

CASE REPORT

Disseminated herpes simplex infection during pregnancy, rare but important to recognise

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ABSTRACT

Disseminated herpes simplex virus (HSV) infection during pregnancy is a rare, but potentially fatal condition. We present a case where prompt treatment with intravenous acyclovir resulted in a successful outcome for both mother and baby.

Keywords: pregnancy, herpes simplex, case report

INTRODUCTION

Disseminated herpes simplex (HSV) virus infection during pregnancy is rare, but important to recognize, as disseminated disease can have a serious outcome for both the mother and neonate.⁽¹⁾ Data from USA and Europe indicate that approximately 2 – 3% of women acquire primary genital HSV infection during pregnancy, and it is well recognized that it is these women who are at highest risk of transmitting HSV infection to their babies.^(2,3) Infants infected intrapartum or postnatally most frequently develop localized mucocutaneous infections (50%), however 33% have involvement of the central nervous system (CNS), and 17% develop disseminated disease, characterized by liver and adrenal dysfunction, shock and coagulopathy, which if not treated carries a mortality rate of up to 85%.⁽³⁾ It is less well appreciated that primary HSV in pregnancy, particularly in the last trimester, can also be complicated by disseminated disease in the mother, although this is rare.⁽⁴⁾ Features of disseminated infection include visceral and central nervous system (CNS) involvement, hepatitis, thrombocytopenia, leucopenia and coagulopathy, and is associated with a maternal mortality of 50%.⁽²⁾

We present a case of primary HSV infection during pregnancy where prompt treatment with intravenous

(IV) acyclovir resulted in a successful outcome for both mother and baby.

CASE HISTORY

A 19 year old primigravida presented at 32 weeks of pregnancy with a two-day history of shooting pain in the symphysis pubis area. A diagnosis of symphysis pubis dysfunction was made and she was discharged on analgesics.

She returned 48 hours later with worsening vaginal and right-sided lower abdominal pain, and abnormal vaginal discharge. On examination, she appeared septic with a temperature of 38.3°C, pulse of 148 per minute, and blood pressure of 97/52 mm Hg.

Her chest was clear to auscultation, with oxygen saturation of 97% on room air. Abdominal palpation revealed only mild tenderness in the right upper quadrant; there was no suprapubic or loin tenderness to suggest urinary tract infection, pyelonephritis nor appendicitis, and no features of peritonism.

A cardiotocography (CTG) was performed on admission, which demonstrated a normal fetal heart rate.

Initial blood results revealed mild pancytopenia; haemoglobin (Hb) 8.6 g/dl (11.5 – 16.5 g/dl), white cell count (WCC) $1.7 \times 10^9/L$ ($4.0 - 11.0 \times 10^9/L$), platelets $94 \times 10^9/L$ ($150 - 450 \times 10^9/L$), coagulation was normal as was renal function with serum creatinine of 45 micromoles/L (53 – 97 micromoles/L). C-reactive protein was elevated at 146.6 mg/L (< 10 mg/L), and there was evidence of liver inflammation with alanine transaminase (ALT) 161 U/L (10 – 35 U/L), however bilirubin was normal. Chest x-ray did not reveal any abnormalities.

A provisional diagnosis of sepsis with no obvious focus of infection was made and broad spectrum antibiotics commenced (piperacillin and tazobactam) after obtaining cultures of blood and urine. A high vaginal swab (HVS), and a throat swab for viral and bacterial screen were also taken. Group A streptococcus (GAS) was grown from the HVS and therefore the possibility of invasive GAS infection was also considered.

No other infective pathogens were subsequently identified from blood, urine or throat swab. Serology for HIV tested at her antenatal screening visit was negative.

Over the next 48 hours she continued to spike high fevers in spite of the addition of clarithromycin, clindamycin and teicoplanin. Arterial blood gases revealed mild acidosis and a fall in oxygen saturation

on air to 87%. Worsening pancytopenia was noted (nadir platelet count $80 \times 10^9/L$, Hb 6.9 g/dl, WCC $1.0 \times 10^9/L$). ALT rose to 385 U/L, however bilirubin and coagulation remained normal. Repeat CTGs recorded a baseline fetal heart rate of 190 bpm with unprovoked decelerations.

Due to the deterioration in maternal condition and pathological CTGs, a decision to proceed to emergency caesarean section was made. In theatre, ulceration around the labia and paraurethral region was noted, and swabs from the ulcers were obtained and sent for bacterial culture and viral PCR screen (including HSV), however acyclovir was not started at this time. A healthy male infant weighing 1700 g was delivered, APGAR scores were 9 at 1 minute and 9 at 5 minutes. The patient was transferred to the intensive care unit for postoperative care and her baby was transferred to the Special Care Baby Unit (SCBU).

As no focus of infection had been identified at this stage, a CT scan of the thorax and abdomen was performed postoperatively. This demonstrated small bilateral pleural effusions and bilateral basal atelectasis; however, the most striking finding was of gross hepatosplenomegaly with no intrathoracic or intra-abdominal lymphadenopathy (see Figure 1).



Figure 1. Abdominal CT scan showing marked hepatosplenomegaly.

A few days later HSV type 2 was identified by PCR from a vulval swab. HSV DNA was also subsequently detected in her serum at very high levels (over 800,000 IU/ml) giving rise to the concern that the patient had experienced a primary HSV infection during her pregnancy. To confirm this hypothesis, a stored sample of serum taken at her initial antenatal clinic visit was tested for antibodies to HSV-1 and HSV-2 by Abbott Architect chemiluminescence. IgG and IgM antibodies to both HSV-1 and -2 were negative, indicating no evidence of previous exposure to HSV, thus confirming the diagnosis of primary HSV infection.

Following the identification of HSV-2 from the vulval swab, IV acyclovir was instituted at a dose of 10 mg/kg 8 hourly. The patient became afebrile within 48 hours and her condition steadily improved. After 4 weeks of IV therapy she was switched to oral valacyclovir (1 g TDS) and discharged from hospital, at which time her ALT had normalized, clotting continued to be normal throughout the course of the illness and her pancytopenia had corrected. She was followed up in the outpatient clinic and oral valacyclovir was continued until serum HSV DNA had been undetectable on two consecutive tests.

Her baby developed mucocutaneous HSV-2 infection shortly after birth however, there was no clinical evidence of any respiratory, CNS or other systemic involvement and therefore no brain scan was performed. He remained in SCBU for two weeks until he had completed two weeks of IV acyclovir and at the time of discharge, was noted to have a good tone, was feeding well and had no neurological deficits.

DISCUSSION

HSV exists as two subtypes, HSV-1 and HSV-2, both of which cause lifelong infections, which can be asymptomatic in immunocompetent individuals. HSV-1 has traditionally been associated more commonly with non-sexual transmission, usually during childhood, with infection manifesting as mucocutaneous lesions, whilst HSV-2 is almost always transmitted sexually, and is responsible for the majority of primary genital infections.⁽⁵⁾ However, accumulating seroprevalence data has shown that HSV-1 is an increasingly important cause of genital infections in developed countries.⁽⁵⁾

Disseminated HSV infection can be severe and life threatening, with CNS and visceral involvement, particularly hepatitis, and deranged coagulation. Immunosuppression, either due to a primary immunodeficiency state or secondary to treatment with steroids or other immunosuppressant medications, is a well-recognised predisposing factor for disseminated HSV infection. It is less well appreciated that women who experience primary HSV infection during pregnancy are also at increased risk of disseminated disease, particularly if infection occurs during the second or third trimester, and there is also a greater risk that they can transmit the virus to their baby. The increased risk of disseminated HSV infection associated with pregnancy is thought to be due to the suppression of cell-mediated and humoral immunity in the mother, which is important to prevent the rejection of the foreign antigens of the fetus and placenta.⁽⁴⁾ Although approximately 2% of women acquire HSV during pregnancy, disseminated HSV is rare. The first case of disseminated HSV infection in

Table 1. Case reports of disseminated HSV infection between 2001 – 2012.

Case no	Age (years) of the patient at presentation	Gestational Age (weeks)	History of immune suppression condition/illness	Type of HSV	Any lesion	Liver transplant performed	Patient survived
1	21	27	No	2	No	No	No
2	25	34	No	–	No	No	Yes
3	32	31	No	2	No	Yes	Yes
4	43	28	No	2	No	No	Yes
5	28	28	No	2	Cervical lesion seen	Yes	No
6	30	30	No	2	No	No	No

pregnancy was described in 1969, and from then up until 2002, only 25 cases have been published.⁽¹⁾

We accessed MEDLINE case reports between 2001 and 2012, using pregnancy and herpes simplex as keywords. Eight cases of disseminated HSV infection associated with pregnancy were identified; two of these cases were duplicates, leaving six cases for review (summarized in Table 1).

The six females described were aged between 21 and 43 years old, and were all in the third trimester of pregnancy (27 weeks in one case, 28 weeks in two cases and 30, 31 and 34 weeks in the remaining cases). All presented with a non-specific clinical picture not suggestive of HSV infection, and all developed hepatitis. None of the women had any history of immunosuppression. There were no lower genital lesions identified in five of the cases, one woman had an atypical lesion over the uterine cervix. HSV type 2 was confirmed in 5 cases, and was not

sub-typed in the sixth case. All cases were treated with IV acyclovir, the preferred drug in disseminated HSV infection. Only three of the six women survived,^(6–8) one requiring a liver transplant. Of the three patients who died, one received a liver transplant.^(1,9–10)

CONCLUSION

It is important to consider HSV infection in the differential diagnosis of a pregnant woman who is febrile and systemically unwell with no localizing signs of infection, particularly if serum transaminases are elevated without a corresponding rise in bilirubin. Absence of classic herpetic mucocutaneous lesions does not exclude the diagnosis. Awareness of this condition, with prompt institution of IV acyclovir in suspected cases can dramatically reduce mortality of both mothers and infants.

REFERENCES

1. Frederick MD, Bland D, Gollin Y. Fatal disseminated herpes simplex virus infection in a previously healthy pregnant woman. A case report. *J Reprod Med.* 2002;47(7):591–596.
2. Anzivino E, Fioriti D, Mischitelli M, Bellizzi A, Barucca V, Chiarini F, Pietropaolo V. Herpes simplex virus infection in pregnancy and in neonate: status of art of epidemiology, diagnosis, therapy and prevention. *Viral J.* 2009;6:40.
3. Kimberlin DW. Neonatal Herpes Simplex Infection. *Clin Microbiol Rev.* 2004;17(1):1–13.
4. Young EJ, Chafizadeh E, Oliveira VL, Genta RM. Disseminated Herpesvirus Infection During Pregnancy. *Clin Infect Dis.* 1996;22(1):51–58.
5. Bradley H, Markowitz LE, Gibson T, McQuillan GM. Seroprevalence of herpes simplex virus types 1 and 2 – United States, 1990–2010. *J Infect Dis.* 2014;209(3):325–333.
6. Allen RH, Tuomala RE. Herpes simplex virus hepatitis causing acute liver dysfunction and thrombocytopenia in pregnancy. *Obstet Gynecol.* 2005;106(5 Pt 2):1187–1189.
7. Nienaber JH, McNamara DR, Banerjee R, Pritt BS, Karre T, Sohail MR. Fulminant gestational hepatitis due to primary herpes simplex type 2 infection: use of serum HSV polymerase chain reaction for noninvasive diagnosis. *Diagn Microbiol Infect Dis.* 2012;72:181–184.
8. Thurman RH, Konig K, Watkins A, Weerasiri T, Permezel M. Fulminant herpes simplex virus hepatic failure in pregnancy requiring liver transplant. *Aust N Z J Obstet Gynaecol.* 2010;50(5):492–494.
9. Luzar B, Ferlan-Marolt V, Poljak M, Sojar V, Stanisavljevic D, Bukovac T, Markovic S. Acute fatty liver of pregnancy – an underlying condition for herpes simplex type 2 fulminant hepatitis necessitating liver transplantation. *Z Gastroenterol.* 2005;43(5):451–454.
10. Nagappan R, Parkin G, Simpson I, Sievert W. Fulminant hepatic failure from herpes simplex in pregnancy. *Med J Aust.* 2002;176(12):595–596.