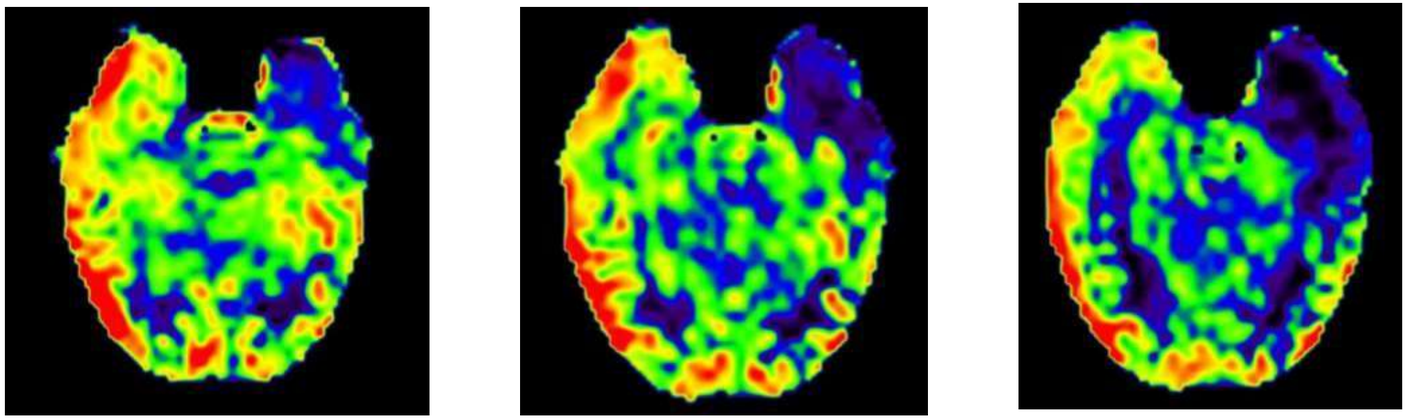
EPSTEIN-BARR VIRUS-INDUCED THROMBOTIC THROMBOCYTOPENIC PURPURA IN A PATIENT WITH REFRACTORY SEIZURE DISORDER: A DIAGNOSTIC CHALLENGE



DARSHAK SANYAL, DR. WEENA STANLEY MD MRCP, DR. SHASHIKALA T.S MD, DR. ARJUN NIDAMBUR BALLAL MD

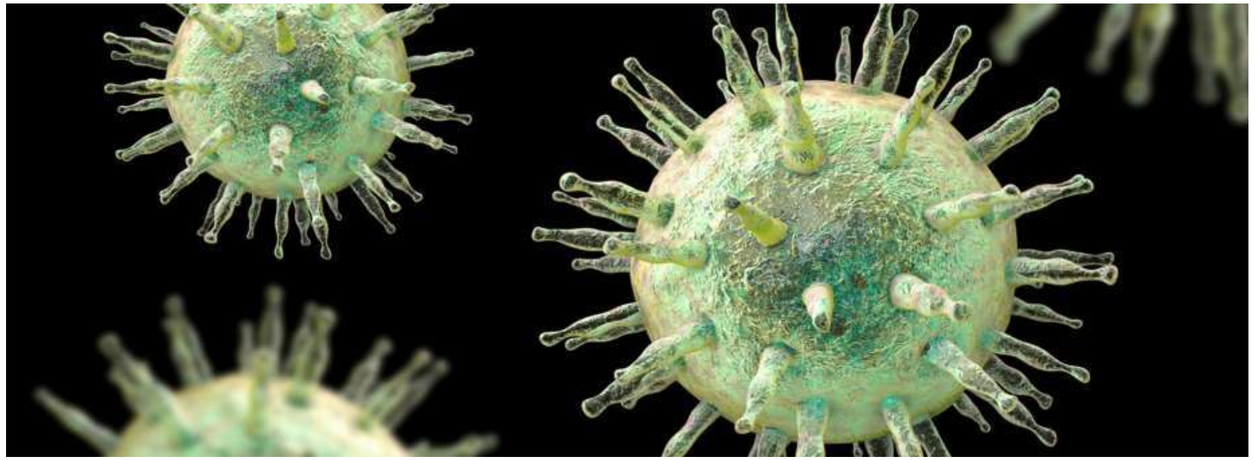
DEPARTMENT OF GENERAL MEDICINE

KASTURBA MEDICAL COLLEGE, MANIPAL

KARNATAKA, INDIA

INTRODUCTION

- Epstein-Barr virus (EBV) is a common viral infection, often presenting as infectious mononucleosis. Patients usually develop fatigue, fever, sore throat, swollen lymph nodes and classically present with splenomegaly. In rare cases, however, EBV can lead to severe complications such as thrombotic thrombocytopenic purpura (TTP), a life-threatening condition marked by microangiopathic hemolytic anemia and thrombocytopenia.



HISTORY

A 61-year-old female with a known history of chronic epilepsy since 2003, presented to the hospital with multiple episodes of tonic seizures occurring between 9:30 PM and 12:30 AM.

The seizure episodes were followed by post-ictal confusion and drowsiness, which persisted until her arrival at the hospital. The patient also reported shortness of breath at the time of presentation. She also became unresponsive soon after.

Her past medical history is significant for epileptic seizures, for which she underwent a lobectomy in 2011. Despite surgical intervention, she has continued to experience seizures and is on long-term antiepileptic medications, including Levetiracetam, Valproate, and Carbamazepine.

The patient was initially admitted to the cardiology department for evaluation of a suspected Non-ST Elevated Myocardial Infarction (NSTEMI). Despite successful management of her cardiac condition, the patient remained unresponsive, prompting a neurology consult.

Due to her low GCS score, she was transferred to the internal medicine department and intubated.

EXAMINATION

Patient was not conscious, cooperative, well oriented to time, place and person.

Moderately built and well-nourished.

PR - 99BPM

BP - 90/56mmHg

RR - 24CPM

No pallor, icterus, clubbing, cyanosis, lymphadenopathy, edema, koilonychia.

Afebrile

GCS - 9/15

Systemic Examination findings were unremarkable

INVESTIGATIONS AND MANAGEMENT

1. Seizure Disorder and Neurological Management:

- Investigations:

- Initial and repeat EEGs were performed due to unresponsiveness following the seizures. The first EEG showed severe encephalopathy, and a later EEG revealed left frontotemporal epileptiform discharge and bifocal epileptiform discharges.

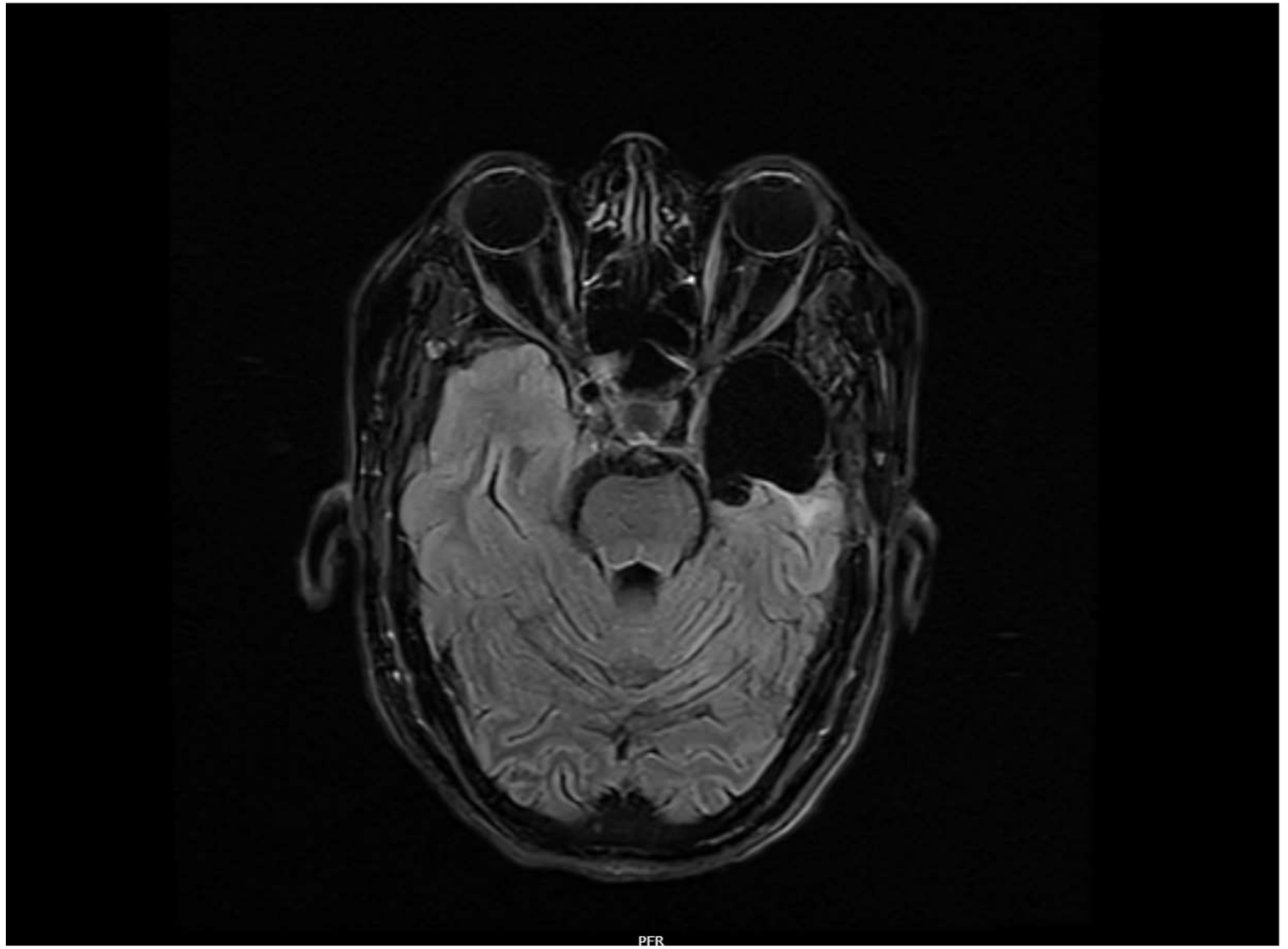
- Management:

- The patient was on chronic antiepileptic therapy with Levetiracetam, Valproate, and Carbamazepine.

- Due to concerns of drug-induced liver injury, Valproate was discontinued, and Midazolam and Topiramate were added to manage seizure activity.

- Antiepileptics were optimized throughout her stay, with close monitoring through EEGs.

- Despite these measures, the patient continued to experience episodes of tonic-clonic movements and tongue bites.



Contrast MRI of brain shows encephalomalacia, with surrounding gliotic changes in the left temporal lobe causing exvacuo dilatation of temporal horn of left lateral ventricle

2. Cardiac Issues and Management:

- Investigations:

- The patient was initially admitted for a suspected Non-ST Elevation Myocardial Infarction (NSTEMI).
- Coronary angiography revealed mild coronary artery disease and myocardial bridging of the Left Anterior Descending (LAD) artery.
- Echocardiogram (ECHO) showed right atrial (RA) and right ventricular (RV) dilatation with normal left ventricular ejection fraction (LVEF).

- Management:

- The cardiac issues were managed conservatively with no intervention required for the mild coronary artery disease.

3. Hepatic Dysfunction and Management:

- Investigations:

- The patient developed fulminant hepatitis, suspected to be multifactorial (?drug-induced, ?ischemic, ?viral).

- Liver function tests (LFTs) showed elevated liver enzymes, and INR was elevated.

- A hepatitis panel was sent to evaluate for viral causes, revealing positive Epstein-Barr Virus (EBV) serology.

EBV Viral Load- (Positive) 2.35 X 10^3 IU/mL

- Management:

- In response to suspected drug-induced liver injury, N-acetylcysteine (NAC) infusion was given for 3 days.

- Vitamin K was administered to correct the elevated INR, which normalized after 3 doses.

- Valproate was discontinued due to suspected liver injury.

4. Coagulation and Thrombocytopenia Management:

- Investigations:

- The patient had persistent thrombocytopenia, with a peripheral smear showing 5-20% spherocytes and 2% schistocytes, indicating hemolysis (Microangiopathic Hemolytic Anemia)

- D-dimer was elevated (>9), but lower limb Doppler ruled out deep vein thrombosis (DVT).

- ADAMTS13 antibodies were sent to evaluate for Thrombotic Thrombocytopenic Purpura (TTP), and LDH was elevated (>1000), consistent with hemolysis.

- Management:

- Unfractionated heparin (UFH) was stopped after ruling out DVT.

- Persistent bleeding from the oral cavity after tongue bites and episodes of coagulopathy prompted further evaluation for a hypercoagulable state.

5. Renal Function and Acute Kidney Injury (AKI):

- Investigations:

- The patient developed acute kidney injury (AKI) during the course of her hospital stay, which was initially improving.

- A repeat renal function test (RFT) during the later stages showed worsening renal function in the context of hypotension.

- Management:

- Supportive care was provided for the AKI, with close monitoring of renal function.

6. Infectious Disease Evaluation and Management:

- Investigations:

- The patient had two episodes of low-grade fever. Procalcitonin and C-reactive protein (CRP) were monitored, both showing a decreasing trend, suggesting no active bacterial infection.

- Blood cultures and endotracheal (ET) cultures were sterile.

- Management:

- Prophylactic antibiotics with piperacillin-tazobactam were continued.

- In view of possible meningitis, ceftriaxone was added at meningitis dosing.

7. Supportive and Critical Care:

- The patient required intubation due to poor Glasgow Coma Scale (GCS) score.

- Hypocalcemia and low vitamin D levels were corrected.

- A lumbar puncture was planned for evaluation of persistent poor sensorium, but it was deferred due to coagulopathy and thrombocytopenia.

FINAL OUTCOME AND DIAGNOSIS

- The patient developed hypotension, requiring escalating doses of noradrenaline for hemodynamic support.
- She went on to experience two cardiac arrests. Cardiopulmonary resuscitation (CPR) was administered according to ACLS guidelines, but the patient was declared deceased after the second arrest.

- The ADAMTS13 factor activity levels were found to be moderately reduced with mildly elevated ADAMTS13 inhibitor levels, confirming the diagnosis of Thrombotic Thrombocytopenic Purpura.

DISCUSSION

- Thrombotic thrombocytopenic purpura (TTP) is a rare and life-threatening condition characterized by thrombocytopenia, microangiopathic hemolytic anemia, neurological abnormalities, renal dysfunction, and fever, though not all features are always present [1]. The pathophysiology typically involves a deficiency of ADAMTS13, a protease responsible for cleaving von-Willebrand factor (vWF), leading to the accumulation of large vWF multimers, platelet aggregation, and microvascular thrombosis [2].
- In this case, the patient's history of refractory seizures complicated the diagnosis. The persistent seizures and associated encephalopathy initially suggested a neurological origin, delaying the recognition of TTP. While neurological symptoms, including seizures, are known in TTP, the severe and refractory nature of her seizures complicated the diagnostic process [4].

- TTP can be triggered by various factors, including infections, autoimmune diseases, malignancies, and medications [5]. The association between EBV and TTP is rare but documented, with EBV potentially triggering an immune response that produces autoantibodies against ADAMTS13 [6, 7]. In this patient, the diagnosis of TTP became more apparent after laboratory findings indicated hemolysis and thrombocytopenia, coupled with positive EBV serology.

- Empirical treatment for TTP is crucial while awaiting ADAMTS13 testing, as delays can result in significant morbidity and mortality [8]. Management typically involves plasma exchange to replenish ADAMTS13 and remove autoantibodies and ultra-large vWF multimers from circulation [9]. Immunosuppressive therapies, such as corticosteroids or rituximab, are often used to inhibit autoantibody production [10]. Unfortunately, despite aggressive management, the patient's condition continued to deteriorate, leading to her death. This case underscores the importance of early recognition and treatment of TTP, particularly in patients with complex presentations involving conditions like EBV infection and refractory seizures [6].

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THANK YOU