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Primary cytomegalovirus infection presenting with itching and obstetric cholestasis like picture in mid-trimester

Osama Eskandar, Georgia Smith

ABSTRACT

Introduction: We present a case of Primary cytomegalovirus infection presented in mid-trimester with itching and obstetric cholestasis like picture. To the best of our knowledge the similarities between primary CMV and obstetric cholestasis, when presenting during pregnancy, have not been highlighted before in the literature. Case Report: A 36 year old lady presented to antenatal clinic at 23+4 weeks gestational age with intense itching. Bile acids and ALT were raised so she was treated as obstetric cholestasis whilst other results were awaited. Cytomegalovirus (CMV) antibodies, immunoglobulin G (IgG) and IgM were positive despite being negative at booking, suggesting an acquisition of CMV at approximately 18 weeks gestation. This article highlights the details of her case including the management and consequences of cytomegalovirus in pregnancy. Conclusion: This case report highlights the importance of the awareness of the clinicians with the condition as a differential diagnosis to obstetric cholestasis. CMV should be considered in the work up investigation of itching and abnormal liver functions in pregnancy.

Keywords: Cytomegalovirus infection, Herpes virus, Primary CMV infection with pregnancy

How to cite this article

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INTRODUCTION

Cytomegalovirus (CMV) is a derivative of the Herpes virus. The virus is present in both developed and developing countries and if an individual is infected, they are usually asymptomatic. Some patients however, may experience a mild flu-like illness during primary infection [1–3]. However, sometimes patients present with itching, fever, splenomegaly and abnormal liver function. Laboratory changes may include elevated liver enzymes, hemolysis, thrombocytopenia, lymphocytosis and raised bile acids, mimicking obstetric cholestasis or HELLP syndrome.

After becoming infected with human CMV, the virus will persist in the body in a dormant form. If the patient is to become immunosuppressed, they are susceptible to reactivation of this dormant virus leading to infection. Pregnancy has been known to reactivate underlying CMV infection and it is thought that this is responsible for 15% of cases of congenital cytomegalovirus in neonates [1, 4, 5].

Cytomegalovirus is a common cause for developmental problems in children diagnosed with congenital infection. Most children whom are congenitally infected with CMV have normal development, however 10% develop abnormally. Their handicap ranges from one feature to multiple problems including sensorineural hearing loss, microcephaly, poor eyesight and developmental delay [4, 6].

Therefore, it is very important to promptly diagnose the CMV infection during pregnancy and pursue further investigations to exclude any potential congenital anomalies. On the other hand, it is necessary to exclude other conditions such as obstetric cholestasis and HELLP syndrome which require prompt management and sometimes elective earlier delivery. Misdiagnosis may subject the patient to unnecessary obstetrical and medical intervention and iatrogenic complications.

CASE REPORT

A 36-year-old female with three previous normal deliveries at term, booked with her fourth pregnancy at 10+5 weeks. She had a routine dating scan, nuchal testing and anomaly scan which were all normal.

At 23+4 she developed intense itching over hands and feet. There was no jaundice or signs of biliary obstruction and she had good fetal movement. Her liver function tests were performed: ALT 49, ALP 77, bili 9, protein 67, Alb 31, LDH 705. Her hemoglobin was 9.3 g/dL. Her bile acids were raised at 22. She was started on ursodeoxycholic acid and vitamin K to treat for obstetric cholestasis, and her viral serology and hepatitis screen were awaited. Meanwhile an upper abdominal ultrasound was performed which showed mild splenomegaly and normal liver and gallbladder.

The patient admitted that two weeks prior to her itching began she had a "cold/flu-like illness" which had resolved. There was no foreign travel and no gastrointestinal symptoms. Her cytomegalovirus antibodies, IgG and IgM were reported as positive. (These were previously negative at booking.)

The results were reviewed and it was estimated that primary infection took place at 18 weeks gestation. Amniocentesis was offered but deferred as the couple were not going to intervene regardless of its result. Fetal measurements and amniotic fluid were normal on detailed ultrasound. The patient was reviewed regularly in the antenatal clinic to ensure adequate development of the pregnancy.

With possiblity of congenital CMV infection, samples from the baby after delivery were requested. These included a urine sample, a viral throat swab and an EDTA blood sample to test for CMV PCR. Evoked potentials and an MRI/USS of the brain were also planed for the neonate. Eyes were to be checked for retinitis. If congenital CMV was confirmed in the neonate, six weeks of valganciclovir was advised.

The patient went into spontaneous labor however, she failed to progress in the first stage of labor due to malposition and had an emergency caesarean section. At birth the 'Apgars' were 8^{1}, 10^{5}. The cord gases were: venous pH 7.335, BE -2.9, arterial pH 7.277, BE -2.8. There were no neurological problems identified on physical examination of the newborn by the pediatrician. Since delivery all investigations have been normal. There is regular pediatric follow-up in place for this infant.

DISCUSSION

Cytomegalovirus is an important cause of itching to identify as it is the commonest congenital infection in neonates, [4] occurring in 0.2–2.2% of all live deliveries [2]. Studies have shown that primary maternal infection provides the highest risk for poor neonatal development [1, 6]. This is particularly evident if the seroconversion occurs during the first trimester [2]. If the mother is seropositive at booking, then this lowers the chance of intrauterine transmission to the fetus and is associated with less potent effects on the neonate if there is reactivation or reinfection with a different CMV strain [7].

It is worth considering the patient's background as studies have shown that immunity to CMV is higher with increasing age, but changes with other factors including ethnicity, geographical location and social status [2, 6].

Yeager (1983) and Adler (1988) studied the transmission of CMV in day nurseries in America, concluding that children in this setting could be a potential source of infection for both parents and childcare staff [8, 9].

Percentages for intrauterine transmission of a primary maternal infection vary amongst studies, but are reported to be from 20-45% [2, 4]. In the neonatal period, 10% of these children go on to develop neurological problems as previously discussed [6]. Of note, research has shown that placental infection can occur without transmission to the fetus [4].

Primary CMV may present with abnormalities of liver function, bile acids, splenomegaly and itching resembles those of obstetric cholestasis and if it is accompanied with thrombocytopenia and hemolysis, it may resemble HELLP syndrome. In symptomatic CMV infection, these changes occur in 10% of patients [10]. Our patient did not exhibit a thrombocytopenia or hemolysis but elevated liver enzymes and bile acids therefore she was initially diagnosed as obstetric cholestasis.

CONCLUSION

Clinicians may encounter difficulty in differentiating between obstetric cholestasis, HELLP syndrome and primary cytomegalovirus (CMV) infection in pregnancy. However, they should be aware with the clinical

presentation of primary CMV during pregnancy and its differential diagnosis. Viral screening and serological tests should be considered promptly. The diagnosis work up for patients present with itching and abnormal liver function test should involve viral serology including CMV PCR and a referral to the results of the booking serology tests or reviewing the stored booking blood sample for further investigations helps in determining the stage of pregnancy at which infection occurs. This enables clinicians to reach a definitive diagnosis and allow them to appropriately council the patient according to the stage of pregnancy.

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Author Contributions

Osama Eskandar – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Georgia Smith – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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