BACTERIAL AGENTS ISOLATED FROM CEREBROSPINAL FLUID OF PATIENTS WITH ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS) AND NEUROLOGICAL COMPLICATIONS

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SUMMARY

Cerebrospinal fluid (CSF) samples from 2083 patients with acquired immunodeficiency syndrome (AIDS) and neurological complications were bacteriologically examined during a period of 7 years (1984-1990). The percentage of patients who had at least one bacterial agent cultured from the CSF was 6.2%. Mycobacterium tuberculosis was the most frequently isolated agent (4.3%), followed by Mycobacterium avium complex or MAC (0.7%), Pseudomonas spp (0.5%), Enterobacter spp (0.4%), and Staphylococcus aureus (0.3%). Among 130 culture positive patients, 89 (68.5%) had M. tuberculosis and 15 (11.6%) had MAC. The frequency of bacterial isolations increased from 1988 (5.2%) to 1990 (7.2%), partly due to the increase in MAC isolations. Bacterial agents were more frequently isolated from patients in the age group 21-50 years and from women (p<0.05).

KEYWORDS: Acquired Immunodeficiency Syndrome; Cerebrospinal fluid; Bacterial agents.

INTRODUCTION

Central nervous system (CNS) complications are a major clinical problem at all stages of human immunodeficiency virus (HIV) infection, and may occur as a result of direct HIV infection, secondary opportunistic infections or neoplasms. Reports on bacterial opportunistic infections of CNS in patients with acquired immunodeficiency syndrome (AIDS) are relatively scarce. Meningeal infections by Neisseria meningitidis serogroup A, Listeria monocytogenes, group G Streptococcus, Streptococcus milleri, and Escherichia coli have been referred only in case reports or short series of patients. More numerous and extensive reports are available for Mycobacterium tuberculosis infections. The nontuberculous mycobacteria included in the Mycobacterium avium complex (MAC) have been cultured from the cerebrospinal fluid (CSF) of a few patients with AIDS.

The frequency of M. tuberculosis meningeal infections in HIV-infected patients has been determined only among patients with tuberculosis. In a study of 199 patients with pulmonary and/or extrapulmonary tuberculosis in the United States, 10% showed meningeal involvement. The same frequency was detected...
in another study of 455 patients with tuberculosis in Spain.

To our knowledge, an extensive search for different bacterial agents in CSF samples of patients with AIDS and neurological complications has not been described. We have performed such search at the "Instituto Adolfo Lutz", a Public Health Central Laboratory of São Paulo State and the National Reference Center for Meningitis in Brazil, during a period of 7 years. The present purpose of the present report is to show the results obtained from 2083 patients studied during this period.

MATERIALS AND METHODS

Patients belonging to the group IV of the AIDS classification made by the Centers for Disease Control and Prevention, Atlanta, U. S. A. 7 and having any neurological symptoms (headache, drowsiness, mental confusion, vomiting, paresis, paresthesia) with or without fever had a CSF sample collected as part of a routine procedure at the "Instituto de Infectología Emílio Ribas", a Public Health Hospital. During a period of 7 years (1984-1990), a total of 2083 patients (1888 men and 195 women, with age ranging from one month to 70 years) was submitted to this procedure.

CSF samples from all 2083 patients were examined by Gram, Ziehl-Neelsen, and auramine staining procedures and cultured at the "Instituto Adolfo Lutz". Chocolate agar (Mueller-Hinton base) and Löwenstein-Jensen (L-J) slants were used as primary culture media and incubated at 37°C for 24-48 h (5-10% CO₂ atmosphere) and 30-60 days, respectively.

Gram-negative rods with a growth that resembled enterobacteria or non-fermenters were subsequently inoculated onto MacConkey agar to verify if there was lactose fermentation and in standard media for biochemical identification 9, 14.

Gram-positive and non-spore forming rods were examined for a characteristic umbrella-like motility in a semi-solid medium and further speciation was performed according to standardized procedures 9.

Gram-positive cocci were submitted to the catalase test and the complete identification was performed according to a previously described methodology 10, 18.

After isolation in L-J medium, mycobacteria were identified according to the criteria described by VESTAL 29 and by DAVID et al 9.

The culture results were statistically analyzed by the chi-square test (Mantel-Haenszel) with regard to the age and sex of the patients.

RESULTS

Among the 2083 AIDS patients, 130 (6.2%) had at least one bacterial agent isolated from their CSF.

<table>
<thead>
<tr>
<th>Bacterial Agent</th>
<th>Number of Patients</th>
<th>Percentage among Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Culture Positive (n=130)</td>
<td>Total (n=2083)</td>
</tr>
<tr>
<td>Mycobacterium tuberculosis</td>
<td>89</td>
<td>68.5</td>
</tr>
<tr>
<td>Mycobacterium avium complex</td>
<td>14</td>
<td>10.8</td>
</tr>
<tr>
<td>Mycobacterium avium complex+ Streptococcus pneumoniae</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Pseudomonas spp*</td>
<td>5</td>
<td>3.8</td>
</tr>
<tr>
<td>Pseudomonas spp** Enterobacter spp**</td>
<td>4</td>
<td>3.0</td>
</tr>
<tr>
<td>Enterobacter spp**</td>
<td>4</td>
<td>3.0</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>7</td>
<td>5.3</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Streptococcus spp</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Listeria monocytogenes</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>1</td>
<td>0.8</td>
</tr>
</tbody>
</table>

* P. aeruginosa and P. putida.
** E. cloacae and E. agglomerans.
samples. Four patients had positive smears (one with Gram-positive diplococcus and three with Gram-negative rods), but negative cultures.

Table 1 shows the frequency of isolation of the different bacterial agents among the patients that were culture positive and among all patients studied. The most commonly isolated agent was *M. tuberculosis*, which was isolated from 4.3% of all patients and 68.5% of the culture positive patients. The second most frequently isolated agent was MAC (0.75% of all patients and 11.6% of the culture positive patients), followed by *Pseudomonas spp* (0.5% of all patients), *Enterobacter spp* (0.4%), and *Staphylococcus aureus* (0.3%). Among *Pseudomonas spp* strains, some were *P. aeruginosa* and others *P. putida* and among *Enterobacter spp* strains, *E. cloacae* and *E. agglomerans* were identified. Five patients had more than one bacterial agent isolated from their CSF.

Acid-fast bacilli were detected in the CSF smears from only one of the 89 patients culture for *M. tuberculosis* and none of the 15 patients with MAC. CSF smears stained by the Gram procedure were positive for 5 of the 27 culture positive patients.

As can be seen in Fig. 1, the frequency of isolation of bacteria from CSF of AIDS patients increased from 1988 (5.2%) to 1990 (7.2%). Among mycobacteria, isolation of MAC but not *M. tuberculosis* increased during this period. As a matter of fact, the frequency of *M. tuberculosis* isolation increased considerably until 1988, but remained steady during the following 2 years.

The distribution of AIDS patients with bacterial agents in CSF according to age and sex is shown in Table 2. Bacterial agents were isolated significantly more from patients belonging to the 21-30 year age group (p<0.05; OR = 1.85 [1.28-2.69]) and from women (p<0.05; OR = 1.85 [1.08-3.12]). The same age group (p<0.05; OR = 2.09 [1.33-3.27]) and sex (p<0.05; OR = 2.04 [1.10-3.74]) showed the highest frequency of *M. tuberculosis* isolation. MAC was isolated only from patients over 21 years of age and there were no

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![Graph](image_url)

**Fig. 1 - Annual frequency of isolation of bacterial agents from cerebrospinal fluid of patients with acquired immunodeficiency syndrome (1985-1990).**

* In 1984 only two CSF samples were examined and both were positive for *Mycobacterium tuberculosis*.

* Symbols: ● = all bacteria; ■ = *M. tuberculosis*; ▲ = *Mycobacterium avium* complex.
significant differences in the frequency of isolation among the different age groups or the sex of the patients.

DISCUSSION

Bacterial agents were detected in the CSF from 6.2% of the 2083 patients with AIDS and neurological complications examined during a 7-year period (1984-1990). A much higher frequency of bacterial isolation from CSF samples (17%) was obtained in a previous study performed at the “Instituto Adolfo Lutz” employing the same methodology but including patients without AIDS.

*M. tuberculosis* was the most commonly isolated bacterial agent from CSF samples of the AIDS patients with neurological symptoms. To our knowledge, there are no published data on the frequency of *M. tuberculosis* isolation from CSF of such patients. The reports on tuberculous meningitis from the United States and Spain included only HIV-infected patients selected for having tuberculosis.

Extrapulmonary tuberculosis occur more frequently in patients with AIDS than in patients with less advanced HIV infection or persons not infected by HIV. This clinical feature can be clearly evidenced when the frequency of tuberculous meningital infection detected in the present study of AIDS patients (4.3%) is compared with the one obtained in the previous study of non-AIDS patients (0.8%).

MAC organisms were the second most frequently isolated bacterial agent in the present study. These organisms are ubiquitous in nature and appear to have a particular predilection for infecting and disseminating within HIV-infected patients. Disseminated MAC infections are more frequent in AIDS patients with high level of immune dysfunction and can involve almost any organ system.

The clinical significance of MAC detection in the CSF of 15 AIDS patients could not be determined in the present study. The fact that 5 patients had more than one CSF sample culture positive for MAC (data not shown) suggests infection of the CNS by these organisms, but histopathological evidence of meningeal involvement was not pursued. Reviewing the records of CSF samples positive for nontuberculous mycobacteria filed in a hospital of the United States, JACOB et al. also identified 15 patients with AIDS or at least one risk factor for AIDS and CSF culture-positive for MAC. Three patients had autopsy data recorded which included CNS lesions.

Recently, BENSON & ELLNER stated that isolation of MAC organisms from normally sterile tissues should be interpreted as indicative of disseminated disease. In the present study, 3 patients with CSF culture positive for MAC also had these organisms isolated from blood and/or bone marrow aspirate (manuscript in preparation). All patients described by JACOB et al. had widespread MAC dissemination.

In the present study, several agents other than mycobacteria were cultured from CSF samples of few or single patients, including *Pseudomonas spp.*
RESUMO

Agentes bacterianos isolados de líquido cefalorraquidiano de pacientes com Síndrome de Imunodeficiência Adquirida (SIDA) e complicações neurológicas

Amostras de líquido cefalorraquidiano (LCR) de 2083 pacientes com Síndrome de Imunodeficiência Adquirida (SIDA) e complicações neurológicas foram examinados durante um período de 7 anos (1984-1990). A porcentagem de pacientes que tiveram pelo menos um agente bacteriano cultivado do LCR foi de 6,2%. Mycobacterium tuberculosis foi o mais frequentemente isolado (4,3%), seguido do complexo Mycobacterium avium ou MAC (0,7%), de Pseudomonas spp (0,5%), Enterobacter spp (0,4%), e Staphylococcus aureus (0,3%). Entre 130 pacientes com cultura positiva, de 89 (68,5%) foi isolado M. tuberculosis e de 15 (11,6%) MAC. A frequência de isolamentos bacterianos aumentou de 1988 (5,2%) a 1990 (7,2%), particularmente devido ao maior isolamento de MAC. Os agentes bacterianos foram mais frequentemente isolados de pacientes na faixa etária de 21-30 anos e de mulheres (p<0,05).

REFERENCIAS


