Invasive meningococcal disease in the university of Malaya Medical Centre, Kuala Lumpur, Malaysia

Raja NS, Parasakthi N, Puthucheary SD, Kamarulzaman A*

ABSTRACT

Background: Neisseria meningitidis (N. meningitidis) remains the leading worldwide cause of acute bacterial meningitis and fatal sepsis in healthy individuals.

Materials and Methods: A total of 12 cases of N. meningitidis from patients with invasive meningococcal infections in University of Malaya Medical Centre, Kuala Lumpur during the years 1987-2004 were reviewed together with details of age, sex, disease, risk factors treatment and outcome of these patients.

Results: Their ages ranged from 10 months to 64 years (median age 29.75 years). The male to female ratio was 1.42:1. Fever, neck stiffness, headache, vomiting and confusion were predominant symptoms. Upper respiratory tract viral infection and Hajj pilgrimage were directly associated with invasive meningococcal disease. Penicillin or ceftriaxone or both in some cases were administered as empirical therapy. All isolates were sensitive to penicillin, ceftriaxone, chloramphenicol and rifampicin. The case fatality ratio was 1:4. One Hajj pilgrim died despite having received polyvalent meningococcal vaccine. Amongst the survivors, two patients had neurological deficit, hearing loss and arthritis.

Conclusion: Early antimicrobial therapy has been shown to reduce these adverse outcomes. Clinicians need to be alerted to the presence the disease in the community and the disease should be made notifiable within 24 hours of detection both for early treatment of cases and to facilitate contact tracing, institution of prophylactic treatment and prevention of secondary cases.

KEY WORDS: Neisseria meningitidis, meningococcal meningitis, bacterial meningitis

Despite the advent of new antimicrobials, meningococcal infections remain a leading cause of morbidity and mortality. Neisseria meningitidis (N. meningitidis), a Gram negative diplococcus, is a major cause of acute bacterial meningitis. Meningococcal disease is relatively uncommon in Malaysia. Serogroups A, B, C, Y and W135 are commonly isolated from patients with acute meningococcal infection. Serogroups B and C of N. meningitidis were predominant in industrialised nations,[1] while serogroup A is an important cause of meningococcal infection in Sub-Sahara Africa especially in the meningitis belt.[2] Serogroup A has recently been associated with an outbreak in Delhi, India with a total of 405 cases and 48 deaths (11.9%).[3] In recent years, however, the infection has gained importance because of the link with the Hajj the Muslim holy pilgrimage. Serogroup W135 has recently been associated with an international outbreak that was directly linked with the Hajj.[4,5,6] Usually serogroup Y affects older adults and is responsible for one third of meningococcal infections in USA.[7] The number of cases involving serogroup Y has increased from 1996 to 1998 and is linked with pneumonia.[8] Meningococcal infections present as two main forms, meningitis and septicaemia or meningococcemia.

However meningococcal infection may rarely present as pneumonia, urcthritis, arthritis, conjunctivitis, otitis media and pericarditis. Meningococcal meningitis resulting from haematogenous spread is similar to other forms of acute purulent meningitis with abrupt onset of fever, headache, neck stiffness, nausea, vomiting, photophobia and confusion.[9] Meningococcemia is often more fatal compared with other meningococcal infections and has a mortality rate of 20%, rising to 50%, if patient is in shock.[10] Serious complications or neurological deficits are common among patients with meningococcal infection. Rosenstein et al[11] reported that 11% to 19% of survivors of meningococcal infections had complications such as disability, loss of limb and damage of the 8th cranial nerve resulting in hearing loss. Improved medical practice based on better understanding of pathogenesis of the disease, nursing care, supportive treatment and administration of prophylactic polyvalent vaccine might contribute more towards decreasing morbidity and mortality rather than new microbes.

Documented meningococcal infections are uncommon in Malaysia. Only seventeen microbiologically confirmed (Isola-
tion of organism from cerebrospinal fluid or blood or antigen detected) cases of invasive meningococcal were seen at University of Malaya Medical Centre (UMMC), Kuala Lumpur between 1987 and 2004. Of the 17 microbiologically confirmed cases, case records were available and retrospectively reviewed in twelve patients and in this report we describe the clinical features and outcome of these patients in addition to the microbiological findings in all 17 cases.

Materials and Methods

Patients with invasive meningococcal infections were identified from the microbiology records of the UMMC from 1987 to 2004. UMMC is a 900 bed, multidisciplinary teaching hospital serving the urban area of Kuala Lumpur and surrounding areas. It has well established units of medicine, surgery, orthopaedics, gynaecology and obstetrics, paediatrics, intensive care units and oncology (adult and paediatrics). Seventeen patients were identified through the microbiology laboratory records and a retrospective analysis of these cases was carried out.

Case Definition

Inclusion criteria for invasive meningococcal infection was Criterion 1. Clinical features of meningitis or sepsicaemia And at least one of the following two criterion Criterion 2. Isolation of N. meningitidis from blood or cerebrospinal fluid (CSF) or other sterile body sites. Or


Patients’ records were reviewed where available and data collected included, patient demographics, clinical presentation including duration of illness and presence of underlying disease, treatment including empirical and definitive, outcome, history of travel or contact with a known case of meningococcal infection, immunization status, and chemoprophylaxis to contacts.

The microbiology data evaluated included body site from which the organism was isolated, antimicrobial sensitivity, serogroup, and antigen detection.

Microbiological methods

From 1987 to 2004, CSF samples received from patients admitted in UMMC were processed by inoculating the sample onto chocolate agar plates, which were incubated in 5-10% CO₂ at 37 °C for two days. Gram stained slides were prepared from CSF soon after receiving the specimen. Latex agglutination (serogroups A-D (Polyvalent), Y, W135 by Wellcogen bacterial antigen kit, Murex Biotech Ltd, UK) was carried out on the CSF samples of some of the patients. In the early part of the study, blood specimens were processed by manual method by subculturing from liquid broth and Robertson’s cook meat medium broth everyday for 7 days. In the late nineties the BACTEC 460 system was used and subsequently BACTEC 9240 (BECTON DICKINSON Diagnostic Instruments Sys-

tems, USA) a continuous monitoring blood culture system was used for processing of blood specimens.

Identification of N. meningitidis was done by conventional bacteriological methods and API NH (BioMerieux, France). Isolates of N. meningitidis were sent to the Institute for Medico Research, Kuala Lumpur for serogrouping. Drug sensitivity was done on chocolate agar plates by Kirby-Bauer disc diffusion method and zone diameters were interpreted according to guidelines established by the British Society of Antimicrobial Chemotherapy.

Results

Demographic Data

Seventeen patients fulfilled the inclusion criteria. The ages of the 16 patients ranged from 10 months to 64 years (mean age 29.75 years). The age of one patient could not be ascertained. There were 10 males and seven females. Of the 17 patients, six were Malays, four were Chinese and five were Indians. Other cases included two foreign workers from a neighbouring country (Indonesia). Patient demographics, clinical features, microbiology findings, antimicrobial treatment and outcome is summarised in [Table 1].

Clinical Features

Five patients’ records were not available and they were excluded from clinical analysis of the cases. Five patients were admitted with meningococcaemia and meningococcal meningitis and one suffered from meningococcaemia only. Six patients presented with meningococcal meningitis. Fever, vomiting, headache and confusion were the commonest presenting complaints while neck stiffness and positive Kerning’s sign were also present in the majority of the cases [Table 2].

Two cases of meningococcal infections were directly linked with the Hajj (Hajj pilgrims) and were part of the Hajj related serogroup W135 outbreak. One patient developed infection one week after returning from Mecca and the second developed signs and symptoms of infection during the eight hour flight from Mecca to Kuala Lumpur. The latter patient was taken directly to the hospital from the airport but she died within 24 hours of admission. Two patients were migrant workers from a neighbouring country who had travelled to Malaysia six months prior to their infection. Another patient was a household contact of a case who died (not in UMMC) due to meningococcal infection. There was no evidence of contact with a known case of meningococcal infection or history of travel in the remaining seven patients. Of the 12 cases, three deaths were recorded giving a mortality rate of 25%. One Hajj related case (patient no 6, [Table 2]) received prophylactic N. meningitidis polyvalent vaccine (A, C, Y, W135), one was an elderly sporadic case (patient no 8, [Table 2]) and the third patient (patient no 3, [Table 2]), a close household contact with a known case of meningococcal disease who was treated elsewhere, did not receive any prophylactic vaccine or chemoprophylaxis.
Table 1: Demographic, clinical features, antimicrobial treatment, outcome, and bacteriological findings of 12 patients.

<table>
<thead>
<tr>
<th>No.</th>
<th>Year</th>
<th>Age (Years)/Sex/Ethnicity</th>
<th>Presenting clinical features</th>
<th>Meningitis/Septicaemia or both</th>
<th>Empiric antimicrobial therapy</th>
<th>Complications</th>
<th>Outcome</th>
<th>Possible risk factors</th>
<th>Culture results/Serogroup</th>
<th>Blood</th>
<th>CSF Culture</th>
<th>Latex agglutination</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2004</td>
<td>14/M/C</td>
<td>Fever Neck stiffness Confusion Vomiting</td>
<td>Meningitis</td>
<td>Ceftriaxone</td>
<td>Nil</td>
<td>Well</td>
<td>Nil</td>
<td>No growth (NG) N. meningitidis (Growth)</td>
<td>Positive (+) Group A-D</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2003</td>
<td>22/M/M</td>
<td>Both</td>
<td>Confusion Neck stiffness Confusion Vomiting</td>
<td>Ceftriaxone Penicillin</td>
<td>Smoker</td>
<td>Growth</td>
<td>Growth</td>
<td>Negative</td>
<td>NG</td>
<td>Growth</td>
<td>Not Done</td>
</tr>
<tr>
<td>3</td>
<td>2003</td>
<td>22/M/C</td>
<td>Fever Headache Ecchymosis Diarrhoea</td>
<td>Meningitis</td>
<td>Nil</td>
<td>ARDS</td>
<td>Died</td>
<td>Smoker</td>
<td>Growth</td>
<td>Poor socioeconomic class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2001</td>
<td>53/F/M</td>
<td>Fever Vomiting Confusion</td>
<td>Both</td>
<td>Ceftriaxone Penicillin Imipenem</td>
<td>3rd nerve palsy Bilateral 7th nerve palsy Hearing loss Nosocomial pneumonia Arthritis</td>
<td>Well</td>
<td>Hajj pilgrimage</td>
<td>Growth W135</td>
<td>Negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>2001</td>
<td>42/F/I</td>
<td>Fever Vomiting Confusion Neck stiffness</td>
<td>Both</td>
<td>Ceftriaxone Penicillin</td>
<td>Poor socioeconomic class</td>
<td>Well</td>
<td>Growth W135</td>
<td>Growth</td>
<td>Negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>2000</td>
<td>58/F/M</td>
<td>Fever Petechiae Apnoea</td>
<td>Both</td>
<td>Penicillin</td>
<td>ARDS Ceftriaxone</td>
<td>Died</td>
<td>Hajj</td>
<td>Growth No Specimen W135</td>
<td>Positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1998</td>
<td>51/F/M</td>
<td>Fever Headache Coma</td>
<td>Meningococcemia</td>
<td>Ceftriaxone Ampicillin</td>
<td>Nil</td>
<td>Well</td>
<td>Respiratory tract infection</td>
<td>Growth W135</td>
<td>No growth</td>
<td>Not done</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>1997</td>
<td>64/M/M</td>
<td>Both</td>
<td>Fever Coma Apnoea</td>
<td>Ceftriaxone Penicillin</td>
<td>ARDS</td>
<td>Died</td>
<td>Smoker</td>
<td>Growth No specimen</td>
<td>Not done</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Demographic, clinical features, antimicrobial treatment, outcome, and bacteriological findings of 12 patients. (Continued)

<table>
<thead>
<tr>
<th>No.</th>
<th>Year</th>
<th>Age (Years)/Sex/Ethnicity</th>
<th>Presenting clinical features</th>
<th>Meningitis/Septicaemia or both</th>
<th>Empiricantibiotic therapy</th>
<th>Complications</th>
<th>Outcome</th>
<th>Possible risk factors</th>
<th>Culture results/Serogroup</th>
<th>Blood</th>
<th>CSF Culture</th>
<th>Latex agglutination</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>1992</td>
<td>10/F/C</td>
<td>Fever Headache</td>
<td>Meningitis</td>
<td>Penicillin Chloramphenicol</td>
<td>Nil</td>
<td>Well</td>
<td>Viral infection</td>
<td>No growth</td>
<td>No growth</td>
<td>Positive</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>1991</td>
<td>27/M/O</td>
<td>Fever Headache</td>
<td>Meningitis</td>
<td>Penicillin Chloramphenicol</td>
<td>Nil</td>
<td>Well</td>
<td>Nil</td>
<td>No growth</td>
<td>Growth</td>
<td>Not done</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>1990</td>
<td>24/F/O</td>
<td>Fever Coma Neck stiffness Confusion</td>
<td>Meningitis</td>
<td>Penicillin Chloramphenicol</td>
<td>Nil</td>
<td>Well</td>
<td>Nil</td>
<td>No growth</td>
<td>No growth</td>
<td>Positive</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>1988</td>
<td>11/M/M</td>
<td>Fever Neck stiffness Confusion</td>
<td>Meningitis</td>
<td>Penicillin Chloramphenicol</td>
<td>Nil</td>
<td>Well</td>
<td>Nil</td>
<td>No growth</td>
<td>Growth Group B</td>
<td>Negative</td>
<td></td>
</tr>
</tbody>
</table>

Microbiology confirmed cases without clinical data

| 13  | 1997 | < 1/M/I                    | -                           | Meningococcemia                | -                         | -             | -       | Growth               | No growth                  | Not done   |
| 14  | 1997 | 34/M/M                     | -                           | Meningococcemia                | -                         | -             | -       | Growth               | No growth                  | Not done   |
| 15  | 1992 | 23/M/C                     | -                           | Meningitis                     | -                         | -             | -       | No growth             | Growth                    | Not done   |
| 16  | 1991 | 20/F/C                     | -                           | Meningococcemia                | -                         | -             | -       | Growth               | No growth                  | Not done   |
| 17  | 1987 | */M/M                      | -                           | Both                           | -                         | -             | -       | Growth               | Growth                    | Not done   |

*Age Unknown Ethnicity, C = Chinese, I = Indians, M = Malays, O = Others
Table 2: Presenting clinical features in 12 patients

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>No. of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>12 (100)</td>
</tr>
<tr>
<td>Confusion</td>
<td>6 (50)</td>
</tr>
<tr>
<td>Coma</td>
<td>5 (42)</td>
</tr>
<tr>
<td>Headache</td>
<td>6 (50)</td>
</tr>
<tr>
<td>Neck Stiffness</td>
<td>8 (67)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>7 (58)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>5 (42)</td>
</tr>
<tr>
<td>Petechial rash</td>
<td>3 (25)</td>
</tr>
<tr>
<td>Ecchymosis</td>
<td>2 (17)</td>
</tr>
</tbody>
</table>

Microbiology
Blood cultures were performed in all 17 patients but N. meningitidis was isolated only from 11 patients. Blood specimens from 15 patients were taken before the initiation of antibiotic therapy and two were taken after the onset of antibiotic therapy. CSF samples were examined in 13 patients. Gram-negative diplococci were seen in the direct smear CSF of five patients. Latex agglutination was done for the detection of antigens of N. meningitidis (A, B, C, Y, W135) on the CSF of eight patients. Although there were two cases where the Latex agglutination test was positive, no organism was isolated from the CSF in both cases. In these two cases, no organism was seen on direct microscopy. In 1988,[14] 2001 and 2003 latex agglutination tests failed to detect antigens of N. meningitidis in one case of group B, two cases of W135 and one case with a serogroup inclusive of A-D (polyvalent sera that only detects serogroups A-D and not the individual serogroup) infections respectively. However, N. meningitidis was isolated from the blood and CSF of these patients. In total, eight CSF specimens yielded N. meningitidis. All isolates of N. meningitidis were sensitive to penicillin, ceftriaxone, chloramphenicol, and rifampicin. Six isolates from blood or CSF were serotyped. Of the six, there were five serogroup W135 isolated in 1987, 1998, 2000 and 2001 and one serogroup B isolated in 1988. Two patients with W135 were linked with Hajj (2000 & 2001) and two cases were sporadic (1998 & 2000).

Antimicrobial Treatment and follow-up
After the onset of symptoms, two of the 12 patients received antimicrobial therapy within the first 8 hours, three within the next 24 hours and two within 48 hours of the onset of the symptoms. Antimicrobial therapy was started in four patients after 48 hours of the start of symptoms. One did not receive any antibiotic therapy. Initial therapy for all cases comprised of intravenous penicillin 0.1-0.3 mega units/kg/day in six divided doses or ceftriaxone 50-100 mg/kg/day in two divided doses up to a maximum of 4 grams per day, pending culture results when definitive antibiotic started. Two patients (case no. 11, 12 [Table 2]) received penicillin as empirical treatment. One patient (case no. 4) who developed nosocomial Klebsiella pneumoniae pneumonia during the stay in hospital was prescribed imipenem along with penicillin and ceftriaxone. In addition, a combination of penicillin and chloramphenicol was administered to two patients (case 9, 10). Ceftriaxone was started as empirical treatment in one patient (Case no. 1). Ceftriaxone and penicillin/ampicillin together were started in six patients (case no. 2, 4, 5, 6, 7, 8) as empirical therapy to cover gram-negative cocci and bacilli causing meningitis. However, two patients received ceftriaxone 3 gram/day for seven days and one of these two patients also received ampicillin one gram six hourly for five days. Intracranial pressure greater than 20 mmHg was seen in seven patients. Other adjunctive therapeutic measures were intravenous mannitol, dexamethasone, and respiratory support.

The majority of the patients responded well and were afebrile after five days of antimicrobial therapy. The follow-up period ranged from one week to six weeks. Rifampicin was prescribed prophylactically to all close contacts of known cases of meningococcal infections.

Clinical outcome
Three patients with invasive meningococcal infection died. These patients were seen in a morbid state, coma grade IV, apnoea and shock. Although vigorous treatment was started, they developed Acute Respiratory Distress Syndrome (ARDS) and died within 24 hours of admission. One fatal case was a patient with ischemic heart disease (IHD). Three patients were chronic smokers including the patient with IHD. On discharge two patients had post-meningococcal infection complications. One suffered from arthritis which is an infrequent complication of meningococcal disease. The second patient had 3rd nerve palsy, 7th nerve lower motor neuron palsy and hearing loss and was readmitted to the hospital with subglottic stenosis secondary to prolonged intubation and ventilation that required a tracheal anastomosis.

Discussion
Meningococcal infections are infrequent in Malaysia and thus documented information on the pattern and management of the disease in the country is lacking. Prompt diagnosis, early treatment with appropriate antibiotic and supportive therapy are highly critical to patient outcome.

Meningococcal infections occur after the transfer of an invasive strain N. meningitidis by an asymptomatic carrier or a known case of meningococcal disease to susceptible hosts.[15] Risk factors for meningococcal disease include household contact with a person with meningococcal disease, institutional crowding, upper respiratory disease, Hajj pilgrimage and their contacts.[6-15] Overcrowding and prolonged exposure to nasopharyngeal carriers among Hajj pilgrims are plausible explanations for the increase of meningococcal infections in Hajj pilgrims. In this study we confirm the significance of these risk factors. However no obvious risk factors were found in four cases. The majority of cases in the present study presented with fever, neck stiffness, confusion, increased CSF opening pressures, low glucose levels and raised protein levels as in a previous study.[19] Of the 12 patients whose medical records were available, three patients had ARDS, which eventually proved fatal. In some cases ARDS developed within a few hours and may have had an impact on outcome.[20] Up to 20% of survivors may suffer from neurological sequelae, ranging from concentration disturbances to sensorineural deafness and seizures. Nevertheless the incidence of neurological sequelae a-
ter meningococcal infection is lower than pneumococcal meningitis.10[23] One patient had neurological sequelae while another suffered from arthritis. The mortality rate of 25% in this series was high when compared with other reports. A study conducted in Singapore showed a 19% mortality rate.39 Delay in the diagnosis and institution of appropriate empirical antibiotic therapy of meningococcal disease when patient did not appear very ill on initial presentation may contribute to a high mortality rate.

In Malaysia, data on the incidence and serogroups of meningococcal disease is not widely available and meningococcal disease is currently not a notifiable disease. In UMMC only a relatively small number of cultures proven cases were treated over a 17 year period and thus the study may not be representative of spectrum of invasive meningococcal disease.Clinicians will have to remain alert for the possibility of cases of meningococcal meningitis and septicaemia. The diagnosis in meningococcal meningitis is straightforward when patient presents with clinical picture of (fever, headache, confusion, positive Kerning’s sign and petechial rash) of bacterial meningitis. There may be a non-specific illness 3 days before the appearance of classical symptoms in meningococcal meningitis. In meningococcal septicaemia, patient presents with severe septicaemia, which progresses more rapidly and has a considerably higher mortality. The hallmark presentation is that of an acute onset of fever with rigors, petechial or ecchymotic rash and rapidly deteriorating sepsis syndrome. Empirical antibiotic treatment should be started promptly because antibiotics are the mainstay of treatment. Administration of benzyl penicillin to the suspected cases before referring to the hospital might lower mortality in meningococcal infections.22 It has also been recommended by the United Kingdom’s Chief Medical Officer to administer antibiotic to the suspected cases on first contact. However, the early start of antibiotic is still controversial in other parts of the world. There is considerable continuing failure to implement this measure probably due to fear of hindrance of microbiological diagnosis and later jeopardizing the management. It has been established that early antibiotic administration does not affect identification of etiologic agent especially when polymerase chain reaction is used as a diagnostic test.23 Delay in the institution of antibiotic therapy will lead to a cascading inflammatory response. N. meningitidis will remain viable in the ischemic lesions that develop during progression of the disease in spite of antimicrobial therapy.24 Adjunctive treatment such as the use of corticosteroids for shock and bacterial meningitis has been increasingly studied. deGan et al reported after conducting a large study in Europe that dexamethasone treatment in adults with bacterial meningitis was linked with a reduction in the danger of death and disability but not hearing loss.25 Internatinal outbreaks of serogroup W135 of N. meningitidis is often linked with the Hajj. Several cases have been reported throughout the world among Hajj pilgrims and their contacts. In 2000, there were several reports of meningococcal infections from Saudi Arabia, USA, UK and France.2 Carriage of N. meningitidis serogroup W-135 increased significantly in pilgrims returning from the Hajj.26 Since the beginning of 2002, it has been a requirement of the Government of Saudi Arabia for all pilgrims to have been vaccinated with quadrivalent meningococcal vaccine (A, C, Y, W135)5 and in Malaysia, it is mandatory for hajj pilgrims to receive the vaccine two to four weeks before travelling. Although the two Hajj pilgrims in this report received quadrivalent vaccine before travelling to perform Hajj, both acquired serogroup W135 of N. meningitidis during their stay in Mecca. Thus breakthrough infection may still occur. Outbreaks of serogroup W135 is mainly associated with the pilgrimage to Saudi Arabia. However, only two of our cases were related to one of the international outbreaks associated with Hajj. Sporadic cases were more frequently identified in our settings. It would be of interest to study the molecular epidemiology of our strains to understand the evolution and spread within our community and globally. Meningococcal disease is associated with high morbidity and mortality. Early antimicrobial therapy has been shown to reduce these adverse outcomes. Thus it is cited that empirical antibiotic therapy with penicillin or ceftriaxone be started promptly upon clinical suspicion of the disease. Clinicians need to be alerted to the presence of the disease in the community and the disease should be made notifiable within 24 hours of detection in Malaysia both for early treatment of cases and to facilitate contact tracing, institution of prophylactic treatment and prevention of secondary cases.

References

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Neisseria meningitidis is an exclusively human bacterium. Its natural habitat is the nasopharynx. Asymptomatic carriage is frequent and affects about 10% of the general population. Transmission occurs through airborne salivary droplets during direct person-to-person close contact. N. meningitidis is responsible for invasive infections that occur as endemic or epidemic cases.

The development of powerful techniques for isolate characterization has improved our understanding of meningococcal epidemiology. Serological typing methods were first employed to determine the antigenic formulas of isolates (serogroup:serotype:serosubtype:immunotype), which are defined by the immune specificities of the capsule, the outer membrane protein PorB, the outer membrane protein PorA, and the lipo-oligosaccharide, respectively. Five of these serogroups (A, B, C, Y, and W135) are most frequently isolated in invasive infections.

N. meningitidis is highly variable and microevolution occurs through horizontal DNA exchange between strains. Genes are randomly associated on the bacterial chromosome. Capsule, PorA, PorB, and LOS are under a strong selective pressure by the host immune response. Variations of these structures reflect adaptation of Nm to its host rather than genetic relatedness between strains. Serological typing is no more adequate for tracking meningococcal strains.

Molecular characterization is now required for tracking microevolution of meningococcal strains and for analyzing the emergence of new clones. Molecular typing methods are usually based on analysis of the polymorphism of meningococcal genes.

In this issue, data described 17 cases on confirmed or probable cases of invasive meningococcal disease from Malaysia during the period 1987–2004. It is unclear how comprehensive the data are. However, this information is interesting as rare data are available from Malaysia. Five cases were owing to N. meningitidis serogroup W135. Only two cases were linked to the Hajj. A clonal outbreak of W135 meningococcal disease has occurred in the year 2000 among pilgrims returning from Saudi Arabia and their contacts. The isolates belonged to the genotype ST-11/ET-37. The presence of such isolates was subsequently reported worldwide. However, these isolates showed continuous diversification. The presence of several local ST-11/ET-37 isolates has been reported since 1970. (Two isolates from Malaysia were isolated before 2000) incomplete sentence. Multifocal emergence of W135 ST-11/ET-37 may be suspected rather than a clonal spread of one particular clone of the ST-11/ET-37 genotype. Therefore, complete characterization of invasive meningococcal isolates from Malaysia is needed, as well as the comparison of these isolates to the Hajj 2000 strain and to other W135 strains.

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