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Diagnostic challenges in neuroinfections: case report and literature review

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ABSTRACT

Meningitis and encephalitis are a group of neuroinfectious diseases that require both correct and early diagnosis and etiopathogenic treatment, because their potential for severe evolution, is often being associated with sequelae. In addition to the detailed anamnesis and clinical examination, it is important to know the specific neurological manifestations at the beginning in order to decide properly the indication to perform the lumbar puncture for identifying an etiopathogenic agent in order to administer a targeted treatment. We present the approach both in terms of diagnosis and treatment, in case of an elderly patient with a favourable evolution, towards healing, without associating neurological sequelae. At the same time, we present a synthesis of the novelties of diagnostic and treatment methods in infectious meningitis and encephalitis.

Keywords: Meningitis, encephalitis, infectious disease, diagnosis, mortality

INTRODUCTION

Meningitis and encephalitis are among the most important causes of morbidity and mortality of infectious diseases, but also of neurologic aetiology. They are associated with severe evolutionary potential and require an early diagnosis, in order to initiate the treatment as quickly and correctly as possible, in order to increase the patient's chances of survival [1].

Viral meningitis is more common than bacterial meningitis and has, most frequently, a self-limiting evolution. The most common causes of viral menin-

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gitis are respiratory and digestive tract infections, the most frequent involved being enteroviruses [2]. Also, frequently involved viruses are Coxsackie virus, herpes simplex virus, urlian virus and West Nile virus. Reported incidence rates of viral meningitis range from 10 to 20 cases per 100,000 children per year [3].

Bacterial meningitis, often, has a very rapid, with potential lethal evolution, the treated patients remaining with sequelae in the neurological sphere. The most common aetiologies are: Meningococcus (Neisseria meningitidis) – the most serious form of meningitis, the prototype of meningitis with purulent CSF; Pneumococcus (Streptococcus pneumoniae) - common in elderly, ethanol-consuming, splenectomised patients or patients presenting sinusitis, otomastoiditis or head trauma; Haemophilus Influenzae B - specific to children under 2 years of age; Group B agalactiae streptococcus – specific to the neonatal period; Listeria monocytogenes - route of transmission is tegumentary, respiratory or digestive [4].

Tuberculous, fungal and parasitic meningitis are specific to immunocompromised patients and, in the absence of early initiated treatment, the evolution is towards death.

CASE REPORT

We present the case of a 70-year-old patient, farmer, hospitalized for fatigue, fever, chills, vertigo, malaise started 4 days ago. From the anamnestic data, the patient has no significant personal pathological history, except for chronic alcoholism and a dental abscess in one of the molars, for which he has been on beta-lactam antibio-therapy for 4 days.

At the clinical examination we identify a conscious, agitated, slightly confused, afebrile patient, new-onset hearing loss [5], with a painful and limited movement of the head flexion, associating also the Flatau and the kiss signs, right submandibular ganglion sensitive to palpation, otherwise, cardiorespiratory balanced, bradycardic AV = 58 bpm and without other subjective symptoms. As meningoencephalitis diagnosis was suspected, brain CT [6] and fundus eye examination were performed. No pathological changes were identified so we proceed to lumbar puncture.

In this case, the cerebrospinal fluid was slightly hypertensive, opalescent, the number of nucleated cells was in the hundreds with mixed cytology with polymorphonuclears and mononuclear in varying proportions, Pandy ++, increased albuminorrhea, low glycorrhea and no bacteria were seen on the smear nor did Biofire identify a pathogen.

Subsequently, the appearance of the identified CSF is specific to a bacterial meningitis "decapitated with antibiotics", most likely secondary to the dental abscess. Neither cultures nor multiplex PCR/BIOFIRE identified a germ, this being due to the fact that the patient had received antibio-therapy previously. Depending on the age of the patient, the mastoid starting point and the epidemiological context (farmer, chronic alchoolism), the most common causative agents incriminated may be *S. pneumoniae* and/or *L. monocytogenes*, which is also highlighted in the literature [7-9].

In the present case, we chose to start etiopathogenic therapy after the puncture, but before finding out the results of the CSF analysis. The etiopathogenic treatment that the patient received after performing the lumbar puncture consisted of Ampicillin, Vancomycin, and third-generation cephalosporin, in doses adjusted for CSF penetration [10], without any evidence for the existence of epidemiological, clinical and paraclinical criteria to justify antiviral treatment. The subsequent evolution was with the rapid improvement of the symptomatology.

DISCUSSIONS

The positive diagnosis of meningitis / encephalitis is based on [11]:

- epidemiological data: from the anamnesis we should identify a pre-existing condition, family contact/epidemic outbreak, travel history or recent vaccination history, various activities with infectious potential
- clinical [12]:
  - → the infectious syndrome is the first and consists of the presence of fever, myalgias, adynamia, sweating, sphygmo thermal dissociation, chills. Chills may be missing from this table.
  - → meningeal syndrome, expressed by manifestations of intracranial hypertension: diffuse, continuous headache "in helmet", "central" type vomiting unprevailed by nausea, bradycardia, photophobia, bulging of the fontanelle (specific to the infant) - the objective component; while the subjective component includes neuroradicular component, expressed by the elements from Table 1.
  - → encephalitic syndrome affecting the cerebral cortex (convulsions, agitation, hallucinations, numbness, coma), pyramidal system (spastic paresis, osteotendinous hyperreflexia), extrapyramidal system (hypertonia, tremor), hypothalamus (central hyperthermia), cerebellum (dysmetria, nystagmus) or temporal lobe (hallucinations, aphasia, oddness).

TABLE 1. Main neurological signs in patients with meningoencephalitis (13-14)

Sign	Description
Neck stiffness	the patient complains of pain and resists trying to bend his head on his chest
Brudzinski of neck	the previous manoeuvre, performed faster, causes knee flexion
contralateral Brudzinski	the patient is positioned in a supine position, the leg is flexed unilaterally on the thigh and the thigh on the abdomen at a right angle, a forced extension movement is pressed, pressing on the knee and raising the heel, you can observe the bending of the contralateral knee
Flatau	the appearance of mydriasis when the head is forced forward
Squires	the appearance of mydriasis caused by the forced extension of the head
Kernig I	Attempting to lift the torso vertically by pushing from the shoulder blades, the patient will feel pain and bend his knees.
Kernig II	the attempt to flex the lower limbs on the abdomen will cause the knees to flex
Amoss	The patient sits leaning only on his hands and with the knees bent
Kiss	Sitting, the patient cannot touch his bent knees with his lips
Magnus-De Klein	Caused by lateral rotation of the head and, if positive, contraction of the ipsilateral extensor muscles in rotation and contraction of the contralateral flexor muscles in rotation
Von Hainiss	Causes pain when exerting pressure on the ring of the adductor muscles of the foot
Binda`s	The mobilization of the head corresponds to the rotation and raising of the shoulder contralateral to the direction of rotation of the head – specific to tuberculous meningitis
Trousseau`s	Obtaining a persistent and delayed red dermografism by passing with a blunt tip on the patient's skin – also specific in tuberculous meningitis
Meningitic line	White line framed by two erythematous stripes, appeared following mechanical excitation with a needle
Lesaj	Reproducible only in new-borns – considered positive if the physiological reflex of pedalling (lower limbs) movement is absent when raising the head with both hands subaxillary supported

- paraclinical [15]:
  - → cerebral imaging: CT, IRM and/or fundus of eye examination, followed by
  - → identification of the etiopathogenic agent in cerebrospinal fluid (CSF) (obtained by lumbar puncture), blood or other fluids
  - → CSF analysis is summarized in Table 2.

In addition to CSF analysis, BioFire® FilmArray® Meningitis/Encephalitis Panel has been developed in the last 5 years, the first FDA-approved multiplex PCR for the evaluation of cerebrospinal fluid samples, capable of identifying 14 organisms in a single test reaction, in only one hour (7 viruses, 6 bacteria, 1 fungus) [16].

Studies show that the ideal management is to initiate etiopathogenic therapy without waiting for the microbiologic results and then, after identifying the causative agent, it is recommended to de-escalate the treatment [17]. In addition, other reasons why

TABLE 2. Cerebrospinal fluid (CSF) characteristics in infectious meningitis (15)

Etiology	Physiological CSF	Viral	Bacterial	Tuberculosis	Fungal/Parasitic
Aspect	Clear, like" rock water"	Clear / opalescent	Turbid /" cabbage juice" / purulent	Clear / opalescent	Clear
Pressure	"Bit by bit"	Normal	Raised	Raised	Normal/ raised
Pandy	-	+/-	+++	++++	+/-
Number of elements/mm^3	0-5	Hundreds	Thousands	Tens	Hundreds
Cytology	Mononuclear	Mononuclear	Polymorfonuclear	Mononuclear monomorphic: Small lymfocites	Mononuclear with polymorph aspect polimorf/ Eosinophils
Proteins (mg/dL)	15-45	+	++	+++	+/Normal
Glucose (mg/dL)	40-60	Normal	--	---	-/Normal
Presence of de bacteria on pe smear	No	No	Yes>50% (Gram staining)	Rare / Yes (Ziehl-Nielsen staining)	Yes (China ink staining)

we did not start treatment before the puncture were that we were in front of a patient in good general condition, balanced both metabolically and hemodynamically, and the patient was already under antibio-therapy, which provided a time reserve until the lumbar puncture was performed and the CSF constants were found.

The anamnesis is a very important point in drawing the diagnosis and guiding the treatment and should help to choose the opportunity to start antibiotic/antiviral therapy, respectively before or after punctures and also before or after finding out the results of biochemical and microbiological analysis of CSF.

Given the increased mortality rate and morbidity of pathogens possibly incriminated in the cause of meningoencephalitis (*S. pneumoniae* 30%, *L. monocytogenes* 4-10%) [1], we believe that initiation of therapy should be started as soon as possible after the lumbar puncture (if there are no contraindications for its performance: idiopathic increased intracranial pressure, bleeding diathesis, hypertension associated with bradycardia etc [18-19], a fact reinforced by the data reported in the literature [20].

Also, both current medical practice and dates from literature show that in patients undergoing empirical therapy, if a deterioration of the general condition is observed with worsening of the present symptoms, it is advisable to escalate the treatment and add another antibacterial/antiviral drug or it is recommended to initiate a new regimen treatment [21-22].

It should be borne in mind that meningoencephalitis may initially have a diverse clinical picture with manifestations in all systems (cardiovascular, metabolic and neurological) and a rapid differential diagnosis should be made so that appropriate and early treatment can be initiated [23].

Any delay in taking a therapeutic decision can lead to neurological sequelae or an unfavourable outcome [24].

CONCLUSIONS

The present case presents the need to initiate empirical etiopathogenic therapy after lumbar puncture (in cases where it can be performed), in patients with suspected meningoencephalitis, prior to the microbiological result of CSF analysis, in order to prevent complications and reduce mortality.

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