EPIDEMIOLOGY OF INVASIVE MENINGOCOCCAL DISEASE IN 13 GOVERNMENT HOSPITALS IN THAILAND, 1994-1999

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Abstract. This study was conducted to elucidate the magnitude of problem and the clinical course of invasive meningococcal infection from 13 government hospitals in Thailand between 1994 and 1999. Thirty-six strains of *Neisseria meningitidis* were isolated from 16 blood and 24 cerebrospinal fluid specimens; 4 patients had positive culture in both blood and CSF. Of the 16 strains, 9 (56.3%) were serogroup B. Seventy-one and eighty-four percent of the isolates were susceptible to penicillin and cefotaxime/ceftriaxone respectively. Five out of six penicillin-nonsusceptible strains were found to be relatively resistant to penicillin with the MIC of 0.125 μg/ml. Of 33 patients whose medical records were available, 21 were males and 12 were females, with a mean age of 11.2 years. Fifteen patients (45.5%) presented with meningococcemia and 18 patients (54.5%) presented with meningococcal meningitis. Hypotension and purpura were found in 24.2% and 33.3% of patients respectively. The overall mortality rate was 9.1%. In conclusion, meningococcal disease is not common in Thailand, meningococcemia is a life-threatening condition whereas meningococcal meningitis is much less severe. The prevalence of meningococci relatively resistant to penicillin seems to be increasing.

INTRODUCTION

Neisseria meningitidis is a cause of endemic and epidemic disease in developed and developing nations (Apicella, 1995). Common clinical presentations of invasive meningococcal diseases include meningococcemia and meningitis. In Thailand, a limited number of cases has been reviewed (Thisyakorn *et al*, 1985; Pancharoen and Thisyakorn 1998). This study was undertaken to elucidate the prevalence and the clinical course of systemic meningococcal infection in Thailand.

MATERIALS AND METHODS

Bacterial cultures of blood and cerebrospinal fluid (CSF) specimens submitted to microbiology laboratories between 1994-1999 were retrospectively reviewed in 13 government hospitals located in various parts of Thailand: Chulalongkorn Hospital (site 1), Chonburi Hospital (site 2), Prapokklao Hospital (site 3), Chiang Mai University Hospital (site 4), Thammasartchalermprakiat Hospital (site 5), Ramathibodi Hospital (site 6), Queen Sirikit National Institute of Child Health (site 7), Vajira Hospital (site 8), Hat Yai Hospital (site 9), Bhumibol Adulyadej Hospital (site 10), Khon Kaen University Hospital (site 11), Siriraj Hospital (site 12) and Pramongkudklao Hospital (site 13). These hospitals are secondary or tertiary care government hospitals admitting pediatric and adult patients (except site 7, a children's hospital) and are located in different regions of Thailand: Bangkok (sites 1, 6, 8, 9, 10, 12, 13), central region (sites 2, 3, 5), northern region (site 4), southern region (site 9), and northeastern region (site 11). Five of these hospitals are university hospitals.

Microbiologic data of *N. meningitidis* isolated from blood and cerebrospirial fluid (CSF) were reviewed in terms of year of specimen collection, type of specimen, serogrouping and antimicrobial susceptibility of the isolates.

Medical records of the confirmed cases of meningococcal disease were reviewed in terms of

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age and sex, year of admission, type of positive specimen, clinical manifestations, laboratory findings, treatment and outcome.

Confirmed cases of meningococcal disease are defined as when meningococcus from blood or CSF is isolated from a person with a clinically compatible illness. Meningococcemia is defined as when meningococcus is isolated from blood from a person with a clinically compatible illness, and co-existing meningitis is defined as the presence of CSF pleocytosis (wbc in CSF ≥ 10 cells/mm^3) and/or positive CSF culture. Meningococcal meningitis is defined as when meningococcus is isolated only from CSF from a person with a clinically compatible illness.

RESULTS

During the 6-year study period, 16 out of 924,635 blood culture specimens and 24 out of 123,178 CSF culture specimens were positive for *N. meningitidis*, accounting for 0.002% and 0.02% of all blood and CSF specimens, respectively. Both blood and CSF specimens were positive in 4 cases resulting in a total of 36 strains isolated from 36 patients.

Of 16 strains tested for specific serogrouping, 2 (12.5%) were serogroup A, 9 (56.3%) were serogroup B, 1 (6.3%) was serogroup C, 1 (6.3%) was serogroups W135, and 3 (18.8%) were serogroups other than A, B, C or W135. The antimicrobial susceptibility tests by the disc diffusion method were performed with 35 isolates and revealed that 25 (71.4%) and 29 (83.9%) were susceptible to penicillin and cefotaxime/ceftriaxone, respectively. The minimal inhibitory concentration (MIC) assay demonstrated that 5 out of 6 tested strains (83.3%) were relatively resistant to penicillin with the MIC of 0.125 μg/ml.

Among 33 meningococcal patients whose medical records were available, there were 21 males and 12 females, 22 children (0-15 years) and 11 adults (> 15 years), with an age range from 2 months to 75 years, a mean age of 11.2 years and a peak age of 0-5 years. A 29-year-old woman had underlying systemic lupus erythematosus and a 1-year-old boy had an indwelling ventriculoperitoneal shunt. Fifteen patients presented with meningococcemia and 18 patients presented with meningococcal meningitis.

Hypotension and purpura fulminans were found in 8 patients (24.2%) and 11 patients (33.3%) respectively and these two manifestations were more commonly found in the patients with meningococcemia. Adrenal crisis was found in three patients and all of them were in the meningococcemia group. Nine patients with meningococcemia had coexisting meningitis. Details of the manifestations of each clinical presentation are shown in Table 1. Three patients with meningococcemia died, with the overall mortality rate of 9.1% of all meningococcal patients and 20.0% of all cases with meningococcemia.

White blood cell (wbc) counts of the patients ranged from 5,800 to 31,200 cells/mm^3 and 90% had leukocytosis (wbc count > 10,000 cells/mm^3).

Table 1
Age and sex, clinical manifestations and outcome of meningococcal patients, classified by each presentation.

	Meningococcal disease	Meningococcemia	Meningococcal meningitis
Number of cases	33	15	18
Mean age (yrs)	11.2	14.4	8.6
Sex (M:F)	21:12	8:7	13:5
Manifestations			
Hypotension	8 (24.2%)	8 (53.3%)	0 (0%)
Meningitis	27 (81.8%)	9 (60.8%)	18 (100%)
Purpura	11 (33.3%)	9 (60.8%)	2 (11.1%)
Petechai	4 (12.1%)	4 (26.7%)	0 (0%)
Adrenal crisis	3 (9.1%)	3 (20.0%)	0 (0%)
Mortality	3 (9.1%)	3 (20.0%)	0 (0%)

Platelet counts ranged from 90,000 to 890,000/mm^3 and 6.7% of the patients developed thrombocytopenia (platelet count < 100,000/mm^3). Spinal tapping was not performed in 4 patients and 3 patients did not have complete data of initial CSF findings. All patients presenting with meningitis alone had CSF pleocytosis, however there were 3 out of 9 patients presenting with both meningococcemia and meningitis, whose wbc in CSF were 10 cells/mm^3 or lower (0, 0, 10 cells/mm^3). The CSF cultures were positive in these three cases and antigen detection was positive in one case.

Penicillin G sodium or ampicillin plus chloramphenicol, or cefotaxime were selected as empirical antibiotics in the majority of cases. Corticosteroids were used in 4 patients.

DISCUSSION

The incidence of meningococcal disease (probable and confirmed cases) in Thailand between 1995 and 1999 was 0.05-0.11: 100,000, and more than half of cases were children (Division of Epidemiology, 1995-1999). Compared with the incidence in the United States and African countries (Riedo *et al*, 1995), this infection is relatively uncommon in Thailand. Our data showed that the frequency of *N. meningitidis* isolated from blood and CSF specimens was extremely low. There were 3 hospitals (sites 5, 10, 11) which did not have any meningicoccus-positive cultures during the 6-year period of study.

As in a previous report (Kusump *et al*, 1997), this study revealed that the most common serogroup of meningococus found was serogroup B, the serogroup that cannot be protected against by the available meningococcal vaccine (Lepow *et al*,1999). Using disc diffusion method and MIC tests, resistant strains of *N. meningitidis* were identified, as previously reported in many countries (Jones and Sutcliffe 1990; Jackson *et al*, 1994; Buck and Adams, 1994) including Thailand (Pancharoen, 1998). The alarming increase of this resistant organism needs to be closely observed. At present, high-dose parenteral penicillin or preferably cefotaxime or ceftriaxone should be recommended as an empirical antibiotic for patients in whom meningococcal disease is suspected.

Our study showed that more than half of meningococcal patients were children and the mean age of the meningitis patients was lower than that of the meningococcemia patients (8.6 years versus 14.4 years). Almost all patients were previously healthy. The overall fatality rate of our patients was not different from that of patients with systemic *Haemophilus influenzae* and *Streptococcus pneumoniae* infections that have been previously studied (Likitnukul, 1994; Pancharoen and Thisyakorn, 2000). However, the mortality was higher among the patients with meningococcemia.

N. meningitidis as an etiologic agent of bacterial meningitis, is not commonly found in Thailand (Chotpitayasunondh, 1994; Pancharoen and Thisyakorn, 2000). The clinical manifestations and CSF findings of the patients with meningococcal meningitis are identical to those seen with the three other most common causative organisms. However, compared with meningitis caused by *Streptococcus pneumoniae, Haemophilus influenzae* and *Salmonella* spp (Chotpitayasunondh, 1994; Pancharoen and Thisyakorn, 1999), this study showed that all patients with meningococcal meningitis survived.

In summary, meningococcal disease is not a common disease in Thailand. Meningococcemia is a serious and life-threatening condition whereas meningococcal meningitis is less serious. Strains of *N. meningitidis* with reduced susceptibility to penicillin were isolated and the prevalence of this organism needs to be closely observed.

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