Management and Outcome of Childhood Meningitis in East Malaysia

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Summary: Between January 1983 and June 1986, 62 cases of meningitis were seen in the Duchess of Kent Hospital, Sandakan, Sabah. The commonest organism were H. influenza (14.5%) Strep Pneumoniae (12.9%) tuberculosis (12.9%) L monocytogenes (12.9%) and N. meningitidis (11.3%). There was a strong association between meningitis and the following: Children under one year of age, from a low socioeconomic group, and from urban dwelling immigrant groups. Mortality was significant (19.4%) but comparable to that in other developing countries. The presence of ampicillin-resistant strains of H. influenza and L. monocytogenes has important bearing on choice of antibiotic therapy for meningitis in this region.

Introduction

Data on childhood meningitis in Malaysia is scarce, and reports have been few.[1] A retrospective analysis of all confirmed or strongly suspected cases of childhood meningitis admitted to the paediatric ward of the Duchess of Kent Hospital, Sandakan, East Malaysia between January 1983 and June 1986 was made to determine the following:

i) the presenting feature of the disease
ii) the outcome of management
iii) sociodemographic data pertaining to the susceptible populations.

Patients and Methods

Childhood meningitis is defined as confirmed or strongly suspected meningitis whether pyogenic, tuberculous of viral affecting children under the age of 12 years. Meningitis due to neoplastic or leukaemic cellular infiltration are excluded from this definition.

All children admitted in the 3½ year-study period were included as cases of bacterial meningitis if the study of cerebrospinal fluid (CSF) analysis revealed a minimum of three of the following:

i) Leucocyte count > 100 cells/cu mm with predominant polymorphs.
ii) Glucose < 50mg% (2.8 mmol/L) or
< 50% that of a simultaneously taken blood sugar
iii) Protein > 75% mg/100ml
iv) Positive direct smear for micro-organisms
v) Positive culture.

In the case of suspected tuberculous meningitis, the diagnosis was accepted if there was CSF evidence of meningitis on biochemistry and in the absence of an identified organism, the following were present:

i) A predominant CSF lymphocyte differential count.
ii) Evidence of tuberculosis radiologically, or the presence of confirmed tuberculous lymphadenopathy or choroid tubercles clinically.
iii) A positive sputum or early morning urine smear.
iv) A mantoux reaction > 12 mm.

Viral meningitis was present if CSF showed the following:

i) Leucocyte count > 100 cells/mm^3 with a predominant lymphocytosis.
ii) CSF protein 75 mg/100ml.
iii) Normal CSF sugar.
iv) No micro organisms seen microscopically or cultured.

Following diagnosis, antibiotic treatment was instituted blind in most cases. In neonates and infants, choramphenicol (25mg – 50mg/kg/day) and ampicillin (250–400mg/kg/day) were given in four daily intravenous doses. Gentamicin (2.5 – 5mg/kg/day) was also often given. In children higher doses of chloramphenicol (100mg/kg/day) and ampicillin (400mg/kg/day) were given intravenously. Once culture results were available, the treatment was continued or appropriate change of antibiotic was made.

In tuberculous meningitis, standard treatment consisting of daily oral Rifampicin (15 mg/kg), Isoniazid (10 mg/kg), Pyrazinamide (25 mg/kg) and Streptomycin (25 mg/kg 1m) were given together with dexamethasone (0.1 mg/kg) orally. Antibiotic treatment was continued for between 10–21 days for bacterial meningitis and for 6–9 months for TB meningitis. Convulsions were treated with intravenous diazepam (0.1 mg/kg) followed by phenobarbitone (3 mg/kg) via a nasogastric tube or orally.

Results

During the 42 month-reporting period, 62 patients who met the diagnostic criteria for acute meningitis were seen. The distribution of the cases by age, sex and age specific fatality ratio are indicated in table 1. The largest proportion (72%) of cases seen were in infants (age 2–12 months), but the highest proportion of deaths occured in those less than two months (30%). The high proportion of patients under one year of age was significantly different from the age group of paediatric cases admitted to the hospital during this period (chi-squared test : $p < 0.001$) and suggests a preponderance of meningitis in those under the age of one.

The frequency of clinical features seen in children who presented with meningitis indicates that fever (72%), convulsions (61%) and listlessness (56%) were the commonest presenting symptoms while neck stiffness (77%) and the presence of accompanying infections at other sites (66%) and focal neurological deficits (63%) were the commonest clinical findings. The mean time from the child being unwell to the time of presentation at hospital was 5.2 days.

Table No. 1 Age	Males	Females	Total Deaths	Age-specific Fatality Ratio
< 2 months	10	10	6	30%
2 – 12 months	13	12	4	16%
> 12 months	8	9	2	11.8%
Total No.	31	31	12	

Table 1
Age, Sex, Fatality Rate of Childhood meningitis

Overall Mortality 19.4%

ETHNIC GROUP	NO.	%
BAJAU	20	32.4
SULUK	13	20.9
SUNGEI	12	19.4
BUGIS	10	16.1
KADAZAN	2	3.2
KAGAYAN	2	3.2
OTHERS	3	4.8
TOTAL	62	100

Table 2
Ethnic Group Breakdown Of all Meningitis Cases Seen

Ethnic group breakdown (table 2) indicates that most cases arise from either the Bajau (32.4%) Suluk (20.9%) or Bugis (16%) populations (table 2), the major groups that constitute the Indonesian and Philippine immigrant population in Sabah. Most of the cases seen are from the lower socioeconomic groups living in poor conditions in the urban areas.

Table 3 gives the breakdown of the causative organisms. The commonest was Haemophilus influenza (14.5%) followed closely by listeria monocytogenes, pneumococcus, and mycobacterium tuberculosis (all 12.9%). A small outbreak of listeria meningitis between February 1985 and May 1986 accounted for the high incidence seen. The cause of this outbreak was not clear and was the subject of a separate paper.[2] Table 4 shows the relationship between causative organism and mortality.

Among the 50 survivors, 10 patients (20%) had a total of 21 neurological sequelae from the meningitis (table 5). The commonest morbid outcomes were motor impairment and epilepsy. Eight out of the 10 children had more than one neurological deficit.

Table 3
Causative Organisms in 62 cases of Childhood Meningitis January 1983 – June 1986

Bacteria		NO.	Percentage	Neonate	Infants	Children
Haemophilus Influenzae	Amp. Sens	5	14.5	+	+	
	Amp. Resis	4				
Listeria	Amp. Sens	1	12.9	+	+	
	Amp. Resis	7				
Pneumococcus		8	12.9		+	
M. Tuberculosis		8	12.9			+
Meningococcus		7	11.3		+	
Acinetobacter		5	8.1	+		
Pseudomonas areuginosa		4	6.5	+		
Viral		3	4.8			+
Staph aureus		2	3.6		+	
Enterobacter		1	1.6			
Streptococci		1	1.6			
Fungal		1	1.6			
Unknown		5	8.1			
		62	(100)			

*N = Neonate <2 mths
I = Infants 2 – 12 mths
+ = Predominant age group affected.
C = Children > 1 yr.
Striped boxes indicate prevalent age group affected.

Discussion

The incidence of meningitis among children in Malaysia is unknown. Meningitis however, accounts for approximately 2% of all paediatric admissions to the Duchess of Kent Hospital each year between 1983 and 1986. Most of the cases (71%) were in children under a year old (table 1). This compares strikingly with the overall hospital admission where only 45% of children were under a year old. Childhood meningitis therefore tends to occur in those under a year of age.

Socio-demographic data from this paper indicate that most of the cases come from urban families of low socioeconomic standing and were mainly among the Bajaus and Suluks who formed a large proportion of the immigrant population in Sabah. There was also however, a considerable proportion of the rural Sungeis (19.4%) who were affected. Although we have no direct evidence, it is tempting to postulate that overcrowding and poor nutrition are important contributing factors to the high incidence of meningitis among these ethnic groups. Similar conclusions have been drawn from comparative studies of meningitis between different ethnic groups in various socioeconomic scales in North America.[3]

Twelve cases died. The overall mortality for childhood meningitis of 19.4% (table 1) is comparable to that from the seven years retrospective study at the University Hospital in Kuala Lumpur which was 15%.[1] As in the Kuala Lumpur study, pneumococcal and haemophilus meningitis topped the list of causes of death, although there was a large proportion of deaths from meningitis of unknown aetiology in our series (table 4).

ORGANISM	NO. died	NO. OF CASES	%
Unkown	4	5	80
Pneumococcus	3	8	37.5
Haemophilus	2	9	22.2
Pseudomonas	1	4	2.5
Listeria	1	8	12.5
Mycobact Tuberculosis	1	8	12.5
TOTAL :	12	43*	

Table 4:
Outcome – Mortality in Relation to Organism

*No deaths were recorded in the other 19 cases of meningitis due to other pathogens.

The overall mortality is similar to that reported from Ethiopia (22%),[4] Saudia Arabia (20%)[5] and in parts of the West[6] although in general, mortality in Western Europe and America tend to be much lower[7,8] (2.9 – 10%). Deaths from meningitis due to unknown organisms (table 7) was very high (80%) in comparison to death from deaths due to other organisms (12.5 – 37.5%). See table 4. The difficulty in making an appropriate choice of antibiotics in the absence of positive CSF gram stain or culture is probably the main reason for the high mortality figures. Wrong treatment brings disastrous consequences in bacterial meningitis. Results obtained from retrospective studies in Cairo[9] suggest that the "unknown" organism in some of these cases may be meningococci although rare organisms like flavobacterium meningosepticum[5] may also occur.

The relatively high mortality from meningitis in our study may be due to a combination of factors namely the inability to culture the pathogen, late presentation, and the large proportion of children under one year of age. All these factors are known to increase both morbidity and mortality. Of the 50 surviving cases, neuroglogical sequlae occured in 18 children (36%). See table 5.

Early diagnosis of meningitis presents a clinical challenge. Late features such as convulsions, opisthotonus and coma make the diagnosis easy but, therapeutic response is likely to be disappointing. In the early stages of meningitis fever, lassitude and irritability may be the only features and a high index of suspicion is necessary to bring the diagnosis to mind. The high incidence of neck stiffness, convulsions and focal neurological deficits seen at presentation in the present series suggest that the children are brought in late.

This is further borne out by the mean time of 5.2 days taken for the children to be seen at hospital. In most of these cases the reasons were unknown but access to the hospital was not a major factor as most of the families lived in town.

The predominant organisms: H. influenza, Strep. pneumoniae, L. monocytogenes, M. tuberculosis and N. meningitidis accounted for nearly two-thirds of all meningitis seen. (table 3). The 'big three' i.e. H. influenza, Strep penumoniae and N. meningitidis were well represented. The high incidence of L. monocytogenes is surprising and is due to a small outbreak that occurred between February 1985 and May 1986 in neonates and infants in the urban and suburban community.[2]

RESIDUAL MORBIDITY	NO.	%
Motor Impairment	7	14
Epilepsy	5	10
Gross auditory impairment	3	6
Visual Impairment	2	4
Gross Intellectual Impairment	2	4
Involuntary movement	2	4
TOTAL :	21*	

Table 5:
Outcome: Morbidity in Survivors

*10 children had a total of 21 neurologic deficits.

A high percentage of tuberculous meningitis occured in non-immune children from rural and immigrant populations above the age of one. Most of these had not received their BCG vaccination. This is in agreement with data reported recently from this region.[10]

The emergence of ampicillin resistance in H. influenza and L. monocytogenes means that ampicillin or penicillin should never be used alone for the initial treatment of childhood bacterial meningitis. It should be combined with chloramphenicol initially. Both drugs achieve good CSF concentration. The risk of bone marrow depression from chloramphenicol is small compared to the seriousness of infections. In bacterial meningitis, the duration of antibiotic therapy ranged between 10–21 days; in most cases it was stopped five days after the patient became afebrile. Following recommendations from various studies[1,11] we do not perform routine lumbar puncture at the end of the treatment as they are of no value in predicting relapses.[10] Further more CSF may remain abnormal for three or more weeks after the end of treatment, and it is not necessary to continue chemotherapy until the CSF returns to normal.

Caution also needs to be exercised with the increasing popularity of third generation cephalosporins for neonatal and infant meningitis. Listeria monocytogenes is resistant to third generation cephalosporins. Its use resulted in the only death in our eight cases of listeria infection.

Conclusion

Childhood meningitis mainly affects children under one year of age and accounts for approximately 2% of all childhood admissions to the Duchess of Kent Hospital, Sandakan. It arises mainly in the urbanised immigrant population belonging to the lower socioeconomic groups. Presentation is often late and the condition

is associated with significant mortality and morbidity. There is also significant proportion of ampicillin resistant strains of H. influenza and L. monocytogenes, and this would suggest that ampicillin should never be used alone in the treatment of childhood meningitis in this region. The significant incidence of listeria meningitis in this region also means that precaution should be taken to exclude listeria before treating meningitis in infant and neonates with third generation cephalosporins. Failure to do so may result in fatality.

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