CLINICAL VIGNETTE

Feeling Stressed? A Case of Varicella Zoster Meningitis in a Healthy Young Adult

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Case Description

A 19-year-old immunocompetent woman with a history of migraines presented to the emergency room (ER) with severe headache for 1 day. She described gradual worsening of head pressure as "the worst headache ever" different in both severity and quality than her usual migraines. She also reported photophobia, phonophobia, chills, myalgias, generalized weakness, neck stiffness, nausea, and vomiting for the past day. She developed a vesicular rash on the right torso 2 days prior to presentation, which was diagnosed as herpes zoster at urgent care. She was prescribed valacyclovir but had not yet started taking the medication. Her mother reported that she received the varicella vaccine, but still developed a mild case of chickenpox as a child. The patient also reported she had been very stressed during college final exams week.

On presentation to the ER, the patient was afebrile with normal vital signs. On physical exam, she appeared fatigued but was awake, alert, following commands appropriately, with intact cranial nerves. Meningismus and photophobia were present. Skin exam, was remarkable for vesicular eruptions in the T3-T5 distribution on the right lateral posterior chest. Basic blood work and CT head were unremarkable. Lumbar puncture was performed in the ER with colorless cerebral sinus fluid (CSF). CSF showed 50 nucleated cells/uL, 14% neutrophils, 69% lymphocytes, 4 red blood cells/uL, 52 mg/dL protein, and 48 mg/dL glucose. Varicella zoster virus (VZV) was detected on the meningitis encephalitis pathogens panel and our patient was diagnosed with VZV meningitis.

She was started on high dose intravenous acyclovir at 10mg/kg three times a day, intravenous fluids, and admitted to the medicine service. Infectious disease and neurology were consulted. The patient had rapid improvement of her meningeal symptoms on IV acyclovir. By hospital day 5, her photophobia and headache completely resolved. She was discharged home on hospital day 6 with oral valacyclovir to complete a total 14-day course of antiviral therapy.

Discussion

VZV infections can cause two different disease processes. Primary VZV infection generally affects the younger population and causes chickenpox characterized by a diffuse vesicular rash. After initial infection, VZV gains access to sensory ganglia and usually remains dormant for decades. The average period of immunity by exposure to VZV was estimated to be 20 years.[1] VZV reactivation results in herpes zoster (HZ or shingles), a painful unilateral vesicular rash that typically occurs in 1-2 contiguous dermatomes. In some patients, VZV reactivation can cause central nervous system infections with meningitis and meningoencephalitis the most common. The mechanism of VZV reactivation is not fully understood, but is known to be affected by a decline in cell specific mediated immunity that is generally seen in the elderly and immunocompromised.

Our patient was young and otherwise healthy, but she reported significant stress during this time. Acute and chronic psychological stress is associated with decreased cell mediated immunity due to increased activity of the sympathetic nervous system and the hypothalamic pituitary adrenal axis. A nationwide population-based study in Denmark previously reported perceived psychological stress leads to increased HZ.[2] They used Cohen's Perceived Stress Scale (PSS) score (range 0–40), measuring chronic stress perceived by an individual in response to various demands of daily life stress. They found people reporting a high PSS score (ie. >18) had a 14% elevated relative risk of HZ after adjusting for age and sex.

VZV is responsible for about 11% of the 26,000-42,000 cases of viral meningitis that require hospitalization each year.[3] Our patient is a great example of VZV meningitis in an immunocompetent individual. Antiviral treatment is crucial and a delay in initiation or insufficient treatment can lead to severe neurological complications such as seizures, coma, cerebral vasculitis, myelitis, and cranial polyneuropathy to name a few. In accordance with the Infectious Disease Society of America (IDSA) guidelines, the recommended treatment for VZV meningitis/ encephalitis is IV acyclovir 10-15 mg/kg three times daily for 10-14 days due to the high acyclovir levels needed in CSF to treat.[4] It was previously reported that with oral administration, the acyclovir concentration in CSF is only 13 to 52% of that in plasma. When sustained and high concentrations of acyclovir in plasma are desirable, improved bioavailability can be achieved with valacyclovir. Valacyclovir is rapidly converted to acyclovir on the first pass through the liver and provides plasma concentrations three to five times higher than after administration of corresponding doses of oral acyclovir.[5] This improved bioavailability of valacyclovir in plasma results in higher concentrations in CSF. Given the complete resolution

of our patient's symptoms, she was discharged home on hospital day 6 with valacyclovir 1,000mg twice a day to complete a 14-day course at home. The theoretical risk of worsening was discussed with the patient but deemed acceptable considering the adverse effects of IV acyclovir, such as nephrotoxicity and continued hospitalization.

Conclusion

Our case highlights two unique lessons. First, VZV reactivation has traditionally been associated with the immunocompromised and elderly patient population. However, even young immunocompetent adults can be susceptible to severe cases of VZV reactivation especially associated with psychological stress, which has been shown to decrease cell mediated immunity.

Second, IV acyclovir is currently the only IDSA recommended treatment for VZV meningitis. Our case adds to the growing body of literature which suggests that patients can be safely transitioned from IV acyclovir to oral valacyclovir for the treatment of uncomplicated VZV meningitis.

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