Case 4

The patient was a 20-year-old female who presented to the emergency room with a 4-day history of fever, chills, and myalgia. Two days prior to this she noted painful genital lesions. On the day of admission she developed headache, photophobia, and a stiff neck. Previously, she had been in good health. She admitted to being sexually active but had no history of sexually transmitted diseases (STDs).

On physical examination, she was alert and oriented. Her vital signs were normal except for a temperature of 38.5°C; pulse rate was 80 beats per min and blood pressure was 130/80 mm Hg. A general examination was unremarkable except for slight nuchal rigidity. Her throat was clear, and there was no lymphadenopathy. A pelvic examination revealed extensive vesicular and ulcerative lesions on the left labia minora and majora with marked edema. The cervix had exophytic (outward-growing) necrotic ulcerations. Specimens were taken to culture for *Neisseria gonorrhoeae*, viruses, and *Chlamydia trachomatis*.

General laboratory tests were unremarkable. The VDRL (Venereal Disease Research Laboratory) test was negative. A lumbar puncture was done. The opening pressure was normal. The cerebrospinal fluid (CSF) showed a mild pleocytosis with a leukocyte count of 41/µl with 21% polymorphonuclear leukocytes and 79% mononuclear cells, a glucose level of 46 mg/dl, and a protein level of 68 mg/dl (slightly elevated). The CSF VDRL test was negative. A rapid diagnostic test was done on the genital lesion and gave positive results. Cultures from the genital lesions and CSF verified the diagnosis 2 days later. By that time the patient's condition had improved after 2 days of intravenous therapy. She was discharged home on oral medication.

1. What is the differential diagnosis of ulcerative genital lesions? Which rapid test was used so that specific therapy could be started?

2. Which complication of her underlying illness did she develop?

3. Which specific treatment did she receive?

4. Is she at risk for recurrences? How should her infection be managed?

5. How would you counsel this patient about recurrences? About what other important issues should she be counseled?

4 Case Discussion

1. The most likely diagnosis is genital herpes. Genital herpes lesions are painful, whereas lesions due to *Treponema pallidum* are usually painless. Genital infections such as chancroid or lymphogranuloma venereum can result in painful or painless ulcers, respectively, but they often result in suppurative lymphadenopathy. The etiologic agent of genital herpes in 70 to 90% of cases is herpes simplex virus type 2 (HSV-2), and in 10 to 30% of cases it is HSV-1. This virus is an enveloped, double-stranded DNA virus. Because it is an enveloped virus, it is spread only by direct contact with contaminated secretions. The diagnosis of HSV infection can be confirmed by isolating the virus in tissue culture cells or by examining scrapings from suspect lesions for HSV antigens by using rapid immunofluorescence techniques.

2. The patient had local and systemic signs and symptoms consistent with a primary genital herpes infection. Up to one-third of patients may develop aseptic meningitis as a complication of primary genital herpes, as occurred in this case. The specific meningeal symptoms she developed included fever, headache, photophobia, and stiff neck.

In contrast to aseptic meningitis associated with genital HSV-2 infection, herpes encephalitis in adults and older children is a more severe illness and is most often due to HSV-1 infection. Herpes encephalitis is a rare, sporadic central nervous system (CNS) viral infection. Patients present with fever, headache, and encephalopathic findings such as altered consciousness, behavioral and speech disturbances, and focal or diffuse neurologic signs. A diagnosis can be confirmed by detecting HSV directly using fluorescent antibody staining of tissue obtained by brain biopsy. Alternatively, less invasive means using PCR (polymerase chain reaction) to detect HSV DNA in the patient's CSF can be used. Babies born to women with genital herpes may develop herpes encephalitis from newly acquired HSV-2 infection. It is not clear why certain patterns of CNS infections with either HSV-1 or HSV-2 result in different CNS manifestations. The age of the patient, the route of viral dissemination (e.g., neural versus hematogenous), preexisting immunity, and/or specific viral properties may be factors.

3. The appropriate therapy is the antiviral agent acyclovir, which has specific activity against HSV. Because of the severity of her episode and her complication of aseptic meningitis, she received intravenous acyclovir followed by oral acyclovir therapy.

4. As with all viruses in the herpesvirus group, latent infections occur. Reactivation of latent viral infections can lead to recurrences of clinical disease. Daily suppressive therapy with oral acyclovir can decrease the recurrence rate. Patients can be successfully managed for several years with suppressive acyclovir.

5. Recurrences of genital herpes are generally milder than the primary episode of disease. This patient should be counseled about her risk for transmitting this infection to sexual partners and newborns. She should also be counseled about her risk

for other STDs (syphilis, HIV infection) and the use of barrier contraceptives. She should be advised to have annual Pap smears since her history of an STD puts her at increased risk for infection with human papillomavirus (HPV). Data, although controversial, suggest an association between infection with certain serotypes of HPV and the development of cervical cancer.

References

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2. **Whitley, R. J., and F. Lakeman.** 1995. Herpes simplex virus infection of the central nervous system: therapeutic and diagnostic considerations. *J. Infect. Dis.* **20**:414–420.