have been reported, but the relationship between the two remains conjectural.

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Anaerobic infection in a neonate

Early detection by gas liquid chromatography and response to metronidazole

There is growing awareness of the importance of anaerobic bacteria in the pathogenesis of infection in adults and older children. As these organisms are frequently found in the female genital tract, it is not surprising that they should be involved in infection of the newborn.

The following case illustrates the difficulties experienced in routine culture of these fastidious organisms, and the use of gas liquid chromatography in the early detection of infection. The use of metronidazole in the treatment of serious anaerobic infection is suggested.

Case report

A female infant, weighing 4.38 kg, was born to a 37-year-old primigravida. Labour had begun spontaneously at term; the membranes were artificially ruptured producing clear fluid. After 7 hours of labour the mother was noted to be pyrexial and the

draining liquor became offensive. She was treated with cephaloridine, and caesarean section was performed because of failure to progress after the membranes had been ruptured for 23 hours.

When the uterus was opened foul-smelling fluid appeared; the infant was apnoeic and hypotonic at delivery. She was intubated at one minute and about 10 ml of frothy, foul smelling white fluid was aspirated from the pharynx and trachea. Spontaneous respiration was initiated by 10 minutes but the infant remained floppy and lethargic. She, too, had an extremely offensive smell and was tachypnoeic with a respiratory rate of 100 per minute. There was abdominal distension and the liver was enlarged 4 cm. During the first few hours of life the periumbilical area became increasingly erythematous and the eyelids became crusted with yellow material. X-ray of the chest showed patchy consolidation of the right basal area and a small effusion; the enlarged liver was also shown. Swabs from eyes, ears, umbilicus, nose, throat, and rectum were sent for culture, as were liquor and pharyngeal aspirate and blood. Standard bacteriological techniques were used for both aerobic and anaerobic growth. The only positive culture was obtained from the liquor specimen which grew slender pleomorphic Gram-negative rods in liquid culture (Robertson's cooked meat medium). These could not be subcultured on to solid media even when an anaerobic chamber (Gaspak*) was used. Gastric aspirate showed numerous pus cells, many Gram-positive cocci and Gram-negative rods, but again yielded no bacterial growth even after prolonged incubation (72 hours) anaerobically and aerobically.

The liquor, and later the cooked meat broth, were subjected to gas liquid chromatography using a Pye Unicam 104, which was programmed to detect the presence of volatile fatty acids. This analysis indicated the presence in both samples of acetic, propionic, and butyric acids, the latter two being associated with the presence of anaerobic organisms (Holdeman and Moore, 1975).

The infant was initially treated with intramuscular ampicillin and cloxacillin (Ampiclox); metronidazole 100 mg (20 mg/kg) intravenously twice daily was added to the medication 4 hours after delivery because of the clinical suspicion of anaerobic infection and the chromatography report. Within 24 hours she was considerably better. After 3 days she was active, alert, and no longer tachypnoeic; the liver size had returned to normal, the umbilical redness was barely visible, and feeds were being taken orally. On the third day metronidazole was given in the form of rectal suppositories 100 mg bd, and by 6

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days she was well and in the care of her mother. Seen after 6 weeks, she had remained well.

Discussion

The literature concerning perinatal anaerobic bacteria and sepsis was reviewed by Chow *et al.* (1974). They showed a mortality of 26% of the 43 pooled cases reviewed and remarked that this high figure is probably misleading as only serious cases were reported, often as single case reports. In their own series, Chow and his co-workers found 89 cases of bacteraemia in 12 689 live births over 3½ years. 23 of these were anaerobic and only 1 infant (4%) with anaerobic bacteraemia died. They concluded that many anaerobic bacteraemic episodes are self-limiting but that anaerobic pathogens may be potential causes of serious infection. This latter conclusion is supported by Harrod and Stevens (1974) who detected 3 serious *Bacteroides* infections in the 278 infants admitted to their special care unit in 1 year. 2 of these infants died and 1 responded to chemotherapy.

Routine bacteriology as shown by our case is often unhelpful. The organisms are difficult to grow and may be sensitive to even brief exposure to air. An improved technique (gassed-out tubes for specimen collection, rapid inoculation of samples, and the use of prereduced anaerobically sterilized media) helps the recovery rate but because anaerobes are often slow to grow early diagnosis of the suspected conditions is hindered.

The observation that anaerobic organisms characteristically release various volatile fatty acid metabolites from glucose into their surrounding environment has led to the development of gas chromatographic techniques to detect their presence. Furthermore, these metabolites may be detected rapidly in biological material such as pus, and will persist even though the organisms have died and cannot be grown subsequently (Gorbach *et al.*, 1976). The liquor in this case produced a chromatographic pattern which indicated anaerobes as the probable pathogens at an early stage in the illness.

Kislak (1972) reported *in vitro* susceptibility of *Bacteroides*, the most likely pathogen in our case, to 24 antibiotics. He showed resistance to semisynthetic penicillinase-resistant penicillins such as cloxacillin, variable sensitivity to penicillin, ampicillin, and cephalosporin, and resistance to aminoglycosides. He found clindamycin to be the most active antibiotic *in vitro* against anaerobes though its use is not without hazards (Tedesco *et al.*, 1974).

There are various reports of *in vitro* sensitivity of *Bacteroides* to metronidazole and of its use as an antimicrobial agent in adults with anaerobic

bacteraemia (Tally *et al.*, 1975). Its use in the neonatal period is not described, but in adults and older children no serious side effects have been recorded (Martindale, 1975), apart from reversible sensory neuropathy from prolonged use (*Drugs and Therapeutics Bulletin*, 1976).

Metronidazole has been observed to cause an increased mutation rate in some bacterial strains (Voogd *et al.*, 1974). Further study is required for full evaluation in the neonatal period, especially in the light of experience with chloramphenicol, novobiocin, and tetracycline.

Summary

A case of presumptive anaerobic infection in a neonate is described to illustrate the use of gas-liquid chromatography in the early detection of these potentially serious pathogens. Metronidazole is suggested as a possibly useful antimicrobial agent in these infections.

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