Neonate with Coxsackie B1 Infection, Cardiomyopathy and Arrhythmias

Jimmy C. Lu, MD; Kelly W. Koay, MD; Christian B. Ramers, MD; and Angelo S. Milazzo, MD
Durham, North Carolina

A neonate with Coxsackie B1 infection who experienced significant congestive heart failure, cardiomyopathy and arrhythmia is reported. Viral myocarditis, an important cause of acquired heart disease in neonates, should be considered in the differential diagnosis of neonatal congestive heart failure and cardiomyopathy. A review of the literature is presented.

Key words: Coxsackie B1 ■ cardiomyopathy ■ myocarditis ■ supraventricular tachycardia (SVT) ■ acquired heart disease

CASE REPORT

A 3,035-g male was delivered at 35 weeks via Cesarean section because of maternal fever and fetal heart rate instability. Following delivery, the infant demonstrated grunting, pallor and signs of hypoperfusion. Echocardiography demonstrated decreased left ventricular function with significant hypokinesis of the posterior left ventricular wall, consistent with cardiomyopathy. Telemetry during the first few days of life revealed premature atrial and ventricular complexes [premature atrial complexes (PACs) and premature ventricular complexes (PVCs)] and, later, episodes of supraventricular tachycardia.

Over the course of several days, the patient demonstrated worsening signs of congestive heart failure, including sustained tachypnea, hepatomegaly, hypotension and mottling of the extremities. He also developed fever, while his mother developed fever and headache. He was treated with oxygen, intravenous fluids, inotropic agents, antipyretics, broad-spectrum antibiotics and antiviral medication. Analysis of the patient's cerebrospinal fluid (CSF) demonstrated a significant white blood cell count. Viral polymerase chain reaction (PCR) assay of CSF confirmed enterovirus infection. The patient's mother tested positive for antibodies to Coxsackie B1 virus.

The patient's clinical course continued to deteriorate, and he eventually experienced ventricular fibrillation. He was resuscitated, and his residual cardiomyopathy was managed with a combination of medications. He experienced no further arrhythmia or significant cardiovascular instability during the remainder of his hospitalization. Following discharge, serial echocardiograms over several months demonstrated improved left ventricular function, with increased mobility of the posterior left ventricular wall.

DISCUSSION

Viral myocarditis, due to any of a number of viruses (Table 1), is an important cause of cardiomyopathy in the neonatal period. Murine studies suggest that the pregnant state increases susceptibility

to enterovirus infection, with an elevated viral load, prolonged viremia and increased mortality, compared to nonpregnant individuals.[1] However, the low incidence of human congenital Coxsackie infection suggests that the placenta serves as a barrier to intrauterine transmission. The onset of maternal infection is another important determinant of disease. If infection occurs more than 5–7 days before delivery, specific maternal antibodies can develop and cross the placenta, often resulting in absent or asymptomatic infection.[2]

Neonatal Coxsackievirus (enterovirus) infection occurs both sporadically and in association with seasonal variation. It can be transmitted vertically or postnatally.[2] In the reported case, the neonate may have acquired the infection in utero from an infected mother, as manifested by maternal fever and fetal heart rate instability during delivery, or both may have acquired it nosocomially after delivery. Laboratory testing on the mother was not performed until after delivery, so her serologic status at delivery is not known.

The clinical expression of Coxsackie disease in the neonate is highly variable (Table 2) and tends to result in increased mortality compared with cases in older children. Disease pattern varies from a steady progression to biphasic illness (anorexia, coryza and loose stools followed in 1–10 days by severe illness) to rapid death within the first 24 hours.[3,4] Fatal cases are often characterized by encephalitis, hepatitis and myocarditis, usually occurring within the first four weeks of life. Some affected newborns, despite the development of significant complications from Coxsackie infection (including myocardial disease), will make a complete recovery.

With profound myocardial involvement, infants can develop respiratory distress, tachycardia, cyanosis and eventual cardiovascular collapse.[5] Electrocardiographic findings are variable and may include ST segment elevation or depression; T-wave inversion or flattening; prolongation of the QRS and corrected QT intervals; atrioventricular conduction abnormalities; ectopy, such as PACs and PVCs; and brady- or tachyarrhythmias. In this case, the ectopy seen in the first two days of life may have been an early indication of myocarditis and not necessarily predictive of future, sustained arrhythmia.

Definitive diagnosis of Coxsackie B infection requires isolation of viral particles from cell culture. However, reverse transcriptase PCR tests directed at the conserved 5' noncoding region of the enteroviral genome have been shown to be consistently more sensitive than viral culture, virtually 100% specific,[6] and can significantly impact patient management when used in a lab with rapid turnaround times.[7] Although serologic testing is commercially available, it is often reserved for retrospective diagnosis of patients already diagnosed by one of the above methods.

Specific treatment is not currently available for neonatal Coxsackie B infection. Intravenous immunoglobulin has been associated with an antiviral effect if the neutralizing antibody titer is ≥1:800, but studies have been inadequately powered to definitively demonstrate clinical benefit.[8] The use of pleconaril, an antipicornavirus drug, has been described in a case report in preterm neonates with myocarditis. Use of this drug was reserved for children with serious, life-threatening enterovirus infections, but it was not available for the treatment of this patient and has now been withdrawn from use by the FDA.[9-11]

Prognosis for neonates who survive the initial course of myocarditis is variable. Many patients achieve complete recovery with no residual cardiac damage. However, there is speculation as to whether Coxsackie infection may result in chronic endocarditis or myocarditis.[3] Patients with associated aseptic meningitis are also at risk for various neurological deficits, such as ocular abnormalities, spasticity, developmental delay and seizure disorder.[4]

Table 1. Viral Causes of Myocarditis in Neonates

Adenovirus
Cytomegalovirus (CMV)
Epstein-Barr virus (EBV)
Enterovirus
  Coxsackie A
  Coxsackie B
Herpes simplex virus (HSV)
Human immunodeficiency virus (HIV)
Parvovirus
Respiratory syncitial virus (RSV)
Rubella
Rubeola

Table 2. Clinical Manifestations of Neonatal Coxsackie Virus Infection

Fever
Irritability
Rash
Pharyngitis
Diarrhea
Jaundice
Hepatitis
Aseptic meningitis
Meningoencephalitis
Myocarditis or pancarditis
Pulmonary hemorrhage
Pancreatitis
Necrotizing enterocolitis
Disseminated intravascular coagulopathy
Circulatory collapse

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