CASE REPORT

Importance of diagnostic work-up of Guillain-Barré syndrome in pregnancy

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SUMMARY

We report a full-term neonate presenting with symptomatic congenital cytomegalovirus (CMV) infection with hepatosplenomegaly, 'blueberry muffin' rash, intracranial calcifications, thrombocytopenia and respiratory distress. Maternal history was relevant for Guillain-Barré syndrome (GBS) during the first trimester of pregnancy. CMV infection is an important cause of GBS; thus, women presenting GBS during pregnancy should be screened for CMV infection. If positive, they may benefit from specialised monitoring and treatment in the antenatal period, which may decrease the risk of major neurodevelopmental sequelae of congenital CMV in the neonate.

BACKGROUND

Cytomegalovirus (CMV) is ubiquitous with 50–80% of reproductive-aged women previously infected.¹ Primary CMV infection during pregnancy is often asymptomatic, but GBS from CMV infection has been reported in rare cases. CMV-induced GBS during pregnancy increases the risk for maternal and fetal morbidity.² Fetal effects include death from CMV placentitis and neonatal Guillain-Barré syndrome.² To the best of our knowledge, this is the first report of congenital CMV infection as a neonatal manifestation following maternal GBS.

CASE PRESENTATION

A male infant was born at 40-week gestation to a gravida 2 para 1 mother aged 32-years. Maternal history was significant for hospitalisation during the first trimester of pregnancy due to bilateral leg weakness, diagnosed as GBS. She was treated with five doses of intravenous immunoglobulin with complete resolution of her symptoms. A prenatal ultrasound was performed during the second trimester, which did not reveal any fetal anomalies. The infant was born by spontaneous vaginal delivery with APGAR scores of 8 and 9 at 1 and 5 min, respectively, and no resuscitation was required. Physical examination revealed an afebrile infant, with pallor and jaundice. Birth weight was 2.7 kg (5th–10th centile) and head circumference was 32.5 cm (5th–10th centile). Abdominal examination was significant for marked hepatosplenomegaly with inferior hepatic and splenic borders 3 cm below the costal margin. There were scattered blue lesions over the face, trunk and extremities (figure 1). At 8 hours of age, the infant was tachypnoeic with desaturations.

INVESTIGATIONS

A complete blood count revealed a haemoglobin of 166 g/L, white cell count of 25 900/mm³ and

Figure 1 Petechial rash with CMV-induced thrombocytopenia. CMV, cytomegalovirus.

platelet count of 22 000/mm³. Maternal platelet count measured 1 day prior to delivery was 235 000/mm³. Conjugated bilirubin was 5 µmol/L, alkaline phosphatase 117 U/L, alanine aminotransferase (ALT) 40 U/L and aspartate aminotransferase (AST) 144 U/L. Head ultrasound performed on the second day of life showed increased echogenicity of the thalamostriate vessels and tiny punctate areas of calcification not related to the vessels (figure 2). Ophthalmologic examination was negative for chorioretinitis. Auditory evoked potentials were absent on the right and normal on the left. Urine and blood RNA PCR was positive for CMV DNA with blood viral load of 23 660 copies per millilitre. Cerebral spinal fluid PCR was negative for CMV. Maternal CMV IgG and IgM were not performed.

TREATMENT

The infant was placed on non-invasive continuous positive airway pressure, treated with ampicillin and tobramycin, and received 50 mL (20 mL/kg) platelet transfusion. After consultation with the

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Figure 2 Head ultrasound findings on second day of life showing increased echogenicity of the thalamostriate vessels particularly on the left and extending laterally; and tiny punctate areas of calcification on the left not related to vessels consistent with intracranial calcifications seen in congenital CMV infection. CMV, cytomegalovirus.

infectious disease team, intravenous ganciclovir was started on day 3 of life. The infant was weaned off non-invasive ventilatory support on day 3 of life and remained on low flow oxygen. Three platelet transfusions were administered to maintain platelet counts $>30\,000/\text{mm}^3$.

OUTCOME AND FOLLOW-UP

The infant was transferred to another facility on day 15 of life for continuation of intravenous ganciclovir to complete a planned total course of 6 weeks and subsequently discharged home with mother. At 2-year follow-up, the child has neurodevelopmental impairment with sensorineural deafness, poor language development requiring the use of sign language and gross motor delay (started walking at 2 years of age).

DISCUSSION

Guillain-Barré syndrome in pregnancy is rare, with an incidence the same as that of the general population, <2 in 100 000 individuals per year.³ To date, <100 cases have been reported on GBS affecting a pregnant patient. More than half of the cases that have a known aetiology have been identified as CMV induced. The majority of these cases were published in obstetrical journals or focused predominantly on maternal morbidity.² However, reports on neonatal outcomes are rare and include normal outcomes, fetal demise and neonatal GBS. To the best of our knowledge, this is the first report of congenital CMV infection as a neonatal manifestation following maternal GBS infection.

CMV infection is the most common congenital infection worldwide, with a prevalence of 0.64% in the general population.⁴ Studies have shown that incidence of developing CMV-induced GBS is similar to that from *Campylobacter jejuni*, currently the most common known cause of GBS.⁵ Unlike with *C. jejuni* infection that affects an older population, CMV-induced GBS commonly affects those of childbearing age.⁵ Recent studies have shown that the timing of CMV infection during pregnancy is a significant factor in neonatal morbidity.⁶ A study by Picone *et al* concluded that acquisition of CMV in the periconceptional period (3 weeks prior to and 3 weeks after the date of conception) was associated with the highest rate of severe symptomatology with 67% of fetuses whose mothers were infected during this period being symptomatic. Although transmission rates increased in the later stages of pregnancy, after 14 weeks of gestation, acquired primary CMV infection yielded no symptomatic newborns.⁶ These findings suggest that primary CMV infections during the first trimester are most worrisome for severe neonatal outcomes. Owing to severity of symptoms caused by the congenital CMV infection, it is highly likely the patient in our case acquired the primary infection

during first trimester. However, a limitation of this case is the possibility that the GBS was caused by another aetiology unrelated to the CMV infection.

Among neonates infected with CMV at birth, symptomatic presentation occurs in 10% of cases and is variable.⁴ Similar to our case, symptoms of congenital CMV infection commonly include hepatosplenomegaly, thrombocytopenia and petechiae–purpura. Neurological involvement, including intracranial calcifications, ventriculomegaly, microcephaly or CMV-positive cerebrospinal fluid PCR study, has been associated with adverse neurodevelopmental outcomes and impose a major health burden.⁷ Chorioretinitis and sensorineural hearing loss are also common manifestations of congenital CMV infection.³ A retrospective study reviewed prenatal ultrasounds of fetuses who were diagnosed with symptomatic congenital CMV infection postnatally to evaluate efficacy of prenatal sonogram in detecting symptomatic CMV. The study showed that the sensitivity of ultrasound in detecting symptomatic congenital CMV is poor as it correctly identifies only 20% of infected babies.⁸

This case highlights that CMV is an important cause of GBS in pregnant women, underscoring the importance of screening for CMV among pregnant women presenting with GBS, particularly during the first trimester. With early identification of CMV infection, therapies such as CMV-specific hyperimmunoglobulin⁹ or valacyclovir¹⁰ should be considered in an effort to potentially improve neonatal outcomes.

Learning points

- ▶ Women presenting with Guillain-Barré syndrome (GBS) during pregnancy should be screened for primary CMV infection.
- ▶ CMV-induced GBS during pregnancy increases the risk for maternal and fetal morbidity.
- ▶ With early identification of CMV infection (preferably in the first trimester), administration of therapies such as CMV-specific hyperimmunoglobulin or valacyclovir should be considered.

Contributors EP-C was involved in the drafting of the manuscript and associated editing. K-SL was involved in the care and follow-up of the patient. K-SL was additionally involved in manuscript revision and approval of the manuscript to be published. K-SL was directly involved in all editing of the manuscript.

Competing interests None declared.

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