Human parvovirus B19 in pregnancy

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Parvovirus B19 infection during pregnancy can have implications for pregnancy outcome. This article aims to review features of B19 infection, and discuss some of the issues of particular relevance to pregnancy. Women should be reassured that a successful outcome will occur in approximately 90% of pregnancy-acquired B19 infection cases. However, owing to the small but recognized risk of pregnancy complications, public awareness of this condition is essential and obstetricians should be familiar with the management options available should they be presented with this clinical problem.

EPIDEMIOLOGY

Parvovirus B19 was discovered in 1975. It is a non-enveloped single-stranded DNA virus which is the only member of the parvovirus family that is pathogenic in humans, where it replicates in erythroid progenitor cells. Parvovirus B19 binds to an antigen in the P-system blood group which is present on erythrocytes, erythroblasts, megakaryocytes, placental cells, and fetal liver and heart cells.

Transmission of the virus is via respiratory droplets and the incubation period after contact is 1 week. This is followed by a period of viraemia lasting approximately 4 days, with subsequent rash appearing at around 16 days following inoculation. The patient is generally no longer infectious by the time the rash appears. Outbreaks of parvovirus infection show seasonal variation with late winter and spring being the times of peak activity. Previous infection (immunoglobulin (Ig) G positive, IgM negative) probably confers lifelong immunity and it is estimated that approximately 50% of women of childbearing age will show evidence of past infection.

CLINICAL FEATURES

In children, parvovirus B19 causes erythema infectiosum, otherwise known as fifth disease. This is a mild influenza-type illness with low-grade pyrexia which, in some cases, is followed by the development of a characteristic facial rash, known as 'slapped cheek' syndrome. In adults, the most common symptom is arthralgia, particularly affecting the hands and knees. Recovery from the infection is usually complete, without complicating anaemia. However, an aplastic crisis with severe anaemia may result in patients with certain haematological conditions. At least 20% of the population will be asymptomatic in spite of laboratory evidence of infection.

DETECTION AND DIAGNOSIS

Maternal serology is the first-line investigation to identify 'at-risk' pregnancies (*Table 1*). The presence of B19-specific IgM, with or without B19-specific IgG, is indicative of recent infection. The presence of B19-specific IgG alone indicates past infection and therefore immunity. Parvovirus B19 cannot be grown easily in conventional tissue culture and this has limited the diagnostic tests available. The fetus is unable to produce measurable quantities of

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TABLE 1. Laboratory diagnosis

Patient	Sample	Investigation
Maternal	Blood	Specific anti-B19 IgM and anti-B19 IgG
Fetal	Blood, amniotic fluid, or ascitic fluid	Viral particles (electron microscopy)
		Viral DNA (in situ hybridization or polymerase chain reaction)

Ig = immunoglobulin

antibodies before 20 weeks gestation, thus limiting the role of fetal serology in the diagnosis of in utero infection.

Diagnosis of fetal infection therefore relies upon direct identification of viral particles by electron microscopy, or of viral DNA by in situ hybridization or polymerase chain reaction. These techniques can be performed on fetal blood, amniotic fluid or ascitic fluid. Tissue histology can be utilized to identify the characteristic intranuclear inclusion bodies, but these will not be present in at least one-third of cases of B19 infection confirmed by other techniques (Rogers et al, 1993; Jordan, 1996).

EFFECT ON PREGNANCY

Fetal loss

Initial reports suggested that the fetal loss rate associated with maternal parvovirus B19 infection was high, but these studies were based on small numbers and the cases identified were as a result of adverse outcome rather than primary infection. Subsequent studies have estimated fetal loss rates ranging from 5 to 16% (Public Health Laboratory Service Working Party on Fifth Disease, 1990; Rodis et al, 1990; Miller et al, 1998).

In the largest group of prospectively followed B19-infected pregnant women a fetal loss rate (spontaneous miscarriage and fetal death >20 weeks gestation) of 14% was reported (Miller et al, 1998). These women were compared with a group of pregnant women with varicella who continued the pregnancy to term and whose fetus escaped varicella damage. Varicella-infected women were chosen because their fetal loss rate is similar to the general population. The fetal loss rate in the first 20 weeks of pregnancy was significantly higher in the parvovirus B19 group (15% *vs* 5%) and this difference was most marked when maternal infection occurred between 9 and 16 weeks of gestation.

It has been suggested that fetal loss rates are higher in B19-infected women who are asymptomatic. The hypothesis is that these women have a reduction in immune response and therefore the potential for an increase in viral load and hence an increased risk of fetal infection. However, the study by Miller et al (1998) found no evidence to support this suggestion, although the focus of their study was on women presenting with symptoms or a history of contact. In order to assess the extent of asymptomatic B19 infection a large group of susceptible women would have to be followed prospectively throughout pregnancy.

Congenital abnormality

Parvovirus infection in animals is associated with characteristic congenital malformations. However, there is no evidence to date to indicate that parvovirus B19 is teratogenic in human pregnancy. There have been isolated reports of multiple eye abnormalities (Weiland et al, 1987; Rodis et al, 1988) but this has not been confirmed in larger series (Miller et al, 1998). Large enough case numbers are not available to detect a rare teratogenic effect of parvovirus B19, but available evidence suggests that the risk of major congenital abnormality is no greater than for the general population. In view of this, maternal infection with B19 is not an indication for termination of pregnancy.

Fetal hydrops

Parvovirus B19 infection is an important cause of fetal hydrops and has been implicated in up to 10% of cases of non-immune hydrops fetalis (Yaegashi et al, 1994). During epidemics of B19 infection, which occur every 2–3 years, the frequency of fetal hydrops is increased. There are two mechanisms underlying B19 associated hydrops fetalis.

First, severe anaemia leads to cardiac failure. Because of the short half-life of erythrocytes, the major target cell of the virus, and the rapid expansion in red blood cell volume the fetus is particularly susceptible to severe anaemia. However, in contrast to immune hydrops, hydrops secondary to parvovirus infection may present at a relatively mild degree of anaemia implying an alternative mechanism in its aetiology.

Second, viral particles have been identified in myocardial tissue and it is proposed that cardiac dysfunction, secondary to viral myocarditis, contributes to the development of cardiac failure. Miller et al (1998) estimated that the risk of hydrops fetalis following maternal infection between 9 and 20 weeks of gestation is 2.9%. The interval between the onset of maternal infection and development of hydrops ranged from 2 to 17 weeks.

Long-term follow-up

Miller et al (1998) have reported a congenital infection rate of 22% based on detection of B19-specific IgG in serum or saliva at 1 year of age. The rate of IgG positivity at 1 year was highest in babies whose mothers had been infected in the second half of pregnancy. Intrauterine exposure to parvovirus B19 infection had no adverse effects on long-term out-

come in this series. The frequency of mild developmental delay (1% at 1 year, and 2% at 7–10 years) was no different from that expected in the general population. Similarly, there was no increase in the rate of iron deficiency anaemia, and no unusual haematological conditions were reported.

MANAGEMENT OF PREGNANCY IN PARVOVIRUS B19-INFECTED WOMEN

Since hydrops fetalis secondary to B19 infection is a potentially curable condition, management of a pregnant woman with parvovirus infection is aimed at detecting those fetuses requiring therapeutic intervention (*Figure 1*). Serial ultrasonography provides the basis for monitoring these pregnancies and aims at detecting signs of hydrops such as scalp oedema, ascites and pericardial/pleural effusions. The placenta often appears large in these cases. Scans are performed at weekly intervals and should be continued for at least 8 weeks from the time of exposure (Rodis et al, 1990).

A longer surveillance period may be appropriate, given the above finding of Miller et al (1998). However, in view of the low rate of fetal hydrops in IgM positive women it has been argued that the clinical value of serial ultrasonography may not justify the financial implications (Harger et al, 1998).

Continued conservative management may be appropriate for some cases of mild fetal hydrops as spontaneous resolution can occur in keeping with the natural history of infection. Failure of the hydrops to resolve, or detection of more severe hydrops, should prompt a more invasive approach. Intrauterine transfusion has been successfully employed in the treatment of anaemia secondary to parvovirus infection. Cordocentesis is performed to assess the fetal haematocrit and facilities for immediate transfusion should be available. Other tests performed should include karyotype, specific anti-B19 IgG and IgM, and detection of viral DNA. A single transfusion is frequently adequate and thereafter non-invasive ultrasound monitoring is essential to ensure resolution.

In our own experience there is transient oligohydramnios in the recovery phase following treatment. Cordocentesis is not without risk to the pregnancy, and owing to the fetal condition the risk is probably higher than that associated with cordocentesis for other indications.

POPULATION SCREENING

Fifty per cent of adults have serological evidence of past infection and this probably confers lifelong immunity. There will therefore be a percentage of pregnant women who are susceptible to parvovirus B19 and the question is how to reduce this risk. Routine antenatal screening for B19 immunity is not current practice since there are no measures available that will eliminate the risk of infection. Vaccines are being developed which may dramatically reduce the sequelae of parvovirus in pregnancy, as has been seen with rubella infection, but this remains an area of future research.

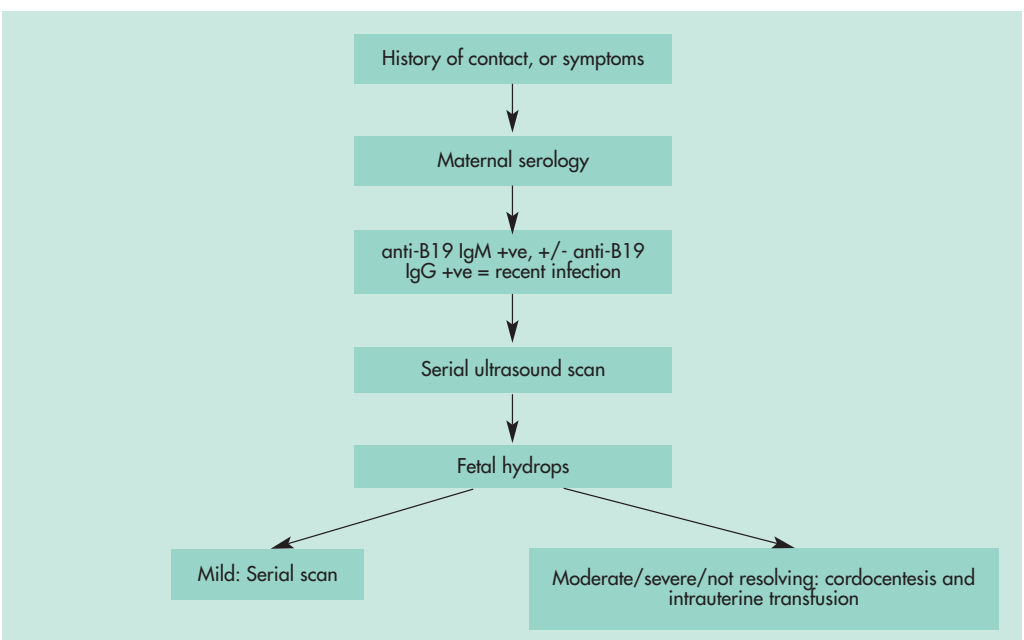

Figure 1. Management of parvovirus B19 infection.

At present, health education to increase public awareness is important, although the impact that this can make on the rate of parvovirus infection in pregnancy remains limited. Those at greatest risk are health-care workers, teachers, and mothers with an infected child in the household, the latter carrying a 50% risk of infection (Plummer et al, 1985). It is not practical to avoid contact in these situations and, since a large proportion of B19 infection is asymptomatic, isolation of affected children or avoiding work cannot eliminate the potential for acquiring infection. Simple hygienic measures such as hand washing will reduce the risk of spread via respiratory secretions.

Patients with aplastic crisis secondary to parvovirus B19 may be highly contagious and should not be nursed by pregnant health-care workers. Women who have been in contact with erythema infectiosum should be offered anti-B19 serology to identify those pregnancies that require closer surveillance.

CONCLUSION

Parvovirus B19 infection can result in an adverse outcome when acquired during pregnancy. However, in the majority of cases a successful outcome can be anticipated. The risk of acquiring parvovirus infection during pregnancy is estimated to be 1 in 400 (Gay et al, 1994), and during an endemic year there would be 2 cases of fetal hydrops and 12 spontaneous miscarriages or intrauterine deaths per 100 000 pregnancies (Miller et al, 1998). These risks are increased during a parvovirus epidemic. Parvovirus B19 should be considered in the differential diagnosis of non-immune fetal hydrops, since it is a potentially treatable condition. **HM**

KEY POINTS

- Epidemics of parvovirus B19 occur every 2–3 years.
- Infection during pregnancy can result in miscarriage or fetal death, but pregnancy outcome will be successful in approximately 90% of cases.
- Infection during pregnancy is not an indication for pregnancy termination.
- Parvovirus B19 should be considered in the differential diagnosis of non-immune fetal hydrops.
- Fetal hydrops can be treated successfully with intrauterine transfusion.

Conflict of interest: None

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