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(CASE REPORT)

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Varicella zoster virus infectious vasculopathy: Case report

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Abstract

A very particular case is described, due to its low frequency and potential effect on morbidity and mortality, of a 20-year-old male with human immunodeficiency virus (HIV) infection with neurological manifestations including first focal epileptic seizure, right amaurosis, left hemiparesis and ipsilateral hyperreflexia. Magnetic resonance imaging revealed absence of contrast filling in the right internal carotid artery, old infarction in the territory of the right middle cerebral artery and laminar necrosis of the left caudate nucleus. The cytochemical analysis of the cerebrospinal fluid was normal, however, the polymerase chain reaction (PCR) was positive for the Varicella Zoster Virus (VZV). The patient was receiving acyclovir and corticosteroid with adequate response to treatment. It is understood then that VZV vasculopathy is part of a broad group of differential diagnoses and that molecular tests in cerebrospinal fluid (CSF) should be included as a sensitive and specific tool.

Keywords: Varicella-zoster virus; Cerebrospinal fluid; Ischemic stroke; Acyclovir; Case report

1. Introduction

The diagnosis of infectious vasculopathy caused by varicella-zoster virus (VZV) is often complex. This is because the typical cutaneous manifestations seen in primary infection are not commonly found in these types of pathologies, and the condition is rarely suspected, as it is neither a frequently described nor common complication of this microorganism[1]. We present the case of a young immunosuppressed patient who consulted due to a florid neurological syndrome. Upon systemic review, cutaneous lesions suspected to be caused by varicella-zoster virus infection were identified, leading to complementary studies, including a lumbar puncture with normal cerebrospinal fluid (CSF) cytochemical findings but a positive PCR result for VZV. What makes this case unique and remarkable revolves around the clinical manifestations, complemented by the finding of a positive PCR for VZV in CSF, suggesting that in such cases, patients may present with normal CSF cytochemical studies and still have an active infection. Therefore, whenever the clinical scenario allows, this entity should be suspected and treated in a timely manner.

Varicella-zoster virus (VZV) is a double-stranded DNA alpha herpesvirus that causes varicella, usually as a primary infection in children, and later causes herpes zoster in adults. After the primary infection, the virus remains latent throughout the nervous system, primarily residing in neurons of the trigeminal ganglia, dorsal root ganglia, and autonomic ganglia, including those located in the enteric nervous system[2].

After a highly variable period, which may last several decades, the virus can reactivate from its latent state. This reactivation is secondary to either primary or secondary immunosuppression, predisposing the patient to one of the most common conditions: herpes zoster. However, herpes zoster is not the only manifestation of viral reactivation. It

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has been described that reactivation can lead to vasculopathy, with productive viral infection of cerebral vessels[2,3]. Moreover, studies have shown that patients with herpes zoster have a higher risk of ischemic stroke as well as cardiovascular conditions[4].

We present the case of a young patient living with human immunodeficiency virus (HIV) who developed neurological manifestations, radiological cerebral involvement, and detection of VZV in cerebrospinal fluid (CSF).

2. Clinical Case

A 20-year-old man with a history of HIV infection (C2 classification) and a previous ischemic stroke, attributed to treated meningovascular neurosyphilis, he showed up at the emergency department with his first focal seizure. A systemic review revealed erythematous, pruritic, and vesicular lesions covering his entire body and a history of periocular blistering lesions on the right side, followed by visual acuity impairment related to retinal detachment.

Clinical examination revealed right-sided amaurosis, left-sided hemiparesis, ipsilateral hyperreflexia, and a positive left Babinski sign, without meningismus or neck stiffness at admission.

Magnetic resonance imaging (MRI) of the brain with contrast showed an area of frontotemporal encephalomalacia and gliosis on the right side, consistent with previous findings, absence of contrast opacification in the right internal carotid artery, and an area suggestive of laminar necrosis in the left caudate nucleus (Figure 1).

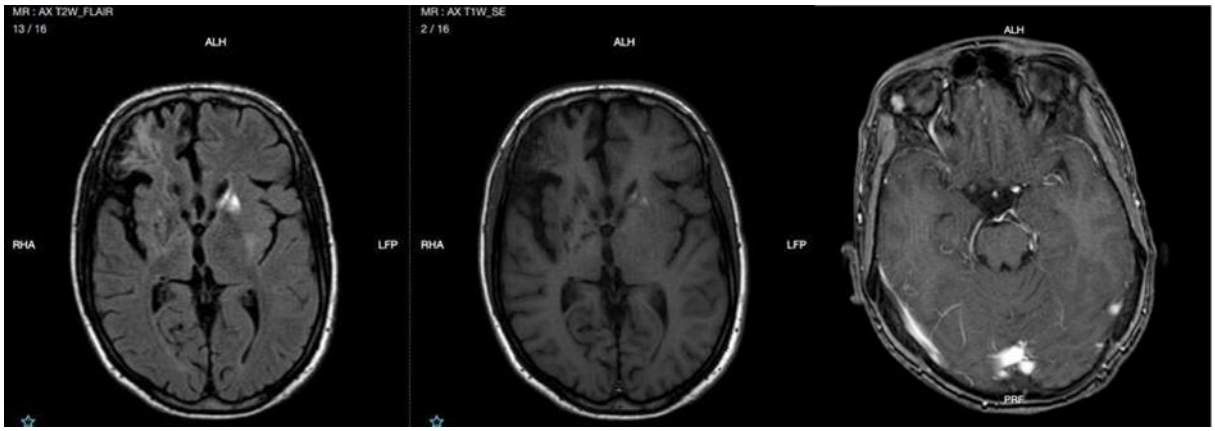

Figure 1 Contrast-Enhanced Brain MRI

A) FLAIR sequence. B) T1 sequence. Gliotic and malacic lesion in the right frontal lobe and right basal nucleus, as well as in the left basal nucleus. Hyperintensity in the left basal nucleus on T1 sequence, suggestive of laminar necrosis. C) Contrast-enhanced T1 sequence. Absence of opacification after contrast administration in the cavernous portion of the right internal carotid artery. No evidence of contrast-enhancing lesions

A lumbar puncture was performed, revealing an opening pressure of 16 cmH2O and normal physicochemical characteristics of the CSF. However, a microorganism identification panel detected VZV by PCR (Table 1).

Table 1 Biochemical Parameters

Parameter	**Result**
Color / Appearance	Clear and colorless
White Blood Cell Count	5/mm^3
Proteins	40.1 mg/dl
Glucose	51.7 mg/dl
Culture	Negative

Others	Gram stain, India ink stain, and ADA: Negative
Simultaneous identification of multiple pathogens by molecular testing/ CSF FilmArray	
Meningitis / Encephalitis panel	Positive
VZV Virus	Detected

Additionally, serology for varicella-zoster virus was requested, with results showing IgG antibodies >1500 (positive) and IgM: 0.2 (negative).

Given the suspicion of right internal carotid artery occlusion, a cerebral digital subtraction angiography (DSA) was performed, documenting a complete occlusion of the right internal carotid artery in its petrous segment, agenesis of the A1 segment of the left anterior cerebral artery, and significant distal vasospasm, with a reduction in lumen diameter of up to 50% in the left middle cerebral artery.

Considering the ischemic cerebral and ocular involvement, as well as the detection of VZV in CSF, a diagnosis of cerebral vasculopathy secondary to VZV infection was established. Treatment was initiated with intravenous acyclovir at 10 mg/kg every 8 hours for 14 days, a short course of corticosteroids with prednisolone at 1 mg/kg/day for 7 days, as well as anticonvulsant and antiplatelet therapy. During hospitalization, the patient showed good clinical response and tolerance to medical management, without complications or adverse effects related to treatment, due to strong adherence to the strategies outlined by the medical team.

3. Discussion

Varicella-zoster virus infection is common and exclusive to humans, affecting more than 95% of the U.S. population. It generally follows a benign course during primary infection but becomes clinically significant and has a worse prognosis during reactivation, occurring in up to 50% of infected patients, particularly in cases of immunosuppression and advanced age. Reactivation in the central nervous system can lead to pathological vascular remodeling and stroke, making VZV reactivation an important risk factor for infectious vasculopathy[5].

Reactivation of latent infections with possible vascular involvement should be suspected in all immunosuppressed patients with neurological deterioration or events of unclear etiology, particularly in those with a recent history of varicella-zoster virus infection, even in the absence of characteristic dermatological lesions from the primary infection[5,6].

The incidence of VZV reactivation is not well documented; however, an association with HIV infection has been noted. Among the 33.4 million people with HIV worldwide, it is estimated that 16% have subclinical VZV infection, and up to 11% may develop ocular and central nervous system disorders, including vasculopathy[7].

This condition encompasses a broad spectrum of vascular abnormalities, including infarcts, aneurysms, pseudoaneurysms, and dissections, which can present with diverse clinical manifestations such as altered consciousness, headache, or neurological deficits, which may be acute or progressively chronic, leading to significant morbidity and healthcare costs[8].

Although infections are considered uncommon causes of stroke, they should be included in the differential diagnosis, especially in young and immunocompromised patients. In a retrospective study conducted in South Africa by Marais et al., involving 87 young adults with HIV infection and ischemic stroke, 37% had evidence of VZV reactivation in the central nervous system. Thus, infectious vasculopathy should always be considered as a potential cause of ischemic stroke in this patient group[9].

Regarding definitive diagnosis, a cross-sectional observational study analyzing 14 cases of VZV vasculopathy found that detecting anti-VZV IgG antibodies was a more sensitive indicator than detecting amplifiable VZV DNA in CSF[9], with sensitivity reaching 80-95% and specificity greater than 95% in immunocompromised patients[10]. Although PCR is useful for detecting VZV in CSF, a negative result does not exclude the diagnosis of vasculopathy. Only when both VZV DNA and anti-VZV IgG antibodies are negative in CSF can VZV vasculopathy be ruled out[11].

Cases of infectious vasculopathy have been reported in the literature. Table 2 describes the different clinical and imaging characteristics of these reports. As in our case, they occurred in immunosuppressed patients, primarily affecting the anterior cerebral circulation, with a variable clinical presentation.

Table 2 Reported Cases of Patients with Infectious Vasculopathy Due to Varicella-Zoster Virus

Authors (Year) - Country	Age	Status	Comorbidities	Primary Infection Diagnosis	Clinical Manifestations	Arterial Involvement	Associated Vasculopathy
Elmståhl et al. (2023) - Sweden[12]	30	Alive	Multiple sclerosis	4 months	Headache, recurrent spasms, hyperreflexia	Right ICA and A1 segment of ACA	Subacute ischemic events in the right basal ganglia and right cerebral peduncle
Liberman et al. (2014) – USA[13]	42	Alive	SLE	2 months	Headache, neck stiffness	M3 segment of the right MCA, left MCA	9 mycotic aneurysms
Saraya et al. (2006) – Japan[14]	36	Alive	HIV	-	Seizures, neck stiffness, dyscalculia, amnesia, monoparesis	Peripheral MCA	Cerebral aneurysms, angioedema
Ahmad et al. (2003) – USA[15]	52	Alive	None	1 month	Headache, hemiplegia, altered consciousness	ICA, ACA, MCA, PCA, Basilar	Mild bilateral diffuse arterial narrowing with multilobar infarcts
Gilden et al. (2002) – USA[16]	71	Alive	Chronic lymphocytic leukemia	2 months	Hemiparesis	Right ACA occlusion and left ACA stenosis	Infarct in the right pericallosal distribution
Takao Hoshino et al. (2019) – Japan[17]	63	Alive	Rheumatoid arthritis	13 days	Hemiplegia	-	Multiple acute infarcts
-	51	Alive	Type 2 diabetes mellitus	24 days	Dysarthria, ataxia, hypoesthesia	No vascular alteration detected	Left lateral medullary infarct
-	38	Alive	SLE	4 months	Dysarthria, ataxia, hemiparesis	Basilar artery stenosis	Ventral pontine infarct
-	54	Alive	SS, Arthritis	1 month	Nausea, vomiting	No vascular alteration detected	Acute infarct in the left lenticulostriate artery territory

Abbreviations

- SLE: systemic lupus erythematosus;
- HIV: human immunodeficiency virus;
- DMT2: type 2 diabetes mellitus;

- SS: systemic sclerosis;
- MCA: middle cerebral artery;
- ACA: anterior cerebral artery;
- PCA: posterior cerebral artery;
- ICA: internal carotid artery.

Patient Perspective

A year before being diagnosed with VZV vasculopathy, I suffered a stroke that left me physically incapacitated. Although I was hospitalized and correctly diagnosed and treated at the time, my skin remained affected with recurrent rashes, making me feel that my illness was still active.

Immediately after receiving acyclovir treatment, I started to feel better. Not only did my body recover, but my spirit improved as well, as I was finally diagnosed and possibly cured of this infectious disease.

4. Conclusion

Infectious vasculopathy, including VZV infection, though considered a rare cause of stroke, should be included in differential diagnoses, especially in immunosuppressed patients such as those with HIV infection. For diagnosis, detecting anti-VZV IgG antibodies in CSF is one of the most sensitive tools, supplemented by a microorganism identification panel via PCR whenever possible.

This case highlights the importance of early identification of this condition in high-risk populations, with a specific clinical approach aimed at implementing timely and individualized therapeutic strategies that impact morbidity and mortality while reducing the risk of complications affecting the patient's quality of life.

Compliance with ethical standards

Disclosure of conflict of interest

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Statement of ethical approval

The authors declare that no human or animal experiments were conducted for this research. The text does not contain any patient-identifying data.

Author Contributions

All authors contributed equally to manuscript preparation, reviewed, and approved the final version of the article.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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