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Meningococcal meningitis in children

J. ELLSWORTH, MD; M.I. MARKS, MD; A. VOSE, RN

Forty-four cases of meningococcal meningitis in children at one hospital between 1971 and 1975 inclusive were studied to document the course and complications of this disease in children in the current therapeutic era. The mortality was 5%. Of the 41 survivors 76% were healthy 1 to 5 years after the episode of meningitis. Permanent severe sequelae (facial palsy, optic atrophy and ptosis) were seen in three (7%) of the survivors, and mild hearing loss, hyperactivity and nervousness were noted in seven (17%). Electroencephalography was not useful in determining management or prognosis. Both the mortality and the frequency of early and late complications among the survivors were lower than those reported from earlier studies.

Quarante-quatre cas de méningite à méningocoque chez des enfants dans un hôpital entre 1971 et 1975 inclusivement ont été étudiés pour documenter l'évolution et les complications de cette maladie chez des enfants dans l'ère thérapeutique actuelle. La mortalité était de 5%. Parmi les 41 survivants 76% étaient en bonne santé 1 à 5 ans après l'épisode de méningite. Des séquelles graves permanentes (paralysie faciale, atrophie optique et ptosis) ont été observées chez trois (7%) des survivants, et une légère hypoacousie, une hyperactivité et une nervosité ont été notées chez sept (17%). L'examen électroencéphalographique n'a pas fourni d'éléments d'intérêt thérapeutique ou pronostique. La mortalité et la fréquence des complications précoces et tardives chez les survivants ont été plus faibles que celles rapportées dans les études précédentes.

From the departments of pediatrics (infectious diseases) and microbiology, McGill University–Montreal Children's Hospital Research Institute

Reprint requests to: Dr. M.I. Marks, Montreal Children's Hospital, 2300 Tupper St., Montreal, PQ H3H 1P3

Haggerty and Ziai[1] and Swartz and Dodge[2] reported mortality rates for meningococcal meningitis in children of 18% and 13% in 1964 and 1965 respectively. Wehrle and colleagues[3] reported an average mortality of 8.4% (range 3.3% to 14.1%) for the years 1961 through 1966. A more recent survey of bacterial meningitis in children in England and Wales documented a mortality of approximately 22% for cases reported in the years 1970 through 1973, but more detailed examination of the records of 265 of the patients from an area in London disclosed a mortality of 11% in this group.[4] Unfortunately data relating to early and late morbidity and clinical and laboratory features of meningococcal meningitis were not provided in this report — nor have these features been described in the modern therapeutic era.

We have followed up children with meningococcal meningitis admitted to the Montreal Children's Hospital between 1971 and 1975 inclusive to document the early and late complications of this disease and to estimate the current mortality. The results of this study indicate a low mortality (5%) and a reduction in the frequency of some complications, compared with earlier data.[1-4]

Methods

The clinical and laboratory features of children hospitalized at the Montreal Children's Hospital with meningococcal meningitis (those in whom *Neisseria meningitidis* was cultured from cerebrospinal fluid [CSF]) during the years 1971 through 1975 were analysed.

Of the 41 survivors 36 were examined at 2 weeks, 2 months, 6 months and 1 year after discharge from hospital. Information about the remainder was obtained from the charts, their physicians and the answers to a telephone questionnaire. Each visit included interval history-taking and physical, neurologic and developmental examination. Audiograms and electroencephalograms (EEGs) were obtained within the first 3 months after the illness and were repeated when abnormal.

Results

There were 44 cases of meningococcal meningitis in 43 children admitted to our hospital between 1971 and 1975. Twenty-six (60%) of the children were male, and the average age was 2½ years (range 2 months to 16½ years). Two patients died. One, a 2-year-old boy, presented with convulsions and hyperglycemia after 6 hours of fever and vomiting. Disseminated intravascular coagulation developed rapidly, and he died 39 hours after admission; histopathologic findings indicated Waterhouse-Friderichsen syndrome. The other was a 7-year-old girl who presented with a 3-hour history of vomiting, fever and delirium, and died in shock 8 hours after admission.

Symptoms were present for an average of 2 days prior to admission (range 4 hours to 7 days). Of the 27 children with petechiae 9 had positive blood cultures; 1 patient had bacteremia without petechiae. All but three children presenting with petechiae manifested other complications later. Eight children presented with convulsions, three were comatose and two were in shock. At the time of admission arthritis was present in four children (all of whom had petechiae and neurologic complications), conjunctivitis in two, cranial nerve palsies in two and pneumonia in one.

The average leukocyte count at the time of diagnosis was 15.5 × 10^9/L (range 4.2 to 34.4 × 10^9/L) in the peripheral blood and 4.1 × 10^9/L (range 0.001 to 21 × 10^9/L) in the CSF. At that time the mean CSF protein concentration was 255 mg/dL (range 15 to 675 mg/dL), and the CSF glucose concentration was 27% (range 0 to 103%) of the peripheral blood glucose concentration (Fig. 1). All patients were treated with intravenous administration of ampicillin or penicillin for 7 to 12 (mean 9.8) days. The average duration of fever (temperature greater than 37.5°C) was 6 days (range 0 to 34 days). Sequential CSF findings are illustrated in Fig. 1. Indications for lumbar puncture included persistent hypoglycorrhachia and CSF pleocytosis.

Two episodes of meningococcal meningitis occurred in a 9-year-old girl with partial lipodystrophy and a low serum concentration of the C3 component of complement. The first episode was uncomplicated, but the second, which occurred 6 months later, was associated with facial nerve palsy. The palsy resolved over the subsequent 6 months. Serogroups of the infecting strains were not known.

Complications were noted in 25 patients during the initial hospitalization and in 14 patients during the follow-up period (Table I). Only one patient with an uncomplicated hospital course was noted to have a complication after hospitalization; in this 3-month-old girl ptosis was noted 2 weeks after discharge. Initially the most common acute problems were

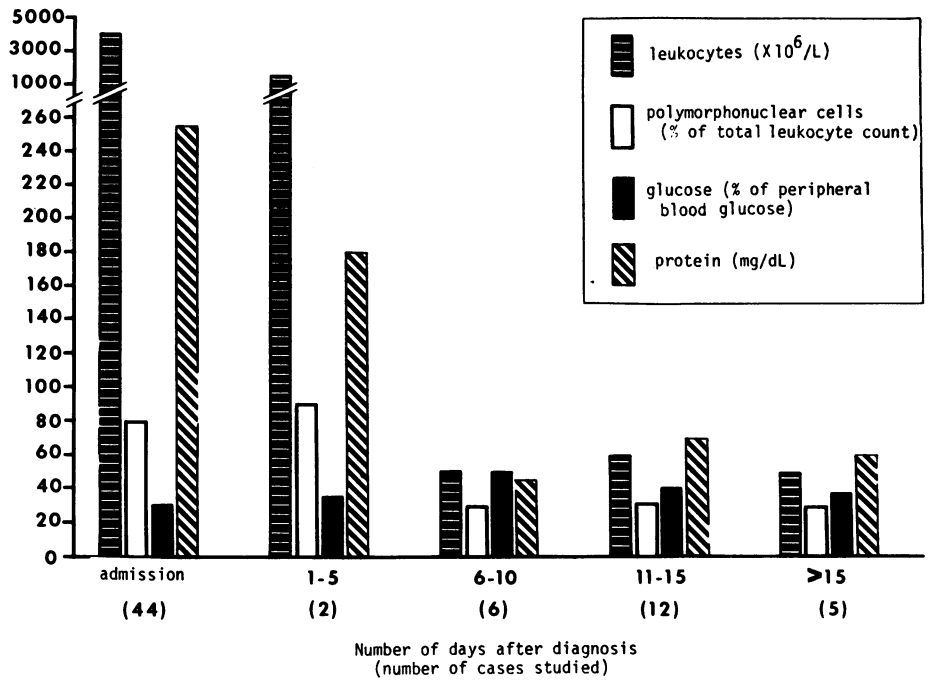

FIG. 1—Characteristics of cerebrospinal fluid in children with meningococcal meningitis; average values indicated.

Table I—Early and late complications of meningococcal meningitis in 43 children during acute stage of disease and 41 children during follow-up

Complication	No. of abnormalities	
	Total	Unresolved
Noted during initial hospitalization	(in 25 patients)	(in 2 patients)
Convulsions	9	0
Palsies	6	1
Cranial nerve VII	3	1
Cranial nerve VI	1	0
Multiple	1	0
Right leg	1	0
Arthritis	4	0
Coma	3	0
Inappropriate secretion of antidiuretic hormone	3	0
Shock	2	0
Renal*	2	0
Conjunctivitis	2	0
Disseminated intravascular coagulation	1	0
Diplopia	1	0
Hydrocephalus	1	0
Optic atrophy	1	1
Subdural effusion	1	0
Cerebral edema	1	0
Apnea	1	0
Pericarditis	1	0
Ileus	1	0
Gastrointestinal hemorrhage	1	0
Hemolytic anemia	1	0
Noted after hospitalization	(in 14 patients)	(in 8 patients)
Psychodevelopmental	8	5
Hyperactivity	3	3
Irritability, nervousness	3	2
Night terrors	1	0
Learning	1	0
Hearing loss	3	2
Ataxia	1	0
Ptosis	1	1
Headache	1	0
Leg weakness	1	1
Finger paresthesia	1	0

*Acute tubular necrosis in one and focal glomerulonephritis in the other.

convulsions (in nine patients), cranial nerve palsies (in five), arthritis (in four) (arthrocentesis was not performed), and coma and inappropriate secretion of antidiuretic hormone (in three each). Complications noted after hospitalization included psychodevelopmental problems in seven children and hearing loss in three. Complications persisted in 10 patients.

Of 35 audiograms 3 were abnormal. One showed bilateral hearing loss 3 weeks after the onset of the illness; the loss had lessened 2½ years later. Another patient had a mild conductive hearing deficit in the high frequency range 2½ weeks after the onset of the illness, but normal findings at 6½ months. The third had a moderate conductive loss 8 months after her illness but was not retested. Hearing aids were not required.

Clinical and electroencephalographic abnormalities correlated poorly in many cases. Electroencephalographic abnormalities consisted of mild to moderate dysrhythmia with few localizing features. Twelve of the 15 patients with abnormal EEGs had neurologic abnormalities: hyperactivity (3), hearing loss and nerve palsies (2 each), paresthesia, optic atrophy, convulsions and ataxia, and nervousness (1 each). Two of the children with epileptiform foci persisting in their EEGs months after hospitalization had had seizures with the onset of meningitis but none subsequently although they were not receiving anticonvulsant therapy. An additional nine children with normal EEGs had similar neurologic abnormalities: nerve palsies and nervousness (two each) and hearing loss, headaches, subdural effusion, cerebral edema and learning problems (one each). Four children with convulsions at the onset of meningitis or shortly thereafter had normal EEGs.

Discussion

The prognosis of meningococcal meningitis in children continues to improve. There were only two deaths in the 44 episodes of meningococcal meningitis treated at our hospital between 1971 and 1975. Both occurred within 48 hours after the onset of symptoms and were related to septic shock and disseminated intravascular coagulation. Stiehm and Damrosch[5] noted the grave prognosis associated with these complications; they suggested that children with meningococcal meningitis who had bacteremia had a higher death rate (8%) than those with meningitis alone (6%). Ten of the children in our series had associated bacteremia. Patients with fulminant meningococcemia but no meningitis have the poorest prognosis.

Although we did not examine the meningococcal serogroups in our study, mortality was not related to the infecting serogroup in other reports.[5,6] Wehrle and colleagues[3] reported only four deaths in 92 cases of meningococcal meningitis in a prospective therapeutic study reported in 1968. Details of patient selection, clinical features and follow-up findings were not provided, although the authors stated that 8 of the 40 patients excluded from the study had died. Other mortality rates have ranged from 22% and 11% recently in England,[4] to 18% and 13% in the 1960s.[1,2] Ross[7] reviewed meningococcal meningitis in adults in 1952 and reported an overall mortality of 16% to 20%, although age-related mortality was not analysed. Death rates were 12% in Africa in 1975[6] and 17% at Boston City Hospital between 1935 and 1972.[8] Since the duration of illness in both of our patients that died was very short (6 and 3 hours respectively), further reduction in mortality may depend on effective vaccination as well as early diagnosis and management of shock.

Only one of our patients had a subdural effusion. In our hospital the subdural space is explored only in children in whom laboratory and clinical features (such as focal neurologic signs) indicate the presence of a significant effusion. Other reviewers (probably using less rigid criteria) have reported frequencies of 15% (2 of 13 patients) and 17% (17 of 100 patients) for this complication.[1,9]

Dodge and Swartz[10] reported that 10% of their patients with meningococcal meningitis had seizures in the acute stage of the disease, an additional 10% had focal cerebral signs, and 15 of the 39 patients had cranial nerve involvement early in the course of the disease. In our study 9 of 44 episodes of meningitis were associated with convulsions in the acute stage, cranial nerve involvement was present in 6 episodes, and other cerebral signs were present in 3 episodes.

Inappropriate secretion of antidiuretic hormone was detected in 4 of 39 patients by Dodge and Swartz[10] and in 3 of 44 episodes in our study. Other acute complications were too few for meaningful comparisons to be made.

Although Ross[7] reported that 30% of survivors of meningococcal meningitis under the age of 16 years had severe residual findings, the prognosis seems to have been much more favourable in the last two decades. None of the patients in the Boston series had postmeningitic epilepsy, persistent focal cerebral signs or unresolved cranial nerve injury.[10] These findings are similar to ours. Deafness has not been a common complication of meningococcal meningitis in the antibiotic era,[11] and none of the children in our study were seriously affected. The improvement in outcome may reflect advances in supportive and pharmacologic treatment. Corticosteroid therapy for shock and cerebral edema, and diazepam treatment of convulsions are two examples. One of our patients had recurrent meningitis. This 9-year-old girl had a complement deficiency associated with lipodystrophy. Other complement deficiencies have been reported in children with recurrent meningococcal meningitis, and these reports have emphasized the role of humoral factors in the pathogenesis of this disease.[12]

Persistence of CSF abnormalities was noted in several of our patients. Since these findings did not correlate with the presence of active infection or with outcome, caution is urged in using CSF findings to guide therapy or to make a prognosis in meningococcal meningitis. Other bacteriologic

and clinical features of the illness need to be considered as well. Further studies are needed to document the sequence of CSF findings in patients with this disease. This problem has also been reported for meningitis due to *Hemophilus influenzae* and *Streptococcus pneumoniae*.[13-15]

The difficulties we encountered in correlating abnormal electroencephalographic findings with clinical outcome in the acute and the late stage of the disease were similar to those for pneumococcal meningitis.[15]

Conclusion

This study has reported the early and late complications of meningococcal meningitis in children in the period 1971 through 1975 in Montreal. Low mortality (5%) and acute morbidity rates were noted, and 76% of the survivors were apparently healthy 1 to 5 years after their illness. Detailed psychologic evaluations are necessary to further define the residual effects of meningococcal meningitis on this and similar groups of children.

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