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Case report

Varicella Zoster Virus Vasculopathy; An HIV adult presenting with multiple strokes

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ABSTRACT

VZV vasculopathy has been associated with granulomatous vasculitis where there is vessel wall damage and transmural inflammation. VZV vasculopathy has been previously called granulomatous angiitis, VZV vasculitis or post-varicella arteriopathy. Intracerebral VZV vasculopathy can occur in children and adults, either after primary infection or after viral reactivation. Where-as varicella primary infection is a common cause of stroke in children, in adults there is an increased risk of stroke after herpes zoster. Here we present a 38-year-old immunocompromised patient who presents to us with multiple cerebral infarcts post primary infection and imaging showing distribution similar to those in children.

Introduction

Varicella zoster virus, a ubiquitous DNA virus, is a member of the human herpesviruses that usually causes varicella (chicken pox) as a primary infection. It remains in the body as a latent infection which can be reactivated and cause herpes zoster (shingles). Varicella infection is a common childhood illness, and the incidence of herpes zoster increases with age and immunosuppression. Herpes zoster is the reactivation of the varicella-zoster virus which has remained dormant within the dorsal root ganglia. Herpes zoster, also known as shingles, is a painful yet self-limiting dermatomal rash. In certain cases, VZV can travel centrally and cause neurological complications such as ischemic strokes, transient ischemic attacks, aneurysms, dissection, and hemorrhages, in both children and adults [1]. In adults, VZV vasculopathy is more common in immunocompromised than in immunocompetent individuals. Studies showed that in HIV infected individuals, VZV vasculopathy occurred more frequently late in the course of infection when there was significant CD4+ depletion [2]. X The risk of stroke is increased after herpes zoster, most commonly in those with ophthalmic-distribution zoster occurring within the first 3 months after the zoster infection, however the risk is still present for up to one year after the herpes zoster [3].

We are presenting a case of a retroviral patient with low CD4 with recurrent strokes after a primary infection.

Case presentation

A 38-year-old Omani female, known case of retroviral infection since 2004. Was initiated on treatment in 2009, with poor compliance to her retroviral treatment and defaulted multiple times to medications and follow up appointments. Her latest viral load was 3,740,000 with a CD4 cell count of 80.

She initially presented to a local health center with a vesicular rash noted on the face, chest, and arms. This was her first attack of varicella after contact with her nephew. She is seen again in a regional hospital 3 months after the primary infection with 2 days history of left sided weakness, left sided upper motor neuron facial palsy and tongue heaviness. She had mild left sided upper limb and lower limb weakness of 4/5, normal reflexes, and tone. Initial CT was done which did not show acute infarct. No MRI was done as it was not available in that hospital. She was discharged after 2 days as symptoms resolved and was kept on dual antiplatelets.

She continued to have poor compliance to her antiretroviral

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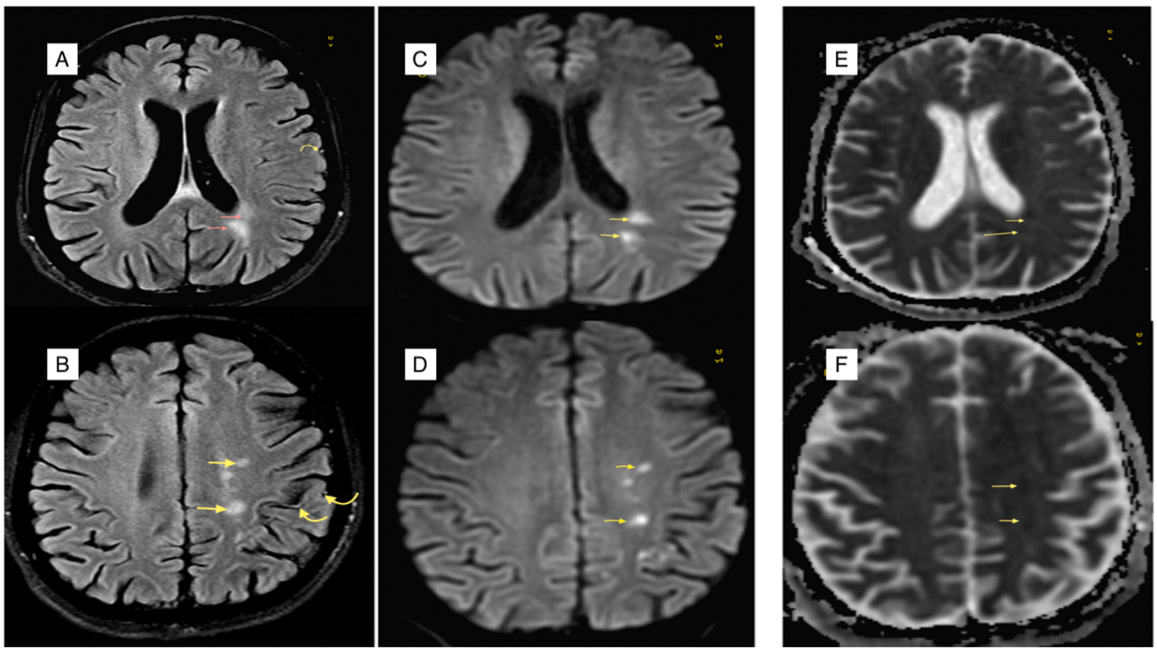

Fig. 1. A and B) axial cut FLAIR image of the brain shows left posterior parietal periventricular white matter and left centrum semiovale foci of FLAIR hyper-intensities (yellow straight arrows). FLAIR hyper intense signal in the cortical branches of the left MCA indicating slow flow or occluded vessel (curved arrows). (C, D) axial Diffusion Weighted images b1000 images showing high signal intense foci at the site of FLAIR hyper intensities corresponding with iso to slightly low signal intensity on Apparent Diffusion Coefficient map (E, F) representing mild restricted diffusion and are suggestive of multiple small subacute infarcts.

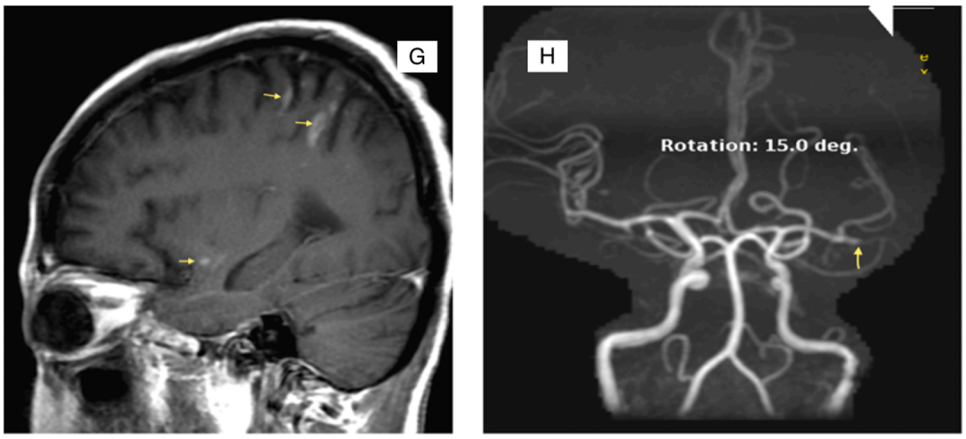

Fig. 2. (G) sagittal post contrast image of the brain shows multiple enhancing foci mainly cortical in the left insular cortex and the left parietal lobe. (H) Time of flight MRA 3D reconstructed image shows abrupt cut off in the left inferior division of the left MCA with attenuated cortical branches of the superior division of the left MCA.

treatment. She was seen again in our hospital 1 year after the primary infection with worsening cough and new onset seizure. There was no documented neurological deficit. Initial non-contrast CT showed no evidence of acute insult. MRI, as seen in Fig. 1, showed multiple foci of mild restricted diffusion seen in the left centrum semiovale, left parietal periventricular white matter, left temporal periventricular white matter and in the right insular cortex, all suggestive of subacute infarcts. Other foci of high FLAIR signal intensity noted in the left parietal cortex, left precentral gyrus and the frontal lobe and insular cortex, representing infarcts more than 10 days old. MRA, as shown in Fig. 2, confirms abrupt cut- off of the inferior division of the left MCA just distal to its origin. There is evidence of irregularities of the superior division of the right MCA with attenuated right opercular branches of the right MCA. An ECHO and EEG were done, both were unremarkable.

We see her again after 1 month with 5 days history of right sided weakness, right upper motor neuron facial palsy associated with slurred speech. Her neurological examination showed normal reflexes and power. There was right mouth angle drop with tongue deviation to the right side. A non-contrast CT was reported as: interval development of hypodensity at left lentiform nucleus corresponding to MCA territory likely to represent acute/subacute ischemic infarction.

Her final admission prior to diagnosis of VZV vasculopathy she initially presented to a regional hospital with history of fever and loose motions. She was treated symptomatically and discharged home. She presented again to the regional hospital with similar symptoms and generalized weakness, labs were collected, and patient was advised admission however she refused and left against medical advice. She was called back to the hospital as her blood culture grew Salmonella species. She was admitted for 2 days, received IV antibiotics and patient signed herself out against medical advice. She then presented to our emergency with symptoms of generalized weakness, mostly worsening of right sided weakness so she was directly referred to our Neurology center

hospital. She was assessed by the Neurology team; she was found to have mild right sided upper and lower limb weakness 4/5 and no further neurological deficit. She had no meningeal signs and no fever. An initial non-contrast CT showed: Multiple small hypodensities are seen in the white matter of the Lt frontal region, Lt centrum semioval, Lt corona radiata, Lt posterior periventricular region, likely chronic infarcts. Questionable hypodensity seen in Lt hemipons [artifact vs small infarct]. A CT angiogram was done and showed occlusion of the inferior division of M2 segment of left MCA [an old finding]. A lumbar puncture was done which initially showed WBC < 2, RBC < 2, CSF protein 28.9, CSF glucose 2.8 and CSF India Ink showed no cryptococcus was seen.

She was then referred to our care, and we proceeded to continue treatment for Salmonella treatment while arranging for an MRI. She was improving generally, symptoms wise however the only obvious symptom she had was emotional lability. We then received a call from central lab that her CSF culture and viral screen was all negative except for a positive VZV DNA PCR.

With this finding, she was initiated on IV Acyclovir and later Prednisolone.

Further input from Neurology team was treat with one antiplatelet agent, in view of the micro-hemorrhage, and no further workup for stroke in young was required as the most likely cause is VZV vasculopathy. She received IV Acyclovir for 18 days and then discharged on oral Valaciclovir for 3 days to complete a course of 3 weeks.

Discussion

It has been widely documented that the most serious complication of zoster is stroke [4] due to VZV vasculopathy, which was first described over 50 years ago [5]. There is relatively very little data on primary varicella infection leading to stroke, the few cases reported are mostly amongst the pediatric age group [6] and few other studies reported cranial nerve palsies as prodromal symptoms of VZV- associated stroke [7].

The exact incidence and prevalence of stroke caused by VZV is unknown, in children it was found that VZV had preceded stroke in 44 % of those with transient arteriopathy of the cerebral circulation [8] while in adults with immunosuppression VZV infection of the central nervous system was detected in 1.5–4.4 % of autopsy cases [9–11].

VZV vasculopathy is diagnosed with detection of VZV IgG or VZV DNA PCR in CSF specimens [12] and radiologically; abnormal findings have been detected on brain MRI, lesions at the grey-white matter junction are typical but abnormalities can be deep cortical in location, involving white/grey matter [13]. Treatment recommendations are a 14- day course of intravenous acyclovir and steroids [1].

Our rare case report here is of an adult immunocompromised patient who developed multiple episodes of stroke, without antecedent cranial nerve involvement, a few months after a primary varicella infection. Looking meticulously into the patient's history, her presenting complaints and her clinical background status, in addition to the workup done such as a lumbar puncture and CSF samples sent for analysis, including viral PCR, MRI brain as reported above; are all suggestive of subacute infarcts due to VZV.

Thus, we conclude that VZV vasculopathy should be considered as one of the rare differentials in patients presenting with neurological signs and symptoms following VZV infection whether it be primary or zoster with or without the typical rash.

CRediT authorship contribution statement

Writing – original draft, M.B. and S.C.; Writing – review & editing, N. P., F.K. and Z.B.; Resources, H.A. and Z.F.; Visualization, A.H.

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Institutional Review Board Statement

Not applicable.

Ethical approval

N/A.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Conflicts of Interest

The authors declare no conflict of interest.

Data Availability Statement

Not applicable.

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