (6). In patients with ophthalmic-distribution zoster, the risk of stroke was increased 3-fold at 5–12 weeks after zoster. Finally, among 55% of zoster patients who received oral antiviral therapy, the stroke risk was reduced compared to that in untreated zoster patients, indicating the value of antiviral treatment in reducing stroke incidence after zoster.

CONCLUSION

In children and adults, VZV is a not uncommon cause of stroke. VZV vasculopathy in children appears to affect large vessels primarily, while stroke after zoster in adults mostly involves large and small arteries. VZV vasculopathy is confirmed by the detection of either VZV DNA or anti-VZV antibody in CSF. Vaccination effectively prevents varicella in

children. While immunization with the current FDA-approved Zostavax vaccine reduces the incidence of zoster and postherpetic neuralgia in adults, a newer subunit VZV vaccine has a remarkable 97.2% efficacy in preventing zoster for 3.2 years, although the duration of its effect is unknown. Finally, VZV appears to trigger the immunopathology of giant cell arteritis. Herpes zoster due to VZV reactivation has been historically perceived as a benign disease, with resolution of rash after several weeks and only rare complications.

BIOGRAPHY

Kerry Badger is a Foundation Doctor currently working at Chelsea and Westminster Hospital NHS Foundation Trust. She achieved a Bachelor of Medical Sciences in 2015 and a Bachelor of Medicine and Surgery in 2017, both from the University of Nottingham. She has a developing interest in neurology and has recently completed a rotation on a combined stroke, neurology and geriatric ward.

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