THE PROBLEM OF DIAGNOSING BACILLARY MENINGITIS (CASE REPORT)

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Abstract: *Mycobacterium tuberculosis continues to be one of the most important etiologies of bacterial meningitis identified in the adults living in Romania; the outcome of the patient, the survival with or without neural and psychical sequels or the cure depends on the early therapy. We present the case of a patient at risk due to chronic alcohol abuse, with improper life conditions, which associated important neurological complications like facial paresis, haemiplegia, strabismus, urinary bladder globe, and who had a slowly favourable outcome under specific therapy.*

Keywords: *Bacillary meningitis – neurological complications – outcome*

Rezumat: *Mycobacterium tuberculosis continuă să reprezinte una dintre cele mai importante etiologii ale meningitelor bacteriene identificate în România, la adult, de a cărei terapie precoce depinde evoluţia cazului, supravieţuirea cu sechele neurospihice sau vindecarea. Prezentăm cazul unui pacient, la risc prin etilism cronic, condiţii precare de viaţă, a cărei evoluţie a fost asociată unor importante complicaţii neurologice-pareză facială, hemiplegie, strabism, glob vezical, cu evoluţie lent favorabilă sub terapia specifică.*

Cuvinte cheie: *Meningita bacilară, complicaţii neurologice, evoluţie*

INTRODUCTION

According to the World Health Organization, bacillary infection is responsible of 8 million new cases every year, among which 2 million deaths.

The meningeal localization of the infection with Mycobacterium tuberculosis represents the most severe form of evolution of this infection.

There are some important variations of the incidence, from one region of the globe to another; in the countries with a poor socioeconomic status, the incidence is associated with the first contact with the bacillus and the diseases appears at about 3-6 months from that moment; in the countries with a higher economical level, the infection is most of the times present in adults, due to a re-activation of the infection.

The **favouring factors** of the TB meningitis are: alcohol abuse, malnutrition, immune depression caused by the long time cortisone therapy, HIV infection, malignant diseases and diabetes mellitus.

The diseases progresses slowly, during one-two weeks, with low fever, fatigability, loss of weight, headache, vomiting; only 2% of the patients present suggestive manifestations for meningitis. In the absence of the proper therapy, the patients start to present conscious disorders, neurological signs like hemiparesis, paraparesis with urinary retention, or tetraparesis, all these being caused by the arteritis and cerebral infarcts, perturbations of the cranial nerves – most frequent III, VI, VII, only rare II, VIII, X, XII; perturbations in the CSF circulation, the obstruction of the basilar cistern, with installation of the hydrocephalus. The eye exam shows most of the times papillary edema, the evolution being sometimes progressive, with optic atrophy, secondary blindness as a consequence of the basal exudates with the optic chiasm compression (optochiasmic arahnoiditis). Other causes of visual disorders are the expression of the tuberculoma on the retina, corioretinitis, granulomatous uveitis, optic nevritis, oftalmoplegia. The inadequate secretion of the anti-diuretic hormone (SIADH), a possible complication of the bacillary meningitis, associates a poor prognosis.

It is essential for the outcome of the patient, for the infection control and for lowering the risk of complications to initiate the specific therapy whenever a suspicion of this disease is being raised (clinical aspects of meningoencefalitis, with clear CSF, low glucose level in the CSF, CT or RMI which show incipient hydrocephalus, basilar meningitis).

TB meningitis can lead to a lot of differential diagnoses, with viral meningitis, bacterial meningitis with clear CSF (Leptospira, Brucella, syphilis of Lyme disease), fungus meningitis (Candida, Cryptococcus, Nocardia), parasite meningitis (Criptococcus, Toxoplasma); there are also other possible differential diagnoses like: Behçet syndrome, lymphomas, thromboses of the cavernous sinus, septic emboli, angeitis, arthritis, Wegener granulomatosa, Vogt-Koyanagi-Harada syndrome.

The diagnosis using cultures from CSF on specific mediums, as Löwenstein, confers the results very late, after 6-8 weeks, the most rapid way of diagnosing being the PCR method; a negative intradermis reaction at tuberculine does not exclude the diagnosis.

The **specific therapy** consists in four

antituberculous drugs: rifampicin, isoniazid, ethambutol and pyrazinamide, immune-modulator drugs, like cortisone therapy, being beneficial in increasing the survival rate, without preventing the severe sequels (abnormal choreo-atetosic movements, hemibalism, mioclonies and cerebellum dysfunctions). The second therapeutic line takes in consideration drugs like ethionamide, cycloserine, PAS, aminoglicozides, capreomicinum, thiacetazone. Fluoroquinolones as ofloxacinum, ciprofloxacinum, levofloxacinum have a good meningocerebral penetration; the results obtained by the administration of rifapentine, isepamicine, oxazolidinone are still in course of evaluation. At the patients with installed hydrocephalus the ventriculoperitoneal shunt is often needed.

Tuberculous meningitis: We present the case of a 44 year old man with medical history of alcohol abuse and gastric ulcer (resolved by surgery 7 years ago), who was brought by his family to the emergency room for conscious disorders – unconsciousness, malaise, fatigability, anorexia, nervousness, no water or food intake for the last day, after an alcohol excess (as related by the family), loss of weight in the last two months. In the ER, he was seen by an internist and a neurologist, who first diagnosed the patient as having an alcoholic encephalopathy. He was treated with Diazepam, Haloperidol, Tiapridal and vitamins B. Brain computer tomography was performed. This demonstrated pan ventricular hydrocephaly. Because he presented fever he returns to the ER and then hospitalized in the Infectious Disease Department with the suspicion of acute meningoencefalitis.

The physical exam, on admission, showed a febrile patient (temperature of 38.0°C), with conscious disorders, grade I coma, with dry teguments, slightly pale mucosa, important weight loss, as compared with the picture from the ID card, hepatomegaly. He had neck stiffness, Brudinzki's and Kernig's signs were present, but he did not have any focal neurological signs. The pupils were bilaterally dilated and unresponsive to light. Other aspects of physical examination were normal.

On these elements, we can establish the **first phase diagnosis**: Febrile syndrome. Grade I coma. Meningeal syndrome. De-hydratation syndrome. Divergent syndrome.

Laboratory evaluation: Complete blood counts: Le **14200-22540** /mm³, Er 5,06-5,11 mil/mm3, Hb 15,3-15,7 g/dl, Ht 46,4-46,7 %, MCV 91,7-91,4 fl, MCH 30,2-30,7 pg, MCHC 33,0-33,6 g/dl **, Tr 594000-525000**/mm3, **Ne 77,9-83,7** %, Ly 6,2-2,1 %, Mo 14,2 %, Ba 0%, Eo 0%, leukocites formula: NN 3%, NS 82%, Ly 2%, Mo 13%, blood glucose 112 mg/dl, urea 30 mg/dl, creatinine 0,7 mg/dl, ESR 5 mm/h, fibrinogen level 275 mg/dl, C-reactive protein 6,5 mg/l, TGO 21 U/l, TGP 19 U/l, **GGT 43** U/l, BD 0,51 mg/dl, BT 0,90 mg/dl, amilases 39U/l, TQ 14,8 sec (65,5%), INR 1,21, APTT 23,1 sec, Na 125,4 mEq/l, K 3,88 mEq/l, Cl 83,9 mEq/l, urinary sample: PRO 1+, KET 2+, UBG 3+, BIL 1+, uroculture: negative.

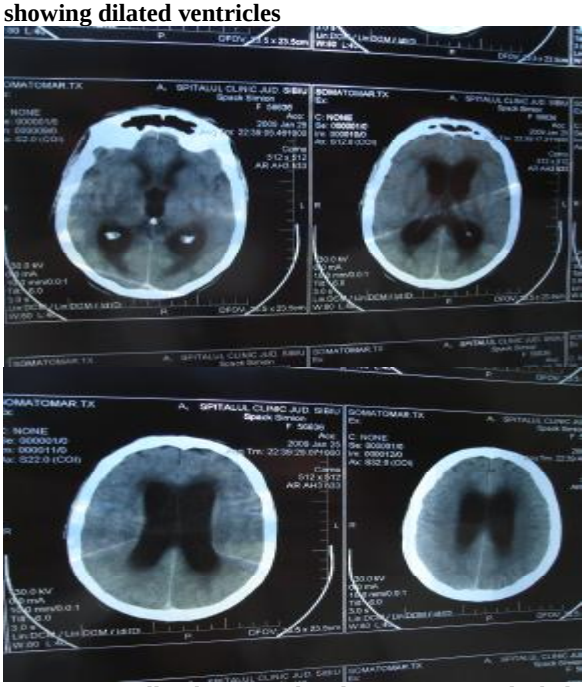
Complementary evaluation: normal ocular funds, IDR at 2 U PPD: negative.

The cerebrospinal spinal fluid (CSF) was performed in dynamics, because of the unfavourable evolution of the patient. In 26.01.2009 the cerebrospinal fluid examination showed a clear CSF liquid with a slightly Pandy positive reaction: CSF protein (4,4 g/l) and reduced CSF glucose (15 mg/dl). The number of elements was 420/mm³. The cytological exam from CSF showed: frequent leukocytes: Ly 99%, Mo 1% and rare red cells. The CSF culture on usual medium was negative and no BK bacilli were isolated from the CSF. The second CSF exam (after 2 days of hospitalization, in 28.01.2009) showed: a clear off color liquid, with a slightly Pandy positive reaction: CSF protein (2.77 g/l) and reduced CSF glucose (8 mg/dl), chlorine level in CSF of 90.3 mEq/l. The number of elements was 150/mm³. The cytological exam from CSF showed also frequent leukocytes: Ly 97%, NS 1% Mo 2% and rare macrophages.

Thoracic X ray showed no pleura-pulmonary lesions.

The brain computer tomography (CT scan) showed panventricular hydrocephalus with moderate hypodensity of the white periventricular substance.

Picture no. 1. Brain computed tomography scan showing dilated ventricles



Initially, because the diagnosis was alcoholic encephalopathy, the patient's course was unfavourable, the patient remained comatose; also, he developed a right hemiparesis and a facial paresis. The clinical features and the CSF aspect suggested an acute meningogoencefalitis with a possible bacillary etiology; so that the initiation of the antituberculosis treatment has been decided (despite of the fact that the cultures from CSF were not yet available).

Positive diagnosis: Acute meningoencephalitis with clear cerebrospinal fluid, of possible Mycobacterium tuberculosis etiology. Grade I coma. Right facial paresis. Right spastic hemiparesis. Acute de-hydration. Electrolyte disarray (hyponatremia). Chronic alcoholic abuse. Panventricular hydrocephaly. Divergent strabismus. Oral candidosis.

The positive diagnosis was sustained by: a patient with a history of alcohol abuse and poor life conditions, fever, weight loss in the last two months, encephalitis signs: nervousness, than coma, neurological signs like facial paresis and right hemiparesis (which often appear in the course of TBC meningitis), a clear CSF, with a cellularity of hundreds of cells, in which there is a predominance of the small, adult lymphocytes, high CSF protein concentration, very low glucose, low concentration of chlorides in CSF.

The differential diagnosis was mainly made with other meningitis with clear CSF, like: *viral meningitis* (clear CSF, cells<300/mm³, polymorph lymphocytes, monocytes, normal glucose level in the CSF, normal of high protein level in the CSF), *Brucellosis meningitis* (it is mainly a professional diseases which appears at people working with animals, vets, zootehnicians; it often associates anemia, leucopoenia, lymphocytosis, important hepatosplenomegaly; exceptionally, Brucella can be isolated from hemoculteres, medulocultures, CSF, ganglions, most of the times, the diagnosis is made serologically), *Leptospirosis meningitis* (antropozoonosis produced by Leptospira, more freqvent in the summer, which associates liver failure, renal failure, intravascular disseminated coagulation, clear CSF, pleiocytosis, hundreds of elements, most of them lymphocytes, with a slightly increased albuminorahia).

Hospital course and treatment: the patient started on antituberculous therapies: rifampicin 600 mg/day, isoniazid 300 mg/day, ethambutol 1600 mg/day, pyrazinamide 1500 mg/day and streptomicine 1g/day. He received intravenous steroids: Dexametazone 3*1viols/day, initially, and, after that, Prednison in decreasing dose. Mannitol was also given as adjuvant therapy to relieve the raised intracranial pressure. He also received gastric protection and antimicotic drugs.

Possible complications: Among the complications of the tuberculous meningitis, the most frequent are those related to the fact that it can affect the cranial nerves, e.g. oculomotor causing strabismus and diplopia, bladder globe, mono-paresis or hemi-paresis; it can also cause hydrocephalus**,** neurological sequels with hearing loss, cerebral paralysis, convulsive crisis, compartmental alterations. We also should consider, as possible complications the adverse events due to anti-tuberculous drugs: toxic hepatitis, chronic renal failure (rifampicin)**,** bacterial infections due to the immune suppression caused by the corticosteroid therapy.

After starting the treatment with anti-tuberculosis drugs, the patient's course was favourable, the patient became conscious, cooperative, appetent and non-febrile. After two weeks of treatment in the Infectious Diseases Department, the patient was transferred in the Pulmonary Diseases Department in order to continue the anti-tuberculosis therapy (9 months)**.** We were informed that the patient's mental and physical status is good and he is continuing his treatment. After 6 weeks, the results of the cultures from CSF on Lowenstein medium confirmed the presence of Mycobacterium tuberculosis.

On short time, the patient's **prognosis** is good, because the patient became non-febrile, conscious, with the amelioration of the general status; long time prognosis is un-known, the risk of possible neurological and motor sequels. TB meningitis is a very critical disease in terms of fatal outcome and permanent sequelae, requiring rapid diagnosis and treatment.

Discussions. The clinical symptoms are installing in a progressive way, with *signs of bacillary impregnation*: low fever, nocturne perspiration, asthenia with loose of weight, no appetite, *neurological signs*: paresis of cranial nerves, paresis of the urinary bladder, *encephalitis signs*: irritability and nervousness, or coma. The diagnosis is usually suggested by the aspect of the CSF, radiological exams, CT or RMN. Generally, the bacillary meningitis is paucibacilal, and the exam made on Ziehl-Nielson smear is, only exceptional positive; the cultures on Löwenstein smear confirm the diagnosis tardily, after 3-6 weeks. The diagnosis would be also possible by using Quantiferon or PCR. The prognosis depends on age, the duration of the infection and the appearance of the neurological sings. The prognosis is also influenced by the virulence of the bacilli which are involved. The course is often lethal, especially at old ages (60%) and in children under 5 years (20%), or in infections with duration of over 2 months. With no specific therapy, death can appear at 3 weeks from the beginning of the disease. The treatment is made with association of 3-4 anti-tuberculous drugs, from which should not miss Isoniaside and Rifampicine, 3 months, corticoids 4-8 weeks. After these 3 months, the anti-tuberculous drugs will be administrated in a program of 3/7 or 2/7, for other 9 months. The neural-surgical intervention can be considered, sometimes, in case of hydrocephalus.

Case particularity: The case was particular because its debut by conscious disorders, confusion, nervousness, agitation at a patient known with chronic alcohol abuse – first diagnosed with alcoholic encephalopathy. As another particularity, we can mention that first, it was impossible to treat the patient with oral drugs, so we had to use intravenous drugs, suppository and even nasal-gastric administration of the anti-tuberculous drugs.

The bacillary meningitis, away of being rare, represents the second cause of bacterial meningitis which was isolated in our department in the last years, so the anti-tuberculous drugs should be considered in the case of un-favourable courses of the patients, with neurological manifestations, especially.

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