hours he was virtually asymptomatic and able to eat solid food, including toast, without pain. In the six months since discharge he has remained completely well.

A subsequent comprehensive investigation of his immunological system failed to show any abnormality. This included serum immunoglobulins (subclasses), T and B cell numbers, helper/suppressor ratio, in vitro lymphocyte proliferative responses, natural killer cell activity, polymorph function, and complement system. He had antibody titres present to various common viral agents, and his specific herpes antibody titres taken on days 3 and 15 showed a rise from undetectable to 1/20.

Discussion

Labial and oropharyngeal herpes in childhood is common, and some children probably have concomitant oesophageal involvement, although this is seldom sought. This case is unusual in that the oesophagus seemed to be the only primary target organ and the oropharynx was completely spared. Upper gastrointestinal endoscopy allowed direct visualisation of the mucosa and the opportunity to obtain tissue for diagnostic purposes. Because of the degree of dysphagia, barium studies may be difficult to perform and as in this case do not always show an abnormality. Although the previous case reports have stated that the children were 'healthy' or 'immunocompetent', this in fact was assumed from

their previous histories and comprehensive immunological studies were not performed.^{5 6} The duration of symptoms, in both children and young adults, receiving symptomatic treatment only has been reported as three to 17 days.¹⁻⁶ Our patient responded to acyclovir in less than 24 hours.

Herpes oesophagitis seems to be an acute, often prolonged, but self limiting condition. We suggest that it should be added to the differential diagnosis of acute oesophagitis, that endoscopy and biopsy examination be the investigation of choice, and that specific antiviral treatment may be beneficial.

References

- Owensby LC, Stammer JL. Esophagitis associated with herpes simplex infection in an immunocompetent host. *Gastroenterology* 1978;74:1305-6.
- Springer DJ, DaCosta LR, Beck IT. A syndrome of acute self-limiting ulcerative esophagitis in young adults probably due to herpes simplex virus. *Dig Dis Sci* 1979;24:535-9.
- Solamadevi SL, Patwardhan R. Herpes esophagitis. *Am J Gastroenterol* 1982;77:48-50.
- Deshmukh M, Shah R, McCallum RW. Experience with herpes esophagitis in otherwise healthy patients. *Am J Gastroenterol* 1984;79:173-6.
- Bastion JF, Kaufman IA. Herpes esophagitis in a healthy 10 year old boy. *J Pediatr* 1982;100:426-7.
- Ashenburgh C, Rothstein FC, Dahms BB. Herpes esophagitis in the immunocompetent child. *J Pediatr* 1986;108:584-7.

Correspondence to Dr E J Eastham, Department of Child Health, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP, England.

Received 22 September 1986

Neonatal candida septicaemia: diagnosis on buffy smear

H E J CATTERMOLLE AND R P A RIVERS

Department of Paediatrics, St Mary's Hospital, London

SUMMARY We report a case of neonatal candida septicaemia diagnosed by examination of a buffy smear. This would seem to be a fairly simple test for a disease where a good prognosis is dependent on rapid diagnosis and isolation using standard culture techniques is notoriously unforthcoming.

Case report

A preterm female baby with a gestation of 25 weeks and a birth weight of 790 g was born by emergency caesarean section and transferred ex utero for intensive care. The baby developed moderate

hyaline membrane disease that required ventilation at maximum pressures of 22/4 cm H₂O and a maximum fractional inspiratory oxygen tension of 0.9. Prophylaxis with antibiotics was with penicillin and gentamicin. Intravenous feeding through a central venous catheter was begun on day 15, ventilatory requirements having fallen. Cefuroxime had been substituted for penicillin due to the isolation of a coagulase negative staphylococcus from tracheal aspirate in association with a lobar collapse.

On day 28 the baby, still ventilated, developed a metabolic acidosis and poor peripheral perfusion, and the inspired oxygen requirement rose again. A chest x ray film was non-contributory and a full septic screen, including culture of suprapubically

aspirated specimens of urine, blood, and cerebrospinal fluid, yielded negative results for bacteria. A scanty growth of candida had been isolated from an umbilical and rectal swab one week previously but not subsequently. Invasive sepsis was suggested by a raised blood immature:total neutrophil ratio (maximum value obtained=0.59, normal=<0.16¹) and a raised C reactive protein concentration (maximum value obtained=47 mg/l, normal=<5 mg/l). The changes in these values are illustrated in Figure 1. Treatment with antibiotics was changed to vancomycin and chloramphenicol and the central venous catheter was removed. Over the next 48 hours the baby continued to deteriorate with worsening hypoxaemia.

On days 31 and 32 blood samples were taken specifically to exclude a diagnosis of candida septicaemia. The initial sample was taken from an indwelling peripheral arterial cannula and the later sample from a separate sterile arterial puncture. Both samples were handled aseptically and processed in identical ways. Each was separated by centrifugation at 400 g for seven minutes and the buffy layer of cells removed with a sterile pipette. The buffy layer was then spotted on to a glass slide cleaned with alcohol and a smear made in the standard manner. A Gram stain was performed and the slides examined under $\times 100$ magnification oil emersion lens. Each smear showed large inclusions within the phagocytic leucocytes, which were stained Gram positive and were oval in shape, characteristic of a yeast. It was possible to see

budding of the yeast cells within some of the leucocytes (Fig. 2). The fact that the yeast was seen intracellularly from two separate samples convinced us that this was a true fungaemia rather than contamination from the skin, of the indwelling cannula, or of the slides during preparation.

Blood samples were sent specifically for culture of

Fig. 2 Leucocytes from a buffy smear visualised on high power light microscopy. A yeast cell that has budded in four places within the leucocyte is shown.

Fig. 1 Total neutrophil counts, immature: total neutrophil (I/T) ratios, and C reactive protein values from 27 days of age through the period of candidal infection. Antifungal treatment was begun on the day of diagnosis.

candida both before and after beginning antifungal treatment. Each blood sample was inoculated into a standard brain-heart infusion broth blood culture system, incubated at 35°, and examined daily.

After visualisation of a yeast on buffy smear the baby was begun on 5-flucytosine and amphotericin at standard neonatal doses, the latter being increased over the first four days. Flucytosine was maintained at therapeutic concentrations (25–80 mg/l). Forty eight hours after the start of antifungal treatment the baby had improved markedly, adding further support to the diagnosis. Candida was only isolated from one blood sample, which had been sent after beginning antifungal treatment, and was identified as *Candida pseudotropicalis*. A repeat buffy smear five days after starting treatment yielded negative results for yeasts and further blood and urine samples also yielded negative results. There was no reoccurrence clinically; the baby was extubated on day 60 and discharged well four months later.

Discussion

Systemic candidiasis is a serious problem in newborn infants who, particularly when severely preterm, are immunologically unprimed and depleted. Maternally derived immunoglobulin G, necessary for candidal opsonisation, is present at particularly low concentrations in the very preterm infant and continues to decline until at least 15 weeks after birth.² Phagocytosis is usually efficient in the preterm baby (as shown in this case) but intracellular killing is often impaired, particularly in stressed infants.

Candida is a particular threat as it is notoriously difficult to isolate rapidly. Involvement of the renal tract is common and examination of suprapubic urine for budding yeasts important in suspected cases.³ Such samples are not easy to acquire, however, in the smallest babies and even if positive do not guarantee systemic involvement. The buffy smear technique permits examination of small blood samples quickly and if positive is diagnostic. Smears

of the buffy layer of cells in peripheral blood have been used previously to diagnose bacteraemia with conflicting reports.^{4,5} The risk of false positive results when diagnosing yeast infections is less, due to their characteristic appearance on microscopy. In one report blood drawn from central venous catheters was positive for candida in three cases involving older children.⁶

Candida septicaemia in this report was diagnosed by an inexperienced observer, illustrating both the simplicity and importance of this test. All cultures yielded negative results before antifungal treatment, and a diagnosis that enabled the start of appropriate treatment was achieved solely using this technique. As recovery from candidiasis seems to rely heavily on early diagnosis and prompt treatment we would strongly advocate that examination of a buffy smear in suspected cases be performed.

We thank the staff of the mycology department, St Mary's Hospital, for their contribution.

This work was supported by grants from Action Research for the Crippled Child and the St Mary's Save The Baby Fund. The work was carried out in the Sam Segal Perinatal Unit.

References

- ¹ Manroe BL, Weinberg AG, Rosenfeld CR, Browne R. The neonatal blood count in health and disease. I. Reference values for neutrophilic cells. *J Pediatr* 1979;**95**:89–98.
- ² Conway SP, Dear PRF, Smith I. Immunoglobulin profile of the preterm baby. *Arch Dis Child* 1985;**60**:208–12.
- ³ Smith H, Congdon P. Neonatal systemic candidiasis. *Arch Dis Child* 1985;**60**:365–9.
- ⁴ Faden HS. Early diagnosis of neonatal bacteremia by buffy-coat examination. *J Pediatr* 1976;**88**:1032–4.
- ⁵ Coppen MJ, Noble CJ, Aubrey C. Evaluation of buffy-coat microscopy for the early diagnosis of bacteraemia. *J Clin Pathol* 1981;**34**:1375–7.
- ⁶ Ascutito RJ, Gerber MA, Cates KL, Tilton RC. Buffy-coat smears of blood drawn through central venous catheters as an aid to rapid diagnosis of systemic fungal infections. *J Pediatr* 1985;**106**:445–7.

Correspondence to Dr H E J Cattermole, Department of Paediatrics, St Mary's Hospital Medical School, London W2 1GP.

Received 10 October 1986