ENTEROVIRUSES AS A CAUSE OF NEONATAL MENINGITIS: DO WE OFTEN MISS THEM?

Azza Morgan¹  Anan Ghazy²  Colin Michie³

ABSTRACT

We describe a newborn with neonatal meningitis caused by an enterovirus. The case illustrated how it may be easy to miss these viruses given the limitation of virological tests. Enteroviruses or EV are RNA viruses broadly divided into polio and non polio groups. Non-polio enteroviruses include echoviruses, coxsackie A and B viruses and a number of unclassified enteroviruses (Bennett, 2009). They are responsible for a range of clinical illnesses with a wide spectrum of clinical manifestations and severity.

Declarations: Nothing to disclose

CASE REPORT

A 5 day-old boy was brought to casualty with a two-day history of fever, irritability and poor feeding. He had wet nappies and passed soft yellow stool regularly. The perinatal history was unremarkable: he was delivered at term by spontaneous vaginal delivery with good Agar score and a birth weight was 3.62kg. The pregnancy had been smooth; his mother had not suffered any fever or unexplained illness. The infant did not require resuscitation, he had been bottle fed and passed meconium at 24 hours. Both parents were healthy and well at the time of delivery. His two elder siblings, both schoolchildren, had suffered febrile illnesses in the weeks before the infant’s presentation, but had not sought medical attention.

Examination, revealed an unhappy, irritable infant, active and well perfused. He was pyrexial (38.7°C) and tachycardic but normotensive with normal respiratory rate and oxygen saturations. There was no rash, petechiae or vesicular lesions. The chest and heart examination was normal. Abdominal examination showed no organomegaly. He had a soft fontanelle, normal

¹ Department of Paediatrics, Ealing Hospital NHS Trust.
² Department of Pathology, Ealing Hospital NHS Trust.
³ Department of Paediatrics, Ealing Hospital NHS Trust.
pupillary responses and no meningism was evident. There were no cataracts, the hips were stable. The umbilical stump was clean. The level of irritability was high and this prompted the clinicians into performing a lumbar puncture.

On investigation, the Hb was 13.6g/dl WBC 6,500/mL, with 32% neutrophils and platelets of 110. The CRP was 7. A capillary gas, electrolytes, liver transaminases and a coagulation screen were normal for his age. The cerebrospinal fluid showed a white blood cell count of 55/ml, with 40% neutrophils and 60% lymphocytes. The cerebrospinal fluid glucose was 3.15 mmol/l with a serum glucose level 4.1 mmol/l and a cerebrospinal fluid protein of 0.94g/l. A chest x ray, ECG and a cranial ultrasound all were within normal ranges. Intravenous fluids, cefotaxime and aciclovir were administered. Clinical improvement was apparent within 48 hours. The infant made a steady recovery and at the age of 3months had an appropriate development according to age with no concern related to hearing. Formal audiological testing was normal.

Bacterial cultures of blood, cerebrospinal fluid, urine and stool were negative However cerebrospinal fluid virology culture and a polymerase chain reaction (PCR) test was positive for a non-polio enterovirus using Roche Light Cyder real time nested detection. The subtype of virus was not examine. PCR was negative for herpes viruses. The case was reported to the Health Protection Authority.

DISCUSSION

In one series Non-Polio enteroviruses (NPEV) were responsible for over 80% of viral meningitis in which the etiologic agent was identified (Gina P.L et al 2006). Neonates younger than 10 days are at higher risk of more invasive disease from these agents. Many may be asymptomatic or have mild response to infection: they may not present to medical services or have other diagnoses made by their families and general practitioners. Many in Hospital recover on resuscitation and do not receive lumbar punctures. Only a small proportion of cases receive investigation with PCR. Some neonates develop a sepsis-like condition that may progress to meningoencepalitis, myocarditis or hepatitis. Meningitis caused by enteroviruses is notifiable in the UK, but not the USA. The rates of long-term complications from NPEV meningitis are thought to be low.

Enteroviruses are non-enveloped single-stranded RNA viruses in the family Picornaviridae. The non polio group include Coxsackie A, B, Echo virus group and EVs. This last group is a particularly common cause of infection in children (Hawkes and Vaudry, 2005). Neonatal infections have been related to a number of indistinguishable EVs, with the exception of polio which gives transverse myelitis and Coxsackie B which may be associated with myocarditis (Zaoutis and Klein, 1998). EVs can survive for days at room temperature and withstand gastric acidity which promotes faecal oral
transmission. The Incubation periods are short, of 2-10 days (Zaoutis and Klein, 1998), supporting the identification of these in our case: the organisms were probably contracted from siblings, rather than in vertical transmission from his mother.

Enterovirus type 71 (EV71) causes a more severe disease spectrum, including aseptic meningitis, encephalitis, acute flaccid paralysis, and acute cardiopulmonary dysfunction. Epidemics of EV71 infection have been reported worldwide (Carlos et al 2007). EV71 strains collected from two UK reference laboratories found that EV71 infection was associated with cases of mild illness, including HFMD, with a subset of cases developing neurological symptoms. UK strains EP/7414/99 and EP/5622/99 were most closely related to an Australian strain (7F/AUS/6/1999) obtained from a patient with meningitis. However UK strains do not possess the VP1 170 (A→V) substitution that appeared to be associated with increased neurovirulence of EV71. Further studies are required to ascertain the role of mutations regarding pathogenesis (Jon M. Bible, 2008).

No specific prevention or control measures are available for NPEV. Adherence to good hygienic practices, such as frequent and thorough hand washing (especially after diaper changes), disinfection of contaminated surfaces by household cleaners (e.g., diluted bleach solution), and avoidance of shared utensils and drinking containers, are recommended to help interrupt transmission (CDC, 2004). Current treatment for enteroviral meningitis is supportive; fluid hydration and antipyretics are the mainstays of care (Singer JI, 1980). Intravenous immunoglobulin may be beneficial in the outcome of myocarditis (Matthias W Freund et al 2010). Other indications include possible efficacy in infection in newborn with agammaglobulinemia (Gaspar BG et al, 2001). Although not approved by US Food and Drug Administration (FDA) the antiviral drug pleconaril may play a role in the treatment plan in future (Desmond, et al 2006).

Enteroviruses are readily found in body fluids and tissues during infection and identification by PCR or virology culture is therefore straightforward. PCR requires a small volume of material for analysis (Herberhold 2009) and is particularly useful in samples of cerebrospinal fluid.

**CONCLUSIONS**

Irritable infants commonly present to paediatric services. Our case illustrates the value of formally checking such cases with a lumbar puncture and requesting PCR for enteroviruses.

**ACKNOWLEDGEMENTS**

We should like to thank the family of this child who consented to our publishing this case history.
REFERENCES