Perinatal Echovirus-11: a potentially fatal infection

This case report details the history of a male infant born at 36 weeks' gestation who presented with necrotising enterocolitis-like signs in the first week of life but was later confirmed to be infected with an enterovirus infection (Echovirus-11). The baby's vague presentation provided a diagnostic conundrum such that he underwent a laparotomy that possibly exacerbated his fragile condition. Despite full supportive therapy, the infant developed disseminated intravascular coagulation and succumbed to massive pulmonary haemorrhage on day 13 of life. This article aims to raise awareness of this potentially fatal group of infections that can mimic common neonatal morbidities.

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Key points

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1. Enterovirus infection with systemic involvement can cause serious morbidity and mortality, which may mimic other conditions leading to missed or delayed diagnosis.
2. Perinatal enterovirus infection should be considered in the work-up of any sick neonate, especially in the case of unexplained sepsis-like syndromes or hepatic failure.

Enteroviruses are a genus of single-strand RNA viruses of which over 70 human serotypes are known. These are sometimes classified into four groups: polioviruses, echoviruses, Coxsackie A and B viruses. Non-polio enterovirus infections are mostly asymptomatic or minimally symptomatic, with no long-term sequelae in neonates. However, they can also present with sepsis, myocarditis, liver involvement, meningitis or encephalitis, with significant morbidity and mortality.

The case

A male infant was born at 36 weeks' gestation by an emergency caesarean section due to maternal abdominal pain and fetal distress. The mother had a history of recent feverish respiratory illness in an otherwise uneventful pregnancy. The baby was born in good condition weighing 2.94kg with Apgar scores of 8 and 9 at one and five minutes, respectively. He was noted to be grunting soon after birth and was admitted to the local neonatal unit with a provisional diagnosis of respiratory distress syndrome. The baby responded well to high flow nasal cannula oxygen and by day 2 of life he was in ambient oxygen and establishing feeds. Sepsis markers and blood cultures were negative. On day 5 the baby developed progressive abdominal distension and respiratory distress, which led to intubation and ventilation by day 8. Blood cultures and C-reactive protein levels were negative. He developed rectal

Parameter	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13
Haemoglobin (g/L)	186	142	79	94	60	79	83
Platelets (x10^9/L)	14	15	49	50	28	59	32
White cell count (x10^9/L)	19.7	30.7	8.1	8.4	5.5	7.3	8.5
Prothrombin time (seconds)	24.2		>180	74.4	27.9	22.8	27.1
Activated partial thrombin time (seconds)	72.1		>240	55.7	38.1	35.2	43.7
Fibrinogen (g/L)			<1	0.9	1.1	1.2	0.9
Alkaline phosphatase (U/L)	322	452	297	260	194		357
Alanine transaminase (IU/L)	79	235	1636	522	288	162	160

TABLE 1 Blood analysis results from day 7 to day 13.

bleeding and was noted to have deranged coagulation and thrombocytopenia; he received blood products accordingly (**TABLE 1**).

On day 9 of life, with a presumed diagnosis of necrotising enterocolitis (NEC), the child was transferred to the tertiary neonatal intensive care unit where an exploratory laparotomy was performed. No evidence of intestinal perforation, volvulus or NEC was seen. However, there was evidence of ascites and the liver was dark and firm with zones of necrosis. The bowel appeared healthy. On return from the theatre, the infant became more unwell, with progressive liver failure and disseminated intravascular coagulation (DIC). Abdominal ultrasound showed an enlarged heterogeneous liver with reversal of portal venous flow (**FIGURE 1**). Cranial ultrasounds were normal.

The infant underwent metabolic and viral screening and remained on antibiotics despite serially reassuring blood cultures. The differential diagnoses of haemochromatosis and haemophagocytic lymphohistiocytosis were considered. On day 10, the baby was diagnosed by serum polymerase chain reaction (PCR) as being enterovirus positive, which was later typed as Echovirus-11. Following discussion with the local liver team, he received immunoglobulin therapy and N-acetylcysteine. The infant became extremely oedematous, with worsening renal function as part of a picture of multi-organ failure. He required escalating ventilatory support and inotropes for hypotension. With ongoing DIC and despite receiving blood products liberally, on day 13 the baby had a massive, uncontrollable pulmonary haemorrhage that led to his death. No post mortem was carried out.

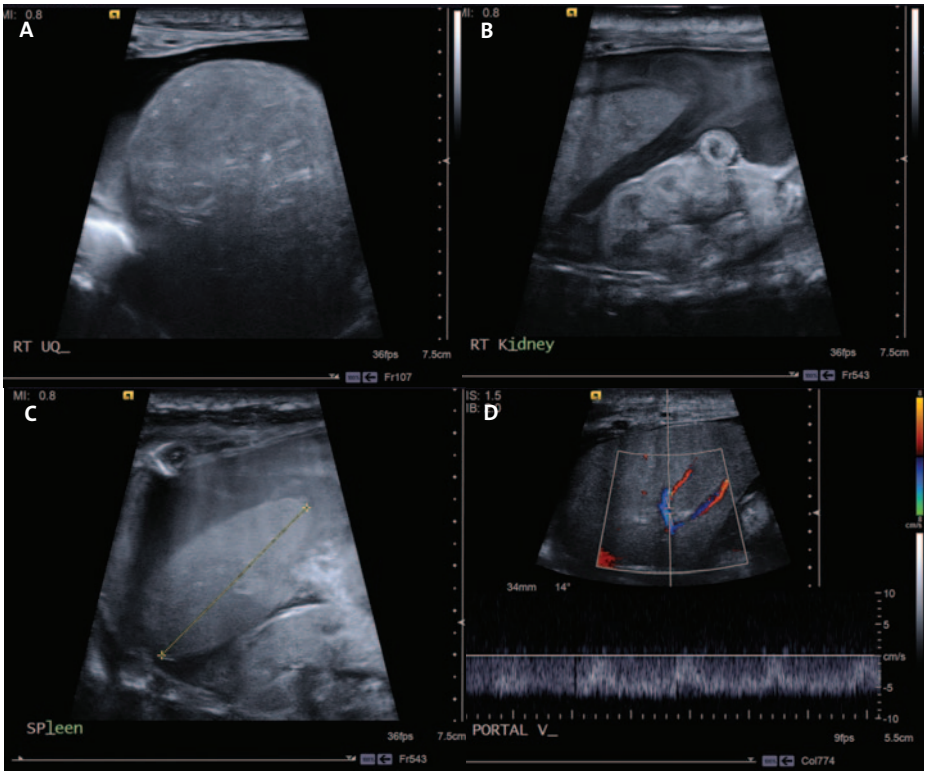

FIGURE 1 Ultrasound scans of the abdomen on day 9 of life. A, B and C demonstrate the ascites/bleed noted in the abdomen. C denotes an echogenic spleen. D shows the enlarged heterogeneous liver with reversal of portal venous flow.

Discussion

Enterovirus infection in newborn infants may be acquired by three mechanisms:

1. through or across the placenta
2. intrapartum, by contact with maternal blood or vaginal/cervical secretions
3. postnatally, including nosocomial transmission.

While mostly asymptomatic (79%),[1] the huge spectrum of disease means that some babies present with non-specific symptoms of fever, lethargy, poor feeding, jaundice, irritability or cough, while others have acute sepsis-like syndromes, meningitis/encephalitis, hepatitis or myocarditis. Among the enterovirus subtypes, Echovirus-11 and Coxsackie virus B are most associated with serious neonatal morbidity and mortality.[1-4] Infection is likely to be more prevalent than believed, with one study reporting detection of enterovirus from throat and stool cultures in 12.8% of neonates,[1] although PCR-based assays are the most sensitive method of detection.

Patients presenting with hepatic necrosis and coagulopathy (HNC) or myocarditis have been found to have high mortality rates[1,3,4] alongside those suffering intracranial and pulmonary haemorrhage. Other associations with poor outcome include maternal illness, prematurity, presentation within the first week of life, anaemia, leucocytosis and multi-system disease.[1,3,4] The patient presented in this report fulfils all of the criteria for enterovirus-associated HNC, and demonstrated many of the above parameters associated with poor outcome.

Treatment of enterovirus is primarily supportive with a few case reports suggesting a role for immunoglobulin.[1,5] Pleconaril (a viral capsid inhibitor) has been used with some minimal success[1,5] but is not licensed in the UK due to concerns around safety and efficacy.

Parental consent

The authors are extremely grateful to the baby's parents who have given consent for publication of their baby's case history and ultrasound images.

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