ORIGINAL ARTICLE

Salmonella Meningitis in the Newborns and Young Infants in Jakarta, Indonesia

by

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Abstract

Experience with salmonella meningitis in the newborn and young infants below the age of 40 days hospitalized during the period 1976 — 1979 was described. They constituted 8,6% of the 324 cases of purulent meningitis in children in approximately 20.000 admissions in the 4-year-period. There was a preponderance of males among the patients and the youngest case was 2 days old. The Salmonella serotypes isolated from cerebral spinal fluid were havana (17 cases) and oranienburg (11 cases). Of particular interest is the fact that 4 of the infants and their mothers showed the identical offending organisms isolated from the spinal fluid and rectal swab. The most common predisposing maternal obstetric complications were fever and premature rupture of the amniotic membranes, whereas the predisposing factors in the infants were infections, asphyxia and prematurity. Ventriculitis, subdural effusion/empyema and hydrocephalus were the most common complications. A brief discussion has been made on the appropriate time to perform ventricular tap.

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Combination of two or more parenterally administered drugs i.e. ampicillin and gentamycin or chloramphenicol in dosages recently recommended as optimal were used in the treatment. Since 1978 intravenous sulphametoxazole/Trimethoprim combination had also been used.

Fifteen (53,6%) of the infants died, and of the six patients who survived and could be followed up regularly, 2 had hydrocephalus and 3 patients are mentally retarded.

Introduction

Despite the use of antibiotics the prognosis of neonatal meningitis is poor. Most reports have stressed the importance of early diagnosis in obtaining good results. Unfortunately early diagnosis is not easy in view of the non specific symptoms that most of these infants manifest.

Meningitis is not often associated with salmonellosis. In Dakar, Senegal, Denis, et al. (1977) reported that among 3658 patients with purulent meningitis, 50 had salmonella meningitis. The frequency of salmonella meningitis had been constant for ten years, but no case had been observed in a baby.

This paper describes our experience with salmonella meningitis in the newborns and young infants below the age of 40 days, hospitalized during the period 1976 — 1979.

Materials and methods

This study is based on a review of the clinical records of all neonates and young infants below the age of 40 days who developed meningitis during the year 1976 to 1979 at the Department of Child Health Cipto Mangunkusumo General Hospital Jakarta. We included in this study patients whose cerebrospinal fluid showed any one of the following criteria: (1) Positive spinal fluid culture, pleiocytosis and decreased sugar content. (2) Positive spinal fluid culture and decreased sugar.

Results

From a review of the records, 103 neonates and infants below the age of 40 days were considered to have developed purulent meningitis.

They constituted 31,8% of the 324 cases of purulent meningitis in children in approximately 20.000 admissions during the 4-year-period.

Twenty eight out of the 103 affected cases had salmonella microorganism isolated from the cerebrospinal fluid. The basal data of the patients is shown in table 1.

Seventeen of the 28 infants were male and 11 cases were female. Seventeen cases occurred within 15 days, eight cases from 15 to 30 days and three cases from 31 to 39 days after birth. The youngest one was 2 days. Two infants were of low birth weight (under 2500 gram). Poor weight gain was observed in 7 cases (cases No. 1, 4, 8, 14, 15, 18 and 26). All of the mothers had rectal swab cultures, with positive findings mentioned in table 1. The salmonella serotypes isolated from cerebral spinal fluid were havana (17 cases) and oranienburg (11 cases).

Of particular interest is the fact that 4 of the infants and their mothers (cases No. 11, 13, 23 and 25) showed the identical offending organisms isolated from the spinal fluid and rectal swabs.

Three out of the 4 cases delivered at home died, two of them (cases No. 2 and 6) were attended by traditional birth attendants and the diagnosis of meningitis

TABLE 1 : *Basal data of salmonella meningitis patients, Cipto Mangunkusumo Hospital Jakarta 1976 — 1979.*

Case No.	Sex	Age (days)		Body weight (gram)		Bacteria		
		at onset	at death	at birth	at onset	CSF	Rectal Swab	
							Infant	Mother
1.	M	39	41	2600	3000	S. oranienburg		
2.	F	5	11	—	2800	S. havana		
3.	F	7	9	2700	2700	S. havana		
4.	M	31	—	2750	3300	S. havana		
5.	F	7	—	3300	3200	S. havana		
6.	M	5	7	—	2850	S. havana		
7.	M	7	9	3100	3200	S. havana		
8.	M	31	50	2000	2600	S. oranienburg		
9.	M	4	4	2550	2600	S. havana		
10.	M	8	12	3600	3650	S. havana		
11.	M	14	19	3750	3800	S. havana	S. havana	S. havana
12.	M	2	—	3100	3100	S. oranienburg		
13.	M	5	—	3300	3350	S. havana	S. havana	S. havana
14.	M	25	—		3600	S. oranienburg		
15.	F	22	35	2600	3000	S. havana		
16.	M	7	—	3500	3600	S. havana	S. havana	
17.	F	27	30	2800	3600	S. oranienburg		
18.	M	26	—	2450	3000	S. oranienburg		
19.	F	6	—	—	3300	S. havana		
19.	M	7	—	2800	2850	S. havana		
21.	F	6	—	3100	3100	S. havana	S. havana	
22.	F	27	30	3200	4000	S. oranienburg		
23.	M	8	—	3500	3550	S. havana	S. havana	S. oranienburg
24.	F	23	—	3000	3600	S. oranienburg		
25.	M	21	22	—	3200	S. oranienburg	S. oranienburg	
26.	M	15	45	3200	3250	S. oranienburg		
27.	F	10	15	3300	3500	S. oranienburg		
28.	F	12	—	3250	3500	S. havana		

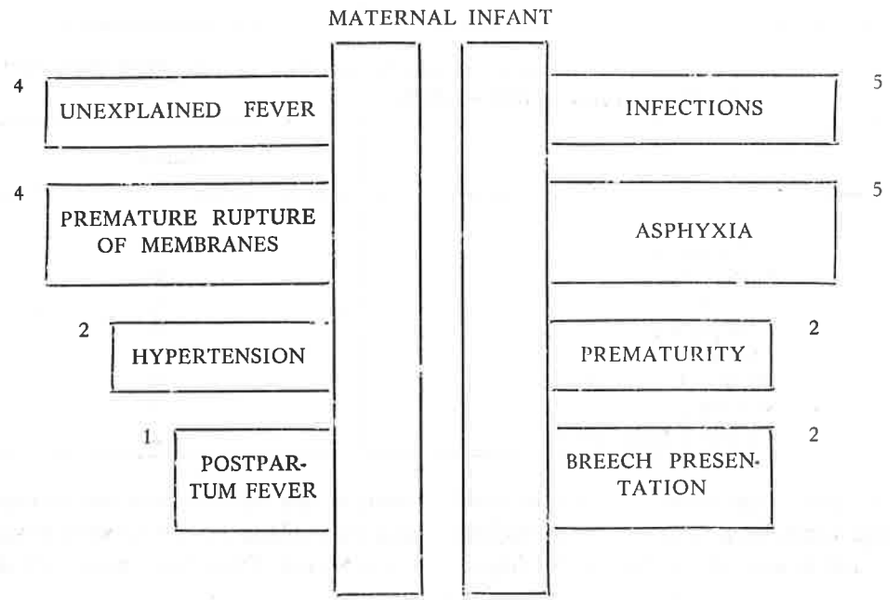
in these two patients was established at the age of 5 days (Table 2).

The predisposing perinatal factors is shown in figure 1.

TABLE 2 : *History of delivery of salmonella meningitis patients, Cipto Mangunkusumo Hospital Jakarta 1976 — 1979.*

Delivered at	Attended by			Total	Died
	Doctor	Midwife	Traditional birth attendant		
Hospital	10	—	—	10	5
Clinic	4	10	—	14	7
Home	—	2	2	4	3
Total	14	12	2	28	15

FIGURE 1 : *The predisposing perinatal factors of salmonella meningitis patients, Cipto Mangunkusumo Hospital Jakarta 1976 — 1979.*



No definite perinatal infections occurred in the mothers, but 4 mothers had unexplained fever during the perinatal period and 1 mother had an unexplained postpartum fever. Premature rupture of the amniotic membranes had occurred in 4 instances. Infections other then those of the central nervous system had occurred in 5 infants before the diagnosis of meningitis became apparent. Five infants were asphyxiated at birth with Apgar scores at one minute of 6 or less. Two infants had a birth weight below 2500 gram and difficult delivery i.e. breech presentation was confirmed in two patients. The presenting symptoms or signs is shown in table 3.

The most frequent initial manifestations of illness were feeding difficulties (15 patients) either refusal of feeds or vomiting. Convulsion occurred in the majority of the infants (13 patients). An impairment of the infant's reactions to stimuli and particularly irritability were frequently observed. These were mostly of short duration lasting 24 hours or less, and were followed by lethargy.

TABLE 3 : *The presenting symptoms or signs of salmonella meningitis patients, Cipto Mangunkusumo Hospital, Jakarta 1976 — 1979*

Presenting symptoms or signs	Number
Feeding difficulties	15
Seizures	13
Lethargy	8
Cyanosis	7
Fever	6
Diarrhea	6
Poor cry	3

TABLE 4 : *The neurological findings of salmonella meningitis patients, Cipto Mangunkusumo Hospital, Jakarta 1976 — 1979.*

Neurological findings	Number
Convulsion	15
Opisthotonus	9
Bulging fontanelle	6
Poor Moro	6
Poor grasp reflex	6
Poor sucking	6
Decreased tendon reflexes	5
Stiff neck	3
Unilateral facial paresis	2

Cyanosis was observed in 7 cases. Six infants had fever, whereas diarrhoea and poor cry were observed in six and three infants respectively.

The neurological findings is shown in table 4.

The signs of meningitis usually seen in older children were infrequent in the neonates. A bulging fontanelle was observed in 6 infants. Nine patients were observed to have opisthotonus, whereas stiff neck was observed in 3 infants. The other neurological findings observed were poor Moro (6 infants), poor grasp reflex (6 infants) poor sucking (6 infants) decreased tendon reflexes (5 infants) and unilateral facial paresis (2 infants). In the majority of the infants (12 patients), symptoms developed during the first week of life and the course of the disease was fulminant, these patients died within several hours to 7 days. In the older infants (cases 8, 15 and 26) who recovered from the initial illness, two died from complication of ventriculitis, and one patient died following repeated shunt procedures for hydrocephalus. The complications of the patients are shown in table 5.

TABLE 5 : *The complications of salmonella meningitis patients, Cipto Mangunkusumo Hospital Jakarta 1976 — 1979.*

Complications	Died	Survived	Total
Subdural effusion/empyema	4	1	5
Ventriculitis	5	—	5
Hydrocephalus	1	2	3
Spasticity	—	3	3

The outcome of treatment of newborn meningitis is not very promising. We gave combinations of two or more parenterally administered drugs in dosages recently recommended as optimal i.e. combined treatment of ampicillin and gentamycin or chloramphenicol. Since 1978 intravenous sulphamethoxazole (SMZ)/Trimethoprim (TMP) combination (Bactrim; Hoffman-La Roche Ag. Basle/Switzerland) had been used in the treatment of neonatal purulent meningitis. The result of the study have been reported separately.

If ventriculitis is present gentamycin is instilled intraventricularly by the neurosurgeon in a total dose of 2 to 2,5 mg daily.

Discussion

Premature rupture of the fetal membranes and maternal infections were the most significant predisposing perinatal factors, in the pathogenesis of the meningitis. In our series unfortunately no proven infection could be detected in five of the mothers. On the other hand in

four asymptomatic mothers in whom bacteriologic diagnosis was made, the organisms was the same as that derived from the infant's spinal fluid. Similar observations have been made by Keitel et al. (1962) who isolated organisms from the cervix of asymptomatic mothers at term which were identical with those subsequently cultured from the spinal fluid of infants with meningitis. These data clearly indicate that the mother is an important source of infection for the infant.

The most common predisposing infant factors in our series were infections such as otitis media (2), bronchopneumonia (2) and omphalitis (1) and asphyxia at birth. The association between meningitis and pneumonia had been noted by Seriki (1970).

Washburn et al. (1965) demonstrated that increased of bacterial meningitis was found in male in all ages, but mostly among newborn infants. They postulated that the preponderance of cases in males is due to a gene locus on the X chromosome which is involved with the synthesis of immunoglobulins. Our findings that 17 out of 28 infants were boys was consistent with their observation.

The most impressive clinical picture in neonatal meningitis is the non specific symptoms and signs. These initial symptoms are vague and thus the diagnosis is often delayed. Hypersensitivity, lethargy, feeding difficulties, respiratory distress, fever, dyspnea, diarrhea are frequent manifestations of systemic illness in the young infant and certainly not the symptoms that one ordinarily associated with meningitis. Most important for early diagnosis is the physician's alertness to the possibility, especially in the neonates, in whom findings may be nonspecific and therapy delay catastrophic. Of the 13 infants with seizures in our series eleven had generalized tonic convulsion, while two had localized clonic fits. In these patients meningitis was suspected at the time of presentation of convulsions. In the majority of the other cases however, the presenting symptoms and signs were non specific and in these patients lumbar puncture was performed only to exclude the diagnosis of meningitis.

The result in our study may partially be explained by the fact that the delay in diagnosis may have occurred because our hospital is a referral hospital.

Early diagnosis of neonatal meningitis had been made in four patients (cases No. 5, 16, 19 and 23) who had apparently a good therapeutic outcome. They had been receiving antibiotics prior to the diagnosis of meningitis for another infection and had been inadvertently treated. While in the others no significant pre-treatment were observed. It cannot be overemphasized that lumbar puncture should be performed before antibiotics are given. In all these infants the spinal fluid examinations were normal, despite the fact that the presence of meningitis was suspected clinically.

Ventriculitis has been shown to complicate meningitis contracted in the neonatal period (Berman and Banker 1966; Salmon, 1972). Lee and co workers (1977) were of the opinion that the most important cause of poor therapeutic response in neonatal meningitis is the failure to recognize the presence of ventriculitis. In their study a ventricular tap was performed in each patient when the diagnosis of neonatal meningitis was confirmed, to determine if there was ventriculitis. Each of the 16 infants in their series had evidence of ventriculitis and in 13 of these infants, a Reeckham ventriculostomy reservoir was subsequently implanted for ventricular instillation of antibiotics.

They were of the opinion that in their study ventriculitis almost invariably complicates neonatal meningitis, even in the early stages of the infection. In conclusion Lee and co-workers claimed that the aggressive approach to diagnosis and therapy of gram-negative bacterial meningitis in the newborn infant seems to be justified. In all of our 5 cases with ventriculitis, ventricular tap had been performed very late and inspite of the instillation of gentamycin intraventricularly all of the patients died.

Fifteen patients (53,6%) of our series died. A figure of 62% had been reported by Denis et al., (1977) in infants with salmonella meningitis in Senegal. After three to four years a follow-up could be done regularly on six out of thirteen patients. Out of those, two have hydrocephalus and three patients are mentally retarded.

It would appear that the solution of the problem lies in the prevention of neonatal meningitis. Improvement in obstetric care, personal and enviromental hygiene and in preparation of infants formula if artificially fed will reduce the incidence of neonatal meningitis, on the other hand the physician's alertness to the possibility of neonatal meningitis in view of the non specific nature of the early symptoms of neonatal meningitis is also important. Lewis and Gupta (1977) were of the opinion that the mode of feeding of the infant immediately after birth may be the most important in the prevention of neonatal meningitis. The specific anti E. coli immunoglobulin A (IgA) known to be present in high titre in colostrum and early breast milk (Ste-Marie et al. 1974) resists proteolytic digestion in the gut but is heat labile.They also pointed out the importance that premature infants, who are recognized as a high risk group, be fed with fresh unsterilized colostrum/breast milk (preferably from the infants' own mother- instead of expressed breast milk that has been heat sterilized.

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