Central nervous system tuberculosis, one of the most challenging of infections

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ABSTRACT We are presented a 35-year-old patient with no previous relevant medical history who was admitted to the emergency department for fever, altered mental status and diffuse abdominal pain. Initial evaluation failed to demonstrate the presence of thoracic or abdominal deep infection. The clinical course was marked by a deterioration of the neurological condition. The cerebral MRI showed diffuse and extensive involvement of the brainstem and cerebellar hemispheres associated with hydrocephalus consistent with tuberculous meningoencephalitis. Antituberculous therapy was started, but no clinical improvement was achieved.

KEYWORDS tuberculous meningoencephalitis, magnetic resonance image

Introduction

Mycobacterium tuberculosis is responsible for approximately 10 million new cases of tuberculosis and 1,3 million deaths annually [1]. Tuberculous meningitis is considered the most severe form of this infection. Tuberculous meningitis disproportionately affects children and HIV patients [2]. The clinical onset of tuberculous meningitis is indolent, which makes diagnosis difficult. Its treatment regimens are still uncertain.

Case report

This is a 35-year-old woman with no previous chronic diseases. She was admitted to the emergency department for fever and altered mental status and personality change 24 hours before hospital admission. She had been previously evaluated by her family doctor for diffuse abdominal pain, vomiting and diarrhoea and received ten days of oral ciprofloxacin twice daily with no clinical improvement. Her recent medical history also revealed the presence of mechanic lumbar pain with a lumbar scanner only showing signs of arthrosis.

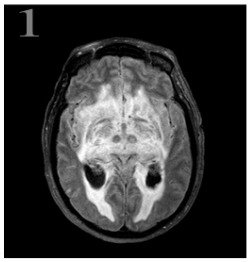
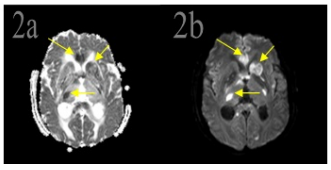


Figure 1: Axial T2 FLAIR shows diffuse and symmetrical edema of white matter and meninges. The ventricles are weakly dilated.

Figures 2a, 2b: On diffusion-weighted imaging and ADC maps, we note a heterogeneous restriction of diffusion in basal nuclei and the genu of corpus callosum (arrows).



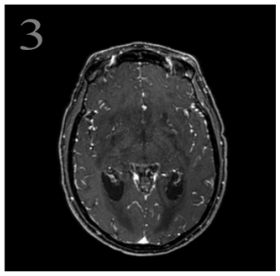


Figure 3: No pathological enhancement was observed on T1-weighted contrast enhanced sequence.

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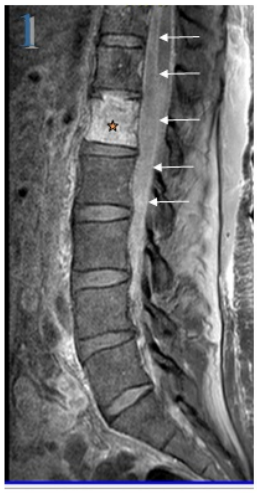

Figures 4: Sagittal and axial views of the T1-weighted sequence with enhanced contrast. The first lumbar vertebra is intensely enhanced (star), associated with an enlargement and inflammatory enhancement of the leptomeningeal space (arrows). The compression of the vertebral canal is responsible for the cauda equina syndrome.

Upon admission at the emergency department, she was febrile, blood pressure 120/70 mmHg and tachycardia. The neurological examination revealed Glasgow coma score was 14/15 and lethargy but no neck stiffness or any other focal neurological sign. The abdomen was diffusely painful, with no masses and the lumbar palpation from L1 to L5 was painful. The cardiorespiratory exam was normal.

Laboratory investigations revealed the presence of inflammatory syndrome, neutrophil hyperleukocytosis (14900 /mm3, neutrophils 60%), protein C reactive (30 mg/L). Coagulation, electrolytes as well as liver and renal function tests were within the normal range. A complete body scanner aiming at detecting a thoracic or abdominal deep infection was performed, but it was normal.

The patient was transferred to the internal medicine department for further investigations. Upon arrival and considering the persistence of altered mental status, a lumbar puncture was performed. It showed 190 white cells/mm3 and 71% lymphocytes, hyperproteinorachie (1.81 g/L) and hypoglycorachie (1.4 mmol/L). Gram stain was PCR on CSF for HSV, VZZ, CMV, EBV and measles were negative as well as the serologies for Lyme disease, CMV, HSV, VZV and EBV. Blood cultures were negative. The electroencephalogram showed no abnormal activity, and the brain scanner was normal.

The diagnosis of bacterial meningitis probably beheaded by recent antibiotic treatment was evoked, and empiric treatment with cefotaxime (2g every 4 h) and vancomycin (22.5 mg/kg q12h) associated to acyclovir was started. However, 72 hours after hospital admission, the patient was still febrile, developed projecting vomiting and Glasgow was 8/15. The patient was intubated and sedated and transferred to the intensive care unit. The brain scanner showed the presence of hydrocephaly in setting of a clinical picture consistent with intracranial hypertension. An external ventricular derivation was placed. This one was surgically changed three times owing to obstruction. Intracranial hypertension was controlled, and sedation was slowly discontinued. However, the neurological course was marked by the absence of awakening state and stereotyped extension of the four limbs to pain. The patient was sent for a brain scanner in order to rule out bleeding or sinus thrombosis, but it only showed the persistence of diffuse and bilateral cerebral edema. The investigations were completed but a cerebral and lumbar magnetic resonance. The cerebral MRI showed diffuse and extensive involvement of the brainstem and cerebellar hemispheres associated with hydrocephalus consistent with tuberculous meningoencephalitis (Fig 1, 2a, 2b, 3). The lumbar magnetic resonance study demonstrated L1 body edema and hyperintensity consistent intradural empyema (Fig 4, 5).

PCR for TB in the LCR and endotracheal secretions were positive as well as Quantiferon. Immediately treatment with Isoniazid, Rimphanpicine, Ethambuthole and Pyrazinamide was started. However, seven days after treatment, no clinical improvement was noted. The risk of a vegetative state and severe sequelae was discussed with the patient's relatives who decided to stop active treatment. The patient passed away 48 hours later.

During the interview the relatives, they stated the patient had been working in a refugee centre four months before

Discussion

Central nervous system (CNS) tuberculosis (TB) includes three clinical categories: tuberculous meningitis, intracranial tuberculoma, and spinal tuberculous arachnoiditis. These categories are frequently encountered in regions where the incidence of TB is high, and the prevalence of post-primary dissemination is common among children and young adults [2]. Tuberculous meningitis accounts for about 1 percent of all cases of TB and 5 percent of all extrapulmonary disease in immunocompetent individuals [3]. Risk factors include: travel to/residence in a country with high TB prevalence, HIV infection, children, elderly, alcoholism, drug abuse, homelessness and exposure to person with pulmonary TB as in our case.

Early recognition of tuberculous meningitis is of paramount importance because the clinical outcome depends significantly upon the stage at which therapy is initiated. Empiric antituberculous therapy should be started immediately in any patient with meningitis syndrome and cerebrospinal fluid (CSF) findings of low glucose concentration, elevated protein, and lymphocytic pleocytosis if there is evidence of TB elsewhere, either clinically or historically, or if prompt evaluation fails to establish an alternative diagnosis as in the case presented.

The patient presented with the so-called meningitic phase follows with more pronounced neurologic features in this case vomiting, lethargy and confusion, but meningismus, protracted headache, and varying degrees of cranial nerve and long-tract signs could also be described. Typically, the CSF formula shows elevated protein and lowered glucose concentrations with a mononuclear pleocytosis as in our case which was initially considered the result of the previous antibiotics treatment and leading to the delay in diagnosis. Besides, early in the course of disease, the CFS formula is often atypical with only a few cells or with polymorphonuclear leukocyte (PMN) predominance. These cases usually quickly develop a lymphocytic cellular predominance if subsequent CSF examinations are performed [4].

Another important useful diagnostic tool is the measurement of the CSF adenosine deaminase (ADA) [4], but unfortunately it was not considered. Its result should be carefully interpreted as elevated CSF ADA level may also be observed in the setting of bacterial infections [5] without clear threshold to distinguish TB meningitis from bacterial meningitis.

The clinical and biological picture was erroneously interpreted as a bacterial meningoencephalitis leading to clinical worsening and delay treatment and diagnosis. Differential diagnosis is comprehensive and includes other causes of basilar meningitis particularly sarcoidosis, endemic fungi, neurobrucellosis and leptomeningeal carcinomatosis.

Antituberculous therapy should be promptly started based on strong clinical suspicion and should not be delayed until bacteriologic proof has been obtained. The patient's clinical outcome depends largely on the stage at which therapy is initiated. Worse outcomes result from delay than from inappropriate therapy as long as efforts are continued to confirm the diagnosis as in our case

Conclusion

The diagnosis of tuberculous meningitis is challenging and the outcomes poor when the diagnosis and treatment are delayed.

Learning points

- Tuberculous meningitis should be considered when the CSF shows low glucose concentration, elevated protein, and lymphocytic pleocytosis if there is evidence of TB elsewhere, either clinically or historically, or if prompt evaluation fails to establish an alternative diagnosis.
- Antituberculous therapy should be promptly started based on strong clinical suspicion and should not be delayed until bacteriologic proof has been obtained.
- Epidemiological data collection is of huge importance in the evaluation of patient with suspected meningitis.

Conflict of Interest

There are no conflicts of interest to declare by any of the authors of this study.

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None

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