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The importance of a correct and prompt diagnostic in a case of bacillar meningo-encephalitis

Marius Costin Chitu[1], Paula-Roxana Raducanu[2], Vlad Dima[3]*, Bianca-Margareta Mihai[3], Teodor Salmen[4], Olivia Andrei[5], Claudia Gabriela Potcovaru[6], Dan Liviu-Dorel Mischianu[7,8], Roxana Elena Bohiltea[9]

[1]Doctoral School, "Carol Davila" University of Medicine and Pharmacy Bucharest, "Matei Bals" National Institute of Infectious Diseases, Bucharest, Romania
[2]Department of Intensive Care Unit, Emergency Clinical Hospital, Bucharest, Romania
[3]Department of Obstetrics, Gynecology and Neonatology, Filantropia Clinical Hospital, Bucharest, Romania
[4]Doctoral School, "Carol Davila" University of Medicine and Pharmacy Bucharest, "N. C. Paulescu" National Institute for Diabetes Mellitus, Nutrition and Metabolic Disorders, Bucharest, Romania
[5]National Institute of Neurology and Neurovascular Disorders, Bucharest, Romania
[6]Doctoral School, "Carol Davila" University of Medicine and Pharmacy Bucharest, National Institute of Rehabilitation, Physical Medicine and Balneoclimatology, Bucharest, Romania
[7]Department of Urology "Carol Davila" University of Medicine and Pharmacy Bucharest, "Carol Davila" Emergency University Central Military Hospital, Bucharest, Romania
[8]The Association of Scientists from Romania, Bucharest, Romania
[9]Department of Obstetrics and Gynecology "Carol Davila" University of Medicine and Pharmacy Bucharest, Filantropia Clinical Hospital, Bucharest, Romania

ABSTRACT

Introduction. Meningitis is the inflammation of the meninges and can be of infectious cause, the most common being viral, followed by bacterial, but which associates a more severe and rapid evolution, even when it is treated correctly and promptly. In infants and children tuberculous meningitis develops more frequently as a complication of progressive primary infection.

Case presentation. A 12-year-old female patient presents to the emergency room with fronto-parietal headache, vomiting, vertigo and lumbar pain, which, despite treatment with oral cephalosporin, returns after 3 days, because the symptoms persist. She is admitted, her treatment is escalated, IV fluoroquinolones and acyclovir are added, along with corticotherapy and cerebral depletives, but within 48 hours the general condition worsens, associating severe headaches, neck stiffness and personality disturbances. Lumbar puncture detects high levels of leukocytes and proteins and low levels of glucose and chlorine, so the patient is transferred to an Intensive Care Unit, intubated and mechanically ventilated. MRI reveals meningoencephalitis with ponto-mesencephalic and cerebellar involvement, with biological minimal leukocytosis with neutrophilia and minimal inflammatory syndrome, the repeated lumbar puncture present the same pathological elements, but the PCR of CSF is positive for Mycobacterium tuberculosis and the diagnosis is of severe tuberculous meningoencephalitis. Under tuberculostatic treatment (isoniaside 5 mg/kg/day, rifampicin 10 mg/kg/day, ethambutol 20 mg/kg/day, pyrazinamide 30 mg/kg/day) associated with vitamin therapy (B1 and B6 – to prevent peripheral neuropathy induced by isoniazid), corticotherapy and cerebral depletives, after 5 days, the evolution was towards healing, which allowed extubation and later discharge, continuing the 7/7 tuberculostatic scheme for 30 days. A subsequent pulmonary assessment is necessary for conversion to 2/7 regime.

Conclusions. Meningitis must be promptly and correctly diagnosed and treated, otherwise the evolution is serious, the patient may develop sequelae or even develop towards death. An important element is the anamnesis, because in the presents case, a member of the patient's family has recently been hospitalized for a respiratory pathology for which he required oxygen therapy.

Keywords: meningitis, tuberculosis, sequelae

INTRODUCTION

Acute meningitis represents the inflammation of the leptomeninges (membranes surrounding the brain and spinal cord), and it can be caused by infections. The evolution of this disease can be severe and constitutes an emergency, which requires correct, early and prompt diagnosis and treatment, otherwise, it may cause sequelae or even death.

Corresponding author:
Vlad Dima
E-mail: dima.vlad@yahoo.com

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Even if there are multiple barriers that interpose (the most important is the blood-brain barrier, which also represents the major anti-infectious and anti-toxic defense factor), meningitis can only be induced by the etiological agent that possesses pathogenic characteristics, under favourable circumstances [1].

Viral meningitis is on the first rank in terms of frequency and has, for the most cases, a self-limiting evolution. Bacterial meningitis, although they are on the second place, has particular the clinical severity, rapid evolution, and sequelae in the neurological sphere, even after the etiopathogenic treatment. Fungal and parasitic meningitis are rare in immunocompetent patients, being specific to patients with comorbidities and altered immune status, and the lack of immediate treatment results in death [2].

Children under the age of five are an important demographic group for understanding the epidemiology of tuberculosis (TB), as TB frequently progresses from primary or latent infection to disease, and severe manifestations of the disease, such as miliary TB and meningitis TB, are more common. in this age group. Therefore, these children serve as sentinel cases, indicating recent and/or ongoing transmission in the community. Most children are infected with TB in the household, especially by parents or caregivers [3].

The clinical presentation of extrapulmonary TB depends on the site of the disease. The most common forms of extrapulmonary disease in children are the lymph nodes and central nervous system TB. Neonates have the highest risk of progression to TB with miliary and meningeal involvement [4,5].

CASE PRESENTATION

We present the case of a 12-year-old female patient, who presented to the emergency room of a city hospital with fronto-parietal headache, two episodes of vomiting, vertigo, and low back pain (bilateral positive Giordano's sign) [6], for which she received antibio-therapy with oral cephalosporin and symptomatic, without remission of the manifestations, which is why, 3 days later, she returns to the hospital, and is admitted as an inpatient.

During hospitalization, after 48 hours, there is an intensification of the headache and the appearance of backache, so a lumbar puncture is performed: clear CSF, Pandy2+, 490 elements/mm^3, rare red blood cells, 96% lymphocytes, 4% polymorphonuclears, proteinorahy 183 mg/dl, glycorahy 22.9 mg/dl, chlorides 6.9 g/l, PCR multiplex CSF (BioFire) [7] negative for bacteria, viruses and fungi, so the treatment is escalated by adding fluoroquinolone IV, acyclovir, corticoid and cerebral depletive, under which the evolution worsens and requires transfer to a hospital unit of upper echelon.

Orotracheal intubation and mechanical ventilation are decided, with cerebral magnetic resonance imaging (MRI) performed, which reveals bilateral meningo-encephalitis with ponto-mesencephalic and cerebellar involvement.

Biologically, minimal leukocytosis with neutrophilia and inflammatory syndrome (PCR, slightly altered Fibrinogen) and hyponatremia with hypokalemia are identified. The repetition of the lumbar puncture noted slightly pinkish CSF, hypertensive, Pandy 2+, 400 elements/mm^3, sediment: 10% polymorphonuclear, 45% small lymphocytes, 40% medium lymphocytes, 5% large lymphocytes, protein 213 mg/dl, glucose 34 mg/dl (serum blood glucose 91 mg/dl), chloride 710 mg/dl, microbiological evaluation and molecular tests from CSF (PCR multiplex, latex agglutination, Burri-Gins stain) were negative, with positive PCR for Mycobacterium tuberculosis.

Considering the positive microbiological result, the diagnosis was of severe form of meningo-encephalitis TB, with neurological dysfunction for which tuberculostatic therapy was initiated (isoniaside 5 mg/kg/day, rifampicin 10 mg/kg/day, ethambutol 20 mg/kg/day, pyrazinamide 30 mg/kg/day) associated with vitamin therapy (B1 and B6 – for the prevention of isoniside-induced peripheral neuropathy) and corticotherapy and cerebral depletives that were already in use. After 5 days, under this therapy, the evolution was towards net improvement, so the patient was extubated and discharged, continuing the tuberculostatic regimen of 7/7 for 30 days, subsequently being evaluated by a pneumologist to state whether to switch to the regimen of 2/7.

DISCUSSIONS

Positive diagnosis of TB meningitis is based on:

→ epidemiological data: from the rigorous anamnesis we were informed that before the onset of the symptomatology by about 2 weeks, a family member was hospitalized for a pathology regarding the respiratory system with the need for oxygen therapy; in addition, the patient came from an environment with poor living conditions [8]

→ clinical [9,10]: subacute evolution with progressive onset:

- Prodromal stage of bacillary impregnation, characterized by fatigability, headache, subfebrility, personality distrubances, weight loss.
- Meningitis stage, with the highlighting of the clinical meningeal syndrome with appearance of neck redness that associates neurological manifestations – cranial nerve palsies (the patient had right central facial palsy and motor deficiency of the right upper limb), confusional syndrome
- Paralytic stage, with appearance of encephalitic syndrome with confusion and coma (the patient had convulsions while hospitalized in the Intensive Care Unit)

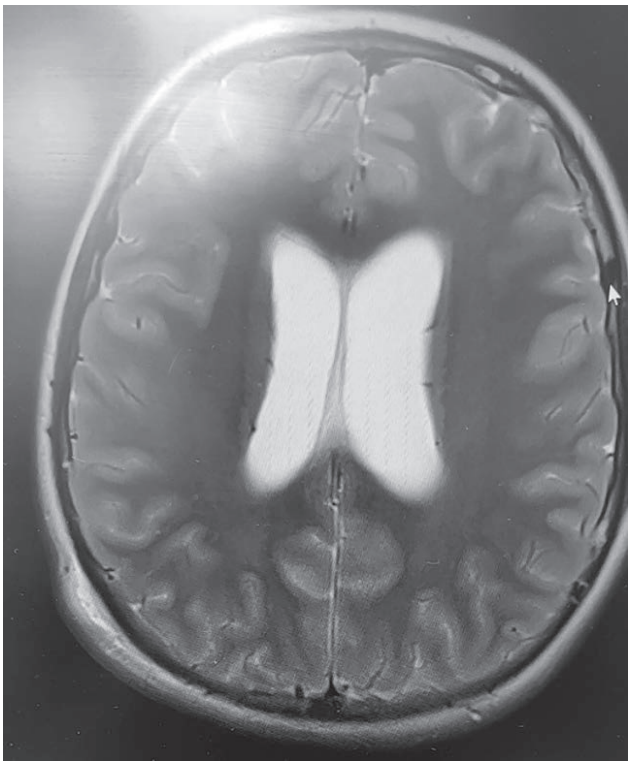

FIGURA 1. Bilateral meningo-encephalitis

→ paraclinic:
- moderate hyponatremia
- pulmonary radiography may reveal TB lesions
- cerebral imaging – CT, MRI (in this case, meningeal enhancement at the level of the cerebellar tentorium and brain stem with interest of the cranial nerves and suggestive aspect of meningitis)
- eye fundus examination could highlight the choroid tubercles
- identification of the etiopathogenic agent in the CSF (obtained by lumbar puncture) or other liquids

The characteristics of CSF in TB meningitis are as follows:
- macroscopic aspect: clear, opalescent or xanthochrome, intensely hypertensive (+++)
- Pandy positive reaction 3+/4+
- the number of cells is of the order of tens, <500/mm^3, of which <30% polymorphonuclear, the rest >70% mononuclear with the predominance of small lymphocytes
- albumin significantly increased 1000-3000 mg/l (left at room temperature will form a veil, because of the many proteins it contains), very low glucose, up close to 0, and low chlorine levels.
- cultures on common growth mediums are negative, while cultures on special solid growth mediums like Lowenstein Jensen are positive, with the great disadvantage that the outcome are available after at least 4 weeks (BACTEC method gives results in 1-3 weeks); the gold standard for etiological diagnosis is the presence of M. Tuberculosis in cultures from the CSF
- PCR Mycobacterium tuberculosis – with result in about 4 hours with specificity around 95%
- antigenic tests – urinary detection of lipoarabinomannan glycolipids of the mycobacterial cell wall (urine LAM test) is recommended by World Health Organization for diagnosis of tuberculosis in HIV patients
- Adenosine deaminase (ADA) – is an adjuvant test that is used for the diagnosis of meningitis TB; an increased level of ADA can also occur in other bacterial infections or neurobrucellosis, with no clear limit to distinguish between TB and other infectious meningitis [11].

Differential diagnosis of TB meningitis can be made with [12,13]:

→ other infectious disease — another meningitis with clear/opalescent CSF:
- viral: HSV 1.2, mumps, varicella-zoster, enteroviruses – lymphocytes have a polymorphic appearance (large and small) compared to the monomorphic aspect (>90% small lymphocytes) in TB meningitis; also, albumin in CSF is slightly increased in viral meningitis, and glucose in CSF is normal
- bacterial: "decapitated" with antibiotic, atypical or bacterial bacteria at onset
- fungal: cryptococcosis, histoplasmosis, blastomycosis – predominance of mononuclear cells, slightly increased proteins,

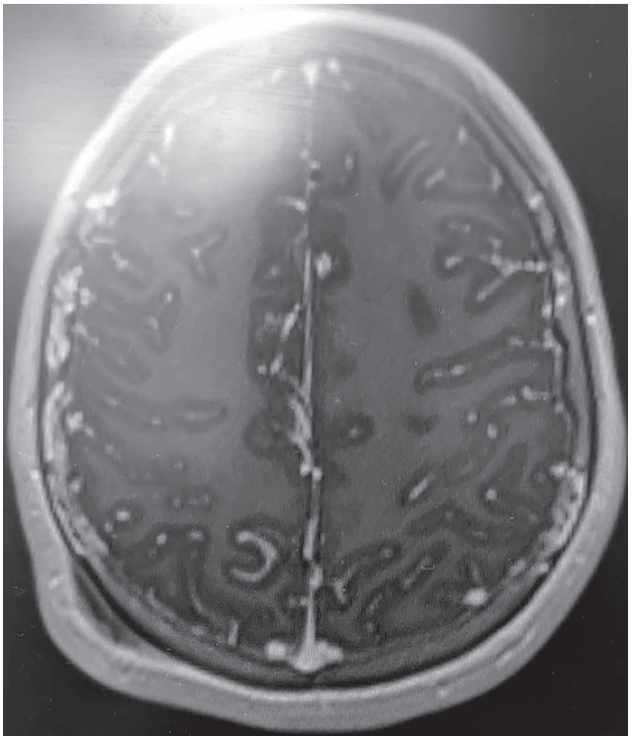

FIGURE 2. Meningeal enhancement

slightly decreased glucose in CSF; the definitive diagnosis is made by the CSF culture
- brain abscess, spinal epidural abscess, sphenoid sinusitis – clinical manifestations of parameningeal infection are nonspecific and subacute; lumbar puncture in most cases is contraindicated, but once obtained CSF (by stereotactically or surgically guided aspiration), it will be with increased protein level, low glucose level and pleocytosis
- neurobrucellosis, neurosiphilis

non-infectious → pathologists:
- Leptomeningeal metastases – most associated with cancers of the breast, lung, and skin; differential diagnosis by the appearance of cerebral MRI – linear and nodular leptomeningeal thickening and CSF aspect – increased pressure, slight pleocytosis, slightly increased proteins and slightly decreased glucose
- Systemic vasculitis, Wegener's granulomatosis, systemic lupus erythematosus.

Complications that can occur in patients with TB meningitis are more common and severe than in those with bacterial meningitis and include:
- stroke – 26% [14]
- hydrocephalus – 80% of those with TB meningitis also show signs of increased intracranial pressure – deterioration of vision and/ or consciousness status – at the appearance of these signs must necessarily be performed cerebral MRI; can be performed and ultrasonography of the optic nerve sheath [15,16]
- seizures – focal seizures, generalized or status epilepticus [17]
- hyponatremia – can occur at any time of TB meningitis; a distinction should be made between patients with inadequate antidiuretic hormone secretion syndrome (SIADH) who are euvolemic and those with central salt loss who are hypovolemic
- vision loss – severely debilitating complication that occurs in a quarter of patients with TB meningitis and many of the survivors have permanent blindness [18]
- transverse myelitis, sensory, motor, behavioral disorders.

CONCLUSIONS

The current case highlights a young patient with severe tuberculous meningoencephalitis who has neurological damage. This condition is not the first pathology that might be suspected, especially considering the patient's less-specific symptoms that are found during his evaluation. Although a disease with progressive onset, it can evoluate towards complications and can lead to irreversible sequelae or even death, so is necessary to make an early and correct diagnosis and treatment for their prevention.

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