21-Year-Old Male Trauma Patient With Skin and Liver Lesions, Hepatitis, and Coagulopathy

(See page 559 for the Photo Quiz.)

Diagnosis: Disseminated Herpes Simplex Virus (HSV) Type 2.

The microscopic findings of the patient’s right thoracic skin lesion were diagnostic of the herpes virus (Figure 1). The patient’s liver biopsy showed necrotic hepatocytes with degenerating nuclei vaguely suggestive of viral changes, but necrosis prevented definitive interpretation. Swabs of the patient’s liver, forehead, and right chest wall pustules were positive for HSV-2 by culture and direct fluorescent antibody testing, and negative for varicella zoster virus (VZV). His blood cultures and subsequent tissue biopsies were negative for bacterial or fungal organisms. Polymerase chain reaction (PCR) performed on DNA from his blood was positive for HSV-2 and negative for HSV-1. Serum testing for HSV-1 and -2 antibodies was positive at 1.92 and >13.40, respectively. His liver and skin lesion cultures were negative for bacteria.

The patient was started on intravenous (IV) acyclovir, 10 mg/kg every 8 hours, and remained on IV acyclovir for 3-1/2 weeks until his transaminases returned to normal and his coagulopathy resolved. He was transitioned to oral valacyclovir and received a total of 14 weeks of antiviral therapy. He continued to do well clinically after discharge from the hospital.

Disseminated HSV with fulminant hepatitis is an uncommon presentation of HSV infection and accounts for 1% of all acute liver failure [1, 2, 3, 4]. It is often associated with disseminated intravascular coagulation (DIC) and can be rapidly fatal. Although reported in immunocompetent patients, this manifestation of HSV is mostly found in immunocompromised patients, especially those with a defect in cellular immunity [1, 5, 6]. In a review of 137 reported cases of HSV hepatitis, 25% of cases were in immunocompetent patients, of which 17% had disseminated disease [2].

HSV hepatitis is characterized by fulminant hepatic necrosis with significantly elevated liver transaminases. Patients tend to be anicteric [4]. Initial symptoms are non-specific but include fever, nausea, vomiting, altered mental states, thrombocytopenia, and coagulopathy [2]. Hepatitis is the most common laboratory abnormality, with an alanine transaminase level 3 times higher than normal [7]. Less than half of cases show the characteristic herpetic mucocutaneous lesions that are seen with this disease [1, 2, 7, 8, 10]. Predisposing factors include pregnancy (later second or third trimester), immunosuppression from organ transplantation, and inhaled anesthetics [6, 9].

Definitive diagnosis can be difficult and is often made post-mortem. Early suspicion with prompt diagnosis and treatment improves survival. Biopsies of involved organs or viral cultures are the most specific means of diagnosis but rely upon the presence of identifiable lesions and cannot differentiate between HSV and VZV. A liver biopsy may confirm the diagnosis in the absence of skin findings [1], but extensive necrosis in the involved organ can obscure viral changes. PCR of the DNA from blood or cerebrospinal fluid is a sensitive method to detect herpes viremia, but it is not always readily available.
Norvell et al report that untreated patients have a mortality of 88% compared to 51% mortality with treatment [2]. Variables associated with death include male gender, age >40 years old, significant liver dysfunction, thrombocytopenia, coagulopathy, encephalopathy, and absence of antiviral therapy [2].

The exact pathophysiology for HSV hepatitis is unknown. Four possible mechanisms include a large HSV inoculum at the time of initial infection, dissemination from mucosal herpetic lesions, impaired T-cell and macrophage immunity, and a hepatovirulent HSV strain with affinity for the liver [6].

This uncommon case describes disseminated HSV with coagulative hepatitis and DIC in an otherwise healthy male, and to our knowledge, it is the only such report of a case that occurred in a combat-related trauma patient. Disseminated HSV hepatitis should be recognized as a cause of significant coagulopathy and should be considered as a possible diagnosis in patients with concomitant fever, altered cognition, hepatitis, and thrombocytopenia. Providers should not rely on the presence of skin findings. Delay in diagnosis and treatment of disseminated HSV is associated with a high mortality rate and often results in a post-mortem diagnosis.

Notes

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