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Clinical and Laboratory Manifestations of Meningococcemia in Children

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Abstract

Lack of vaccination and modern health care facilities in many countries including Iran let meningococcemia 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 meningococcemia 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, *Meningococcemia, Pediatrics, Meningitis, Iran*

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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 meningococcemia 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-*

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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 meningococcemia 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.

Meningococcemia 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/mm^3 (if aged> 1 mo), or recovery of *N. meningitides* from a blood culture alone but with a CSF pleocytosis of ≥ 10 WBCs/ mm^3 (if aged > 1 mo). Because neonates (≤ 1 mo of age) may normally have CSF pleocytosis of ≤ 25 WBC/ mm^3, these patients had meningitis according to the aforementioned criteria if they had a CSF pleocytosis > 25 WBC/ mm^3 (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. Meningococcemia 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 meningitis*.

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.

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

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/mm3)	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		Number of positive culture	25 (71.4)
	White blood cell counts	<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	4 (7.6)
		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 meningococcemia observed in children studied

Complications	Complication type	n (%)
Early	Headache	26 (38.2)
	Neck stiffness	5 (7.4)
	Rash	7 (10.3)
Late	Septic arthritis	3 (4.4)
	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 hospital with meningococcemia 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-

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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.

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