Herpes simplex virus meningitis complicated by ascending paralysis

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A case of herpes simplex virus (HSV) meningitis complicated by ascending paralysis with almost complete recovery following antiviral treatment is reported. We present this case to illustrate the importance of including HSV-induced neuropathy in the differential diagnosis of acute neurologic symptoms following the viral illness.

Both types of herpes simplex virus (HSV) have been known to cause various neurologic syndromes, including meningitis (1–3). HSV-1 remains the most common cause of sporadic encephalitis, while HSV-2 infections of the central nervous system (CNS) mostly are restricted to aseptic meningitis. We report a case of HSV meningitis complicated by ascending paralysis caused by HSV to illustrate another neurological complication that can be treated with antiviral medication.

CASE DESCRIPTION

A 30-year-old African American woman presented to the emergency department (ED) with severe headache, fever (100.8°F oral), chills, photophobia, and tinnitus for 3 days preceded by several days of sore throat and nasal congestion. She was exposed to lead as a child and tested positive but never developed symptoms. She was cognitively intact. Her neck was markedly rigid. She had no skin or genital lesions. Her cranial nerves were intact. She ambulated to her car independently and without difficulty en route to the ED. She was admitted to the hospital and started on broad-spectrum antimicrobial coverage for suspected meningitis. Her initial workup at the ED and after admission is summarized in the *Table*. The cerebrospinal fluid (CSF) was positive for HSV by polymerase chain reaction with 540 viral copies/mL. A diagnosis of HSV meningitis was made, and antimicrobial coverage was narrowed to acyclovir.

Two days after admission, she developed bilateral lower-extremity weakness. She could barely break gravity on the left lower limb and could fight resistance briefly on the right side; she was weaker distally compared to proximally on both sides. Her bilateral deltoids were slightly weak, with full distal strength in the upper extremities. Her reflexes were brisk, including ankle jerks, and her toes were downgoing bilaterally. She had sensory loss to cold in her lower limbs to the knee with intact vibratory sensation. Within 2 weeks, the patient had significant improvement of weakness in the right lower extremity with complete return of sensation on that side. The left lower extremity, the more severely affected side, had only slight improvement in strength and had continued sensory deficits requiring inpatient rehabilitation.

A nerve conduction study (NCS) and electromyogram (EMG) 11 days after the onset of lower limb symptoms showed bilateral severe peroneal nerve axonal neuropathy, more marked distally and greater on the left than the right side. The remainder of the motor nerves tested (left median, left tibial, right tibial, and left ulnar) had velocities and amplitudes within the normal range. The F-waves were normally present in the left median and right tibial locations. EMG showed diffusely reduced recruitment in all muscles tested (left anterior tibialis, left gastrocnemius, left vastus lateralis, right anterior tibialis, and right gastrocnemius). A repeat NCS and EMG in the rehabilitation facility 35 days after symptom onset showed an overall improvement in amplitudes. She had a repeat CSF analysis for recurrent headache about 5 months after initial symptom onset, which was completely normal. One year after her initial presentation, she was fully ambulatory with rare sensation of tingling in her left leg. She was fatigued with prolonged exertion but did not require any assistive devices and had returned to work.

COMMENTS

Herpetic diseases were probably first described by Hippocrates (4). HSV-1 most commonly causes oral mucosal and facial skin lesions. HSV-2 is known for causing genital mucosal ulceration and is one of the most prevalent sexually transmitted infections worldwide. Persons with HSV-2 infection do not necessarily develop clinical disease, but most intermittently shed virus from the genital tract (5). The clinical manifestations of HSV infections are known to be diverse depending on the

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Table. The patient's test results upon initial workup

Test	Result
Cerebrospinal fluid	
Protein (mg/dL)	237
Glucose (mg/dL)	52
White blood cells (per µL)	975 (62% lymphocytes)
Gram stain	Negative
HSV PCR (copies/mL)	540
West Nile virus Ab	Negative
VDRL	Negative
Other labs	Negative for adenovirus, Epstein-Barr virus, varicella-zoster virus, coxsackie Ab, cytomegalovirus, cryptococcal antigen
Blood	
White blood cells (per µL)	14,800
Blood culture	No growth
HIV	Negative
Rapid plasma reagin	Negative
HHV6 PCR	Negative
Mycoplasma IgM	Negative
Lyme Ab	Negative
Monospot	Negative
TSH/Folate/B12	Within normal limits
Urine protein electrophoresis	Negative
Serum protein electrophoresis	Negative
Heavy metal screen	Negative
24-hr urine lead	Negative
Imaging	
CT scan head	Normal with possible maxillary sinuses
MRI brain/spine with contrast	No acute abnormalities

Ab indicates antibody; CT, computed tomography; HHV6, human herpesvirus 6; HSV, herpes simplex virus; MRI, magnetic resonance imaging; PCR, polymerase chain reaction; TSH, thyroid-stimulating hormone; VDRL, Venereal Disease Research Laboratory test.

organ system afflicted. HSV establishes latency in sensory ganglia following initial acquisition, causing an infection that persists for life (6, 7). Both HSV-1 and HSV-2 have been associated with various neurologic syndromes, including meningitis (1–3). The CSF profile typically includes a lymphocytic pleocytosis, a normal CSF glucose concentration, and elevated protein. HSV DNA detection by polymerase chain reaction in the serum and/or CSF is the most sensitive and specific method for detecting HSV meningitis (8).

Patients with HSV meningitis can develop peripheral nerve involvement. HSV-1 has been implicated in at least one case of atypical lumbosacral pain, weakness in ankle dorsiflexion, and scattered hyperesthesia in L4 to S1 dermatomes unilaterally (2). Paresis of the bladder and anus, paresthesia of the buttocks and lower limbs, and symmetrical weakness in the lower limbs lasting 1 to 9 days (9) have been described with HSV-2. One year after HSV-2 infection, some patients developed paresis of the bladder and rectum as well as lower-extremity weakness even after clinical signs of meningitis had resolved. Given the array of neurological morbidities associated with HSV CNS infections, during the acute episode and following resolution, causes of acute neuropathies from HSV should be considered along with other more common entities, such as Guillain-Barré syndrome (GBS) (2, 4, 9–11).

Mononeuritis multiplex (MNM) is used to group multiple disorders with varying mechanisms of injury that cause damage to two or more separate peripheral nerves. MNM typically presents asymmetrically initially. It can become symmetrical with progression of the disease and can include damage to sensory, motor, and autonomic nerves (12). Causes of MNM include vasculitis, diabetes mellitus, amyloidosis, paraneoplastic syndromes, rheumatoid arthritis, and systemic lupus erythematosus.

Another consideration in our patient was GBS given the apparent ascending nature of the weakness. GBS can be protean in its presentation. Due to its multiple variants, GBS can simulate symptoms of other pathological conditions, making it difficult to reach a definitive diagnosis. The most common and classic description is the ascending paralysis seen in acute inflammatory demyelinating polyradiculoneuropathy. The disease is characterized by symmetrical weakness starting in the lower limbs, with or without sensory symptoms, progressing over hours or days to the upper body. Lower cranial nerves might be affected, leading to oropharyngeal dysphagia and respiratory failure. Sensory symptoms often include deep aching pain in weakened muscles, loss of proprioception, and areflexia (13). Acute motor and/or sensory axonal neuropathy are subtypes manifesting with motor and sensory symptoms with severe respiratory and bulbar involvement. Rarer subtypes include the Miller-Fisher variant, which presents with ophthalmoplegia, sensory ataxia, and areflexia. The pharyngeal-cervical-brachial variant presents with proximal descending weakness. In milder forms of the disease, only the cranial nerves might be affected (14). Acute pandysautonomia is another variant of GBS, which manifests with sympathetic and parasympathetic failure (13–15). GBS is often treated based on history and clinical examination. Spinal fluid and electrophysiological findings are corroborative, but often nondiagnostic. These tests may be limited because of the disease stage and presence of preexisting neuropathies.

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