88-Year-Old Man With Mental Status Changes and Vesicular Lesions

Hidong Kim, MD, PhD; Nicole M. Gentile, MD; and Thomas H. Poterucha, MD

An 88-year-old man with a remote history of rectal carcinoma after abdominoperineal resection, Parkinson disease treated with carbidopa-levodopa, and a recent diagnosis of left-sided parotitis presented to his local urgent care center with a 24-hour history of vesicular lesions involving the left side of his forehead. The following day, he began to experience confusion, visual hallucinations, urinary incontinence, and unsteady gait and presented for admission to the hospital.

On presentation to the emergency department, his vital signs were as follows: pulse rate, 80 beats/min; blood pressure, 134/51 mm Hg; oxygen saturation, 93% while breathing room air; respiratory rate, 18 breaths/min; and temperature, 37.0°C. He was awake and interactive and answered questions appropriately. Approximately 3 hours later on the general medicine ward, the patient appeared ill with altered mental status. He was obtunded, somnolent, minimally responsive to vigorous sternal rub, and unable to provide history. Bilateral periorbital edema and erythema along with vesicular and crusted lesions were noted predominantly on the left side of the forehead and scalp, with no lesions on the nose. Scattered lesions were also noted on the right side of the forehead, and crossing the midline on the trunk and back. The neck was rigid. He did not have photophobia, and his pupils were equal and reactive to light with bilateral conjunctival injection noted. No facial asymmetry was seen.

Computed tomography of the head revealed moderate preseptal and periorbital soft tissue swelling, greater on the left. No acute intracranial abnormalities were seen. Initial laboratory studies revealed the following (reference ranges provided parenthetically): white blood cell count, 9.6 × 10^9/L (3.5-10.5 × 10^9/L); hemoglobin, 12.0 g/dL (13.5-17.5 g/dL); serum creatinine, 1.1 mg/dL (0.8-1.3 mg/dL); alanine aminotransferase, 21 U/L (7-55 U/L); aspartate aminotransferase, 25 U/L (8-48 U/L); and total bilirubin, 0.3 mg/dL (≤1.2 mg/dL).

1. Which one of the following is the most likely etiology for this patient’s rash and mental status changes?
   a. Acute atopic dermatitis
   b. Varicella-zoster virus (VZV) infection
   c. Normal pressure hydrocephalus (NPH)
   d. Parkinson disease progression
   e. Bacterial meningitis

Vesicular and crusted lesions may be seen in inflammatory skin conditions, such as acute atopic dermatitis. Scaling is a more common presentation, but vesicular lesions can also be seen. The face is commonly affected in atopic dermatitis. Our patient’s neuropsychiatric symptoms, however, were not typical for atopic dermatitis.

Infectious etiology in the form of herpes zoster caused by reactivation of latent VZV infection was strongly considered because of the vesicular and crusted lesions distributed predominantly in a single dermatome. The patient’s skin lesions were seen mostly in the left cranial nerve (CN) V \textsubscript{1} dermatome. Varicella-zoster virus infections may also present with neuropsychiatric symptoms. The patient’s neurologic symptoms of confusion, gait instability, and urinary incontinence could be compatible with NPH, a condition of decreased absorption of cerebrospinal fluid (CSF). Although gait instability, urinary incontinence, and dementia constitute the classic symptom triad for NPH, the patient’s vesicular rash was not typical for NPH. In addition, ventriculomegaly was not detected on computed tomography of the head.

Cognitive decline and dementia are observed in patients with Parkinson disease and often manifest late in the course of the disease. The acuity of onset of mental status changes in this patient was less suggestive of progression of
Parkinson disease. Also, skin lesions are generally not characteristic of Parkinson disease.

Bacterial meningitis usually presents with fever, neck rigidity, and mental status changes. Although the patient had a rigid neck and mental status changes, his normothermia was less consistent with bacterial meningitis. Patients with acute bacterial meningitis are rarely normothermic.

The patient’s condition was also consistent with delirium because he presented with altered mental status, inattention, and abnormal level of consciousness. Although the patient had long-term predisposing risk factors for delirium, including advanced age and Parkinson disease, the examination finding of vesicular rash suggested a new acute medical condition as a precipitating risk factor for delirium. After initial assessment, the most likely etiology for this patient’s presentation was suspected to be herpes zoster.

2. At this time, which one of the following is most appropriate in establishing the patient’s diagnosis?
   a. Culture from swab of the base of a lesion
   b. Real-time polymerase chain reaction (PCR) on CSF
   c. Tzanck smear
   d. Serologic IgG testing
   e. No further testing because this is a clinical diagnosis

Further testing to establish the diagnosis of VZV infection may be indicated in an immunocompromised individual with atypical or absent skin lesions. Results of cultures of the lesion base swab or CSF can take up to 2 weeks, which may be untimely for diagnosis and treatment planning. In addition, the sensitivity of cultures declines as lesions progress toward crusting. Testing of skin lesions and CSF samples with PCR can provide rapid confirmation of VZV infection and is more sensitive than viral culture. In our immunocompetent patient, however, PCR was not needed to confirm VZV infection.

Tzanck smears taken from the base of a vesicular lesion can aid in identification of herpes infections if the diagnosis is in question. Multinucleated giant cells are seen in a positive Tzanck smear. Results cannot, however, differentiate between different herpes viruses, eg, VZV vs herpes simplex virus, and Tzanck smears are less sensitive than other diagnostic tests such as PCR.

Serologic IgG testing for anti-VZV antibodies can be used to detect previous varicella exposure or response to varicella vaccination. It is not useful for diagnosis in a new case of herpes zoster.

The skin findings were highly characteristic of VZV infection, which is normally a clinical diagnosis in immunocompetent hosts. In such patients, diffusely widespread lesions are seen in chickenpox (primary VZV infection), whereas lesions restricted to a particular dermatome are seen in herpes zoster (reactivation of latent VZV infection). No further laboratory testing was required to make the diagnosis of VZV infection in this patient.

3. Given the information obtained thus far, which one of the following is the best diagnosis for this patient?
   a. Ramsay-Hunt syndrome type 1
   b. Ramsay-Hunt syndrome type 2
   c. Herpes zoster ophthalmicus (HZO)
   d. Chickenpox
   e. Disseminated herpes zoster

Ramsay-Hunt syndrome type 1, or progressive myoclonus ataxia, is characterized by severe myoclonus, progressive ataxia, mild epilepsy, and cognitive change. Ramsay-Hunt syndrome type 1 was unlikely because our patient did not have motor neurologic symptoms. Ramsay-Hunt syndrome type 2 is reactivation of VZV involving the geniculate ganglion or CN VII and is characterized by ipsilateral facial palsy, and oral and tongue lesions. The patient’s diagnosis of left parotitis before admission was initially suggestive of Ramsay-Hunt syndrome type 2 but was considered unlikely because of the absence of facial motor deficits or tongue lesions.

The patient’s presentation was marked by vesicular lesions in the left CN V1 dermatome. Herpes zoster ophthalmicus is reactivation of latent VZV infection in the trigeminal ganglion with involvement of CN V1. It typically presents with a prodrome of headache, malaise, and fever. Onset of vesicular skin lesions can also be accompanied by conjunctivitis, episcleritis, and lid droop. Herpes zoster ophthalmicus can place patients at risk for eye involvement, notably keratitis and subsequent vision changes. It was not the appropriate diagnosis for our patient.
because his lesions extended far beyond the CN V1 dermatome.

Chickenpox is a manifestation of primary VZV infection usually seen in childhood. The characteristic clinical presentation of chickenpox is a generalized vesicular rash on the face, trunk, and extremities. Although the patient had vesicular lesions on various regions of his face and body, the lesions were heavily concentrated in a single dermatome (left CN V1), less consistent with the more generalized distribution of lesions in chickenpox.

The most likely diagnosis for our patient was disseminated herpes zoster, defined as 20 or more vesicular lesions occurring outside the primary affected dermatome and its immediately adjacent dermatomes. Dozens of scattered lesions were seen on the right side of the patient’s forehead, and bilaterally on his chest, abdomen, and back. Disseminated herpes zoster is a risk factor for development of herpes zoster encephalitis. Central nervous system involvement by VZV is most commonly associated with herpes zoster of the head and neck because of the anatomic proximity of these dermatomes to the central nervous system.

4. Which one of the following physical examination findings would be most concerning for herpes zoster involvement of the eye and warrant immediate ophthalmologic consultation?
   a. Periorbital vesicular lesions
   b. Periorbital edema
   c. Conjunctival injection
   d. Vesicular lesions on the tip, alae, or root of the nose
   e. Yellow crusting or discharge

Herpes zoster ophthalmicus comprises about 10% to 25% of all herpes zoster cases and may involve the globe of the eye. Approximately 2.5% of all herpes zoster cases are associated with eye complications. Among patients with HZO, 50% will develop eye complications including keratitis, iritis, and scleritis, often presenting with pain and/or blurred vision. In cases of HZO, periorbital vesicular lesions and edema do not necessarily indicate involvement of the globe. Conjunctival injection is also a nonspecific sign that does not involve the globe itself.

Vesicular lesions on the tip, alae, or root of the nose are known as Hutchinson sign. These areas of skin are innervated by the nasociliary branch of CN V1. The nasociliary nerve ramifies to the long ciliary nerves that provide sensory innervation to the globe. Lesions involving any branch of the nasociliary nerve may therefore indicate VZV involvement in other branches including the long ciliary nerve innervating the globe. Hutchinson sign is a strong predictor of ocular inflammation and warrants immediate ophthalmologic consultation. Involvement of both the external nasal (lower nose cutaneous innervation) and infratrochlear (upper nose cutaneous innervation) branches of the nasociliary nerve is associated with 100% development of ocular inflammation in patients with HZO. Yellow crusting or discharge may indicate secondary Staphylococcus aureus infection. It does not necessarily indicate VZV involvement of the globe.

The patient did not have vesicular lesions on his nose characteristic of Hutchinson sign. He was evaluated by an ophthalmologist who noted no keratopathy by fluorescein staining. Herpes zoster lesions of the eye may cause ulcerations of the corneal epithelium. Such corneal lesions are apparent by examination of the fluorescein-stained eye under ultraviolet light.

5. Which one of the following is the best initial treatment for this patient?
   a. Oral acyclovir
   b. Intravenous acyclovir
   c. Oral valacyclovir
   d. Oral prednisone
   e. Intravenous foscarnet

Although acyclovir is the drug of choice for initial treatment of herpes zoster, its oral bioavailability, approximately 15% to 30%, makes this route of delivery less effective for treatment. For disseminated herpes zoster, the preferred initial treatment is intravenous acyclovir because of its complete bioavailability.

Valacyclovir is a prodrug of acyclovir with oral bioavailability of approximately 55%. Valacyclovir is equally as effective as acyclovir in treating non-disseminated herpes zoster. The oral bioavailability of valacyclovir is still less than that of intravenous acyclovir. Therefore, intravenous acyclovir is preferred over oral valacyclovir for initial treatment of disseminated herpes zoster.

Combined therapy with acyclovir and prednisone can improve quality of life in patients 50...
years of age or older with localized herpes zoster. Prednisone alone, however, is not an appropriate treatment for herpes zoster. Foscarnet may be used to treat disseminated herpes zoster but only in the setting of acyclovir-resistant strains of VZV. Foscarnet is used primarily in the treatment of ganciclovir-resistant cytomegalovirus infections in patients with AIDS or transplants.

On admission, the patient was given acyclovir, 1000 mg intravenous every 8 hours. On the sixth day of admission, the patient’s clinical condition improved with decreasing periorbital edema, return of mental status to baseline, and encrusting of herpetic lesions. Intravenous acyclovir was stopped, and oral valacyclovir was administered at 1000 mg every 8 hours. The patient completed a total 14-day course of treatment and recovered.

DISCUSSION
Herpes zoster is a commonly encountered disorder. In the general population, 1 in 5 individuals will have herpes zoster during their lifetime. In the United States, there are approximately 1 million new cases of herpes zoster each year, with 25% of patients experiencing complications. The incidence of complications is strongly correlated with age, with two-thirds occurring in patients 50 years of age or older. The most common complication is postherpetic neuralgia (PHN), defined as the presence of herpetic pain for more than 90 days after rash onset. Before the introduction of VZV vaccine, PHN occurred in 18% of all adult patients with herpes zoster and in 33% of all patients with herpes zoster who were 79 years old or older. Eye complications are the second most common complication of herpes zoster, occurring in about 5% of patients 65 years of age or older.

In addition to PHN and eye issues, other complications of disseminated herpes zoster include pneumonia, hepatitis, meningitis, and bacterial superinfections possibly leading to necrotizing fasciitis. The most concerning potential complication in the present case was ocular involvement due to CN V1 dermatome involvement of the rash. The examination for Hutchinson sign is often focused on the tip of the nose, which is innervated by the external nasal branch of the nasociliary nerve. The nasociliary nerve, however, also innervates the upper part of the nose via its infratrochlear branch. It is important, therefore, to assess the entire nose for Hutchinson sign in the HZO examination for possible globe involvement.

The patient responded well to antiviral therapy with progressive resolution of his cutaneous lesions and improvement of his mental status back to baseline. This case illustrates the importance of early and prompt recognition of herpes zoster by clinicians in order to prevent potentially devastating complications of the disease including globe involvement. Because of the disease burden and complications attributable to herpes zoster, the Centers for Disease Control and Prevention recommends vaccination in immunocompetent adults ages 60 years and older. In this age group, the herpes zoster vaccine has been shown to reduce the incidence of herpes zoster by 51.3% and the incidence of PHN by 66.5%.

Correspondence: Address to Thomas H. Poterucha, MD, Division of Primary Care Internal Medicine, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (poterucha.thomas@mayo.edu).

REFERENCES

CORRECT ANSWERS: 1. b. 2. e. 3. e. 4. d. 5. b.