Short reports

Relapsing *E. coli* K1 antigen meningitis in a newborn

Neonatal meningitis is still associated with a high mortality, and a high incidence of sequelae among survivors. Yet early diagnosis, prompt and adequate treatment, and careful attention to supportive measures, such as assisted ventilation when necessary, can improve this situation (McCracken, 1972; Lorber, 1974). There has been renewed interest in *Escherichia coli* meningitis recently with the discovery that strains invading the cerebrospinal fluid (CSF) of newborn infants are encapsulated, and that over 80% of them possess the capsular polysaccharide K1 antigen (Robbins *et al.*, 1974; Schiffer *et al.*, 1976). Ventriculitis is a well known accompaniment of neonatal meningitis (Berman and Banker, 1966), making it essential that adequate levels of the antibacterial drugs used in treatment reach this area. A case of relapsing *E. coli* K1 antigen meningitis in a newborn infant is presented which illustrates these points.

Case report

A male infant was born elsewhere at 32 weeks' gestation to a primiparous Sikh woman who had been treated with ampicillin for a suspected urinary tract infection and whose postdelivery high vaginal swabs grew *E. coli*, later discovered to be resistant to ampicillin.

The infant cried at birth; birthweight 1830 g and head circumference 29 cm were both near the 50th centile. Transfer was requested at 52 hours after increasingly severe apnoeic episodes; mechanical ventilation via a tightly fitting face mask was necessary for the journey and for the next 26 hours. On arrival he was pale and ill-looking, but apyrexial. The skin around the umbilicus was inflamed but not indurated. The anterior fontanelle was small and not under tension.

Investigations showed Hb 15.9 g/dl; white blood count $8.3 \times 10^9/l$ ($8300/mm^3$) (56% neutrophils); CSF clear; white blood count $400/mm^3$ ($0.4 \times 10^9/l$) (90% polymorphs); red blood count $20/mm^3$ ($20 \times 10^{12}/l$). Apparently capsulated Gram-negative rods were seen. Culture grew *E. coli* carrying an R factor

determining resistance to ampicillin, but sensitive to all other antibiotics tested. The strain showed the following slide-agglutination reactions with two sera provided by the Standards Laboratory, Colindale.

Serum	Suspension	
	Live	Boiled
<i>E. coli</i> 018 ac Meningococcal group B	Faint	Rapid and complete
	Rapid and complete	Faint

Umbilical, rectal, and throat swabs all grew *E. coli*; blood culture (peripheral vein): *E. coli*; urine showed no pus cells, sterile on culture; chest x-ray showed no evidence of aspiration pneumonia.

As soon as Gram-negative rods were seen on the CSF film, treatment was started. Ampicillin 50 mg/kg and gentamicin 2.5 mg/kg were given 12-hourly intravenously and gentamicin 1 mg instilled daily into the lumbar theca. On the third treatment day (age 6 days) ampicillin was stopped when *E. coli* cultured from the CSF was reported to be resistant to this drug. On the same day lumbar puncture failed, and chloramphenicol 12.5 mg/kg was given 12-hourly because of its good CSF penetration. Subsequent lumbar punctures produced sterile CSF and a total of 9 intrathecal doses of gentamicin were given. The systemic therapy was changed to 8-hourly on the 7th postnatal day and continued for 16 days in all (see Fig.). Serum gentamicin levels on the fourth treatment day, 2 and 12 hours after a dose, were 6.5 µg/ml and 3.5 µg/ml; and CSF levels 24 hours after an intrathecal dose ranged from 4 µg/ml to 7 µg/ml (Fig.).

On the 25th day of life (6 days after stopping systemic therapy) he was noted to be irritable and had one small vomit. Lumbar puncture showed turbid CSF with a raised white cell count and cultured *E. coli* with the same characteristics as before. Gentamicin 1 mg was instilled immediately and the 8-hourly chloramphenicol and gentamicin restarted. A ventricular tap showed heavily infected fluid and 2 mg of gentamicin were instilled at a mantle depth of 30 mm. After 2 doses of chloramphenicol and gentamicin, intravenous sulphamethoxazole 15mg/kg-trimethoprim 3 mg/kg 12-hourly was substituted and continued for 7 days when a further 8 days of

Fig. Clinical course of illness. Conversion: SI to traditional units—WBC: $1.0 \times 10^9/l \approx 1000/mm^3$. Glucose: $1 \text{ mmol/l} \approx 18 \text{ mg/100 ml}$.

oral therapy was given. Gentamicin 2 mg was instilled daily into the left and right lateral ventricles alternately for 8 consecutive days with rapid sterilization of the ventricular CSF, the levels 24 hours after a dose ranging from 4 $\mu\text{g/ml}$ to 9 $\mu\text{g/ml}$ (Fig.).

The infant was discharged well at 40 weeks' gestational age behaving normally and weighing 3010 g (10–25th centile) and head circumference 33 cm (25–50th centile). At 3½ months (8 weeks post-term) he had been smiling for 6 weeks and was behaving and growing normally.

Discussion

This case illustrates, first, the paucity of signs in early serious neonatal bacterial infection, and emphasizes the importance of considering meningitis if any abnormal behaviour is noted; in this case apnoea was the presenting sign. Second, the *E. coli* isolated from the CSF had the characteristics of the K1 antigen in its immunochemical relationship to the capsular polysaccharide of *Neisseria meningitidis* Group B. The K1 antigen is one of a hundred K antigens presently known, and Schiffer *et al.* (1976),

in showing its importance for invasiveness and a higher incidence of complications in *E. coli* meningitis in the newborn, have also shown maternal transmission, and have estimated that 10% of adult *E. coli* urinary tract infections are of the K1 variety. Although the maternal vaginal isolate of *E. coli* in this case was unfortunately not available to us for serotyping, the early onset of the infant's illness makes this route of infection very likely.

A third important point is the persistence of ventriculitis and the efficacy of antimicrobial therapy in this condition. It is likely that this infant had a low grade ventriculitis when the lumbar fluid became sterile initially, and when it showed even 24 hours after instillation adequate levels of gentamicin. It has been reported that in neonatal meningitis caused by Gram-positive organisms the CSF is sterilized promptly, in contrast to the significantly longer duration of positive cultures when Gram-negative organisms are involved (McCracken, 1972). An important reason for this may be that conventional doses of systemic penicillin for example, give levels in the CSF 10 to 100 times higher than the minimum inhibitory concentration (MIC) required for the commoner Gram-positive organisms, whereas the aminoglycosides in similar circumstances may only just reach the MIC for Gram-negative organisms (McCracken, 1972). Kaiser and McGee (1975) have shown in adults and older children that lumbar instillation of gentamicin does not give adequate ventricular levels, presumably because the direction of CSF flow is from above downwards. Thus if the aminoglycosides are to be used successfully in neonatal meningitis, given the organisms' susceptibility, they should be instilled directly into the lateral ventricle at least initially. In the case reported here, when the relapse was diagnosed repeated punctures were performed with ease alternating from the left to the right lateral angles of the anterior fontanelle. Though such a procedure may not be without the hazards of needle tracks and subsequent intracerebral cysts (Lorber and Emery, 1964), in early diagnosed cases it may be needed for a short time only, and may be preferable to the siting of a Salmon-Rich ventriculostomy reservoir for the sampling of CSF and instillation of drugs (Salmon, 1972). The ratio of cerebral mantle depth to head circumference can be used to estimate gentamicin dosage (Salmon, 1972). Finally, attention should be drawn to the use of sulphamethoxazole/trimethoprim in the treatment of neonatal meningitis. This drug has been shown to produce high concentrations in CSF, and has been used successfully in infant meningitis after other therapy had failed (Sabel and Brandberg, 1975). Though possible side effects exist, they may be less

serious in the early weeks of life than those of chloramphenicol, which has to be used in relatively high systemic dosage to achieve adequate CSF levels.

Summary

A male infant of 32 weeks' gestational age who presented with recurrent apnoea on the second day of life was shown to have an *Escherichia coli* K1 antigen meningitis. Relapse occurred 6 days after an adequate systemic course of gentamicin and chloramphenicol and intrathecal gentamicin. This was successfully treated with intraventricular gentamicin and systemic cotrimoxazole. The need to maintain a high index of suspicion for meningitis in the newborn period and to treat adequately the frequently accompanying ventriculitis is emphasized.

I am most grateful to Drs. Naomi Datta, Ruth Mitchison, W. Henderson, and J. H. Darrell of the Department of Microbiology, Royal Postgraduate Medical School, for allowing me to quote their investigations, and to Dr. Pamela Davies for help in preparing this report.

References

- Berman, P. H., and Banker, B. Q. (1966). Neonatal meningitis: a clinical and pathological study of 29 cases. *Pediatrics*, **38**, 6-24.
- Kaiser, A. B., and McGee, Z. A. (1975). Aminoglycoside therapy of Gram-negative bacillary meningitis. *New England Journal of Medicine*, **293**, 1215-1220.
- Lorber, J. (1974). Neonatal bacterial meningitis. *Medicine (Medical Education, London)*, **27**, 1579-1582.
- Lorber, J., and Emery, J. L. (1964). Intracerebral cysts complicating ventricular needling in hydrocephalic infants. *Developmental Medicine and Child Neurology*, **6**, 125-139.
- McCracken, G. H. (1972). The rate of bacteriologic response to antimicrobial therapy in neonatal meningitis. *American Journal of Diseases of Children*, **123**, 547-553.
- Robbins, J. B., McCracken, G. H., Gotschlich, E. C., Ørskov, F., Ørskov, I., and Hanson, L. A. (1974). *Escherichia coli* K1 capsular polysaccharide associated with neonatal meningitis. *New England Journal of Medicine*, **290**, 1216-1220.
- Sabel, K.-G., and Brandberg, Å. (1975). Treatment of meningitis and septicaemia in infancy with a sulphamethoxazole/trimethoprim combination. *Acta Paediatrica Scandinavica*, **64**, 25-32.
- Salmon, J. H. (1972). Ventriculitis complicating meningitis. *American Journal of Diseases of Children*, **124**, 35-40.
- Schiffer, M. S., Oliveira, E., Glode, M. P., McCracken, G. H., Sarff, L. M., and Robbins, J. B. (1976). Relation between invasiveness and the K1 capsular polysaccharide of *Escherichia coli*. *Pediatric Research*, **10**, 82-87.

P. J. HELMS

Department of Paediatrics and Neonatal Medicine, Hammersmith Hospital, 150 Du Cane Road, London W12 0HS.