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CASE REPORT

Varicella zoster vasculopathy presenting as lateral medullary syndrome

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Introduction

Stroke is the second leading cause of death above the age of 60 years and the fifth leading cause in people aged 15 to 59 years old (WHO 2012). While established risk factors such as hypertension, diabetes, obesity, and hypercholesterolemia have been identified and are targets for stroke prevention, viral infections have also emerged as risk factors for stroke (Nagel et al. 2010). In the post-human immunodeficiency virus (HIV) era, not only acquired immunodeficiency syndrome (AIDS) but other opportunistic infections like cytomegalovirus (CMV) and varicella zoster virus (VZV) have been implicated and also proven as causative factors of stroke. This needs to be looked into diligently in patients who present with atypical history of stroke or an infective prodrome preceding stroke. Infections being causative of vasculopathy have been shown in a recent case series (Gilden et al. 2009). We report an interesting case presenting with posterior circulation stroke following zoster rash, which improved with definitive treatment, and discuss the current knowledge on the subject.

Case presentation

A 48-year-old female, right handed, working as midwife with no previous morbidity, presented with a rash in the left arm and chest for 7 days, headache and vomiting for 2 days, and sudden-onset numbness of the left half of the face and right arm, trunk, and leg with unsteadiness and swaying to the left while walking for the same duration. She also had intractable hiccups. There was no history of previous hospitalization/surgery/blood transfusion. On examination, she was moderately built, normotensive, afebrile, and with healing vesicular eruptions with some scabbing in left C8, T1, and T2 distribution. She was conscious, oriented, and cooperative. She had nystagmus to the left, with absent corneal reflex on the left side and impaired fine touch and pain in left V1 and V2 distribution. Palatal movements were sluggish with deviation of the uvula to the right. There was mild weakness of the left side with decreased pain and temperature in the right half of the body. The deep tendon jerks were brisker on the left side and left plantar was extensor. She had past pointing in the left side with truncal ataxia.

A provisional diagnosis of posterior circulation stroke–lateral medullary syndrome was made. A non-contrast CT head was normal. MRI brain revealed left lateral medullary infarct (Figs. 1 and 2). The MR angiography was normal. Cerebrospinal fluid examination revealed 40 cells (predominantly polymorphs) with raised protein (132 mg/dL) and low sugar of 49 mg/dL (corresponding blood sugar, 128 mg/dL). PCR analysis revealed no amplifiable herpes simplex virus (HSV) or VZV DNA or antibody to HSV, but an enzyme-linked immunosorbent assay of cerebrospinal fluid revealed an extraordinarily high titer (26.10 [normal, 0–3.4 mg/dL]) of anti-VZV IgG antibody.

She was given acyclovir and aspirin with symptomatic treatment for vomiting and hiccups. Her further workup revealed positive serology for HIV, her CD4 count being 211/μL. Thus, a final diagnosis of herpes zoster with left lateral medullary syndrome with VZV-associated vasculopathy with AIDS was made.

She was treated with acyclovir in divided doses as infusion over 1 h for 14 days combined with prednisone 60–

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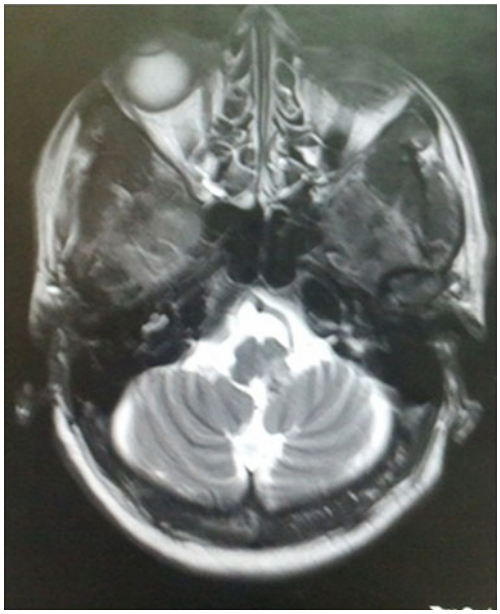

Fig. 1 T2 axial image showing hyperintense signal in the left medullary area including the left inferior cerebellar peduncle

80 mg/day for 3–5 days along with institution of antiretroviral therapy. She had complete recovery of her deficits over the next 2 months.

Discussion

The clinical diagnosis of VZV vasculopathy is usually based on a history of recent zoster rash followed by neurologic symptoms and signs; imaging abnormalities indicating cerebral ischemia, infarction, or hemorrhage; angiographic evidence of narrowing or beading in cerebral arteries; and a CSF pleocytosis (Nagel et al. 2008). In a young patient presenting with zoster and complications, the clinician should investigate for an underlying immunocompromised condition including HIV and also ask if the patient has had chickenpox at less than 4 years of age (since these patients can present with early zoster). VZV vasculopathy patients do not always have VZV DNA in CSF, but diagnosis can be confirmed by finding anti-VZV antibody in CSF, along with reduced serum/CSF ratios of VZV immunoglobulin G (IgG) compared to albumin or total IgG. Even when VZV vasculopathy develops months after zoster, antiviral treatment is often effective (Gilden et al. 2002). In a case series of 14 subjects, 100 % had anti-VZV IgG antibody in their CSF, whereas only four (28 %) had VZV DNA (Nagel et al. 2007). Therefore, a positive PCR for VZV DNA in CSF is helpful, but a negative PCR does not exclude the diagnosis of VZV vasculopathy. Only when the CSF is negative for both VZV DNA and anti-VZV IgG antibody can the diagnosis of VZV vasculopathy be reliably excluded.

In transient cerebral arteriopathy of childhood, stroke is preceded by varicella in 44 % of cases (Braun et al. 2009). However, in adults, VZV vasculopathy is more common in immunocompromised than in immunocompetent individuals. Our patient did have a history of zoster rash preceding the vascular event, which suggested the probable etiology, but the involvement of posterior circulation was uncommon and she had a normal angiography. Large-vessel disease is most common in immunocompetent individuals, whereas small-vessel disease usually develops in immunocompromised patients. In some patients, both large and small vessels are involved (Mareedu et al. 2011). In immunocompromised adults, VZV infection of the CNS was detected in 1.5 to 4.4 % of autopsy cases (Gray et al. 1994). In 37 % of cases, there is no history of rash (Nagel et al. 2008). The association of varicella zoster and brainstem strokes has been described in a few case reports (Romero López et al. 1990; Ortiz et al. 2008; Patrick et al. 1995).

Our patient was also subsequently found to be HIV positive, and VZV vasculopathy was the first manifestation. VZV can present with a wide spectrum in immunocompromised and HIV-positive patients (Corral et al. 2003). HIV-infected patients with a history of AIDS or low CD4 cell counts have

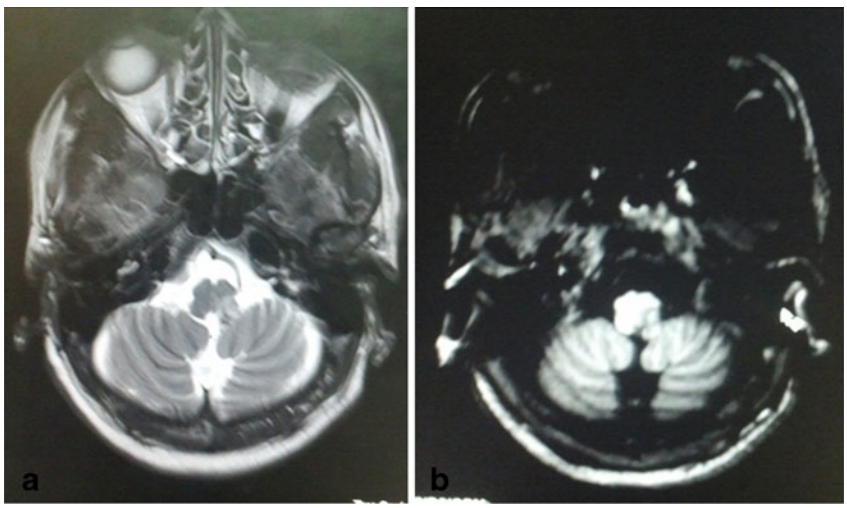

Fig. 2 **a** Axial Fluid Attenuation and Recovery (FLAIR) showing hyperintense signal in the left medullay area and **b** diffusion-weighted image showing a bright signal in the same area

impaired VZV-specific CMI responses and remain at risk for herpes zoster (De Castro et al. 2011). On the other hand, HIV per se and other opportunistic infections like CMV have also been implicated in vasculopathy (Cutfield et al. 2009). However, in an autopsy series, infarcts in HIV-infected patients are rare in the absence of cerebral non-HIV infection, lymphoma, or embolism (Connor et al. 2000). The titer of circulating antibody against CMV has been found to be higher in subjects undergoing vascular surgery for atherosclerosis than in matched control subjects (Adam et al. 1987).

Our case depicts an interesting presentation of both VZV vasculopathy presenting as a posterior circulation stroke and also the presenting feature of AIDS. In the post-HIV and antiretroviral era, early detection and treatment of both the above conditions is warranted for a better outcome.

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