

Original Article

Bacteriology and Sensitivity Patterns of Acute Adult Bacterial Meningitis: A Seven-Year Overview

Behnam Zamanzad, Hedayatollah Shirzadeh, Mohammad Reza Naficy

Department of Microbiology and Immunology, Shahrekord University of Medical Sciences, Shahrekord, Iran

Kuwait Medical Journal 2003, 35 (2): 122-125

ABSTRACT

Objectives: Bacterial meningitis is a potentially fatal infection and its rapid diagnosis has an important role in the prognosis of the disease. The objective of this study was to determine the microscopic, bacteriologic and clinical characteristics of adult bacterial meningitis in Chaharmahal province of Iran over a period of seven years.

Materials and Methods: Thirty-one patients with bacterial meningitis in Shahrekord Kashani Hospital were observed in a period of seven years (Oct. 1993 - Sept. 2000). The clinical findings, type of bacteria isolated from cerebrospinal fluid (CSF) samples, CSF leucocyte counts, CSF cultures and the antibiotic sensitivity profile of the common bacterial isolates were evaluated.

Results: The annual incidence of the disease was about 0.64 per 100,000 inhabitants. Neck stiffness and impairment of consciousness were seen only in a half of

the cases. In 50% of patients, the CSF leucocyte counts were 1000-10,000/mm³, while in 26% of the cases the count was below 500/mm³. Eighty-three percent of CSF cultures were reported positive. *Streptococcus pneumoniae* (58%), *Neisseria meningitidis* (19%) and Gram negative enteric bacilli (6%) were the most common isolates. Gram's stain of sedimented CSF helped in the presumptive identification of the causative bacteria in 80% of the cases. Fifty percent of the pneumococcal isolates were resistant to penicillin and 13% were resistant to chloramphenicol.

Conclusions: A combination of CSF culture and microscopic examination is highly specific for early diagnosis of bacterial meningitis, and performing an antibacterial sensitivity test is recommended before any antibiotic therapy.

KEY WORDS: bacterial meningitis, CSF culture, microscopy

INTRODUCTION

Bacterial meningitis is an infectious disease of the central nervous system due to bacterial growth in the vicinity of leptomeninges. Although a variety of bacteria can cause meningitis, *Streptococcus pneumoniae*, *Neisseria meningitidis* and *Haemophilus influenzae* are responsible for more than 80% of adult bacterial meningitis^[1-3]. In contrast, infections due to Gram negative enteric bacteria are usually associated with brain abscesses, head trauma and some neurosurgical procedures^[1]. Fever and impairment of consciousness usually are constant clinical findings of the disease. Headache with nausea and vomiting, neck stiffness, convulsions and coma are also observed^[1,4].

Cerebrospinal fluid (CSF) culture is the best diagnostic method and is positive in the majority of the cases. But the use of antibiotics by patients usually causes problems in isolating the infective agents. Blood culture in bacterial meningitis is positive in 40-60% of patients and may provide the only definitive clue to the causative agents if CSF culture is negative. Furthermore Gram's stain of

sedimented CSF permits presumptive identification of the causative agents in most cases^[1,2]. The CSF cellular changes are valuable in diagnosis. However, despite the presence of bacteria it is possible that in the early stages of meningococcal meningitis with acute meningococemia or rarely in pneumococcal meningitis these changes are not remarkable^[1].

Resistance of meningitis bacterial agents, especially *S. pneumoniae* to some antibiotics is an important clinical problem and intermediate and high level resistance of pneumococcal isolates to penicillin has been reported by many investigators. Fever and impairment of consciousness usually are constant clinical findings of the disease. Headache with nausea and vomiting, neck stiffness, convulsions and coma are also observed^[5,6,7].

Due to the rapid course and the potentially fatal nature of meningitis, careful and rapid diagnosis of the clinically relevant organisms and early application of appropriate therapy are two of the most outstanding tasks of the physicians and laboratory staff^[8]. The use of ineffective antibiotics

Address correspondence to:

Zamanzad B. MD, Department of Microbiology and Immunology, Faculty of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran. Fax: 0098 381 3335776, E-mail: Bzamanzad@yahoo.com

by most of the patients and sometimes, different features of the disease, produce many problems in clinical and paraclinical diagnostic procedures. This investigation was carried out in Kashani Hospital of Shahrekord city of Iran in a period of seven years to evaluate the bacteriologic patterns of the infection and to find the shortcomings of the common diagnostic procedures in the bacteriologic laboratories for the diagnosis of the disease. The antibiotic sensitivity profile of the isolated *S. pneumoniae* strains to penicillin and chloramphenicol was also examined.

MATERIALS AND METHODS

This cross-sectional study was performed on 31 patients above 12 years old with bacterial meningitis, admitted over a period of seven years (Oct. 1993- Sept. 2000) to the infectious diseases ward of Kashani Hospital of Shahrekord (reference center of infectious disease in Chahar-mahal province of Iran). The sample consisted of 18 (58%) males and 13 (42%) females. The median of their age was 24 years. No patient had a past history of diabetes mellitus, head trauma or neurosurgical complications. Clinical findings, type of bacteria isolated from CSF cultures and CSF leucocyte counts were evaluated. Three samples of CSF from each patient were collected and immediately transported to laboratory for bacteriologic and cell count examinations. The samples were first centrifuged at 1500g for 15 minutes and the sediment were then used for Gram's stain and culture and sensitivity. The CSF sediment was directly inoculated on 5% sheep blood agar (oxid) and chocolate agar plates. For isolation of Gram negative enteric bacilli a selective medium, such as MacConkey agar (oxid), was also used. Agar plates were incubated at 37 °C in humid atmosphere with 5% CO₂ (candle jar). Suspicious colonies thought to be *S. pneumoniae* were tested for either bile solubility or susceptibility to optochin (Padtan teb Co. Tehran, Iran). Besides, colonies suspected to be *N. meningitidis* were identified by performing oxidase test and evaluation of carbohydrate utilization patterns of the bacteria using cystine trypticase soy agar (CTA) (oxid) with 1% glucose, maltose, lactose and sucrose. Growth of the organism on modified Thayer-Martin medium (oxid) were also examined. Oxidase test, nitrate reduction test and glucose fermentation test were performed to identify the Gram negative enteric bacilli.

Blood cultures were performed using standard blood culture tubes obtained from Padtan teb Co. Tehran, Iran. The tubes incubated at 37 °C for at least seven days and examined routinely for any bacterial growth. Furthermore, the sensitivity of *S. pneumoniae* isolates to both penicillin (disks: 10

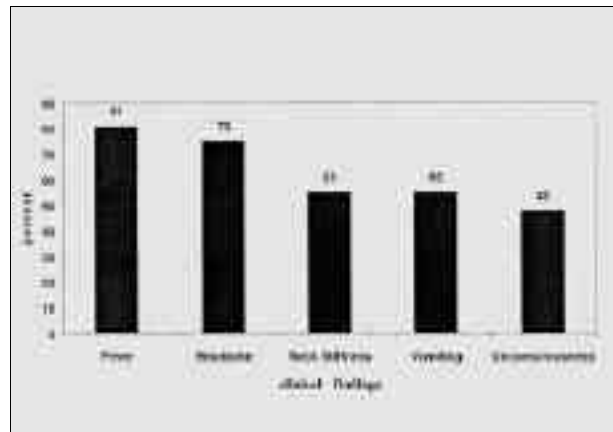


Fig. 1: The percentage of common clinical findings in studied patients

Units) and chloramphenicol (disks: 30 µg; both disks obtained from Padtan teb Co. Tehran, Iran), were examined using disk diffusion (Kirby-Bauer) method. The performance of disk diffusion test was routinely monitored by periodically testing recommended quality control strains *Staphylococcus aureus* (ATCC 25923), *Escherichia coli* (ATCC 25922), and *Pseudomonas aeruginosa* (ATCC 27853). Approved resistant pneumococcal strains (Health Institute of Tehran medical University), were also tested. Standard bacterial suspension (turbidity of 0.5 Mc Farland turbidity standard) was prepared, then inoculated on the Mueller Hinton agar plates (oxid) plus 5% sheep blood and incubated overnight at 35 °C in 5% CO₂. After the incubation period, strains showing a growth inhibition zone of < 19 millimeter around penicillin disk were regarded as resistant. Zone size < 12 millimeter for chloramphenicol disk was also reported as resistant. Gram stains of sedimented CSF were tested by general light microscopic examinations. All methods were carried out according to reference nine.

RESULTS

Our results showed that the annual incidence of the disease was 0.64 per one hundred thousand inhabitants. The most commonly observed clinical findings are shown in Fig. 1. Fever and headache were more prevalent among the patients with meningococcal meningitis. Chronic otitis media was observed in six and frontal sinusitis in nine patients with pneumococcal meningitis. Sixty-eight percent of the patients had blood leucocyte counts of more than 10,000/mm³, from which 35% was higher than 20,000/mm³. Blood leucocyte counts in 10 patients (32%) were normal.

As shown in Fig. 2, the range of CSF leucocyte counts were < 500 to > 10,000/mm³. Gram's stain of sedimented CSF helped the presumptive identification of clinically relevant bacteria in 80% of the cases. While CSF cultures in 83% of the cases

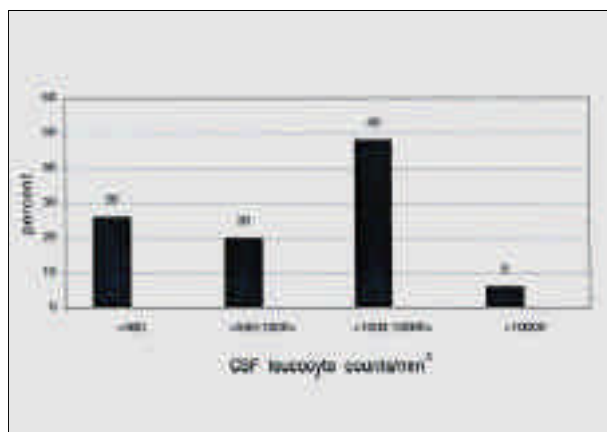


Fig. 2: The percentage of leucocyte counts/mm³ of patients CSF samples

were reported positive, only 6% of the blood cultures were positive. We noted that 26% of the patients had antibiotics during 72 hours before taking the samples. Ampicillin, cephalexin and trimethoprim-sulfamethoxazole were the antibiotics used orally by 16%, 6.5% and 3.5% of the patients respectively. Penicillin G (24 million units intravenously each day in eight divided doses) or ampicillin (18 g daily IV in divided doses) was prescribed by the physicians. For patients allergic to penicillin, chloramphenicol (4 g daily IV in divided doses) was prescribed. In 12 patients with inappropriate therapeutic responses, ceftriaxone (2 g IV/day) was included to the therapeutic regimens.

We found that *Streptococcus pneumoniae*, *Neisseria meningitidis* and Gram negative enteric bacilli were the most common bacterial agents isolated from the CSF samples (58%, 19% and 6% respectively). Infection in more than 90% of the 12 to 22 years old group was caused by *Streptococcus pneumoniae*. The fatality rate was 19% and it was the highest for patients with pneumococcal meningitis. The important factors of mortality were as follows: abrupt onset of the disease, late admission and impairment of consciousness on admission.

Antibiogram tests performed on the isolated *S. pneumoniae* strains revealed that 50% of these isolates were resistant to penicillin and 13% were resistant to chloramphenicol.

DISCUSSION

Although the clinical findings in our patients were generally in accordance with the classic features of meningitis, unconsciousness and neck stiffness were only observed in 48% and 55% of patients respectively. This showed that in many instances the presentation may be atypical and may lead to diagnostic difficulties in the early stages of the disease.

The CSF leucocyte counts of 26% of the cases were below 500/mm³ indicating that even though CSF leucocyte count is a valuable finding for the

diagnosis of meningitis, the CSF cellular response in early stages of the disease can be unremarkable. The high sensitivity (80%) of Gram's stain for CSF sediment, makes it a valuable test for early diagnosis of bacterial meningitis. In our study the CSF cultures were positive in 83% of the cases, which is comparable to previous reports^[11,12]. In contrast the rate of positive blood cultures in our study was lower (6%) than that of another report^[1]. Previous administration of antibiotics may have been the main cause of negative blood cultures.

The types of bacteria isolated from the CSF of patients were almost similar to those reported by other investigators^[13,14,15]. Isolation of Gram negative enteric bacilli in adult bacterial meningitis has been also reported by some studies^[1,11,16]. While the role of Gram negative enteric bacteria in pathogenesis of adult meningitis is commonly associated with some neurosurgical procedure and head trauma^[1] none of our patients had a past history of head trauma or neurosurgical complications.

Despite the important role of penicillin and chloramphenicol in the treatment of meningitis^[17] many investigators have reported a resistance rate from 6-36% to penicillin and 6% to chloramphenicol in isolated pneumococcal strains^[6,7,18]. In another study none of the most common bacterial isolates were resistant to chloramphenicol^[12]. In contrast, in our investigation the results of antibiogram on *S. pneumoniae* revealed a resistance of 50% to penicillin and 13% to chloramphenicol. These drug-resistant bacteria complicate the treatment of bacterial meningitis. Despite the opinion that bacterial meningitis cannot be excluded on the basis of the CSF leucocyte counts in combination with any clinical and biochemical parameters^[19], we found that the combination of CSF culture and microscopic examinations of Gram-stained sedimented CSF can be highly specific in early diagnosis of bacterial meningitis. Further, due to the high resistance of the pneumococcal isolates to penicillin and chloramphenicol, performing the antibacterial sensitivity test before any antibiotic therapy is recommended.

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