GROUP B STREPTOCOCCAL INFECTION IN THE NEWBORN

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INTRODUCTION

In recent years, group B streptococcus has emerged as an important cause of severe neonatal infection. Although precise documentation of an increased incidence of group B streptococcal infection in newborn is lacking, many neonatal units in the United States and Europe had experienced an increase in infection caused by this organism. Epidemiologic studies revealed an incidence of 2 per 1,000 live births and a mortality of 1 per 1,000 live births as being due to neonatal group B streptococcal infection (Franciosi *et al.*, 1973). In fact it ranked second only to *E.coli* as a cause of neonatal septicaemia and meningitis (Barton *et al.*, 1973; Baker *et al*, 1973; Reid, 1975). There is no epidemiological data about this organism among pregnant women and newborns in this country and we believe the problem has not been recognised before.

This paper reports a case of neonatal group B streptococcal infection in Malaysia and discusses the epidemiology, clinical manifestations, treatment and the prevention of it.

CASE REPORT

Baby N.M., a full term 3.09 kg Malay girl, was born on 31st January, 1979 to a 23 years old years old mother, Gravida 2, Para 1, Abortion 1. The pregnancy and delivery was normal with ruptures of membranes 11 hours prior to the delivery At 3 hours of age the infant was noted to have slight grunting with cyanosis and mild respiratory distress. Chest X-ray revealed mild reticular changes in both lung fields and was diagnosed as mild respiratory distress syndrome of newborn. The grunting persisted and by 24 hours of age, she developed low grade fever (rectal temperature 38.4°C) and was noted to be lethargic, ill-looking with ashen grey colour of the skin. There was marked abdominal distension and bulging frontanelle. Laboratory investigations revealed Hb 12.5 gm%, Wbc 11,200/ul (68% neutrophils, 29% lymphocytes, 3% monocytes); lumbar CSF was turbid with 10,000 RBC/ul, 420 WBC/ul (14% neutrophils, 84% lymphocytes), protein 116 mg%, sugar 12 mg% and Gram-positif cocci was present. Ventricular CSF showed 180 RBC/ul, 1,500 WBC/ul., (99% neutrophils, 1% lymphocytes), sugar 5 mg%, protein 270 mg% and Gram-positive cocci also. The blood sugar was 90 mg%, serum bilirubin 8.4 mg%, serum electrolytes and blood urea were normal. Radial arterial blood Astrup showed pH 7.10, pCO_2 40 mmHg, pO_2 37 mmHg. She was diagnosed as neonatal septicaemia with pyogenic meningitis and was given oxygen, intravenous penicillin (200,000 units/kg/day) and intramuscular gentamycin (7.5 mg/kg/day). She also had three daily intraventricular instillations of gentamicin totalling 6 mg for the ventriculitis. The blood, CSF and ventricular fluid cultures all grew beta-haemolytic streptococci. Lancefield grouping was performed by using a rapid latex test kit (*Streptex*, Wellcome Reagents Ltd, England). All the 3 strains belonged to Lancefield Group B and subseqent typing of the strains by Streptococcus Reference Laboratory, London, found them to be type IIR. Group B Streptococci belonging to the same serotype was also isolated from the vagina of the mother. The patient was discharged well after 3½ weeks treatment and follow up 3 months later revealed a relatively normal child with no obvious neurological deficit.

COMMENTS

It is important to consider the diagnosis of B streptococcal infection in all neonates presenting with respiratory distress syndrome as the infection freqently manifests as such in the early stages. There should be minimum delay before the commencement of antibiotics as the morbidity and mortality is closely related to the timing of the treatment. (Alojipan and Andrew, 1975). Meningitis is also a frequent clinical manifestation of group B streptococcal infection and lumbar puncture should be routine in the "septic work-up" of these

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patients.

THE ORGANISM

Group B streptococci (*Streptococcus agalactiae*) were originally isolated from cows with mastitis and distinguished from group A streptocci by Lancefield in 1934. Infection in pregnancy and in the newborn was first described by Hood *et al.*, (1961); and subsequently Eickhoff *et al.* (1964) revealed that group B streptococci was the leading cause of neonatal sepsis at their hospital accounting for 25% of the cases. The organism is Gram-positive, arranged in chains and morphologically indistinguishable from other streptococci or the pneumcocci. It produces a mucoid colony of 1-1.5 mm in diameter with a narrow zone of beta-haemolysis on sheep blood agar. Various laboratory tests, immunofluorescent and counterimmunoelectrophroresis techniques are available to distinguish group B streptococci from other streptococci (Edwards and Larson, 1973; Romero and Wilkinson, 1974). Immunochemically, they can be differentiated on the basis of their type-specific polysaccharides into types Ia, Ib, Ic, II and III.

EPIDEMIOLOGY

The epidemiology of group B streptococci is not well understood. The organism is widely distributed in humans as well as in cows and is found in the nasopharynx of asymptomatic carriers, the female genital tract, the rectum (the most common site) and the male urethra (Patterson and Hafeez, 1976). Due to differences in culture technique and site of swabbing, the vaginal carriage rate of group B streptococci among asymptomatic pregnant women varies from 4.6% to 29% (Franciosi *et al.*, 1973; Baker and Barrett, 1973, 1974; Reid, 1975; Schauf and Hlaing, 1976). However in the non-pregnant women of child-bearing age, the vaginal carriage rate is lower varying from 5% to 14% (Franciosi *et al.*, 1973; Monif, 1974). Not surprisingly, if the husbands of female carriers are examined, about half will have the organism in the urethra. More interestingly, nurses working in the nursery or obstretrical delivery suite appear to have a higher carriage rate than those in other parts of the hospital (Yow, 1975).

CLINICAL MANIFESTATIONS OF GROUP B STREPTOCOCCAL DISEASE

Maternal Disease

The vast majority of vaginal carriers of group B streptococci during pregnancy and puerperium are asymptomatic, but abortion is found to be more frequent among the carriers. Urinary tract infection, wound infection, puerperal sepsis, endocarditis, ostemyelitis and meningitis have also been described in the adult patients (Reid, 1975).

Neonatal infection

In recent years, beta-haemolytic group B streptococci has emerged as an important cause of neonatal septicaemia and in some studies is as common as Gram-negative infection (Howard and McCracken, 1974; Reid, 1975; Ablow *et al.*, 1976). Group B streptococcal infection is more common among the premature and low birth weight infants, after prolonged rupture of membranes, obstretrical manipulation and foetal asphyxia (Baker and Barrett, 1973, Lloyd and Baker, 1976). Although a significant number of pregnant women have group B streptococci in their vagina, only 1.9% of their infants are colonised and 0.27% of the infants showed signs of illness (Lloyd and Reid, 1976). The combined morbidity and mortality in their group of infants is estimated to be 50% (Horn *et al.*, 1974). The reasons why the carrier rate of group B streptococci in the pregnant women is so high and yet the rate of colonisation and infection in the neonates is so low, are not known. The low infection rate (0.78%) in the infant by his carrier mother is also observed with entero pathogenic E.coli (Lam, 1978).

Neonatal infections due to group B streptococci have been described into 2 main clinical syndromes based on the age of onset (early or late) and the types of infection (septicaemia or meningitis) (Table I).

Characteristic	Form of Disease	
	Early onset	Late onset
Time of onset	10 days	10 days-12 weeks
Obstetrical complications	+ + +	+
Prolonged rupture of membranes	+ + +	–
Clinical presentation	rapid onset, severe fulminating multi-systemic illness, with septicaemia, shock, pneumonia, apnoea and meningitis.	insidious onset, presenting with meningitis and septicaemia.
Mortality	58 – 71%	14 – 21%
Transmission	maternal genital tract (intra-partum)	Nosoconial (post-partum)
Isolation of organism from sites other than blood and CSF	86%	14%
Serotypes of streptococcus	variable (usually type Ia)	type III

Table I Neonatal group B streptococcal disease

Early Onset Disease

This occurs in approximately 2 to 3 infants per 1,000 live births and manifests within the first few hours of life as a rapid onset fulminating septicaemia with symptoms of respiratory distress and shock. It carries a high mortality of 58-71% inspite of treatment (Baker *et al.*, 1973). Baker (1978) reported that 60% of 58 infants with early onset group B streptococcal infection had symptoms within 12 hours of birth and apnoeic episodes were the most common initial signs observed. The other common clinical manifestations were pneumonia and meningitis. The early onset of pneumonia causing respiratory distress may so closely mimic hyaline membrane disease in both the radiological and clinical features that they may be indistinguishable (Albow *et al.*, 1974). However, associated high risk factors which favoured group B streptococcal infection may be present, namely, prolonged rupture of maternal membranes; chorioamnonitis manifesting as peripartum maternal fever and in the infant, early onset of apnoea, septicaemia, shock-like state and respiratory distress; presence of Gram-positive cocci and pus cells in the gastric aspirate and a positive high maternal vaginal swab for group B streptococci. The infection is acquired in utero from the aspiration of infected amniotic fluid or cervical secretions possibly as a result of micro or macroscopic rupture of membranes prior to labour with resultant extensive pulmonary infection at birth or possibly contamination by maternal faeces at birth (Baker, 1978). The pathogen can be cultured from multiple sites including the blood, cerebrol spinal fluid, nasopharynx, skin and meconium of the infants.

Early onset disease can be caused by all subtypes of group B streptococcus but it is most commonly associated with type Ia but type III has also been isolated from one third of the cases. Type III is more frequently encountered in the late onset illness described below.

Late Onset Disease

The onset of the illness is usually insidious and most commonly presents as meningitis after 10 days of age but may occur as late as 12 weeks. The infants are not as severely ill as those with early onset disease. They have a lower mortality rate of 14-21% but the survivors frequently have neurological sequelae (Baker and Barrett, 1974). The pathogenesis of late onset disease is not fully established and is not associated with maternal infection or obstetrical complications. It has been suggested that the pathogens are acquired post partum from the mothers' or the infants' attendants. Virtually all the infants have purulent meningitis and group B streptococcus type III is isolated in 90% of the cases (Franciosi *et al.*, 1973; Barton *et al.*, 1973).

TREATMENT

Early diagnosis is imperative especially in those with early onset disease because of the high mortality associated with group B streptococcal infection. As many of these infants present with respiratory distress it may be difficult to differentiate from hyaline membrane disease and the diagnosis may be missed. Thus, a high index of suspicion is necessary especially when clinical features and risk factors for group B streptococcal infection are present.

Intravenous penicillin is the drug of choice and ampicillin is the alternative. The dosage of penicillin is 150,000-250,000 units/kg per day and that of ampicillin 100-200 mg/kg/day (McCracken and Feldman, 1976). Penicillin is known to have a synergistic effect with the aminoglycosides (Schauf *et al.*, 1976). Combinations of penicillin or ampicillin with the aminoglycosides (kanamycin/gentamycin) are frequently used in the treatment especially when the possibility of Gram-negative infection cannot be excluded.

Supportive therapy with fresh whole blood transfusion, oxygen and ventilation are often indicated in the acute form illness. In the patient with purulent meningitis, it is important to do a ventricular tap to rule out ventriculitis which if present, should be aggressively treated with intraventricular chemotherapy (Lee *et al.*, 1977).

PREVENTION

Until an effective vaccine against group B streptococcal infection is developed, there is a need to examined other preventive measures against this serious neonatal infection which has a high mortality rate in spite of appropriate antimicrobial therapy. The various preventive methods advocating antimicrobial agents are still very controversial. The treatment with penicillin of all pregnant women colonized by this organism and thier "positive" spouses had been suggested (McCracken, 1973, Franciosi *et al.*, 1973). The practicability of this method had been questioned as the number of infected infants are so small compared with the high incidence of vaginal carriers; besides, there is also a significant failure to eradicate maternal genital colonization on mucous membrane by antimicrobial drugs and infection may recur even after successful treatment. Recently, Yow *et al.*, (1979) recommended the screening of pregnant women at 34 to 36 weeks gestation in areas where group B streptococcal disease is prevalent and by treating

Others recommend a single dose of intramuscular procaine penicillin to the baby as it had been observed that this method given prophylactically to all newborns for prophylaxis against neonatal gonococcal ophthalmia have resulted in an absence of early onset group B streptococcal disease. This procedure must be evaluated with great caution as we do not know what it will do to the colonized newborns (Steigman *et al.*, 1975). It has also been suggested that prophylactic penicillin be given to all infants with respiratory distress at birth as it may not be possible to distinguish between hyaline membrane disease and group B streptococcal septicaemia (Miller, 1977). However, others have condemmed the indiscriminate use of antimicrobial agents in respiratory distress syndrome of the newborn as the vast majority do not need them (McCracken, 1973). Recently, Lloyd *et al.*, (1979) reported a marked reduction in early onset neonatal group B streptococcal septicaemia in their nursery when they routinely administered 50,000-100,000 units crystalline penicillin/kg/day to all infants less than 2500 grams or less than 35 weeks gestation. Penicillin was given by 2 hours of age and was continued for 10 days if group B streptococci were isolated but was stopped at 48 hours if all cultures were negative.

These methods of prevention are impractical in this country as the facilities and resources are limited. We also do not advocate routine prophylactic antibiotics to all premature newborns with respiratory distress syndrome. However, in those infants at high risks for group B streptococcal disease and having respiratory distress, we recommend treatment with penicillin (100,000-200,000 units/kg/day) and kanamycin (15-20 mg/kg/day) after cultures are taken from the infant and the mother. The antibiotics are discontinued after a 5 days course if the cultures are negative and to continue for 10 days if group B streptococci or other organism are isolated.

It is also important to prevent cross infection in the hospital as nursing personnel and doctors have a colonisation rate of 15-43% (Yow, 1975). It is very easy to transmit organisms from one patient to another via the hands or our stethoscopes. Thus, routine hand washings with soap in between patients and disinfection of stethoscopes periodically are important preventive procedures. Other measures to prevent cross infection in the nursery are described elsewhere (Lam, 1978).

Finally, the future approach would be to immunise all females against the organism. Since type III accounts for the majority of all disease, immunogenic antigen derived from this organism have been prepared by Baker *et al.* (1978). Passive transfer of these antibodies to newborns should protect the infant until 3 months of age. However further studies are needed to demonstrate the safety and immunogenicity of the vaccine in man.

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