Primary meningitis caused by *Bacteroides fragilis* and *Fusobacterium necrophorum*

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Summary

A fatal case of meningitis due to *Bacteroides fragilis* and *Fusobacterium necrophorum* is reported. This appears to be the first case in which meningitis due to these organisms was not secondary to a disease elsewhere in the body. The organisms are difficult to culture and strict anaerobic methods should be used whenever they are suspected. Intravenous metronidazole is probably the antibiotic of choice.

Introduction

Meningitis due to anaerobic bacteria is rare and is usually secondary to an adjacent septic lesion, particularly otitis media, or to a distant site of infection causing bacteraemia. The authors report a case of *Bacteroides fragilis* and *Fusobacterium necrophorum* meningitis which occurred as a primary illness in an otherwise healthy adolescent.

Case report

A previously well 13-year-old girl of West Indian parents was admitted to Whipps Cross Hospital with a 3-day history of headache, vomiting and fever. She had had no significant previous illnesses. On examination she was drowsy and restless, with a temperature of 40°C. She had severe neck rigidity, positive Kernig's sign and she developed fixed dilated pupils and a right sixth nerve palsy. She had $19.7 \times 10^9/l$ leucocytes (94% neutrophils) in her peripheral blood.

The cerebrospinal fluid (CSF) pressure was 260 mmH₂O. The protein concentration was 0.9 g/l, glucose 6.1 mmol/l (simultaneous plasma glucose 12.4 mmol/l), and there were $160 \times 10^9/l$ leucocytes (95% polymorphs). Gram stains showed a few Gram-negative bacilli, but culture was negative after 6 days aerobic and anaerobic incubation. Blood cultures were also sterile.

She was treated with benzyl penicillin 2.5 Mu. and ampicillin 2 g i.v. 4-hourly, as well as mannitol and

dexamethasone. Her condition deteriorated and she became apnoeic. She was intubated and mechanically ventilated but died 24 h later.

At post-mortem examination, the right cerebral hemisphere was covered with foul-smelling, thick, yellowish pus which was mainly in the subdural space but also in the subarachnoid space (Fig. 1). The right cerebral hemisphere was superficially necrotic and there was an early right occipital abscess which was not apparent macroscopically. There was no evidence of a septic focus elsewhere in the body.

Gram stains of the pus showed scanty Gram-negative bacilli. Culture yielded a heavy growth of *B. fragilis* and *F. necrophorum* after only 48 hr incubation on the pre-reduced anaerobic plates. *B. fragilis* was sensitive to metronidazole, clindamycin, chloramphenicol and tetracycline but resistant to penicillin, ampicillin and erythromycin. *F. necrophorum* was sensitive to all the above antibiotics except erythromycin.

Discussion

Bacteroides and *Fusobacterium* spp. form part of the commensal flora of the mouth, gut and female genital tract. *Bacteroides* has been increasingly recognized as a pathogen in wounds and after abdominal surgery where contamination with gut organisms is the probable source of infection (Finegold, 1974; Feathers *et al.*, 1977; Griffiths *et al.*, 1976; Galland *et al.*, 1977). *Fusobacterium* is occasionally pathogenic in these situations, but its role in causing a wide variety of necrotic lesions (necrobacillosis) in man (e.g. empyema, lung abscess, liver abscess, tubo-ovarian sepsis and septic arthritis) is well recognized (Alston, 1955; Finegold, 1974).

Both organisms are important pathogens in brain abscesses (Owen and Spink, 1948; Markham and Kershaw, 1956; Sanders and Stevenson, 1968; Bartlett, 1974; DeLouvois, Gortvai and Hurley, 1977), and as recently reported, *B. fragilis* was found in 8 of 9 cases of brain abscess (Ingham,

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Fig. 1. Brain section showing acute leptomeningitis with extensive subdural exudation (HE, $\times 90$).

Selkon and Roxby, 1977). In these series, infection was always associated with an adjacent septic focus, usually otitis media.

Meningitis due to *Bacteroides* and *Fusobacterium* is much rarer. It, too, is usually associated with otitis media; but it has also been seen in cases of haematogenous spread from respiratory infections, and following gastrointestinal operations, and in patients with cancer and bacteraemia (Lifshitz, Liu and Thurn, 1963; Cooke, 1975; O'Grady and Ralph, 1976; Feldman, 1976). *Bacteroides* meningitis has also occurred in one neonate with no source of infection but for whom the membranes had been artificially ruptured before delivery (Dysart *et al.*, 1976).

The present case is unique in that the meningitis occurred despite no septic focus, bacteraemia, operation or evidence of immunosuppression. The organisms may have gained access *via* the cribriform plate from the naso-pharynx. The predominantly subdural site of infection is interesting and unusual. It is likely that the pia arachnoid (leptomeninges) was the primary site of infection with subsequent extension of infection mainly to the subdural site (Fig. 1). It is avascular, and this probably favours the growth of these obligate anaerobes. Both organisms are pathogenic by themselves, in the presence of coliforms, or in combination with facultative/obligate anaerobic Gram-positive organisms, such as *Streptococcus milleri*. It is possible

that together they exerted a synergistic effect against the host defences or, conversely, that they both invaded the same tissues because the local conditions were favourable.

Both organisms are difficult to culture and strict anaerobic methods, using pre-reduced blood agar plates and thioglycollate broth, are necessary. If an initial CSF specimen shows organisms on direct film but a culture yields no growth or negative bacteriology findings in a patient (with an adjacent septic focus, particularly otitis media) who clinically probably has bacterial meningitis, a second specimen should be obtained for strict anaerobic culture. An early diagnosis of this case of anaerobic meningitis could have been made by using direct gas-liquid chromatography of CSF after suitable extraction procedures (Philips, Tearle and Willis, 1976).

The patient was treated with penicillin and ampicillin in high dosage since the findings of Gram-negative bacilli on direct film suggested the presence of a *Haemophilus* sp., and in the absence of any predisposing condition anaerobic infection was not suspected; in retrospect, it is felt that chloramphenicol instead of ampicillin would have been a better choice. However, *Bacteroides* and *Fusobacterium* infections of meninges and brain respond better to metronidazole than to penicillin, clindamycin, lincomycin or chloramphenicol (Feldman, 1976; O'Grady and Ralph, 1976), as metronidazole crosses the blood/brain barrier better, and

CSF/pus levels above the minimal bactericidal concentrations are readily achieved (Feldman, 1976; Ingham *et al.*, 1977). Intravenous metronidazole should be considered where lumbar puncture shows Gram-negative organisms that have failed to grow on culture or when the features of bacterial meningitis are present in a case with an adjacent septic focus, particularly otitis media.

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