IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 14, Issue 10 Ver. X (Oct. 2015), PP 37-40
www.iosrjournals.org

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

Dr. Mahendra Wawhal[1], Dr. Vajed Mogal[2], Dr. Jafar Tadvi[3]
[1]*Senior Consultant and Associate Professor ,MD (General medicine) in the Department of Medicine, Mahatma Gandhi Mission's Medical College and Hospital, Aurangabad, Maharashtra, India — 431003.*
[2]*Associate consultant-Intensivist, MD (General Medicine) at Wockhardt Hospital, Nashik, Maharashtra, India*
[3]*Junior resident in department of community medicine, M.G.M. Medical college, Aurangabad, Maharashtra.*

Abstract: *We report a rare case of a young women 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 immunocompetent[14]. 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 pneumonia 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 adults[1]. Herpes simplex virus (HSV) associated pneumonitis & hepatitis is an uncommon complication of HSV infection[2]. 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 death[3]. 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 distress[4].

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 aggrevating or alleviating factors. She also had maculopapular rash over face, neck & back. Five days before admission, he 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 100^0F, 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 mm^3, 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

(PaCO2) 5.3 kPa. Herpes simplex Direct fluorescent antibody (DFA) screening was positive foe herpes simplex virus 1 & 2. Bedside chest X-ray obtained on admission showed interstitial and alveolar infiltrates in the left lower lobe, and the left diaphragm was elevated (fig. 1). Her ultrasound showed hepatomegaly with moderate ascites. The chest computed tomography (CT) showed no evidence of pulmonary thromboembolism and extensive patchy ground glass opacities in both lungs consistent with possible pulmonary edema, ARDS, or severe pneumonitis.

No focus for infection was found, and she was presumed to have a viral illness with a systemic inflammatory response syndrome (SIRS). She was treated with intravenous fluid administration, and she was given broad-spectrum antibiotics

to cover for any bacterial pathogen that may be causing her SIRS.

The imaging was considered consistent with hepatitis. She was initially thought to have liver dysfunction due to prolonged hypotension on presentation resulting in hepatic ischemia. Acyclovir IV 800 mg 3 times daily was started for herpes infection. Piperacillin/tazobactum 3.375 g twice daily, levofloxacin 750 mg once daily, and methylprednisolone 40 mg twice daily were continued. After 10 days of treatment, she improved & her rash start disappearing after administration of acyclovir & repeat chest radiogram showing resolution of pulmonary infiltrates (fig:2). In view of financial issue, she left AMA and was referred to another hospital. After 15 days, the patient's breathing became labored and tachypneic, and she was intubated due to respiratory failure. Her acyclovir were discontinued and she suffered with multiple organ failure and septic shock and died on ICU day 18 (four weeks after admission to primary hospital).

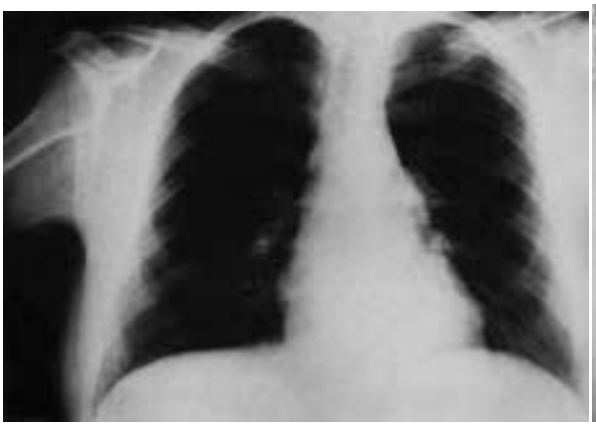

Fig : 1= Interstitial and alveolar infiltrates In the left lower lobe

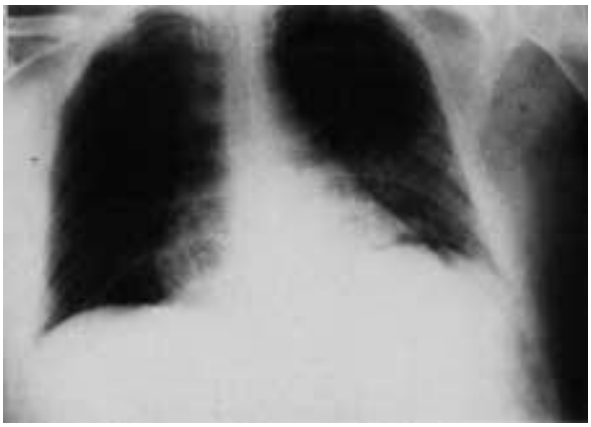

Fig :2= Resolution of pulmonary infiltrate after acyclovir treatment

III. Discussion

Herpes Simplex Virus (HSV) is a double-stranded DNA virus which exists in either a lytic or latent phase of infection[5]. 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[6] and hepatitis[7]. In NHANES III (midpoint 1991), the seroprevalences of HSV-1 and HSV-2 were 68% and 22%, respectively[8]. The hallmarks of HSV infection are periodic symptomatic reactivation and asymptomatic viral shedding.

Herpes simplex pneumonitis was first described in 1949[9]. 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[10]. 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[11]. The first reported case of HSV hepatitis was in 1969[12] ; 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)[13]. 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[14].**

Four mechanisms for HSV dissemination and resultant hepatitis & pneumonitis have been hypothesized[15] : (1) a large HSV inoculums 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[16]. HSV hepatitis presents with nonspecific flu-like symptoms including fever, myalgias, and abdominal pain. Only 30–50% show characteristic herpetic skin lesions[17]. Laboratory investigations often show leucopenia, thrombocytopenia, and coagulopathy[18] . Renal failure is not uncommon in these patients , and it has been shown to occur in up to 65% of patients with HSVrelated 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[19]". Anicteric hepatitis refers to a liver profile showing a significant increase in transaminases (100–1000 fold) with a relatively normal or low bilirubin. There may be a marked elevation of AST greater than ALT.

Leukopenia has been reported in 43% of cases with HSV-associated hepatic failure, accompanied by thrombocytopenia (45%), and elevation of transaminases and bilirubin[20].

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[21]. Antemortem diagnosis of HSV hepatitis is difficult and is considered in only 23–42% of cases prior to autopsy[22]. 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.

Currently, the major laboratory tests used for diagnosis of HSV are liver biopsy, viral culture, antigen detection tests (enzyme immunoassay or immunofluorescence on smears), and nucleic acid detection with polymerase chain reaction[23] (PCT/RT-PCR).

The spectrum of symptoms of the disseminated HSV infection resembles the clinical picture of a bacterial sepsis, which is reflected by analogies in inflammatory host response.

In a recent study, Berrington et al. examined the clinical correlates of HSV1/2 in 951 serum or plasma samples. 4% of those patients had detectable levels of HSV-1/2 in PCR analysis and were observed to have a high mortality rate[24].

Scheithauer et al. reported 191 patients with pulmonary diseases suspected to be of viral origin with 32.5% of the respiratory specimens tested positive for HSV-1 by PCR[25].

Approximately 60% of immunosuppressed and 33% of immunocompetent individuals died after HSV was detected in the peripheral blood. **The most common cause of death was sepsis followed by multi-organ failure.** The high mortality seen in this study raises a number of questions. Is HSV the primary cause of sepsis and multi-organ failure, or does detectable HSV in the blood stream represent viral reactivation in an individual whose immune system is impaired by ongoing sepsis syndrome by another causative organism or other underlying disease[26].

The nucleoside analogues acyclovir, valacyclovir, and famciclovir inhibit HSV-1 and HSV-2 replication through specific inhibition 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

t.i.d. for one week) is considered to be the treatment of choice[21]. 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 acyclovir plays a large role in its effectiveness,

but outcomes probably improve with earlier initiation of therapy[27].

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[28]. 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[29]. This study would suggest that, in general, herpes infections do not have an independant effect on prognosis and outcome.

IV. Conclusion

We present here a case of herpes simplex caused pneumonitis and hepatitis in an immunocompotent 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

[1]. Chase RA, Pottage JC Jr, Haber MH, Kistler G, Jensen D, Levin S. Herpes simplex viral hepatitis in adults: two case reports and review of the literature. Rev Infect Dis 1987; 9:329-333.

[2]. Ramsey PG, Fife KH, Hackman RC, Meyers JD, Corey L. Herpes simplex virus pneumonia. Clinical, virologic and pathologic features in 20 patients. Ann Intern Med 1982; 97: 813–820.

[3]. Prellner T, Flamholc L, Haidl S, Lindholm K, Widell A. Herpes simplex virus - the most frequently isolated pathogen in the lungs of patients with severe respiratory distress. Scand J Infect Dis 1992; 24: 283– 292.

[4]. Norvell JP, Blei AT, Jovanovic BD, Levitsky J. Herpes simplex virus hepatitis: an analysis of the published literature and institutional cases. Liver Transpl 2007; 13:1428-1434.

[5]. Whitley, RJ. Herpes Simplex Virus. In: Knipe, DM.; Hensley, PM., editors. Fields Virology. Vol. 4th ed. Vol. Vol. 2. Philadelphia: Lippinscott, Williams, and Wilkins; 2001. p. 2461-2506.

[6]. Feldman S, Stokes DC. Varicella zoster and herpes simplex virus pneumonias. Semin Respir Infect 1987 Jun;2(2):84–94.

[7]. Czartoski T, Liu C, Koelle DM, Schmechel S, Kalus A, Wald A. Fulminant, acyclovir-resistant, herpes simplex virus type 2 hepatitis in an immunocompetent woman. J Clin Microbiol 2006 Apr;44(4):1584– 1586.

[8]. Schillinger JA, Xu F, Sternberg MR et al. National seroprevalence and trends in herpes simplex virus type 1 in the Unites States, 1976-1994. Sex Transm Dis 2004;31:753-60.

[9]. Morgan HR, Finland M. Isolation of herpes virus from a case of atypical pneumonia and erythema multiforme exudativum: with studies of four additional cases. Am J Med Sci 1949; 217: 92–95.

[10]. Torphy DE, Ray CG, McAlister R, Du JNH. Herpes simplex virus infection in infants: a spectrum of disease. J Pediatr 1970;76:405-8**.**

[11]. St Geme JW Jr, Prince JT, Burke BA, Good RA, Krivit W. Impaired cellular resistance to herpes-simplex virus in Wiskott-Aldrich syndrome. N Engl J Med 1965;273:229-34.

[12]. Flewett TH, Parker RGF, Philip WM. Acute hepatitis due to Herpes simplex virus in an adult. J Clin Pathol 1969**;** 22:60-6.

[13]. C.Riediger,P.Sauer,E.Matevossian,M.W.M ¨ uller, P. B¨ uchler, and H. Friess, "Herpes simplex virus sepsis and acute liver failure," Clinical Transplantation, vol. 23, no. 21, pp. 37–41, 2009.

[14]. J.P.Norvell,A.T.Blei,B.D.Jovanovic,andJ.Levitsky,"Herpes simplex virus hepatitis: an analysis of the published literature and institutional cases," Liver Transplantation, vol. 13, no. 10, pp. 1428–1434, 2007.

[15]. Miyazaki Y, Akizuki S, Sakaoka H, Yamamoto S, Terao H. Disseminated infection of herpes simplex virus with fulminant hepatitis in a healthy adult: a case report. APMIS 1991; 99:1001-7.

[16]. Sherry MK, Klainer As, Wolff M, Gerhard H. Herpetic tracheobronchitis. Ann Intern Med 1988; 109: 229– 233.

[17]. J. Polson and W. M. Lee, "AASLD position paper: the management of acute liver failure," Hepatology,vol.41,no.5,pp. 1179–1197, 2005.

[18]. D. J. Peters, W. H. Greene, F. Ruggiero, and T. J. McGarrity, "Herpes simplex-induced fulminant hepatitis in adults a call for empiric therapy," Digestive Diseases and Sciences, vol. 45, no. 12, pp. 2399–2404, 2000.

[19]. D. V. Glorioso, P. J. Molloy, D. H. Van Thiel, and R. J. Kania, "Successful empiric treatment of HSV hepatitis in pregnancy. Case report and review of the literature," Digestive Diseases and Sciences, vol. 41, no. 6, pp. 1273–1275, 1996.

[20]. G. Biancofiore, M. Bisa, L. M. Bindi et al., "Liver transplantation due to Herpes Simplex virus-related sepsis causing massive hepatic necrosis after thoracoscopic thymectomy," Minerva Anestesiologica, vol. 73, no. 5, pp. 319–322, 2007.

[21]. Straus SE, Rooney JF, Sever JL, Seidlin M, NusinoffLehrman S, Cremer K. Herpes simplex virus infection: biology, treatment and prevention. Ann Intern Med 1985; 103: 404–419.

[22]. S. Sharma and M. Mosunjac, "Herpes simplex hepatitis in adults: a search for muco-cutaneous clues," Journal of Clinical Gastroenterology, vol. 38, no. 8, pp. 697–704, 2004.

[23]. Van Doornum GJ, Guldemeester J, Osterhaus AD, Niesters HG. Diagnosing herpesvirus infections by real time amplification and rapid culture. J Clin Microbiol 2003; 41: 576-580.

[24]. W. R. Berrington, K. R. Jerome, L. Cook, A. Wald, L. Corey, and C. Casper, "Clinical correlates of herpes simplex virus viremia among hospitalized adults," Clinical Infectious Diseases, vol. 49, no. 9, pp. 1295–1301, 2009.

[25]. S. Scheithauer, A. K. Manemann, S. Kr ¨uger et al., "Impact of herpes simplex virus detection in respiratory specimens of patients with suspected viral pneumonia," Infection, vol. 38, no. 5, pp. 401–405, 2010.

[26]. Johnston C, Magaret A, Selke S, Remington M, Corey L, Wald A. Herpes Simplex Virus Viremia during Primary Genital Infection. The Journal of infectious diseases 2008 May;9.

[27]. M. Montalbano, G. I. Slapak-Green, and G. W. Neff,"Fulminant hepatic failure from herpes simplex virus: post liver transplantation acyclovir therapy and literature review," Transplantation Proceedings, vol. 37, no. 10, pp. 4393–4396, 2005.

[28]. Fleming DT, McQuillan GM, Johnson RE, et al. Herpes simplex virus type 2 in the United States, 1976 to 1994. N Engl J Med 1997; 337:1105-1111.

[29]. Tuxen DV. Prevention of lower respiratory herpes simplex virus infection with acyclovir in patients with adult respiratory distress syndrome. Chest. 1994;106(1 suppl):28S-33S.