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Ischemic and hemorrhagic stroke secondary to HSV-1 encephalitis

Fiorella Sotomayor Villanueva
University of Maryland, fiorellasv89@gmail.com

Mounika Angirekula
Saint Agnes Hospital, mounika.angirekula@ascension.org

Martha Baker
Saint Agnes Hospital, martha.baker1@ascension.org

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Abstract

Background HSV is the most common cause of encephalitis, and although rare, it can lead to cerebrovascular manifestations such as ischemia or hemorrhage, which can sometimes overlap. The mechanism behind cerebrovascular pathology is not well understood, and further research is needed to fully comprehend it.

Case Report A35-year-old patient that presented with AMS, focal deficit and meningeal signs. Patient was admitted with diagnosis of meningoencephalitis and lumbar puncture (LP) revealed Herpes simplex type 1. Given focal deficit, MRI of the brain was performed and showed presence of multifocal ischemic stroke with associated petechial hemorrhage. After being started on proper therapy, mental status returned to baseline and she no longer presented focal deficit.

Conclusion Herpes encephalitis, although rare, it can lead to cerebrovascular manifestations. Delay in diagnosis can lead to significant morbidity or even mortality.

Keywords

Herpes simplex virus, herpes encephalitis, ischemic stroke, hemorrhagic stroke, infectious stroke.

Conflict of Interest Statement

None of the authors have any conflict of interest with this manuscript.

Cover Page Footnote

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Introduction

Herpes simplex virus (HSV) is a member of the Herpesviridae family, and it is the cause of acute viral encephalitis in 50-70% of cases. Both HSV-1 and HSV-2 can cause encephalitis, affecting predominantly the temporal lobe and the limbic system. Cerebrovascular disease can occur as a complication of multiple central nervous infections. However, the relationship between cerebrovascular complications and HSV is not well studied. We present a not previously reported case of encephalitis with multifocal brain ischemia and associated hemorrhage due to HSV-1.[1,2]

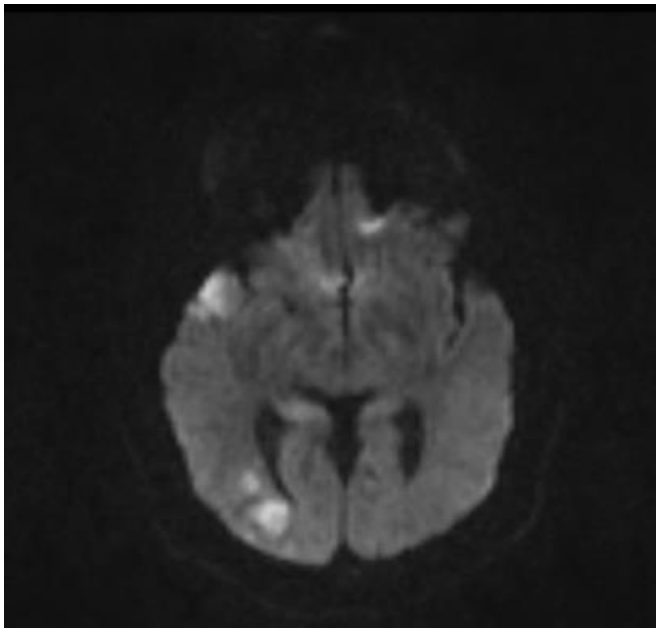
Case presentation

35-year-old African American female with past medical history of human immunodeficiency virus (HIV) on highly active antiretroviral therapy (HARRT) that arrived at the emergency department from a group home for altered mental status (AMS). Per group home staff, the patient had been complaining of left sided weakness, which led her to have 2 recent falls, frontal headache and increased confusion. Vital signs on admissions were positive for fever, with temperature of 103.0, heart rate of 110 bpm, respiratory rate of 22, with blood pressure of 126/76 mmHg and oxygen saturation of 98% on room air. Physical exam was positive for dry mucous membranes, nuchal rigidity, and somnolence and 3/5 left side weakness in both proximal and distal muscles groups of upper and lower extremities; the rest of the physical exam was unremarkable. Initial laboratory exam showed WBC of 12.0 (4.0-11.0 K/uL), Sodium of 127 mEq/L (136-145 mEq/L), bicarbonate of 10mEQ/L (22-32mEq/L), glucose of 422 mg/dL (65-105mg/dL), beta-hydroxybutyrate of 4.30mM (<0.3mM), 3+ ketones in urine, and lactic acid of 4.90mmoL (0.5-1.6mmoL). EKG showed sinus tachycardia and CXR was unremarkable, but head CT showed hypoattenuation in the right temporal lobe as well as small regions of hypoattenuation in the right frontal lobe and right occipital lobe. Patient was started on therapy for bacterial and viral meningitis and started on diabetes ketoacidosis (DKA) protocol. Lumbar puncture revealed clear CSF with WBC of 137 (0-10), glucose of 162 mg/dL (40-70mg/dL) and protein of 59 mg/dL (15-45 mg/dL) and less than 5 RBC/mm^3; BioFire revealed Herpes simplex 1 infection. Furthermore, MRI/MRA brain was done and showed multiple acute infarcts seen within the right frontal lobe, right centrum semiovale, the right parietal cortex, the right temporal lobe, and the right occipital lobe with associated cytotoxic edema and small petechial hemorrhages seen in the right posterior parietal/frontal region; no signs of vasculitis were noted on MRA (Figure A-D). Transthoracic echocardiogram showed a normal ejection fraction, no wall motion abnormality and a negative bubble study. Patient improved and returned to baseline mental

status and had no focal deficit by the end of her hospitalization. She was ultimately discharged on a 21-day course of IV Acyclovir and on Keppra for seizure prophylaxis.

Figures A and B. Diffusion weight imaging (DWI) showing multiple acute infarcts in the right frontal, parietal, temporal and occipital lobes.

A.



B.

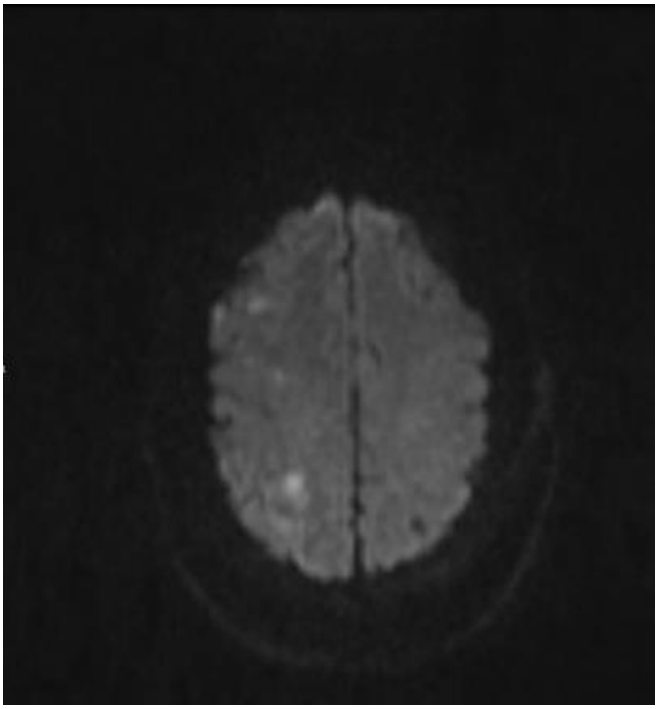


Figure C. MRI brain showing presence of acute Infarct with cytotoxic edema in the parietal and occipital lobe.

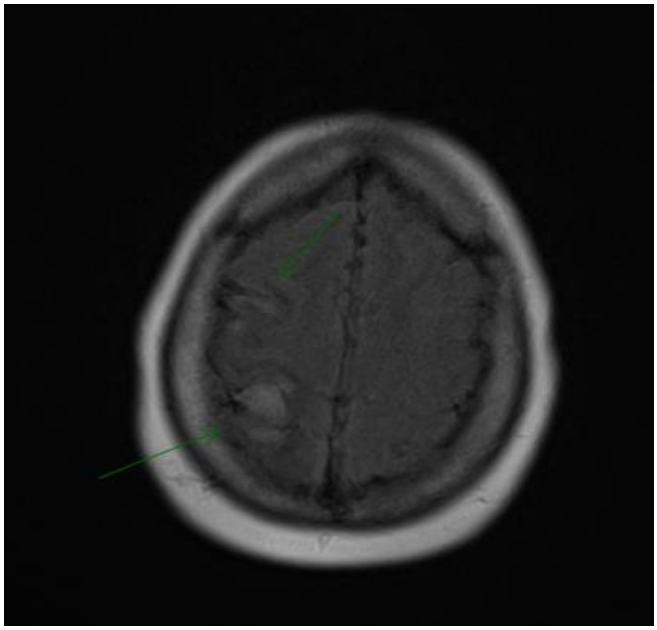
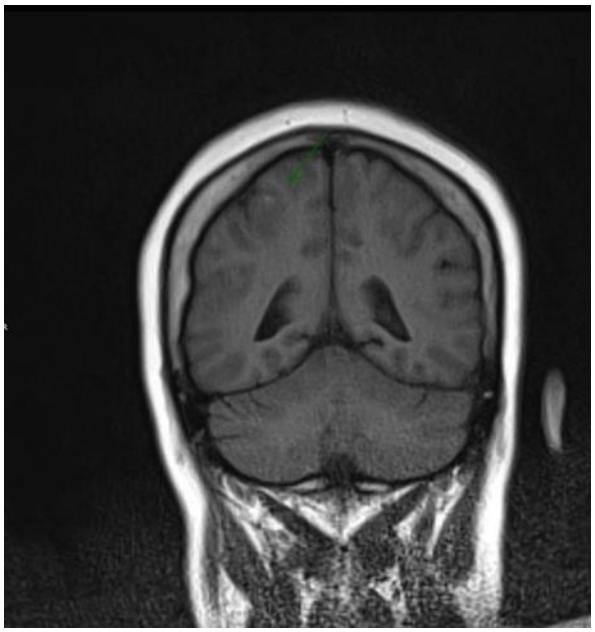


Figure D. Brain MRI (coronal view) showing gyriform petechial high signal seen in the right posterior frontal/parietal region in the zone of acute infarct.



Discussion

Our patient presented with AMS, fever and meningeal signs concerning for and ultimately diagnosed with HSV-1 meningoencephalitis. In addition, the report of focal weakness prior to admission led us to pursue brain imaging studies, which revealed multifocal ischemia with presence of petechial hemorrhage. *Snider et al* also reported a case of hemorrhagic and ischemic stroke secondary to HSV meningitis, however, unlike our patient, it was caused by HSV-2.[1] Similarly, *Zhang et al* reported a case of a 68-year-old female patient that presented with a holocephalic headache, left sided numbness and brief period of hallucinations that was admitted for stroke after MRI showed three areas of acute stroke.[2] After 3 days, she developed slurred speech and right-sided facial droop; given MRI did not show worsening ischemia, LP was done and the patient was diagnosed with HSV-2 encephalitis.[2] After proper treatment was started, symptoms improved and she remained neurologically intact by discharge.[2]

Mak et al reported a case of HSV-2 infection presenting as multifocal hemorrhagic stroke.[3] In their report, the hemorrhage was located in the right cerebellar and right frontal lobe, and was initially attributed to hypertension and the patient was discharged on hypertension medication.[3] Shortly after discharge, the patient's condition deteriorated, which led to readmission and further work up and ultimate diagnosis of HSV infection.[3] The delay in diagnosis and treatment led to a poor outcome, and eventually the patient died.[3]

Hauer et al conducted a systematic review of published cases of cerebrovascular manifestations of HSV between January 2000 to July 2018.[4] They analyzed a total of 36 manuscripts comprising 38 patients, 10 of which presented with cerebral infarction.[4] The patients with ischemic manifestations were predominantly women (70%), the initial clinical presentation was encephalitis in 50% of patients, and stroke and meningitis 30% and 20% respectively.[4] Brain infarction was detected on the first brain imaging in 50% of cases, and hemorrhage preceded infarction in 10% of cases.[4] Furthermore, multiple ischemic lesions were found in 90% of cases.[4] Lastly, HSV-2 was present in 50% and there was evidence of vasculitis in 63% of patients.[4] On the other hand, they analyzed 26 patients with hemorrhagic manifestations, with 25 having parenchymal hemorrhage and only one having petechial hemorrhage.[4] Hemorrhage was seen predominantly in men (55%), and, unlike patients with ischemic manifestation, patients with hemorrhage were more likely to be diagnosed with HSV-1 (59% of cases).[4] What distinguishes our patient from the patients in this study and other studies which were reviewed is that she is female with overlapping ischemic and hemorrhagic manifestations (which has not previously been reported), although predominantly ischemic, and was diagnosed with HSV-1.

The mechanism behind the development of ischemia and hemorrhage in the setting of HSV encephalitis remains unclear. It is postulated that ischemia is primarily caused by vasculitis, although, as discussed by *Hauer et al*, it may not always be evident in imaging studies. Moreover, the mechanism of herpes simplex induced vasculitis is also unclear and there is no evidence that treatment such as steroid would be helpful. On the other hand, hemorrhage is thought to be caused by inflammation of vessels, leading to edema, inflammatory vascular remodeling and finally necrosis and hemorrhage.[4] Timely diagnosis of HSV infection is important, as delay can lead to significant morbidity and even death; furthermore, it is considered a treatable cause of stroke and hence proper treatment can lead to reversal of neurological deficit such as in our patient.

Conclusions

HSV is the most common cause of encephalitis. Although rare, it can lead to cerebrovascular manifestations such as ischemia or hemorrhage, or like in the case of our patient, both. Further studies need to be done to have a better understanding of the pathogenesis, but also a high index of suspicion is also needed to identify a potentially treatable cause of stroke.

Conflict of interests

None of the authors have any conflict of interest with this manuscript.

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