



MORNING REPORT

WHEN A FEVER TURNS DEADLY: HERPES
SIMPLEX ENCEPHALITIS IN THE ELDERLY

Ayla Pelleg, MD; Shahla Baharlou, MD

Dr. Pelleg (Ayla.pelleg@mssm.edu) is a clinical educator and practicing geriatrician and palliative care physician at the Icahn School of Medicine at Mount Sinai in the Brookdale Department of Geriatrics and Palliative Medicine in New York. Dr. Baharlou (Shahla.baharlou@mssm.edu) is a clinician educator and a practicing geriatrician at the Icahn School of Medicine at Mount Sinai in the Brookdale Department of Geriatrics and Palliative Medicine in New York.

An 89-year-old female presented to clinic with a sore throat and weakness for one day. She was incidentally found to have a fever of 101.3°F. She denied confusion or urinary symptoms. Past medical history included atrial fibrillation, hypertension, hypothyroidism, cholelithiasis, and mild cognitive impairment. Patient denied sick contacts. She had traveled to Connecticut one day prior to presentation. Physical exam revealed a well appearing older woman with a slow, wide-based gait; euthymic, non-anxious affect, and tangential speech. Labs included: white blood cell count (WBC) 8.1 (WBC 4.5-11 $\times 10^3/\mu\text{L}$) with 59.5% neutrophils (neutrophils % 40-78%), platelets 141 (platelets 150-450 $\times 10^3/\mu\text{L}$), potassium 3.1 (potassium 3.5-5.2 MEQ/L), and sodium 132 (sodium 135-145 MEQ/L). Chest X-ray was unremarkable. The patient's weakness and fever persisted the next day. She was admitted to a hospital at home program for intravenous fluids with presumed upper viral respiratory infection and dehydration. Using an interdisciplinary team approach, our urban academic center's hospital at home program cares for patients with acute illnesses, such as pneumonia, cellulitis, congestive heart failure exacerbations, in their home by providing intravenous support, oxygen, X-rays, labs, and daily medical visits. This program has decreased readmission rates, caregiver burden, costs, and improved clinical outcomes.¹

Serious illnesses in older patients often present atypically. Due to homeostasis, treatable infections in older adults with complex medical problems or frailty can become sentinel health events. When evaluating older adults with fever, it is critically important to consider a broad differential diagnosis, including meningitis and encephalitis, while investigating the cause of presenting symptoms.

On day three, the patient was referred to the emergency department (ED) for ongoing fever and altered mental status (AMS). In the ED, she was awake but not

alert, did not follow simple commands, and had nuchal rigidity. Labs included: WBC 12.6 with 87.3% neutrophils, platelets 131, potassium 3.2, and sodium 136. CT head showed chronic microvascular changes and parenchymal volume loss without hemorrhage or infarct. Multiple attempts for bedside lumbar puncture (LP) were unsuccessful. She was started on acyclovir, vancomycin, cefepime, and ampicillin for presumed meningitis. On day four, the patient became more altered and agitated with 101.5°F fever and WBC count of 13. Urgent Interventional Radiology (IR) guided LP showed clear cerebrospinal fluid (CSF), glucose 66mg/dL (glucose 40-70 mg/dL), protein 108.2 mg/dL (protein 15-45 mg/dL), RBC 280/ μL (RBC 0/ μL), and WBC 12/ μL (WBC 0-5/ μL) with 59% lymphocytes (lymphocytes $\geq 70\%$). Suspicion was high for Herpes Simplex Encephalitis (HSE); acyclovir was continued at 10mg/kg q12 hours.

Approximately 2-4 cases per million of HSE are reported worldwide annually.² HSE can cause significant morbidity and, without treatment, mortality rates are as high as 70%.³ HSE diagnosis can be challenging, particularly in older patients, resulting in potentially dangerous treatment delay. HSV PCR is a rapid CSF test that can quickly identify HSE; however, it has low sensitivity and specificity. CSF HSV culture is the gold standard diagnostic test, but the time requirement can delay diagnosis. Brain MRI is non-invasive and helpful as it can show hyperintensity in the temporal lobes, but is also limited by its low specificity.

On day five, the patient's mental status worsened. She was no longer responsive to verbal or tactile stimuli. Her respiratory status declined. She was intubated and admitted to the Intensive Care Unit (ICU). On day five, CT head showed a left middle cerebral artery (MCA) territory hyperintensity, depicting an acute infarct. On day seven, MRI brain showed hyperintensity signals along left insular cortex, anterior and medial left temporal lobes,

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and left cingulate gyrus. This MRI suggested HSE as well as an evolving left MCA infarct. On day eight, CSF polymerase chain reaction (PCR) detected HSV1- 5,400 copies/mL (HSV1 not detected <50 copies/mL), confirming the diagnosis of HSE.

HSE case reports are associated with ischemic strokes, intracerebral hemorrhage, and cerebral venous sinus thrombosis.⁴ Often originating as cerebral hematomas, cerebral hemorrhages due to temporal lobe vessel disruption occurred more in HSV-1 cases. HSV-2 cases were more frequently associated with infarcts and multifocal ischemia caused by large vessel vasculitis and related occlusions.⁵ The patient's initial CT head did not show an infarct. However, repeat imaging supported a diagnosis of acute MCA infarct, further complicating the clinical diagnosis. Cerebral hemorrhages and infarcts on imaging are not always seen initially and can have a radiographic delay of up to 10 days on average.

Due to worsening prognosis, goals of care were readdressed on day nine. Code status was updated to Do Not Resuscitate (DNR)/Do Not Intubate (DNI) on day 12. She was transferred to the palliative care unit for palliative extubation and died on day 20.

When older adults present with a fever, weakness, and AMS, a broad differential diagnosis should be considered, including encephalitis. If a workup is negative and a patient remains symptomatic despite empiric treatment, clinicians should maintain a heightened index of suspicion and avoid any anchoring biases because decompensation can occur rapidly.

References

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