TUBERCULOUS MENINGITIS – CLINICAL AND EPIDEMIOLOGICAL CONSIDERATIONS (A RETROSPECTIVE STUDY 2008 - 2011)

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TUBERCULOUS MENINGITIS – CLINICAL AND EPIDEMIOLOGICAL CONSIDERATIONS (A RETROSPECTIVE STUDY 2008 - 2011) (Abstract): Tuberculous meningitis represents one of the most severe forms of tuberculosis and is often a difficult diagnostic and therapeutic problem. The objective of this study is to analyze the cases of tuberculous meningitis in our region. Material and Methods We retrospectively analyzed 76 observation sheets of patients aged 4 months to 84 years, diagnosed with tuberculous meningitis, admitted to Infectious Diseases Hospital Iaşi during 2008 to 2011. Results: Tuberculous meningitis has affected mostly males (65.7%). Only a small proportion of patients (23.68%) had tuberculosis in their personal history. 26.2% were diagnosed also with other localization of tuberculosis (mostly pulmonary). Fever was identified in only 43.4% of cases; 40% of patients had an altered conscience at admission. The outcome was favorable in all cases. Conclusions: Tuberculous meningitis predominantly affects males, almost equally affects patients with other focuses of TB and those with a history of tuberculosis disease. Key words: QUANTIFERON, CEREBROSPINAL FLUID, MENINGITIS

Tuberculosis remains a frequent disease in our country (1, 2). Tuberculous meningitis represents one of the most severe forms of tuberculosis (3).

MATERIAL AND METHODS
We evaluated 76 cases of tuberculous meningitis admitted in the Hospital of Infectious Diseases Iaşi between 2008 and 2011, taking into account the clinical and biological aspects. We studied the incidence of new cases and the distribution of these cases according to age, gender, the way they were diagnosed and according to evolution under specific treatment.

We have taken into account the following aspects (as they result from the admission paper) - age, sex, a personal history of tuberculosis, a diagnosis of tuberculosis at other site than CNS, the presence of other diseases (cancer, diabetes, other conditions that can cause immunosupression), the clinical presentation, laboratory exams – the CSF direct exam, culture results, the Quantiferon test.

We also evaluated the treatment – time elapsed between admission and the initiation of specific therapy, the evolution of CSF parameters with treatment and the adverse effects.

RESULTS
Tuberculous meningitis affected mostly male patients (50 cases / 65.7%).
The distribution according to age groups was as follows: 9 patients (11.84%) with ages between 0 and 20 years, 18 patients (23.68%) with ages between 21 and 30 years, 12 cases with ages between 31 and 40 years (15.78%), 7 cases with ages between 41 – 50 years (9.21%), 12 patients with ages between 51 and 60 years (15.78%), 6 cases (7.89%) with ages between 61 and 70 years and 12 cases (15.78%) with ages over 71 years.

We notice a higher incidence of tuberculous meningitis among teenagers and young adults. 18 patients (23.68%) had a personal history of pulmonary tuberculosis (but not active pulmonary disease). 20 patients had simultaneous tuberculous with other localization (different from CNS), as follows – 16 patients (21.05%) with pulmonary tuberculosis, 3 patients (3.94%) with pleural tuberculosis, one patient with both pulmonary and pleural disease and one patient with tuberculous arthritis of the left knee.

Three patients had a personal history of neoplastic disorders (multiple myeloma, melanoma, Hodgkin’s disease); 3 patients had a personal history of diabetes mellitus.

The time elapsed between the onset of symptoms that could be related to meningitis and admission varied, but for the majority of patients (53 - 69.73%), this period had an average duration of 14 days. The period of time between the suspicion of tuberculous meningitis and the moment when the specific therapy was initiated was usually one or two days.

Fever was present in 33 (43.42%) patients. In 35 (40.50%) cases, we identified an altered conscience. 59 (77.63%) had meningeal signs. The degree of neurological involvement was variable. 40 (52.63%) were admitted with no neurological disturbances, 24 (31.57%) had minor neurological signs (cranial nerve involvement) and 12 (15.80%) had major neurological disturbances - seizures, major motor deficits (paresis or plegia).

The exam of the cerebrospinal fluid (CSF) has an important diagnostic value. In 6 (7.89%) patients, at the direct exam of the CSF was noticed the presence of Mycobacterium tuberculosis (using the Ziehl Neelsen stain). Furthermore, CSF cultures were positive in 37 patients (46.68%). The plasmatic Quantiferon test was positive in 16 patients (21.05%) (tab. I).

<table>
<thead>
<tr>
<th>TABLE I</th>
<th>The number of CSF elements at admission</th>
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<tbody>
<tr>
<td>No. elements/mmc</td>
<td>No. cases</td>
</tr>
<tr>
<td>1 – 200</td>
<td>37</td>
</tr>
<tr>
<td>201 – 500</td>
<td>27</td>
</tr>
<tr>
<td>&gt;500</td>
<td>12</td>
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At the time of the first control evaluation (by spinal tap) the number of elements in CSF varied as follows in Table II.

<table>
<thead>
<tr>
<th>TABLE II</th>
<th>The dynamic of CSF elements</th>
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<tbody>
<tr>
<td>No. elements / mmc</td>
<td>No. cases</td>
</tr>
<tr>
<td>1 – 200</td>
<td>46</td>
</tr>
<tr>
<td>201 – 500</td>
<td>15</td>
</tr>
<tr>
<td>&gt;500</td>
<td>15</td>
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Etiological treatment – all patients received the quadruple association of antituberculous drugs Isoniazide - 50 mg/kg b.w./day, Rinfapicin - 10 mg/kg b.w./day, Etambutol – 15 to 25 mg/kg b.w./day, Pirazinamid - 20 to 25 mg/kg b.w./day, for the duration of hospitalization (a average duration of 21 days), with the recommendation of continuing the treatment up to 1 year. The pathogenic treatment - with in-
travenous corticosteroid therapy (Dexamethasone) in all cases, with an average duration of 8 days.

**DISCUSSION**

The outcome is influenced by age (more severe in extreme age groups), the evolutional state of meningitis at admission, the neurological status of the patient, the progression of CNS involvement and the co-morbidities (4).

Most of the patients in this study had ages between 20 and 60 years, which could explain the favorable evolution. Furthermore, most of the patients were admitted with no major neurological involvement.

In this study there were no deaths (although two patients were transferred in ICU wards). Because The Clinical Hospital of Infectious Diseases Iași receives patients from the entire North-East region of the country, the discharged patients do not always come back for check-up, so we cannot have a clear picture of their evolution.

Tuberculous meningitis is the most severe form of *M. tuberculosis* infection. It is also the most common form of CNS tuberculosis (3).

An early diagnosis and a rapid specific treatment can reduce mortality and associated morbidity (5, 6). The treatment is usually no less than 9 months. The pathogenic treatment with dexamethasone, although still controversial, is successful in reducing morbidity (7), especially in HIV-positive patients.

An increased mortality can be seen in patients with other major diseases, in those patients with severe neurological involvement at the time of the admission, in patient with a rapid evolution and in extreme age groups (8).

**CONCLUSIONS**

The incidence of tuberculous meningitis is influenced by the tuberculosis epidemics. In our study, the disease was most common at the young adult, affecting more frequently the male sex.

Only a small proportion of patients (23.68%) had tuberculosis in their personal history.

Although the tuberculous meningitis does not evolve as fast as other bacterial meningitis, the antituberculous therapy must be initiated at the first suspicion of *M. tuberculosis* infection. Any delay can influence the outcome. The suspicion of tuberculous meningitis appears in the presence of clinical signs (meningeal signs, gradual involvement), laboratory findings (the CSF exam, with a number of elements usually between a few hundreds and one thousand, with increased proteins and decreased glucose) and epidemiological data (a personal history of tuberculosis or contact with a known case of pulmonary tuberculosis).

A rapid diagnostic and an early treatment are essential in reducing the mortality and morbidity of this formidable disease.

**REFERENCES**

Tuberculous meningitis – clinical and epidemiological considerations


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**PLANTS USED IN AYURVEDIC AND TRADITIONAL CHINESE MEDICINE MODULATE AMYLOID PRECURSOR PROTEIN**

Alzheimer’s disease, the most common form of dementia, is characterized by memory and cognitive impairment, speech loss and personality changes. The main pathological event is the accumulation of neuritic plaques composed of β-amyloid peptide (Aβ). This peptide is generated through the proteolysis of a transmembrane glycoprotein named amyloid-β-precursor protein (APP). The non-amyloidogenic cleavage of APP leads to α soluble APP (sAPPα), p3 peptide and APP intracellular domain (AICD) while the amyloidogenic cleavage generates soluble APPβ (sAPPβ), Aβ and AICD. As it is estimated that 115.4 million people will suffer from this disease by 2050, numerous efforts are done to discover new therapeutic agents that reduce Aβ accumulation. This study reports on *in vitro* screening on APP modulation of 15 herbs used in Ayurvedic and Traditional Chinese medicine for the treatment of cognitive disorders. N2a-SweAPP cells (mouse neuroblastoma N2a cells that have been stably transfected with human Swedish mutant APP) were treated with different doses of ethanolic extracts of tested herbs; the Aβ levels in the supernatant were determined by ELISA. The extracts showing a significant inhibition on Aβ production, namely extracts of *Polygonum multiflorum* Thunb. roots and *Convolvulus pluricaulis* Choisy. leaves, were further subjected to an APP modulation assay. In this respect, their effects on sAPPα and sAPPβ were studied through western blot analysis. Only the extract of *Polygonum multiflorum* Thunb. roots showed APP modulation activity by up-regulating sAPPα and down-regulating sAPPβ. This result justifies not only the traditional uses of the plant but also further investigations on the therapeutic potential of this species. (Liu L-F, Durairajan SSK, Lu J-H, Koo I, Li M. *J Ethnopharmacol* 2012; 141: 754-760).

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