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POST HERPETIC BASAL GANGLIA STROKE IN AN ADOLESCENT GIRL: BRIEF REVIEW OF LITERATURE AND A CASE REPORT

Izehiuwa Gertrude Enato, FMCPaed[1,2]**; Paul Ehiabhi Ikhurionan,** FWACPaed[2,3]

[1]Department of Paediatrics, College of Medical Sciences, Edo State University, Uzairue, Edo State, Nigeria
[2]Institute of Child Health, University of Benin, Benin City, Edo State, Nigeria
[3]Department of Childhealth, University of Benin Teaching Hospital, Benin City, Edo State

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Corresponding Author:
Enato Izehiuwa Gertrude
Department of Paediatrics, College of Medical Sciences, Edo State University, Uzairue, Edo State, Nigeria
+2348035673681
izehiuwa.enato@edouniversity.edu.ng; izyenato@gmail.com

ABSTRACT: Herpes simplex encephalitis (HSE) is a leading cause of sporadic, non-epidemic viral encephalitis in children and adults. We report a very rare case of HSE complicated by multiple ischaemic infarcts involving both basal ganglia in a 15-year-old female adolescent admitted with complaints of headache and fever, irrational behavior and seizures. On clinical examination patient was unconscious with signs of raised intracranial pressure, right hemiparesis and meningeal irritation. She had elevated temperature (38.7°C), and anaemia (packed cell volume of 25.0%). Magnetic resonance imaging showed features of Multiple non-enhancing hypodensities in both basal ganglia with mild dilation of the 3rd and lateral ventricles. She was managed as a case of Post-encephalitis Basal ganglia stroke. The patient subsequently developed a repeat vascular event, with suspected haemorrhagic transformation after 4 weeks and succumbed to the illness.

Keywords: Basal ganglia stroke, Herpes simplex encephalitis, encephalitis, haemorrhagic transformation of ischaemic stroke.

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INTRODUCTION

Encephalitis is a severe neurological syndrome characterized by inflammation of the brain parenchyma. It presents a significant diagnostic challenge due to its diverse aetiologies, ranging from infectious to autoimmune causes. Clinical manifestations vary widely, including altered mental status, seizures, focal neurological deficits, and behavioural changes. The diagnostic process is often complex, requiring careful evaluation of clinical, laboratory, and neuroimaging features to distinguish encephalitis from other mimicking conditions.[1-2] A distinct subset of encephalitis cases involves abnormalities in the thalamus and/or basal ganglia, which can be identified through advanced neuroimaging techniques such as MRI.[3] These regions of the brain are particularly vulnerable due to their high metabolic demand and dense vascular supply, making them susceptible to ischaemic events following inflammatory processes.[4] Ischemic stroke following encephalitis in adolescents is rare but carries significant morbidity and mortality. This complication is believed to result from a combination of direct viral invasion, immune-mediated mechanisms, and vascular injury leading to thrombotic events.[5] The literature reports few cases of basal ganglia ischemic strokes secondary to encephalitis, particularly in younger populations, highlighting the need for heightened clinical vigilance and prompt intervention.[6] In this case, we present a 15-year-old girl who developed a basal ganglia ischemic stroke following a severe episode of encephalitis. The report discusses her clinical presentation, including acute onset of hemiparesis and altered consciousness, which prompted a diagnostic workup. This included an MRI, revealing characteristic findings of both encephalitis and subsequent ischemic stroke. The management of such cases involves a multidisciplinary approach, integrating antiviral therapy, immunomodulation, and anticoagulation, tailored to the underlying etiology

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and pathophysiology.[7] Despite aggressive treatment, the prognosis remains guarded due to the high risk of neurological sequelae, such as haemorrhagic transformation. This report underscores the importance of early recognition and comprehensive management to improve outcomes in adolescents with this rare but serious complication of encephalitis.

CASE REPORT

We present AA, a 15 year old girl, who presented to the emergency room with complaints of cough and catarrh of 14 days; headache and fever of 7 days duration; irrational behavior, neck stiffness and inability to walk of 3 days and progressive unresponsiveness to calls, and seizure noticed at presentation.

Headache was said to be severe, the nature and location of the headache could not be ascertained by caregiver; headache was transiently relieved by paracetamol. Fever was low grade, intermittent, and relieved by acetaminophen tablets. Neck stiffness was characterized by extension of the neck with drooling of saliva. No seizures, no blurring of vision, no vomiting, no history of trauma, no use of hard drugs nor substance abuse. Caregiver claims she is not sexually active and she is not aware of her immunization record. Her mother died from a cerebrovascular accident (CVA) when she (index patient) was an infant; relatives could not recall the details of her mother's death. She was then adopted by her maternal grandmother. She was in her first year of senior secondary school; her performance level was graded as average with no specific concerns. She attained menarche at 12 years and her last menstrual cycle started 2 days prior to presentation.

At onset of illness, she was given antimalarial and cefuroxime tablats purchased from a patent medicine store. However, at onset of unresponsiveness to calls, she was brought to our

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facility for expert care. On examination, she was acutely ill looking, pale, with severe neck stiffness, unconscious with Glascow coma scale (GCS) of 6/15. She had focal neurologic signs (partial seizures, tremor, chorea, long tract signs, and aphasia) with muscle weakness on the right side of the body; her muscle power on the right side was Grade 1, as she had just flicker of muscle contractions in her right arm and lower limp; there was no facial palsy, but she was drooling saliva. Brudsinksy was positive and kernigs sign was not assessed (probably due to her comatosed state and right sided hemiparesis); she had features suggestive of raised intracranial pressure (occulomotor nerve palsy, with anisocoria). Her blood pressure was 99/67 mmHg; pulse rate was 124bpm, regular and bounding. She was tachypnoeic, not dyspneoic and breath sounds were vesicular with no added abnormal sounds.

An assessment of Meningo-encephalitis with cerebral abscess was made; a differential diagnosis of intracerebral space occupying lesion, possibly infratentorial tumour was also added. An urgent Magnetic resonance imaging (MRI) and other ancillary blood tests were requested; a lumbar puncture for cerebrospinal fluid analysis was deferred. She was managed as an unconscious patient, with regular turning, and prevention of pressure ulcers. Feeding via nasogastric tube with fortified pap was commenced, and hydration was maintained as well. Intravenous ceftriaxone, mannitol, phenobarbitone, chloramphenicol and antimalarial therapy were also administered.

The Full blood count showed leukocytosis with neutrophillia, anaemia (packed cell volume of 25%) and thrombocytopenia. Her calcium level was low, other electrolytes, urea and creatinine was essentially normal. Her prothrombin time (PT), and activated partial thromboplastin time (APTT) were prolonged. Blood film for malaria parasite confirmed parasitaemia; her urine microscopy and culture yielded no growth. Her blood sugar was

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normal and her Haemoglobin genotype AA. MRI done showed: Multiple non-enhancing hypodensities in both basal ganglia with mild dilation of the 3rd and lateral ventricles, the 4th ventricle appeared normal [Figure 1]. The usual symmetry of brain anatomy without evidence of mass effect or significant volume loss was maintained, there was no evidence of focal cerebral parenchymal mass or haemorrhage. The brain stem and cerebellum show no evidence of focal lesion or hematoma. The cerebral sulci and basal cisterns were normal. The cranial vault and skull base showed no signs of fracture, sclerotic or lytic bone lesions, with no extra-axial collections. There was collection in the frontal, maxillary and ethmoidal sinuses [Figure 1]. The other paranasal sinuses, middle ear clefts and mastoid air cells were unremarkable [Figure 1]. A conclusion of Post- menigoencephalitic Basal ganglia ischaemic stroke was made by The Paediatric Neurologist, and then patient was managed for stroke. Antibiotics, antimalarial, fluid therapy, and anti-seizure therapy were continued; while acyclovir, Vitamin B, C and E, calcium, blood transfusion and physiotherapy were commenced. Due to the presence of thrombocytopenia, repeated anaemia (following blood transfusion), and in view of haemorrhagic transformation, the use of antithrombotic agents was withheld.

Over the next three weeks, she improved significantly as she gained consciousness fully, but her speech and swallow reflex were poor, thus gavage feeding was continued, with intermittent direct oral feeds. Muscle power on the right side of the body improved to grade 4, but she could not walk. Guardian refused professional physiotherapy but performed other forms of therapy.

On the 4th week on admission, she was noticed to be suddenly unresponsive, with irregular eye movement. On examination, she had rotary eye movement, GCS of 3/15, she was pale, in

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cardiovascular shock (pulse was fast and thready, blood pressure was 80/40mmHg), her respiration was slow but regular and oxygen saturation was 90-95%. An assessment of a second Basal ganglia CVA with haemorrhagic transformation was made. Immediate resuscitation commenced with antishock (using 0.9% normal saline), supplemental oxygen and vaso-pressors. Despite all resuscitative efforts, her condition continued to deteriorate and she succumbed to the illness.

DISCUSSION

Cerebrovascular complications associated with herpes simplex encephalitis have been well-documented in adults, particularly in those with underlying cardiovascular diseases.[8] However, acute ischemic strokes following herpes encephalitis are exceedingly rare in children.[9] Most paediatric cases of herpes simplex virus (HSV) infection are either asymptomatic or present with mild symptoms such as fever.[10] Hemorrhagic transformation is one of the most common complications following herpes encephalitis, often leading to significant neurological deficits.[11] However, in this particular case, the patient developed fever but notably did not exhibit any signs of hemorrhagic transformation at onset, and this was confirmed by a Brain MRI. However, the second cerebro-vascular event, which was fatal, was most likely a haemorrhagic type, following haemorrhagic transformation. The common complications of herpes encephalitis in children are typically non-specific neurological symptoms, and cerebrovascular events like ischemic stroke are very rare. In this case, we reported a rare case of an ischaemic stroke and bilateral basal ganglia infarction leading to hemiplegia in an adolescent following viral encephalitis.

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The pathophysiologic mechanisms leading to cerebral infarction following viral encephalitis are not yet fully elucidated. However, several potential mechanisms have been proposed, including direct viral invasion, immune-mediated vascular injury, and secondary inflammatory responses that result in endothelial damage and thrombosis.[12] In this case, the HSV infection likely precipitated an inflammatory cascade that led to stroke. Specifically, the patient developed cerebral infarction three days after exhibiting fever from the infection, indicating rapid disease progression. Post-infection, herpes simplex virus (HSV) may trigger a cytokine cascade reaction and endothelial cell dysfunction, leading to an inflammatory response, thrombocytopenia, and coagulation abnormalities.[13] This could account for the thrombocytopenia and anaemia found from her complete blood count analysis at presentation. Damage to endothelial cells and coagulation dysfunction may result in the formation of microthrombi, which can subsequently cause ischemic stroke.[14] Furthermore, elevated inflammatory markers or other indicators of severe systemic involvement could signal the progression of herpes encephalitis into a severe and critical stage. Recently, Zhang et al. (2023) reported a case of acute heamorrhagic necrotizing encephalitis in a previously healthy child with herpes simplex infection, suggesting that even in the absence of underlying risk factors, HSV encephalitis in adolescent females can potentially lead to a fatal outcome as seen in this index case.[15] This highlights the need for vigilant monitoring and aggressive treatment, even in patients who initially appear to be at low risk for severe complications.

Early recognition and treatment of encephalitis are crucial in preventing severe complications and improving outcomes. Common symptoms include fever, vomiting, headache, and lethargy, which occur in 80-100% of patients.[16] Seizures are reported in 40-60% of cases, while nuchal rigidity is present in 25-50% of patients.[17] Focal neurologic findings such as

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paresis, partial seizures, tremor, chorea, long tract signs, and aphasia are observed in 15-25% of cases.[18] These features, including focal neurologic signs were observed in our index case. Cerebrospinal fluid (CSF) analysis typically shows leukocyte counts ranging from 0-1,500 cells/mm³, with a lymphocytic predominance. Most cases report CSF leukocyte counts in the range of 50-500 cells/mm³, although approximately 30% of patients have counts outside this range.[19] Our patient was unusual in that the focal neurologic deficits commonly reported with viral encephalitis, such as hemiparesis, were not transient. This differs from typical cases, where deficits often resolve quickly. In a study on herpes encephalitis, 9% (14/151) of patients developed acute hemiparesis.[20] Of these 14 patients, 12 experienced rapid recovery, suggesting that the focal weakness in some cases may have been postictal in etiology.[20] Research indicates that central nervous system infections caused by herpes simplex virus predominantly affect medium-sized vessels, often leading to infarctions in the basal ganglia.[21] This pattern is consistent with the infarction locations observed in our case, supporting the hypothesis that herpes simplex virus has a predilection for causing cerebral infarctions in the basal ganglia of paediatric patients.

Identifying specific predictors for the early detection of cerebral infarction as a complication of herpes encephalitis could significantly improve the prognosis in affected children. Studies have suggested that a marked increase in proinflammatory markers, such as C-reactive protein (CRP) and interleukin-6 (IL-6), is associated with a hypercoagulable state related to herpes simplex viral infection.[22] Additionally, certain factors like haemoglobin genotype SS (sickle cell anemia), thrombocytopenia, and elevated D-dimer levels have been identified as potential risk factors for cerebral infarction in the context of viral infections.[23] In our case, D-dimer levels were not assessed, but platelet levels were below normal; prothrombin time (PT)

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and activated partial thromboplastin time (APTT) were deranged, suggesting a possible risk for thrombosis. Routine laboratory tests, including complete blood count (CBC), platelet count, PT, APTT, and fibrinogen levels, are crucial in identifying hypercoagulable states in patients with herpes encephalitis.[24] Thrombocytopenia, in particular, might be an important marker of cerebral infarction risk in patients with herpes encephalitis. Therefore, for children, especially adolescents presenting with persistent fever lasting more than three days and any abnormalities in platelet counts, heightened vigilance for hypercoagulability and the potential for cerebral infarction is warranted. Timely coagulation function tests, along with early utilization of cerebral and neurovascular imaging, such as MRI or Computerised tomography angiography, can be critical in assessing the risk of stroke and potentially improving the prognosis of the disease.[25] Prompt intervention based on these findings could reduce the risk of long-term neurological sequelae in pediatric patients.

The use of antiviral therapy, such as acyclovir, is the standard of care for HSV encephalitis and has been shown to significantly reduce mortality and morbidity when initiated promptly.[26] However, in cases where stroke occurs as a complication, additional therapeutic interventions are necessary to optimize patient outcomes. Management may include anticoagulants to prevent further thromboembolic events, anti-inflammatory therapies to reduce cerebral edema, and continued antiviral treatment to control the viral infection.[27] Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) may also be considered to protect against secondary vascular damage.[28] Early administration of aspirin has been associated with lower mortality rates in patients with stroke secondary to HSV encephalitis, possibly due to its antithrombotic effects.[29] On the other hand, studies have shown that early administration of aspirin increases the risk of haemorrhagic

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transformation.[30-31] In this case, in view of a possible haemorrhagic transformation, the use of aspirin was withheld; our treatment strategy encompassed acute phase management, including measures to reduce intracranial pressure and anti-inflammatory treatments, alongside supportive therapies such as hydration and nutritional support. During the recovery phase, rehabilitation, including physiotherapy and speech therapy, was crucial in helping the patient regain lost functions and improve overall outcomes.[32] Furthermore, it is important to highlight the latest consensus from the Paediatric Infectious Diseases Society on the management of herpes encephalitis in children, which emphasizes the importance of early antiviral therapy, close monitoring for complications such as cerebral infarction, and the integration of multidisciplinary care, including rehabilitation services, to enhance recovery.[33] Notably, this report has some limitations. First, it is based on a single case study, limiting generalizability. Second, cerebrospinal fluid analysis was deferred at onset of illness due to raised intracranial pressure and focal neurologic signs; also a repeat MRI could not be done to confirm our diagnosis of a haemorrhagic transformation of post-encephalitis ischemic stroke.

CONCLUSION

This case underscores the critical importance of vigilant monitoring and swift intervention in children, particularly those with prolonged fever, presenting with encephalitis, due to the risk of severe complications such as cerebral infarction. Effective management requires prompt treatment to reduce intracranial pressure and inflammation, alongside continuous rehabilitation, which are essential for recovery. Additionally, clinicians must maintain a high level of suspicion for the possibility of recurrent strokes.

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