Herpes Simplex Virus associated Pneumonitis and Hepatitis in an immunocompetent host: A case report and a brief review of literature:

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Abstract: We report a rare case of a young woman who presented with pneumonitis and hepatitis caused by herpes simplex virus infection, which responded successfully to acyclovir treatment. Up to 25% of patients who develop HSV hepatitis are immunocompetent⁴. Hepatitis secondary to infection with herpes simplex virus (HSV) type 1 or 2 is a rare, frequently fulminant disease typically affecting patients with impaired immunity. Herpes simplex pneumonitis may develop as a primary infection or as a reactivation of latent infection during an acute illness, especially respiratory failure. Mortality rates associated with herpes simplex virus with pneumonitis & hepatitis are high, and early diagnosis and treatment with acyclovir may produce a favourable outcome.

Key Words: Herpes simplex virus (HSV), Pneumonitis, Hepatitis, Acyclovir

I. Introduction:

Hepatitis and pneumonitis are unusual manifestations of herpes simplex virus infection. HSV associated hepatitis & pneumonitis is a difficult diagnosis, and the infection is often fatal. Herpes simplex virus infections cause typical dermal and mucosal lesions in children and adults¹. Herpes simplex virus (HSV) associated pneumonitis & hepatitis is an uncommon complication of HSV infection². The diagnosis is often delayed due to the lack of specific signs or symptoms. Primary or recurrent HSV infection can result in disseminated infection leading to respiratory & hepatic failure, or death³. Most cases have been reported in immunocompromised patients (HIV infection, recipients of bone marrow transplantation, malnutrition, malignancy, burns and the elderly), or in subjects with severe respiratory distress³⁴.

Here, we report a rare case of HSV associated hepatitis & pneumonitis in an immunocompetent patient. Herpes simplex virus must be considered in all patients presenting with liver & respiratory failure of unknown cause. If suspected, prompt treatment with acyclovir should be initiated.

II. Case Report

A 30-year-old women was admitted to hospital because of progressive dyspnoea and fever. She had been well until three weeks previously when he began to have dry cough, headache, myalgia and malaise. She also had mild epigastric abdominal pain, yellowish discolouration of skin & urine, nausea & vomiting for the previous 7 to 10 days with no aggravating or alleviating factors. She also had maculopapular rash over face, neck & back. Five days before admission, she experienced the onset of fever, that rose as high as 40°C, and increasing dyspnoea. Her head and neck examination was unremarkable. She denied any diarrhoea or constipation. She had no history of smoking, exposure to animals, recent travel, use of intravenously administered drugs, homosexual practices or blood transfusions. She had performed household work and his past clinical history was unrevealing. She was alert, oriented with a GCS of 15 and was able to give a history of her illness.

Her vital signs were as follows : heart rate 110 beats per minute, blood pressure 140/90 mm of Hg, respiratory rate 24 breaths/min, temperature 100°F, O2 saturation 92% on room air. On examination she was mildly dyspneic and diaphoretic. She had diffuse inspiratory crackles were heard in the lower lobes of both lungs. Her abdomen was soft, mild tenderness, hepatomegaly. Heart and genitalia were normal.

Her labs were as follows : haemoglobin 10 g/dl, white blood cell 14,450/uL, hematocrit 36.4%, platelet count of 100,000 per mm³, normal electrolytes, creatinine 1.9 mg/Dl, glucose 104 mg/Dl, INR 1.3, total bilirubin 6.8 mg/Dl, albumin 2.5 g/Dl, alanine aminotransferase (ALT) 1200 IU/L, and aspartate aminotransferase (AST) 1000 IU/L. Her ANA was negative and dsDNA was also negative. Her hepatitis profile (Hepatitis A,B,C,E) was negative. Urine examination was normal. The arterial blood gases whilst breathing room air showed: pH 7.48; arterial oxygen tension (PaO2-1) 5.1 kPa and arterial carbon dioxide tension
Herpes Simplex Virus (HSV) is a double-stranded DNA virus which exists in either a lytic or latent phase of infection. Newly acquired or reactivated infections cause either ulcerative gingivostomatitis (typically with HSV-1) or genital ulceration (typically with HSV-2) in children and adults. Manifestations include meningitis, encephalitis, pneumonitis and hepatitis. In NHANES III (midpoint 1991), the seroprevalences of HSV-1 and HSV-2 were 68% and 22%, respectively. The hallmarks of HSV infection are periodic symptomatic reactivation and asymptomatic viral shedding.

Herpes simplex pneumonitis was first described in 1949. It has been considered as a rare entity and has been reported only in immunosuppressed patients. Pulmonary HSV infection has frequently been associated with intubation or mechanical ventilation in subjects with chronic disorders.

Hepatitis secondary to HSV infection occurs primarily in neonates and malnourished children and is usually fatal. Fulminant hepatitis due to HSV is rare in adults. It can occur in apparently immunocompetent adults; however, it is primarily a disease of patients with impaired immunity. The first reported case of HSV hepatitis was in 1969; it occurred in a pregnant patient.

HSV hepatitis is rare and accounts for only 1% of all acute liver failure cases and only 2% of all viral causes of acute liver failure (ALF). It occurs most commonly in organ transplant patients, in the third trimester of pregnancy or in patients who are otherwise immunocompromised, but up to 25% of patients who develop HSV hepatitis are immunocompetent.

Four mechanisms for HSV dissemination and resultant hepatitis & pneumonitis have been hypothesized: (1) a large HSV inoculum at the time of the initial infection may overwhelm the defense system and result in visceral dissemination; (2) pneumonitis & hepatitis may occur as a result of dissemination from mucosal herpetic lesions because of an impairment in macrophages, cytotoxic T lymphocytes, and...
delayed-type hypersensitivity reactions; (3) the virulence of HSV may be enhanced by activation of a latent virus possibly in association with reinfection by a second strain of HSV; and (4) there may be some strains of HSV that are hepatovirulent.

HSV lower respiratory tract infection can present either as focal necrotizing pneumonitis through extension of herpetic tracheobronchitis, or as disseminated pneumonia due to haematogenous dissemination from oral or genital mucocutaneous disease. Clinically, the patients have fever above 38.5°C, cough, dyspnoea and mucocutaneous lesions, which appear after or at the same time. HSV hepatitis presents with nonspecific flu-like symptoms including fever, myalgias, and abdominal pain. Only 30–50% show characteristic herpetic skin lesions. Laboratory investigations often show leucopenia, thrombocytopenia, and coagulopathy. Renal failure is not uncommon in these patients, and it has been shown to occur in up to 65% of patients with HSV-related ALF. Disseminated intravascular coagulopathy is frequently reported, and encephalopathy is a late sign of the disease. Ninety percent of patients with HSV hepatitis have a characteristic liver profile, known as “anicteric hepatitis”. Anicteric hepatitis refers to a liver profile showing a marked elevation in transaminases (100–1000 fold) with a relatively normal or low bilirubin. There may be a significant increase in transaminases and bilirubin.

Leukopenia has been reported in 43% of cases with HSV-associated hepatic failure, accompanied by thrombocytopenia (45%), and elevation of transaminases and bilirubin. Diagnosis of HSV pneumonia is usually based on cytological and histological findings and confirmed by viral culture or serological methods. Tissue culture is the most sensitive and specific diagnostic test. Investigations to aid in the diagnosis for HSV hepatitis are limited. Viral serology cultures are extremely sensitive and can be used as a screening tool but are very poorly specific. Viral PCR testing may be useful but is often not rapidly available. Although not always possible due to coagulopathy, the gold standard for diagnosis is liver biopsy.

In the review of all the reported HSV cases, 49 (36.6%) of 134 patients received acyclovir treatment. Antiviral treatment with acyclovir has been used successfully. The extent of disease at the initiation of treatment of a virally encoded thymidine kinase. More than 2 decades of experience with acyclovir has demonstrated that these compounds are safe and effective for treatment of HSV reactivation. Acyclovir or vidarabine treatment, as well as other supportive measures such as oxygen or ventilatory support, have been recommended. Today, acyclovir (800mg oral 5 times a day for one week, or 10–15 mg·kg\(^{-1}\) t.i.d. for one week) is considered to be the treatment of choice. When given early, it alters the course of infection, improving the survival and shortening the evolution.

Antiviral treatment with acyclovir has been used successfully. The extent of disease at the initiation of treatment plays a large role in its effectiveness, but outcomes probably improve with earlier initiation of therapy. In the review of all the reported HSV cases, 49 (36.6%) of 134 patients received acyclovir treatment. Patients who received treatment were less likely to die. Tuxen studied the effects of prophylactic acyclovir in patients requiring prolonged mechanical ventilation and demonstrated that this antiviral medication could reduce the frequency of herpes recovery from the lower respiratory tract but did not change outcomes. This study would suggest that, in general, herpes infections do not have an independent effect on prognosis and outcome.
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IV. Conclusion

We present here a case of herpes simplex caused pneumonitis and hepatitis in an immunocompetent host. Herpes simplex should be suspected and if positive, treatment can be instituted in time and further morbidity & mortality can be avoided. Herpes simplex virus must be considered in all patients presenting with liver & respiratory failure of unknown cause. If suspected, prompt treatment with acyclovir should be initiated.

References