

Clinical and Laboratory Manifestations of Meningococemia in Children

S Mamishi¹, S Mostashfi habibabadi¹, *B Elahi¹

¹Dept. of Pediatrics, Faculty of Medicine, Tehran University of Medical Sciences, Iran

(Received 1 Jul 2006; accepted 25 Oct 2006)

Abstract

Lack of vaccination and modern health care facilities in many countries including Iran let meningococemia to remain as a serious challenging disorder especially among children and in spite of improved diagnosis and earlier treatment its prognosis is still dismal. This study describes 68 cases (54.4% male) of proved meningococemia hospitalized since 1992 up to the end of 2002 in Children Medical Center Hospital, Tehran, Iran. Infants of 6 to 12 month old were a major concern in number (14.7%) and severity of disease. 5.9% of the cases have had at least two hospitalization history for meningococcal septicemia and 19.1% of the patients had Systemic Lupus Erythematosus (SLE), nephrotic syndrome or chronic liver disease in their past medical history. Meningeal irritation signs were seen in 55.9% and cerebrospinal fluid (CSF) smear was positive in 71.4% and culture was positive in 48.5% of patients. Meningococcal septicemia ended in shock (38.2%), Disseminated intravascular coagulation (DIC) (7.4%), thrombocytopenia (10.3%), arthritis (4.4%), ocular complications (2.9%), pericarditis (2.9%) and seizure (8.8%) in 51 of the cases, and death occurred in 7 patients. This study shows that the manifestation of the disease is similar to those described elsewhere except for lower pneumonia and no seasonal variations.

Keywords: *Neisseria meningitides, Meningococemia, Pediatrics, Meningitis, Iran*

Introduction

Meningococcal infections continue to kill and disable many children (1-7). There are few published data available explaining the morbidity, mortality, and different presentation of this fatal disease in Iranian patients.

Rates of meningococcal disease in the US have remained relatively stable, at approximately 0.9 to 1.5 cases per 100, 000 persons per year, or 2500 to 3000 cases per year but in the sub-Saharan "meningitis belt" region where consists of the countries extended from Senegal to Ethiopia in Africa, serogroup A poses a recurrent threat to public health, with attack rates up to 500 to 1000 cases per 100, 000 population (8-10). Other studies have also shown occurrence of the highest attack rate among young children which is probably due to immaturity of their immune system in production of protective antibodies (1, 5, 11).

Infection by *Neisseria meningitides* may cause overwhelming sepsis, typically characterized by

shock and a hemorrhagic exanthema, or central nervous system involvement (12, 13), purpura fulminans and hemodynamic deterioration continues to have a mortality of more than 50% (14, 15).

This high mortality and morbidity makes timely and correct diagnosis of acute febrile children with meningococemia a dilemma for considerate clinicians, while lack of vaccination and modern diagnostic tools in many developing countries give additional significance to clinical manifestation as a tool for detecting the culprit agents especially in affected children.

Unluckily, there are few published data available from Iran including mortality rates and serotypes of meningococcal infections (16), however; published data have shown similarity between nature of this infection in Iran and neighboring countries.

In this study, we tried to describe the clinical and laboratory manifestations of *Neisseria meningiti-*

dis sepsis, as well as the mortalities and disabilities we are coping with in fighting this life threatening disease.

Material and Methods

In this retrospective case series study, we reviewed children (defined as patients younger than 13 yr old) admitted in one of the major affiliated children's referral hospitals of Tehran University of Medical Sciences, Iran. We identified children from April 1992 to April 2002 with either primary or final diagnosis of meningococemia confirmed by positive microbiological findings of meningococcal infection.

We extracted the demographic information, clinical manifestations, laboratory results, complications, and outcome to standardized data collection sheets for further analysis.

Meningococemia is considered in patients with at least one positive blood culture. Clinical signs of meningitis (neck stiffness or low level of consciousness) were observed in 38 patients. Lumbar puncture for CSF smear and culture was performed in 52 patients. "Meningitis" was defined as the recovery of *N. meningitides* from samples of the CSF in association with a CSF pleocytosis of ≥ 10 WBCs/mm³ (if aged > 1 mo), or recovery of *N. meningitides* from a blood culture alone but with a CSF pleocytosis of ≥ 10 WBCs/mm³ (if aged > 1 mo). Because neonates (≤ 1 mo of age) may normally have CSF pleocytosis of ≤ 25 WBC/mm³, these patients had meningitis according to the aforementioned criteria if they had a CSF pleocytosis > 25 WBC/mm³ (17).

Pericardial effusion was diagnosed by means of echocardiography. Seizure activity was determined based on a description in a progress note or a discharge diagnosis.

Permanent or long-lasting complications of the disease were registered including scarring secondary to localized skin loss, partial or complete amputations, conjunctivitis, arthritis, and neurological impairments, including seizures. Epilepsy considered as a complication of meningococcal disease if patients were discharged on

anticonvulsant medication. Unfortunately, lack of proper audiometric evaluation resulted in inconclusive information about hearing loss.

Patients with an altered immune status owing to the use of immunosuppressive drugs or splenectomy, diabetes mellitus, nephrotic syndrome or chronic liver disorders were considered immune compromised, as were patients infected with the human immunodeficiency virus or those with recurrent meningococcal infections.

Results

We identified 68 children (54.4% male and median age of 5 yr old) with culture proven meningococcal disease; all of them had clinical signs for overt meningococcal disease. Lumbar puncture (LP) was done on 52 patients, of whom 35 had neck stiffness and meningeal irritation signs, while 16 patients underwent LP without any sign of meningeal irritation, on the other hand there was two patients who had neck stiffness but LP was not done or failed to extract enough CSF sample for analysis. *Neisseria meningitidis* isolated in CSF smear of 25 (71.4%) patients with neck stiffness or other meningeal irritation signs and CSF culture was positive among 17 patients of whom 11 had both positive CSF smear and culture for *N. meningitidis*.

In our study, 20.6% of our patients were between 4 to 6 yr old (median 5 yr) and 14.7% were between 6 to 12 mo. Meningococemia were presented with rash, shock and meningitis on admission (Table 1). Seasonal change on disease occurrence was insignificant (Chi-square $X^2=0.92$) with the lowest occurrence of disease between July and November.

Thirteen patients had altered immune system with chronic conditions such as chronic liver disorders, SLE or nephrotic syndrome and four patients had recurrent infections with *Neisseria meningitidis*.

Complications occurred in a major number of the patients (Table 2.). Seven patients died (10.3%); two of them had meningeal signs and 5 had severe sepsis and respiratory failure.

Table 1: Results of the blood culture and smear CSF examinations and clinical signs in patients with meningococemia

| Clinical or Laboratory Findings | | Measured or Observed Variables | n (%) | |
|------------------------------------|-------------------------|---|-------------|------------|
| Symptoms at presentation | | Headache | 38 (55.9) | |
| | | Neck stiffness | 38 (55.9) | |
| | | Rash | 44 (64.7) | |
| | | Shock | 26 (38.2) | |
| Blood count and sedimentation rate | | ESR (>30mm/hr) | 7 (10.3) | |
| | | Leucopenia (WBC <1500/mm ³) | 14 (20.6) | |
| | | Thrombocytopenia (platelet<150000) | 10 (14.7) | |
| Positive blood culture | | Number of positive culture | 68 (100) | |
| Positive CSF culture | | Number of positive culture | 17 (48.5) | |
| Positive CSF smears | White blood cell counts | Number of positive culture | 25 (71.4) | |
| | | <250 cells/mm ³ | 12 (23.0) | |
| | | 251-500 cells/mm ³ | 4 (7.6) | |
| | | 500 cells/mm ³ < | 36 (69.2) | |
| | | CSF inflammation Indexes | CSF protein | 0-25 mg/dl |
| | | 26-50 mg/dl | 9 (17.3) | |
| | | 51-200 mg/dl | 22 (42.3) | |
| | | 200 mg/dl < | 17 (32.6) | |
| | | CSF glucose | 0-30 mg/dl | 26 (50) |
| | | | 31-50 mg/dl | 9 (17.3) |
| | | | 50 mg/dl < | 17 (32.6) |

Table 2: Number of the early and late complications of meningococemia observed in children studied

| Complications | Complication type | n (%) |
|---------------|-------------------|-----------|
| Early | Headache | 26 (38.2) |
| | Neck stiffness | 5 (7.4) |
| | Rash | 7 (10.3) |
| | Septic arthritis | 3 (4.4) |
| Late | Conjunctivitis | 2 (2.9) |
| | Pericarditis | 2 (2.9) |
| | Epilepsy | 6 (8.8) |

Discussion

This study elucidated the common manifestations and outcomes of patients admitted to hos-

pital with meningococemia as their primary or final diagnosis. 38.2% patients admitted with septic shock and 7 patients (10.3%) died, case fatality rates reported in other studies was 7 to 14% (1, 6, 18- 21) comparable to what we found. Most of our cases were children 4 to 6 yr old and the second peak occurred in children 6 to 12 mo as we expected from previous studies (1, 7). Many studies have shown seasonal variation in the number of their patients with a nadir of cases in summers, especially September, but in this study we did not detect statistically significant variation (1, 6, 7, 19, 20).

Seizure (8.8%), septic arthritis (4.4%), and conjunctivitis (2.9%) were the most prominent complications. While in one study performed in Canada the most common complication regis-

tered was amputation and skin defects (22). This discrepancy originated from the different periods of follow-up. At the present study, we considered immediate and delayed complications, which had occurred during admission or on the first post admission visit.

Meningitis has been reported to occur in 57%-93% of patients with meningococcal disease (1, 3, 6, 18, 19). We found 55.9% of the patients with clinical and laboratory signs of meningitis. Rash was observed in 64.7% of the cases, while this sign had a range of 7.3% to 100% of the cases in other studies (18,23) in a recently published article in New England journal of Medicine occurrence of rash was significantly related to unfavorable outcome among patients with meningococcal meningitis(24).

We found 25% of the patients with the background history of recurrent meningococcal infections (5.9%), or a chronic debilitating disorder (nephrotic syndrome, chronic liver disease, or SLE) (19.1%).

However, lack of appropriate serological diagnostic test and poor economic condition in developing countries limit this study in many aspects. Unsuspected meningococcal infection which consists of those cases who had managed out patiently did not include in this study. Also we did not have enough data concerning the serogroup of N. meningitides in our patients.

In brief this study reviews meningococcal disease in children at one of the academic pediatric referral hospitals in Tehran for 10 yr; although the majority of patients had meningitis, the full range of the manifestations was also seen. Manifestations of the disease were similar to those described elsewhere, with the exception of the pneumonia and seasonal variations, which we rarely observed.

Acknowledgments

Authors want to thank Professor A Siadati, for his kind guidance and for his continued support of our work, and we also thank Professor Bavarian and Dr Elahi for their precious consulta-

tions and revision of the manuscript. This study was conducted without any external funds and was accepted for poster presentation in Medicine and Health in Tropics, Marseille- France September 2004.

References

1. Jafari HS, Perkins BA, Wenger JD (1997). Control and prevention of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep*, 46: 1-10.
2. Singh J, Arrieta AC (2004). Management of meningococemia. *Indian J Pediatr*, 71(10): 909-13.
3. Kirsch EA, Barton RP, Kitchen L, Giroir BP (1996). Pathophysiology, treatment and outcome of meningococemia: a review and recent experience. *Pediatr Infect Dis J*, 15:967-79.
4. Riedo FX, Plikaytis BD, Broome CV (1995). Epidemiology and prevention of meningococcal disease. *Pediatr Infect Dis J*, 14: 643-57.
5. American Academy of Pediatrics, Committee on Infectious Diseases; Canadian Paediatric Society, Infectious Diseases and Immunization Committee (1996). Meningococcal disease prevention and control strategies for practice-based physicians. *Pediatrics*, 97:404-12.
6. Whalen CM, Hockin JC, Ryan A, Ashton F (1995). The changing epidemiology of invasive meningococcal disease in Canada, 1985 through 1992. Emergence of a virulent clone of *Neisseria meningitidis*. *JAMA*, 273: 390-94.
7. Mok Q, Butt W (1996). The outcome of children admitted to intensive care with meningococcal septicaemia. *Intensive Care Med*, 22: 259-63.
8. Singh J, Arrieta AC (2004). Management of meningococemia. *Indian J Pediatr*, 71: 909-13.

9. Rosenstein NE, Perkins BA, Stephens DS, Popovic T, Hughes JM (2001). Epidemiologic Features of Meningococcal Disease. *N Engl J Med*, 344(18): 1378-88.
10. Meningococcal disease in the African Meningitis Belt (WHO website) (2002). Available from: <http://www.who.int/disease-outbreak-News/n2002/april/10april2002.html>.
11. Jackson LA, Wenger JD (1993). Laboratory-based surveillance for meningococcal disease in selected areas, United States, 1989-1991. *MMWR CDC Surveill Summ*, 42: 21-30.
12. Kirsch EA, Barton RP, Kitchen L, Giroir BP (1996). Pathophysiology, treatment and outcome of meningococemia: a review and recent experience (see comments). *Pediatr Infect Dis J*, 15:967-78.
13. Wong VK, Hitchcock W, Mason WH (1989). Meningococcal infections in children: a review of 100 cases. *Pediatr Infect Dis J*, 8: 224-27.
14. Havens PL, Garland JS, Brook MM, Dewitz BA, Stremski ES, Troshynski TJ (1989). Trends in mortality in children hospitalized with meningococcal infections, 1957 to 1987. *Pediatr Infect Dis J*, 8: 8-11.
15. Giraud T, Dhainaut JF, Schremmer B, Rognier B, Desjars P, Loirat P et al. (1991). Adult overwhelming meningococcal purpura: a study of 35 cases, 1977-1989. *Arch Intern Med*, 151: 310-16.
16. Emami Naeini A (2005). Importance of Scoring Systems in Prognosticating Meningococemia. *Journal of Research in Medical Sciences*, 1: 34-37.
17. Gotoff SP (2000). Infections of the neonatal infant: laboratory diagnosis. In: *Nelson textbook of pediatrics*. Eds Behrman RE, Kliegman RM, Jenson HB, W. B. Saunders. 16th Ed, New York, pp. 548-49.
18. Wang VJ, Kuppermann N, Malley R, Barnett ED, Meissner HC et al. (2001). Meningococcal Disease among Children Who Live in a Large Metropolitan Area, 1981-1996. *Clin Infect Dis*, 32(1): 1004-9.
19. Edwards MS, Baker CJ (1981). Complications and sequelae of meningococcal infections in children. *J Pediatr*, 99: 540-45.
20. Jackson LA, Wenger JD (1993). Laboratory-based surveillance for meningococcal disease in selected areas, United States, 1989-1991. *MMWR Morb Mortal Wkly Rep CDC Surveill Summ*, 42: 21-30.
21. Havens PL, Garland JS, Brook MM, Dewitz BA, Stremski ES, Troshynski TJ (1989). Trends in mortality in children hospitalized with meningococcal infections, 1957-1987. *Pediatr Infect Dis J*, 8:8-11.
22. Erickson L, De Wals P (1998). Complications and sequelae of meningococcal disease in Quebec, Canada, 1990-1994. *Clin Infect Dis*, 26(5):1159-64.
23. Mandl KD, Stack AM, Fleisher GR (1997). Incidence of bacteremia in infants and children with fever and petechiae. *J Pediatr*, 131(3):398-404.
24. Van de Beek D, de Gans J, Spanjaard L, Weisfelt M, Reitsma JB, Vermeulen M (2004). Clinical Features and Prognostic Factors in Adults with Bacterial Meningitis. *N Engl J Med*, 351(18):1849-59.