Netherlands
The Journal of Medicine

CASE REPORT

Herpes simplex virus oesophagitis in a pregnant woman

H.H.F Remmelts[1*], J.W. van den Brink[2], R. Laan[2], D.J. Bac[1]

Departments of [1]Internal Medicine and Gastroenterology and [2]Gynaecology and Obstetrics, Gelderse Vallei Hospital, Ede, the Netherlands, *corresponding author: tel.:+31 (0)318- 43 43 43, fax: +31 (0)318-61 39 44, e-mail: interneaaremmeltsh@zgv.nl

ABSTRACT

Herpes simplex virus (HSV) oesophagitis is well described in immunocompromised patients. In immunocompetent individuals HSV oesophagitis is rare. We present a case of HSV oesophagitis in a pregnant woman. A possible explanation for HSV oesophagitis during pregnancy is the decreased cellular immunity, leading to an increased frequency and severity of viral infections. Antiviral therapy is advocated in pregnancy.

KEYWORDS

Herpes simplex virus, oesophagitis, pregnancy

What was known on this topic?
Herpes simplex virus oesophagitis is a well-known phenomenon in immunocompromised hosts. In immunocompetent individuals this condition is rare.

What does this add?
We present a case of herpes simplex virus oesophagitis in a healthy, pregnant woman, which has never been described before. A possible explanation is the decreased cellular immunity during pregnancy, leading to an increased frequency and severity of viral infections.

INTRODUCTION

Herpes simplex virus (HSV) oesophagitis is a well-known phenomenon in immunocompromised hosts. In immunocompetent individuals this condition is rare. HSV oesophagitis during pregnancy has never been described before in the English literature. We present a case of a pregnant woman with HSV oesophagitis, together with an overview of the characteristics of HSV oesophagitis, within the scope of pregnancy.

CASE REPORT

A 25-year-old woman, gravida 2 para 0, was admitted to our hospital at 22 5/7 weeks gestation with a four-week history of epigastric pain. One week before hospitalisation she noted fever, together with aggravation of the epigastric pain radiating to the back. Intake of food was hampered by odynophagia and vomiting. The medical history revealed nephrolithiasis. Antacids and laxative suppositories were prescribed for the symptoms, next to antibiotics because of a supposed cystitis. Advanced ultrasonography at 20 weeks had shown no signs of congenital abnormalities.
Physical examination revealed a tachycardia of 104 beats/min and a body temperature of 39.2 °C. There was epigastric tenderness on palpation. Blood testing showed elevated inflammatory markers: leucocytes 13.4 /nl and C-reactive protein 101 mg/l. There were no signs of preeclampsia or HELLP syndrome. Ultrasonography of the upper abdomen showed no abnormalities. Oesophagogastroduodenoscopy revealed mucosal erythema and multiple fibrin exudates of the entire oesophagus, which became partially confluent in appearance (*figure 1*). Biopsies were taken for histopathological analysis and culture. Histopathology showed multinucleated giant cells and Cowdry's type A inclusion bodies (*figure 2*). Immunohistochemical stains were positive for HSV (*figure 3*), fungal stains were negative. HSV type 1 was cultured from the oesophageal tissue.

Figure 1. *Oesophagogastroduodenoscopy showing HSV oesophagitis. There is extensive ulceration throughout the oesophagus, volcano-like in appearance, with raised edges*

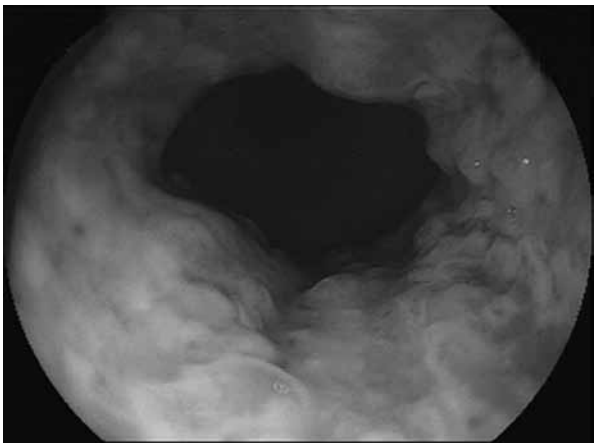


Figure 2. *Histopathology of HSV oesophagitis. There are multinucleated giant cells showing characteristic nuclear inclusion bodies*

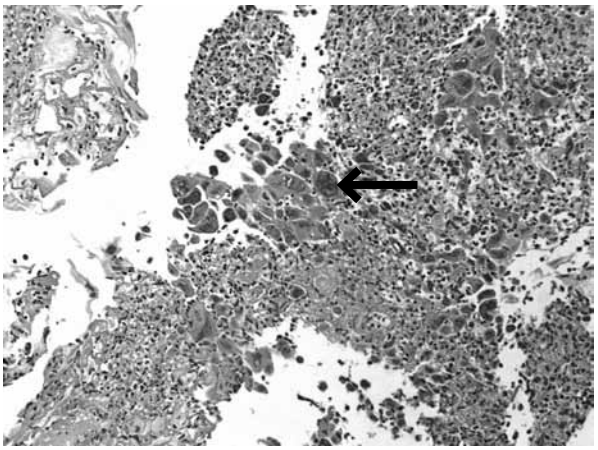
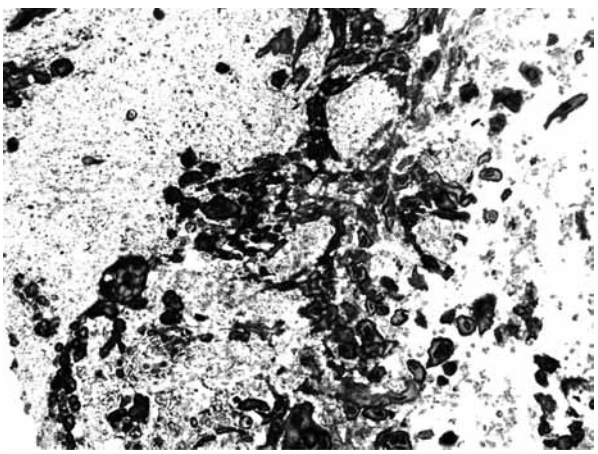


Figure 3. *Positive immunohistochemical stains for HSV in the oesophagus*



She was treated with acyclovir intravenously for seven days (15 mg/kg in four doses). Within two days she was able to drink and eat a soft diet. Complete relief of symptoms was achieved in five days. She was discharged from the hospital on the 13th day. Serology for HSV showed seroconversion, indicating primary infection. The patient had no history of HSV infection and no genital lesions were seen during gynaecological inspection. Retrospectively, her partner had had possible orolabial HSV lesions several weeks before, indicating a possible source of infection. Human immunodeficiency virus serology was negative.

At 41 2/7 weeks gestation she delivered a healthy daughter of 3280 gram with Apgar scores of 9 and 10 at one and five minutes, respectively. No congenital abnormalities were noticed. At follow-up three months postpartum she had normal levels of serum immunoglobulins. T-lymphocyte quantitation revealed high-normal values: CD4 lymphocyte count 2.15 x 10^9/l (0.56-1.49 x 10^9/l), CD8 lymphocyte count 1.17 x 10^9/l (0.26-0.99 x 10^9/l). The CD4/CD8 lymphocyte ratio was 1.84 (normal).

DISCUSSION

HSV type 1 (HSV-1) and 2 (HSV-2) belong to the human herpes viruses.[1] Orolabial herpes infections are usually caused by HSV-1.[2] As a consequence HSV oesophagitis is also predominantly caused by HSV-1 while HSV-2 is mostly responsible for genital herpes infections.[2,3]

The incidence of HSV oesophagitis is 1.8% in autopsy patients.[4] Most of these patients were immunocompromised. In immunocompetent individuals HSV oesophagitis is rare. HSV oesophagitis may represent primary disease or reactivation of a latent infection. The characteristic patient is a young adult male with the acute onset of the triad odynophagia, retrosternal chest pain and fever.[3] Prior exposure to a family member with possible HSV lesions has been reported in about 20% of the cases.[3,5]

Oesophagogastroduodenoscopy is the diagnostic procedure of choice. HSV oesophagitis has typical endoscopic findings.[5] In the early stage vesicles are seen, which then deepen and confluence to form discrete, circumscribed ulcers with raised edges. These lesions may have a punched-out or volcano-like appearance. Cobblestoning can be seen when the lesions coalesce. Exudates are present in a substantial number of patients. Biopsies from the ulcer edges should be obtained for histopathology and viral culture to make the definitive diagnosis. The histological characteristics of HSV oesophagitis are ground-glass appearance in the nuclei, Cowdry type A nuclear inclusion bodies and multinuclear cells.[6]

During pregnancy significant changes occur in the maternal immune system. The alterations are initiated at the placental site by the hormones of pregnancy. Sridama *et al.* demonstrated a decrease of CD4 lymphocytes throughout pregnancy which is responsible for the maternal immunodeficiency.[7] This mechanism may be important for the protection of the foetus. However, due to the decreased levels of CD4 lymphocytes, pregnant women have a higher risk of viral infections and severity of symptoms.[1,7] After pregnancy, the CD4 lymphocyte levels normalise within five months.

In case of a primary HSV infection in pregnancy the risk of intrauterine transmission is less than 5%.[1] After intrauterine transmission there is an increased risk of disseminated infection of the foetus which may lead to early embryonic or foetal damage, intrauterine growth restriction, preterm birth, major developmental or congenital anomalies, or even miscarriage or stillbirth.[1]

Treatment of HSV oesophagitis with acyclovir, a nucleoside analogue, is well established in immunocompromised patients.[8] In immunocompetent individuals HSV oesophagitis is generally a self-limiting disease. However, to prevent complications such as bleeding or perforation and to hasten recovery, it is advisable to initiate antiviral therapy in an early stage of disease also in immunocompetent patients, particularly in those with severe odynophagia.[8,9]

The essence of treatment of HSV infections in pregnancy should be prevention of vertical transmission of HSV to the foetus or neonate. Acyclovir crosses the placenta and is excreted by the foetal kidney, but there is no accumulation in the foetus.[10,11] Stone *et al.* have studied the effects of systemic acyclovir administration during pregnancy.[12] The risk of birth defects of live births exposed to systemic acyclovir during first trimester is 3.2% and for exposures during any trimester is 2.6%. As the expected rate of congenital abnormalities in the general population is 3.2%, no difference is seen in the acyclovir versus the general population and acyclovir is therefore classified as a category B drug.[1] Pregnant women are relatively immunocompromised and therefore antiviral therapy is indicated in case of HSV oesophagitis.

In conclusion, HSV oesophagitis is a rare occurrence in pregnancy. It should be considered in patients with odynophagia, retrosternal chest pain and fever. Oesophagogastroduodenoscopy with biopsy for histopathology and viral culture should be performed to confirm the diagnosis. Antiviral therapy is advocated in pregnancy.

ACKNOWLEDGMENTS

The authors thank T.E.G. Ruijter (MD) of the Department of Pathology, Gelderse Vallei Hospital Ede, for his comment on the histopathological images.

REFERENCES

1. Avgil M, Ornoy A. Herpes simplex virus and Epstein-Barr virus infections in pregnancy: consequences of neonatal or intrauterine infection. Reprod Toxicol. 2006;21(4):436-45.
2. Ficarra G, Birek C. Oral Herpes Simplex Virus infection in pregnancy: what are the concerns? J Can Dent Assoc. 2009;75(7):523-6.
3. Galbraith JCT, Shafran SD. Herpes simplex oesophagitis in the immunocompetent patient: Report of four cases and review. Clin Infect Dis. 1992;14(4):894-901.
4. Itoh T, Takahashi T, Kusaka K, Kawaura K, Nakagawa Y, Yamakawa J, et al. Treating reflux oesophagitis: Herpes simplex oesophagitis from 1307 autopsy cases. J Gastroenterol Hepatol. 2003;18:1407-11.
5. Ramanathan J, Rammouni M, Baran J, Khatib R. Herpes simplex virus oesophagitis in the immunocompetent host: an overview. Am J Gastroenterol. 2000;95(9):2171-6.
6. Kato S, Yamamoto R, Yoshimitsu S, Shimazaki K, Ogawa S, Itoh K, et al. Herpes simplex oesophagitis in the immunocompetent host. Dis Oesophagus. 2005;18(5):340-4.
7. Sridama V, Pacini F, Yang SL, Moawad A, Reilly M, DeGroot LJ. Decreased levels of T helper cells: a possible cause of immunodeficiency in pregnancy. N Engl J Med. 1982;307(6):352-6.
8. Kurahara K, Aoyagi K, Nakamura S, Kuwano Y, Yamamoto C, Iida M, et al. Treatment of herpes simplex oesophagitis in an immunocompetent patient with intravenous acyclovir: a case report and review of the literature. Am J Gastroenterol. 1998;93(11):2239-40.
9. Rongkavilit C, El-Baba MF, Poulik J, Asmar BI. Herpes simplex virus type I oesophagitis in an immunocompetent adolescent. Dig Dis Sci. 2004;49(5):774-7.
10. Frenkel LM, Brown ZA, Bryson YJ, Corey L, Unadkat JD, Hensleigh PA, et al. Pharmacokinetics of acyclovir in the term human pregnancy and neonate. Am J Obstet Gynecol. 1991;164(2):569-76.
11. Andrews EB, Yankaskas BC, Cordero JF, Schoeffler K, Hampp S. Acyclovir in pregnancy registry: six years' experience. The acyclovir in pregnancy registry advisory committee. Obstet Gynecol. 1992;79(1):7-13.
12. Stone KM, Reiff-Eldridge R, White AD, Cordero JF, Brown Z, Alexander ER, et al. Pregnancy outcomes following systemic prenatal acyclovir exposure: conclusions from the international acyclovir pregnancy registry, 1984-1999. Birth Defects Res A Clin Mol Teratol. 2004;70(4):201-7.