Reminder of important clinical lesson

Enterovirus—a double act

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Summary

This case report describes twins presenting approximately 24 h apart both with enterovirus meningoencephalitis. The presenting symptoms are described along with laboratory results. Both had extremely high white cell counts in cerebrospinal fluid, which were predominantly lymphocytes. Clinical course and outcomes are described. There was a potential delay in diagnosis of the second twin given the pathology of the twin sibling and the symptoms presented.

BACKGROUND

Neonates may present with non-specific symptoms in the early phase of an infective illness. The second twin in this case report displayed similar symptoms to those of his twin with proven meningoencephalitis and his parents voiced their anxiety about this. Despite this they were discharged, only to re-present hours later with an ill baby who had identical pathology. It is important to take into consideration likely infective pathogens, especially in twin siblings who are often in very close physical proximity in the newborn period.

CASE PRESENTATION

Twins were born 36+5 week via emergency caesarean section for fetal tachycardia. Routine antenatal investigations were normal. Mother's medical history included asthma and anxiety. There was no history of maternal pyrexia, prolonged rupture of membranes or group B streptococcus. The first twin weighed 2030 g (2nd to 9th centiles) and had Apgars of 7¹ and 9⁵. The second twin weighed 2310 g (9th to 25th centiles) with identical Apgar scores. The twins were managed on the postnatal ward; both had blood glucose monitoring as per local protocol. The first twin was seen by the paediatric foundation year 2 doctor and an advanced neonatal nurse practitioner because of two episodes on day 2 of cyanosis and pallor post-feed. It was assumed he had choking-type episodes. He examined normally at the time. He lost 11.4% of birth weight by day 3 and was kept in for a further day to establish feeding. Mother felt that he was at times jittery; blood glucose measurements were within normal range and she was reassured. The second twin did not have any such problems. Both twins were discharged home on day 4.

On day 5, the parents presented with both twins to accident and emergency. The first twin had been increasingly jittery, was feeding poorly and felt feverish. On questioning, the parents were themselves well; there was no history of cold sores. Their older toddler had been feverish 24 h previously but with no other symptoms and was felt to be

teething. The first twin's temperature was 39°C, he was alert and hyperphagic but also hypertonic and irritable. On examination he had a full fontanelle. In view of age and pyrexia, a full septic screen was performed.

During this time, the second twin was present and initially was entirely well. The twins had been sleeping in the same cot in the postnatal ward and at home. He was with the mother in the special care baby unit (SCBU) the night the first twin was admitted. The following day he was also present in the nursery. The parents raised concerns regarding the jitteriness and somewhat poor feeding over the day and he was reviewed by an advanced neonatal nurse practitioner who felt he looked well and feed volumes were reasonable. Calcium, magnesium and phosphate blood tests were performed for jitteriness and he was allowed home. Later that evening they re-presented as the second twin felt feverish and had vomited. On examination he was jittery, distressed, hyperphagic and had a full fontanelle. Otherwise he was well-perfused and active. An infection screen was performed.

INVESTIGATIONS

The first twin's cerebrospinal fluid (CSF) biochemistry revealed increased protein (1.27; reference range 0.25–0.95) and reduced glucose. CSF white cell count (WCC) on microscopy was markedly elevated at 800/ml³ and 90% were lymphocytes. No organisms were seen. Blood parameters, including urea and electrolytes, and liver function tests were normal. C reactive protein (CRP) was 3 (reference range 0–10 mg/litre). Plasma WCC was 14.7 (reference range 6–18 × 10⁹/litre) with 5.2 lymphocytes (reference range 3–13 × 10⁹/litre). Other investigations, including urine microscopy and chest x-ray, were normal.

The second twin had a CSF white count of 1129/ml³ with raised protein (1.38; range 0.00–0.95) but normal glucose. Ninety-five per cent of the white cells in CSF were lymphocytes. CRP was 4, WCC 16.7 (reference range 6–18 × 10⁹/litre) and 8.8 lymphocytes (reference range 3–13 × 10⁹/litre).

The laboratory technician commented that such high WCCs in CSF were extremely rare.

TREATMENT

The first twin was started on benzylpenicillin and gentamicin and intravenous dextrose. Aciclovir was added once the CSF results were known. He was admitted to an isolated bay in SCBU. He remained pyrexial and tachycardic and received one 10 ml/kg bolus of 0.9% saline for tachycardia. The following morning the antibiotics were changed on microbiology advice to cefotaxime and amoxicillin to better cover *Listeria*.

The second twin was started on cefotaxime, amoxicillin and aciclovir but remained enterally fed.

OUTCOME AND FOLLOW-UP

Both twins remained on antibiotics and aciclovir for 48 h, after which the antibiotics were discontinued as blood and CSF bacterial cultures were negative. CSF viral analysis revealed enterovirus on PCR after 48 h for the first twin and after 24 h for the second twin. Unfortunately further subtyping at the national reference laboratory proved technically impossible. Aciclovir was discontinued after this result was known. Both still had intermittent low grade pyrexia for 3 further days. Both had normal cranial ultrasounds. They were in SCBU for 8 and 9 days, respectively, and discharged home with routine follow-up. Parents raised concerns regarding the potentially delayed diagnosis in the second twin and were counselled appropriately. The twins are now thriving without neurological sequelae.

DISCUSSION

Enteroviruses, a group of single-stranded RNA viruses, are commonly encountered in infants and children. Coxsackie and echovirus are the main non-polio enteroviruses implicated. Widespread outbreaks are not uncommon, particularly over summer and autumn months. Neonatal sepsis and encephalitis are recognised presentations. In older children, a vague coryzal illness may be the only sequelae. Transmission of the human form is most commonly faeco-oral; respiratory and oral-oral may occur in crowded living conditions. Incubation period is 3–10 days. Infants younger than 10 days are unable to mount a significant immune response and are at higher risk of a serious infection. Overall mortality is extremely low, but greatest in those presenting with neonatal sepsis.¹ From a cohort of 2544 neonates over a 20-year period, reported death rate was 11%.²

A history of a maternal febrile illness, often with gastrointestinal symptoms around the time of delivery, is commonly reported in the history. This was not a feature in our

case, although one wonders of the significance of the ‘teething toddler’ at home. It is plausible that the first twin infected the second twin and that the infection had been passed on from an unknown, clinically well, source within the hospital or indeed a well-meaning visitor.

Treatment is supportive although bacterial pathogens would inevitably be treated until culture results became available. The role of aciclovir is limited, although its role in herpetic viral meningitis and encephalitis is well proven; therefore, one might argue that until herpes is disproven it is reasonable to treat as such.³ Immunity is type-specific and natural infection confers life-long immunity. Good hand hygiene is important in reducing transmission and infection control strategies for nursing infected infants include isolation and barrier nursing.⁴ Immunoglobulin may have a role in treatment of severe infections.⁵

There are case reports describing the neurological sequelae of enterovirus encephalitis in infants which is more severe than isolated meningitis. There are no recent case reports about twins acquiring the infection simultaneously in the newborn period.

Learning points

This case report highlights:

- ▶ The need to always take parental concern seriously and to have a low threshold for screening the non-specifically unwell neonate for infection.
- ▶ The virulence of enterovirus between close contacts, which should be taken into account in evaluation of infants with infectious contacts.
- ▶ The greatly elevated WCC in CSF, which may result from viral meningitis (as opposed to assuming bacterial meningitis).

Competing interests None.

Patient consent Obtained.

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Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Smith JK, Al-Essa S, Ramlingham S. Enterovirus—a double act. *BMJ Case Reports* 2010;10.1136/bcr.01.2010.2635, date of publication

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