Fetal viral infection: a pragmatic approach to recognition and management

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Abstract

Viruses can be transmitted from a pregnant woman to her fetus via the placenta and can affect development and growth. Maternal infection is often asymptomatic or mild. The implications for the fetus are dependent on gestation, stage of organogenesis, the presence of maternal immunity and the virus type. Fetal infections are a potentially preventable cause of perinatal morbidity and mortality. Prenatal diagnosis is often initiated due to exposure of mother to an infectious contact. Management involves confirmation of maternal infection and careful consideration of the risks and benefits of fetal diagnosis, fetal surveillance, intrauterine treatment and possibly termination of pregnancy. Empathic and effective counselling of the parents is crucial and a multidisciplinary approach is important for optimal care. This case based review follows three pregnancies to illustrate a pragmatic approach to the prenatal diagnosis and management of three common fetal viral infections.

Keywords chickenpox; congenital infection; cytomegalovirus; parvovirus B19; prenatal diagnosis; vertical transmission

Introduction

Fetal infections are a potentially preventable cause of perinatal morbidity and mortality. Viruses such as rubella, cytomegalovirus, parvovirus and varicella-zoster virus can be transmitted vertically from a pregnant woman via the placenta and can affect fetal development. The likelihood of fetal infection, and indeed the consequences of infection for the fetus, via transplacental transmission are dependent on the presence of maternal immunity and gestational age. This review discusses three fetal infections in detail, highlighting current approaches to prenatal diagnosis and management. Routine serum screening is carried out at booking for syphilis and hepatitis B. Viral testing is otherwise initiated, for example for cytomegalovirus, parvovirus B19 and varicella zoster, if markers of fetal infection are identified on a routine ultrasound scan or in response to maternal exposure to infection and, rarely, symptoms of maternal infection. Knowledge of the methods available for prenatal diagnosis, and their benefits and limitations, is essential for accurate counselling and treatment of affected pregnant women.

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Case 1 (Parvovirus)

A 26-year old woman presents to you in the antenatal clinic at 22 weeks gestation. She has been referred by her community midwife because she works in a nursery and two children there have been diagnosed with parvovirus infections. She is very anxious about the well-being of her baby.

What would you do?

Firstly, you should confirm that the patient has had significant contact by taking a targeted history.

Up to 50% of women are non-immune and thus susceptible to parvovirus infection. Significant contact is defined as being in the same room for over 15 minutes, or face-to-face contact of any duration. Parvovirus is infectious prior to the development of the rash and clarification is therefore needed as to when the patient was in contact with the infected children. Transmission of parvovirus B19 most commonly occurs through respiratory secretions and hand-to-mouth contact. The incubation period is 4–14 days following exposure; the infected person generally is infectious for 7–10 days after exposure, prior to the onset of the rash. The person is no longer infectious one day after the rash appeared. The rash can appear up to 18 days following exposure. The transmissibility of the virus is found to be approximately 50–90% among susceptible household contacts.

The lady has been confirmed as having significant contact. What would you do next?

Serum should be collected as soon as possible after contact to investigate for evidence of parvovirus. The laboratory will test for parvovirus and rubella despite the clinical history. Investigation of the serum will facilitate determination of whether the patient has had a previous infection, is still susceptible, or has had an acute parvovirus infection (Figure 1). Serum stored from booking blood can be tested for evidence of past infection to help assess the likelihood of an acute seroconversion.

Adults are frequently asymptomatic, although they may present with erythema infectiosum (fifth disease) – transient fever, arthralgia and malaise. Transient maternal aplastic crises can occur in patients with sickle cell anaemia, thalassaemia, spherocytosis and pyruvate kinase deficiency. Children have a mild illness presenting with the 'slapped cheek' facial rash and fever. Although fetal infection does not appear to cause teratogenicity it can, however, cause profound fetal anaemia through transient bone marrow suppression which can result in cardiac failure, non-immune hydrops and potentially intrauterine death.

The likelihood of fetal infection and damage to the fetus is not dependent on whether maternal infection is asymptomatic or symptomatic. The risk of adverse outcome to the fetus may be reduced by active management of the pregnancy when maternal seroconversion has occurred.

The presence of IgG is evidence of previous infection and confers lifelong immunity. Approximately 50–60% of adults will

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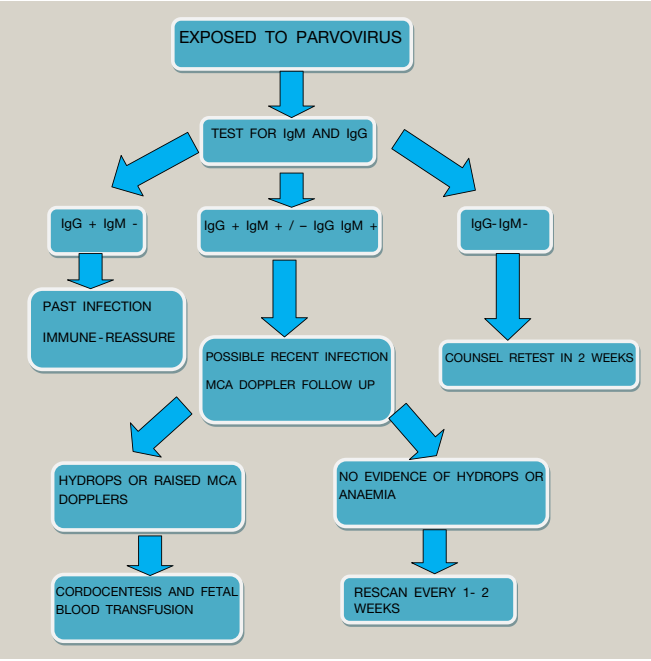

Figure 1 Serology testing for parvovirus.

have evidence of previous infection. The seroconversion rate in pregnant women is an indirect measurement of the primary infection rate and is approximately 1% per year.

The lady should be advised to avoid contact with other pregnant women and people who are immunosuppressed until she is no longer infectious.

Her recent serology is reported as IgG positive and IgM positive for parvovirus B19 infection. Her antenatal screening serology was negative for both IgG and IgM. What is your ongoing management?

She has had an acute parvovirus infection and her care should be discussed with the regional Fetal Medicine Unit. She may need to be managed there rather than her district hospital, depending on local scan expertise.

A multidisciplinary team including virology, neonatologists and fetal medicine specialists should be involved.

How should a woman in this situation be counselled regarding the potential risks to the fetus, and how should the pregnancy be managed?

The risk of maternal infection crossing the placenta to the fetus is 15% from 5 to 15 weeks, 25% after 15 weeks and increasing up to 70% towards term. Infection before 20 weeks can lead to intrauterine death, with a 5–10% fetal loss rate. Infection after 20 weeks results in a 0.5% fetal loss rate. There is a 3–10% risk of hydrops developing over the next eight weeks following parvovirus infection, resulting in fetal death in approximately 50% of cases. The key mechanism causing hydrops is the development of severe fetal anaemia as the human parvovirus B19 targets rapidly dividing cells, thereby interrupting red cell production. This, combined with a shorter half-life of fetal red blood cells, leads to the severe anaemia, hypoxia, high output cardiac failure associated with fetal hydrops. A prospective study showed that 7.5% of third trimester fetal deaths *in utero* were positive for parvovirus B19 in the placental tissues. Thus, testing for parvovirus B19 should be offered in this scenario.

Weekly ultrasound monitoring is necessary to identify fetal anaemia, ascites and hydrops (accumulation of fluid in 2 compartments) for up to 12 weeks after maternal exposure (Figure 2 a and b).

Doppler ultrasound measurements of the middle cerebral artery peak systolic velocity (MCA-PSV) are used to help predict fetal anaemia. (Figure 3). A study assessing the predictive value of MCS-PSVs reported that these Doppler studies had 100% sensitivity for predicting fetal anaemia in the presence of parvovirus.

The Fetal MCA Doppler peak systolic velocity suggests anaemia. What are the options?

30% of cases with fetal hydrops will spontaneously resolve. However, there is no robust method to distinguish these cases from those that will progress to intrauterine death. Thus active management is considered in all cases.

Cordocentesis is used for fetal blood sampling to diagnose fetal anaemia. It should be done with full facilities available for immediate intrauterine blood transfusion if fetal anaemia is confirmed.

Cordocentesis can be performed from 18 weeks onwards. There is a 1–2% risk of procedure-associated miscarriage. The preferred transfusion site is at the umbilical vein insertion into the placenta, but the intrahepatic umbilical vein, or the cardiac

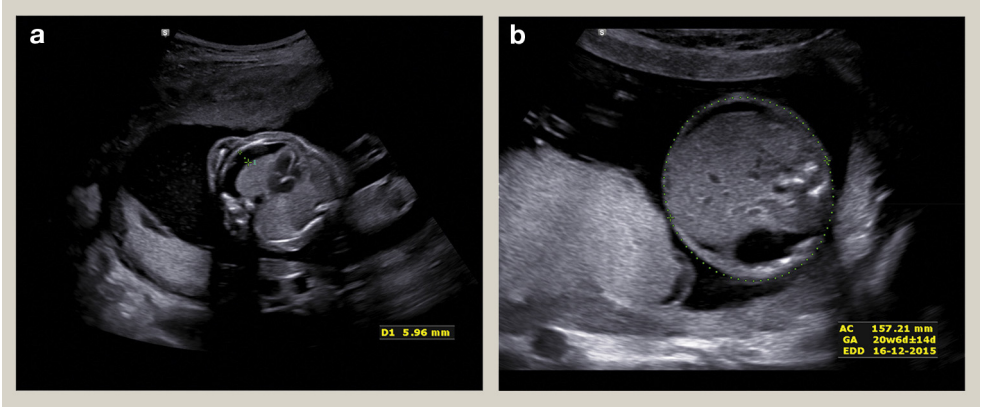

Figure 2 (**a**) Pleural effusion; (**b**) Ascites.

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