Recurrent Herpes Simplex Virus Type 2 Meningitis in Elderly Persons

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Objective: To review the ages of patients with recurrent herpes simplex virus type 2 (HSV-2) meningitis.

Design: Case report and literature review back to 1970.

Setting: Referral Veterans Affairs hospital.

Results: Our patient developed his first episode of recurrent HSV-2 meningitis at 78 years of age, 57 years after his only episode of genital herpes simplex infection. Of 223 patients in the literature with recurrent HSV-2 meningitis, 5% occurred in patients older than 60 years and 19% in patients older than 50 years.

Conclusions: Although recurrent meningitis due to HSV is primarily seen in young, sexually active adults, a surprising number of episodes of HSV meningitis can develop in older age. Meningitis due to HSV-2 should be in the differential diagnosis of aseptic meningitis in older patients.

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Herpes simplex virus type 2 (HSV-2) meningitis primarily develops during or following a primary genital HSV-2 infection that was acquired from sexual contact. As such, the initial infection typically occurs in sexually active adults. After the primary viral infection, the virus becomes latent in the sacral sensory ganglia. During the initial symptomatic genital herpes episode, 28% of women and 17% of men develop symptoms of meningitis. Eighty-nine percent of patients with HSV-2 genital herpes have at least 1 recurrence of genital herpes in the following year. If a patient develops HSV-2 meningitis, there is a 19% chance that recurrent meningitis will occur over their lifetime.

Most articles describe recurrent meningitis episodes within 10 years of the initial infection. We describe a 78-year-old man who developed 2 episodes of HSV-2 meningitis 56 years after his only episode of genital herpes. We then reviewed the literature to examine the distribution across different age groups of recurrent HSV-2 meningitis.

REPORT OF A CASE

In 1952 a 32-year-old man in the military had unprotected sex in Japan and subsequently developed his only episode of genital herpes infection characterized by vesicles on his penis. Results of tests for other sexually transmitted diseases were negative. He did not develop meningitis, and the infection cleared within a few weeks. He has never had recurrent genital herpes. He has been monogamous and married to his second wife for 36 years and has been in good health.

At 78 years of age he developed a severe headache and low back pain without leg radiation. He was hospitalized on the fourth day of severe headache. On admission he had a fever of 101.6°F and a white blood cell count of 9900/mm³. The physical examination showed normal mental status, no meningismus, no genital lesions, and normal cranial nerves, limb strength, sensation, and stretch reflexes. Testing of the cerebrospinal fluid (CSF) demonstrated a white blood cell count of 141/mm³ (70% mononuclear cells, 2% eosinophils, and 18% neutrophils); blood glucose, 49 mg/dL (to convert to millimoles per liter, multiply by 0.0555); protein, 0.281 g/dL (to convert to grams per liter, multiply by 10.0); and negative Gram stain and bacterial cultures. The CSF polymerase chain reaction for HSV-2 DNA was positive at 1955 copies per milliliter and negative for HSV-1. Results of other CSF tests for enteroviruses, fungi, and Venereal Disease Research Laboratory (syphilis) were negative, and serologic tests for arboviruses were negative. Findings of cranial computed tomography were normal. He did not receive acyclovir, and the headache and backache resolved during the next 6 days.

Four months later, he returned with another severe headache and backache and was readmitted to the hospital. He was afebrile, with a white blood cell count of 8500/
mm\(^3\). Results of neurologic examination were normal. Testing of CSF showed a white blood cell count of 90/ mm\(^3\) (52% neutrophils and 48% mononuclear); protein, 117 mg/dL; and negative bacterial cultures. Polymerase chain reaction using CSF for HSV-2 DNA revealed 303 copies/mL and was negative for HSV-1. Cranial computed tomography was again normal. He was treated with 800 mg of acyclovir twice a day for 10 days. The headache resolved in 5 days. Since discharge more than 7 months ago, he has not had any further episodes.

**METHODS**

Articles in English of recurrent meningitis, herpes simplex meningitis, and Mollaret meningitis were searched using PubMed (1970-2010). The age and sex of all reported patients with recurrent meningitis proven to be caused by HSV-2 were analyzed.

**RESULTS**

A total of 223 cases of recurrent HSV-2 meningitis were identified in the literature. The mean age of all patients was 38.9 years (men, 40.2 years; women, 38.0 years; and unidentified, 40.3 years). Distribution by sex, excluding patients of unidentified sex, showed 70% women and 30% men. The sex distribution for patients older than 60 years was 5 women, 4 men, and 3 unknown. The age and sex distribution of all cases is shown in the Figure. Two percent of patients were older than 70 years; 5%, older than 60 years; and 19%, older than 50 years. The oldest reported case was 83 years.\(^6\)

In the United States, approximately 1 in 5 adults are infected with HSV-2, and adults older than 70 years have a seroprevalence of 28%.\(^7\) A study in Finland reported the prevalence of recurrent lymphocytic meningitis associated with HSV-2 to be 2.2 per 100,000 persons.\(^8\)

Surveys of 3142 patients with genital herpes simplex infections report that the mean age of the first episode is 27 years for women and 31 years for men but 4% were older than 50 years when they developed the initial episode.\(^9\) This is consistent with our finding that most patients with recurrent HSV-2 meningitis are young adults; yet, 5% of the reported patients are older than 60 years. The current understanding is that once HSV-2 becomes latent in the sacral ganglia, it remains there for the life of the patient. Although the virus is persistently latent, there is evidence that the frequency of meningitis recurrences slowly declines during the 10 years following the initial genital infection or meningitis.\(^1,10\) However, our patient and other elderly patients with recurrent HSV-2 meningitis demonstrate that, although the frequency of recurrences declines, it does not fall to zero. The duration of recurrent HSV-2 meningitis is reported to range up to 22 years.\(^10,11\) In our patient, there was an interval of 56 years between the initial genital herpes episode and the first recurrent HSV-2 meningitis. In summary, it is important to keep HSV-2 meningitis in the differential diagnoses in elderly patients who present with aseptic meningitis.

**COMMENT**

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**REFERENCES**