Acute Neurologic Complications And Long Term Sequelae Of Bacterial Meningitis In Children

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Citation

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Abstract

Mortality and morbidity rates are high among children with acute bacterial meningitis, especially in young ages. A im: to determine the most common neurologic complications during the acute phase of childhood bacterial meningitis and long term sequelae. Material and methods: A total of 277 children (aged 0-16years) were evaluated for acute neurologic complications following bacterial meningitis at the Infectious Diseases Clinic in Prishtina (Kosovo) in years 1997-2002. The authors have analyzed the sequelae that persisted during the three year follow-up period. Results: Of the 277 children treated for bacterial meningitis, 60 children developed neurologic complications (22%) and 15 died (5%). The acute neurologic complications observed were: subdural effusion (35), seizures (31), hydrocephalus (7), 2 cases of subdural empyema and single case of spinal abscess, quadriparesis, vision loss, cerebritis, subdural hematoma and intracerebral hemorrhage. Fifteen children (5%) underwent neurosurgical intervention: 6 children with subdural effusion, 5 with obstructive hydrocephalus, 2 with subdural empyema and one child with subdural haematoma. Long term sequelas were observed in 28 patients (10%): late seizures (24), hydrocephalus (5), deafness (3) neuropsychological impairment (3) and a single case with quadriparesis and partial amaurosis. Conclusion: Neurologic complications of bacterial meningitis are frequent with subdural effusion being the most common during the acute phase of meningitis. Half of neurologic complications resolved within three years of follow up: only 10% of children were left with long term sequelae with late seizures being the most common.

INTRODUCTION

Bacterial meningitis is a severe infection responsible for high mortality and disabling sequelae. Early identification of patients at high risk of these outcomes is necessary to prevent their occurrence by adequate treatment as much as possible. Despite effective antimicrobial and supportive therapy, mortality rates remains high (from 20-30%) with significant long-term sequelae in survivors[1,2,3]. The risk of death or developing complications is related to the age and underlying condition of the patient, the etiologic agent, the severity and duration of illness at the time of presentation, and, occasionally, delays in the initiation of antibiotic therapy[4]. As many as 50% of survivors experience neurological sequelae, such as hearing impairment, seizure disorders and learning and behavioral problems[5,6,7]. Neurological complications of BM in children include subdural effusion or empyema, cerebral abscess, seizures, hydrocephalus, focal deficits (hearing loss, cranial nerve palsies, hemiparesis or quadriparesis), cerebrovascular abnormalities, neuropsychological impairment, and developmental disability. Seizures are more often seen during the acute stage of the disease[8,9,10,11].

MATERIAL AND METHODS

A retrospective study of 277 children (aged 0-16 years, median 2 years, 162 boys) treated for BM at the Infectious Diseases Clinic in Prishtina (Kosovo) in years 1997-2002. All the data for cases of bacterial meningitis in children were gathered prospectively while the analysis was done retrospectively. Patients included: 7 neonates, 108 infants, 37 children aged 1-2 years, 56 aged 3-5 years, 45 aged 6-10 years and 24 aged 11-16 years. With exeption of some neonates treated in neonatology ward, every bacterial meningitis case in a child < 16 years from Kosovo was send to our department. The diagnosis of bacterial meningitis was based on WHO criteria: clinical symptoms (e.g. fever, meningeal signs) and changes in cerebro-spinal fluid (CSF): pleocytosis (>100 /mm^3) and either direct (positive blood or CSF culture) or indirect (positive latex agglutination test or CSF Gram stain) confirmation of bacterial presence. The etiology was confirmed by culture in 124 cases (45%); 71 mengococcus, 22 H.influenzae, 17 pneumococcus and 11 gram-negative bacilli cases were observed. The diagnose of neurologic complications was made by neurological examination, neuroimaging, electroencephalografy and by

neurologist and psychologist evaluation. Head compjuted tomography (CT) scans were performed in all 109 children with prolonged fever, focal neurologic deficits, convulsions, or worsening clinical status to detect all visual neurologic complications. A brain CT was perfomed on either weeks 1 or 2 and after one month. Elecroencephalogram was performed in 60 cases who presented seizures during the acute phase of bacterial meningitis and in 24 cases who presented late seizures in follow up for three years. "Sequelae" was defined as a complication that resulted from childhood bacterial meningitis that was present at or developed after the time of discharge and persisted during the years follow-up period. Sequelae included hearing loss, vision loss, cognitive delay (including mental retardation and learning disabilities) and motor delay and impairment.

STATISTICAL ANALYSIS

Data were analyzed using computer program Stata 9.0. The statistical parameters analyzed were the structure index, mean, standard deviation, and relative risk with 95% confidence intervals.

RESULTS

Sixty of 277 children (22%) developed neurologic complications, while there were 15 deaths, resulted in an overall mortality rate of 5%. The neurologic complication observed during the acute phase of meningitis were: subdural effusion (35), seizures (31), hydrocephalus (7), 2 cases of subdural empyema and single case of spinal abscess, quadriparesis, vision loss, cerebritis, subdural hematoma and intracerebral hemorrhage. Many of these acute neurologic complications were resolved within a month by conservative treatment while 15 patients underwent surgical intervention. On admission, by clinical examination was observed the presence of neurologic deficit in 44 patients: cranial nerves palsies 34, hemiparesis 3, paraparesis 2, and a single case of monoparesis and quadriparesis. The observed neurologic deficit was reversibile in all patients except in one left with quadriparesis.

62 children out of 109, in whom a head compjuted tomography was performed, had abnormalities, most commonly subdural effusion (35/109) . Other subdural abnormalities included 2 patients with subdural empyema and 1 patient with of subdural hematoma; all three patients underwent surgical burr hole drainage.

Subdural effusion occurred most often in infants (29/108) and relative risk 7.6 (3.2-17.6, CI 95%), was the highiest for this age group (Table 1).

Figure 1

Table 1. Relative risk for Subdural effusion by age group

Age-group	N° of patients	Subdural effusion	%	Relative risk (95% CI)
0-1 months	7	-	-	0.47 (0.03 - 7.10)
2-11 months	108	29	26.85	7.56 (3.24 - 17.61)
1-2 years	37	4	10.81	0.83 (0.31-2.22)
3-5 years	56	1	1.78	0.12 (0.01-0.82)
6-10 years	45	1	2.22	0.15 (0.02-1.10)
11-16 years	24	-	-	0.14 (0.00 to 2.26)
Total	270	35	12,63	

There were only 6 cases of subdural effusion in older children including 4 cases in age group 1-2 year. No case of subdural effusion in the 11-16 years age group (24 children) was observed.

Six children with subdural effusion underwent surgical treatment during the first week of treatment (mean time, day 5) due to worsening clinical presentation with space-occupying symptoms and signs: progression of altered mental state to coma, recurrence of seizures, and worsening of neurological deficit. The surgical techniques applied were surgical burr hole drainage in five patients and the placement of a subduroperitoneal shunt in one patient.

The etiology of subdural effusion was confirmed in 27/35 children. Causative pathogens were: Neisserria meningitidis (11), Haemophillus influenzae (6), Streptococcus pneumoniae (6), Staphylococcus aureus (2) and gram negative bacilli (2). Repeated head CT scans in 29 children treated conservatively showed spontaneous remission of subdural effusion. All 35 children with subdural effusion were observed for 3 years, and the only complication and sequelae observed were late seizures in 2 children, both treated conservativly.

Of the 277 patients treated for bacterial meningitis, 7 patients were diagnosed by head CT scan as internal hydrocephalus. In consultation with neurosurgent 5 patients underwent external drainage and later placement of permanent ventriculo-peritoneal shunt. Two patients were diagnosed as communicating hydrocephalus and were treated with conservative treatment.

There was only one patient diagnosed for spinal intramedullary abscess in thoraco-lumbar region (Th 12, L 1-2) following bacterial meningomyelitis. The diagnose was confirmed by myelography and the patient underwent successfully surgical treatment (laminectomy and evacuation of abscess).

Late seizures duration >72 hours manifested 31 children; 22 children manifested generalized seizures and 9 haemiseizures. The incidence of late seizures was the highest in first year of life, 23/108. This age-group had also the highest incidence of neurologic complications (Table 2).

Figure 2

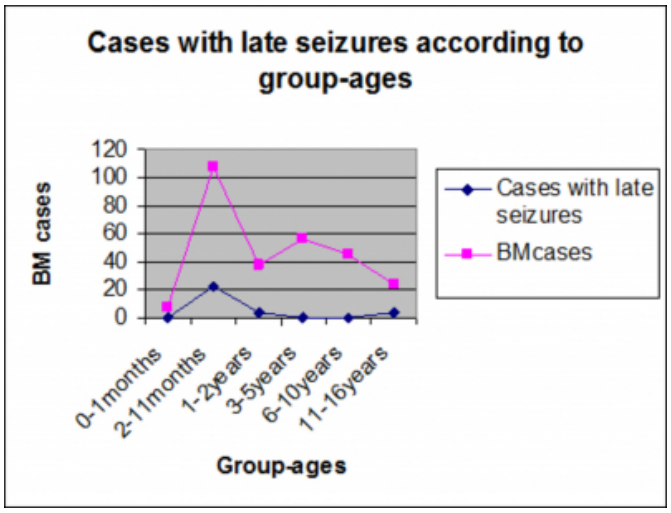
Table 2. The outcome of cases with bacterial meningitis according to age-groups

Age group	n	% of study sample	Patients with Neurologic complications (n)	Deaths (n)
0-1 months	7	3	1	5
2-11 months	108	39	42	8
1-2 years	37	13	7	1
3-5 years	56	20	4	-
6-10 years	45	16	2	1
11-16 years	24	9	4	-
Total	277	100	60	15

In age-group from 11-16 years of age there were 4/24 with late seizures and 4/37 in second year of life. Children aged 3 -10 years didn't manifest late seizures (Figure 1).

Figure 3

Figure 1. Presentation of cases with late seizures by age-groups



Patients with late seizures manifested abnormalities in electroencephalograms (EEG) and in consultation with neurologist were treated with antiepileptic drugs.

During a follow up for three years the long term sequelae observed in children were: late seizures (24), hydrocephalus (5), deafness (3) neuropsychological impairment (3) and a single case with quadriparesis and partial amaurosis.

24 children due to the EEG abnormalities were classified as secondary epilepsy. In all of them was continued the antiepileptic therapy for three years of follow up.

The worst outcome has patients with obstructive hydrocephalus (5); three of them had neuropsychological impairment and on of them was left with quadriparesis. A child with intracranial bleeding in occipital lobe was left with partial amaurosis.

The three most common pathogens isolated by CSF cultures in the included children were Neisseria meningitidis (71 cases), Haemophilus influenzae (22 cases), and Streptococcus pneumoniae (17 cases). Neurologic complications developed more frequently in patients who were infected with H. influenzae (11/22) than in patients who were infected with S. pneumoniae (5/17) or N. meningitidis (15/71).

DISCUSSION

We found that the incidence of neurologic complications was high during the acute phase of the disease: 60 children (22%) developed acute neurologic complications with subdural effusion being the commonest one.

Subdural fluid collection is a classic complication of bacterial meningitis in infants. When a diagnosis is based solely on subdural puncture, subdural effusion prevalence is estimated to be as high as 50%[14,15]. In our study, where we used a more reliable technique (CT), subdural effusion was diagnosed less often, in 13% children only, but still being the most frequent short-term complication of bacterial meningitis. Similar results were obtained with cranial sonography. Arrumugham et all. (1994) observed subdural effusions in 6% of infants and Han at all. (1985) in 26/78 patients (newborn to 2 years old) with clinically proved bacterial meningitis[12,13]. As far as age is concerned, subdural effusion was most common in infants (26,9%), while it occurred in only six older children (4%). Similarily as in previous publications, where subdural effusion was found in infants mainly[12,13,14,15,16,17]. Haemophillus influenzae b is generaly thought to be the most common causative pathogen of subdural effusion, although some newer reports published after the universal use of the anti-H.Influenzae vaccine point N.meningitidis [16,17]. In Kosovo, where universal vaccinations

against the three major pathogens of bacterial meningitis in children (meningococcus, H. influenzae b and pneumococcus) are not implemented yet, N.meningitidis is the leading cause of bacterial meningitis in children and in our study Neisseria meningitidis was the most common etiologic agent of subdural effusion, and H. influenzae was the next. Of the 109 children who underwent a head CT scan one in three children was diagnosed with subdural effusion. Other subdural collections complicating bacterial meningitis were rare; two patients with subdural empyema and one with subdural hematoma. Six out of 35 children with subdural effusion underwent surgical treatment. The results of surgical intervention in our patients were similar to other studies[18].

Almost half of the acute neurologic complications (n=60) were resolved within a month by conservative or surgical treatment while 28 patients (10%) were left with long term sequelas such as: late seizures (24), hydrocephalus (5), deafness (3) neuropsychological impairment (3) and a single case with quadriparesis and partial amaurosis.

Rates of severe or moderate disability reported in one large study of long-term effects in infants ranged from 9% for meningococcal meningitis to 24% for pneumococcal meningitis (Bedford et al, 2001)[24]. Oostenbrink R. et al. reported a 2% case-fatality rate in children with bacterial meningitis and a 13% rate of sequelae among survivors[25].

Our study was nationwide and, therefore, we were able to study a representative sample of children with acute bacterial meningitis. Furthermore, our prospective approach allowed us to collect comprehensive data on signs and symptoms, clinical course, and outcome. The main strength of our study comes from the involvement of the whole Kosovo pediatric population, diagnosis of neurologic complications using a reliable method (CT) and long follow up (3 years) which allows us to assess reliabe figures of prevalence of neurologic complications in bacterial meningitis.

Our study has one important limitation: the etiology was confirmed only in 45% of patients. This is part of previous antibiotic treatment (n=100) and due to non-functioning of our Microbiology Institute which works only during working hours from 7am-3pm. Negative cerebrospinal fluid cultures occur in 11 to 30 percent of patients with bacterial meningitis[8,19,20,21,22,23]. The three leading causes of bacterial meningitis are vaccine preventable, and routine use of conjugate vaccines could help on the prevention of childhood meningitis cases, deaths and disability.

In conclusion Neurologic complications of bacterial meningitis are frequent with subdural effusion being the most common during the acute episode of meningitis. Half of neurologic complications resolved within three years of follow up: only 10% of children were left with long term sequelae with late seizures being the most common.

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