A Rare Presentation of Tubercular Meningitis as Persistent Neutrophilic Meningitis

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To cite this article: Ralot T, Bafna C, Singh S, Sharma S. A rare presentation of tubercular meningitis as persistent neutrophilic meningitis. Malays J Med Sci. 2017;24(6):103–106. https://doi.org/10.21315/mjms2017.24.6.13

To link to this article: https://doi.org/10.21315/mjms2017.24.6.13

Abstract

Persistent neutrophilic meningitis is an atypical form of chronic meningitis defined as clinical meningitis with a cerebrospinal fluid (CSF) analysis suggestive of neutrophilic pleocytosis that persists for more than one week despite giving empirical antimicrobial therapy. The predominant presentation of tubercular meningitis is with CSF lymphocytic pleocytosis and even if early phase of the disease presents with neutrophilic pleocytosis, no persistence is usually observed for more than one week.

We hereby report the case of an immunocompetent man aged 25 years with tubercular meningitis manifesting as persistent neutrophilic meningitis which is very rare as an entity in tubercular meningitis (TBM). Patient was started on anti-tubercular therapy based on the granulomas in magnetic resonance imaging (MRI) of the brain after which there was a reduction in total cell count in CSF but persisting neutrophilic predominance. Patient improved clinically and was given a full course of anti-tubercular treatment (ATT) thereafter.

Keywords: tubercular meningitis, anti-tubercular treatment, persistent neutrophilic meningitis, lymphocytic pleocytosis, granulomas

Introduction

Persistent neutrophilic meningitis is a variant of chronic meningitis which is vaguely described and is characterised by the neutrophilic persistence in the CSF over prolonged periods of time (more than one week) in association with negative CSF cultures for bacteria and other pathogens with evidence of ongoing meningeal inflammation (2).

There are number of other uncommon infectious and noninfectious causes have been described for persistent neutrophilic meningitis and among them the bacterial pathogens like Streptococcus pneumoniae, Hemophilus influenzae, Group B streptococci and Neisseria meningitidis account for vast majority of cases (5, 6). Other causes include fungal and viral infections like Herpes Simplex Virus (HSV). The initial management of neutrophilic meningitis usually consists of antimicrobial therapy directed against one or more of these common pathogens (5, 6, 9).

We hereby report a case of meningeal tuberculosis manifesting as persistent neutrophilic meningitis. This is to our knowledge the first case report of such a rare presentation of TBM as persistent neutrophilic meningitis in our region.

Case Presentation

Mr X, a 25-year-old man, previously a healthy patient presented to us with chief complaints of fever, headache, vomiting and seizures for four days for which he was admitted in a hospital in his native place and diagnosed as bacterial meningitis based on the Computed Cerebral Tomography (CCT). The patient’s complaints of fever, headache, vomiting and seizures continued for another four days despite the treatment for bacterial meningitis. The patient was referred to our hospital for further evaluation.

On admission, the patient was febrile and had a headache. Neurological examination revealed Kernig’s sign and Brudzinski’s sign. The results of the initial investigations were suggestive of aseptic meningitis. The patient was treated with intravenous ceftriaxone and metronidazole for aseptic meningitis. However, the patient continued to have fever and headache. The CSF analysis showed a total cell count of 5000 cells/µL with 80% neutrophils. The patient was started on anti-tubercular therapy based on the granulomas in the MRI of the brain. The patient improved clinically and was given a full course of anti-tubercular treatment (ATT) thereafter.

Case Report

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Tomography (CT) scan and CSF findings and was put on vancomycin and ceftriaxone for two weeks. Patient did not show signs of recovery for which patient was referred to our hospital. Patient had right hemiparesis and aphasia when he was brought to our hospital. We did MRI of the brain which showed multiple conglomerate peripheral enhancing lesions in left occipital lobe likely representing inflammatory granulomas (Figure 1 and Figure 2).

CSF showed Total Leucocyte Counts (TLC) of 700 µL with 70% polymorphs and sugar was 28 mg/dL with elevated protein levels (Table 1). CSF was negative for Acid Fast Bacilli (AFB) and Indian ink staining. Cultures for bacteria including *Mycobacterium tuberculosis*, fungus were not positive. HSV (Herpes simplex virus) PCR was also negative.

Patient was evaluated with a diagnostic possibility of partially treated meningitis and ATT and anti-epileptic drugs were started in view of the granulomas and seizures. After 10 days of therapy, patient still had low grade fever. Repeat CSF analysis showed reduction in TLC to 400 µL with 70% polymorphs (Table 1). After two weeks repeat, the MRI of the brain showed resolution of the granulomas (Figure 3). Repeat CSF at that time showed further reduction in cell counts to 240 µL with 40% polymorphs still persisting. Ruling out all other possible diagnostic probabilities with a good clinical response to ATT and also keeping in view the prevalence of tuberculosis in our region, patient was advised to complete a full course of ATT, AED and review. After a year of ATT regimen patient had fully recovered to his previous healthy state.

**Table 1.** CSF Analysis (in chronological order)

| Date     | Cell count (/µL) | Polymorphs (%) | Lymphocytes (%) | Protein (mg/dL) | CSF Sugar (mg/dL) | Blood sugar*(mg/dL) |
|----------|------------------|----------------|-----------------|-----------------|-------------------|--------------------|
| 2.6.11   | 3400             | 92             | 8               | 58              | 36                | 85                 |
| 15.6.11  | 700              | 70             | 30              | 28              | 95                | 88                 |
| 27.6.11  | 400              | 70             | 30              | 29              | 39                | 93                 |
| 2.7.11   | 270              | 60             | 40              | 27.7            | 111.7             | 87                 |
| 2.8.11   | 200              | 0              | 100             | 27.0            | 100               | 115                |

*Corresponding Blood sugar at the time of CSF analysis
However, neutrophilic pleocytosis is frequently seen, especially in the early phases of disease (5, 6, 9). If serial CSF analysis is undertaken in patients with early neutrophilic tuberculous meningitis, conversion to a lymphocytic pleocytosis usually ensues within seven days (9). Still occasional reports have documented the persistence of a neutrophilic pleocytosis for longer than one to two weeks (4, 10). In fact, some authors have emphasised that marked variability in the CSF cell count with transient increases in CSF neutrophils during the early stages of disease should suggest the diagnosis of tuberculous meningitis (6–8).

Our patient presented with clinical features highly suggestive of meningitis which was labelled to be of tubercular etiology with a strong suspicion keeping in view the appearance of inflammatory granulomas in radioimaging studies and prevalence of disease in our country. A lack of improvement in CSF parameters suggests either the therapy has been inadequate (suboptimal drug activity, dosage or CSF penetration; resistant organism) or a neurologic complication has developed (5, 6). If this lack of improvement in CSF parameters manifests as a persistent neutrophilic CSF profile, especially if bacterial cultures of CSF remain negative, then the clinician is faced with an uncommon and frequently puzzling clinical problem.

Discussion

Tuberculosis is a very rampant disease entity and one of the most common cause of chronic morbidity as far as Indian health conditions are taken into account. This statement is evident from the very fact that India accounts for a TB burden which is highest in the world (21%) accounting for an incidence of almost 1.9 million cases annually as compared to a global incidence of 9.23 million having a substantial socioeconomic impact (3).

Meningeal tuberculosis stands out as the most common form of central nervous system tuberculosis (TB) and has very high morbidity and mortality. The symptoms of this subacute disease may persist for weeks before it is diagnosed. CSF analysis typical of TBM include a pleocytosis which is lymphocytic-predominant, high protein, and decreased glucose (4–6). Nucleic acid amplification of the CSF by PCR is highly specific but suboptimal sensitivity precludes ruling out TBM with a negative test. CSF AFB smear and culture have relatively low sensitivity but yield is increased with multiple, large volume samples. Treatment for TBM should be initiated as soon as clinical suspicion is supported by initial CSF studies Initial CSF evaluation along with early clinical suspicion warrant treatment initiation (4).

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Figure 3. MRI brain FLAIR sequence in the axial plane after two weeks of receiving anti tubercular treatment showed significant reduction in the peri lesonal vasogenic edema and ring enhancing lesion in the splenium of corpus callosum is no longer visualised.
In our patient all the usual and unusual causes of persistent neutrophilic meningitis were effectively ruled out by running all possible tests comprising bacterial, fungal cultures and viral markers which did not show any significant results. Keeping in mind the presence of inflammatory granulomas and endemicity of tuberculosis in our region, we diagnosed and treated him as TBM.

Conclusion

To conclude, neutrophilic pleocytosis in CSF can be seen in TBM even beyond one month in rare circumstances and the patient should be treated as early as possible on the basis of clinical and radiological findings. Further clinical research is still required to give a deeper insight to such rare finding.

Authors’ Contributions

Analysis and interpretation of the data: SHS
Drafting of the article: CB, SS
Critical revision of the article for important intellectual content: TKR
Final approval of the article: TKR

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