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# Chronic Neutrophilic Meningitis in Tuberculous Infection: A Rare Case Presentation and review of the literature

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## Background

Persistent neutrophilic pleocytosis syndrome is a rare form of tuberculous meningitis that is defined as the persistence of neutrophils in cerebrospinal fluid for more than 7 days, in association with the clinical features of meningitis (headache, fever, and positive meningeal signs).[1] The exact pathogenesis of this syndrome is not well known yet, and it has many diverse etiologies, including infectious and noninfectious ones. among infectious ones: bacteria such as Nocardia and Actinomyces, and systemic mycoses such as Aspergillus and the zygomycetes, as well as mycobacterium.[2] This entity is very rare in immunocompetent patients, and most of the cases are due to infectious causes in those who are immunocompromised. The usual scenario in such cases is initiating broad-spectrum antimicrobial agents without any improvement, therefore the diagnosis is difficult initially and often delayed. Therefore, the epidemiologic features and clinical profile may offer clues to the etiologic agent, especially in the immunocompromised host.[3]

## Case report:

Ms. M, a 35-year-old woman who had been previously healthy and had no significant medical history or chronic drug use, was pregnant in her first trimester; her fetus was the product of in vitro fertilization (IVF). She presented with clinical features of meningitis, including headache, fever, and neck stiffness, as well as an unintentional weight loss of more than 10 kilograms over the last month. On examination, she was febrile, her temperature was 37.9°C. meningeal signs were positive, fundoscopy was normal, there was a skew eye deviation, brain magnetic resonance imaging (MRI) was unremarkable, and CSF gram stain and cultures were obtained, which demonstrated no organisms or growth, respectively. There was neutrophilic pleocytosis, high protein, and low sugar on 5.4.2021 as shown in the Table (1). She was diagnosed as having pyogenic meningitis but with no clinical response to one week duration of each of ceftriaxone and vancomycin, due to the persistence of symptoms and lack of signs of recovery, the antibiotics were changed to meropenem vial without response and follow up CSF study on 13.4.2021 showed an increment of cells

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from 140 to 1280, with 71% being neutrophils. Five days later, the patient developed focal convulsions with loss of consciousness, left-sided weakness, and a new CT scan was done, which showed hydrocephalus with right thalamic infarction Figure (1) and Figure (2). Assuming she has TB meningitis, anti-tubercular medicines and steroids were started an external drain was performed for her. CSF meningitis PCR panel was sent; the PCR for TB came out positive Figure (3). The last CSF was done on 21.4.2022 and again showed 80% neutrophils. On follow-up She and her child both survived, however she was able to walk with some assistance and her baby had a low birth weight. She also suffered mild to moderate weakness and spasticity in both her upper and lower limbs.

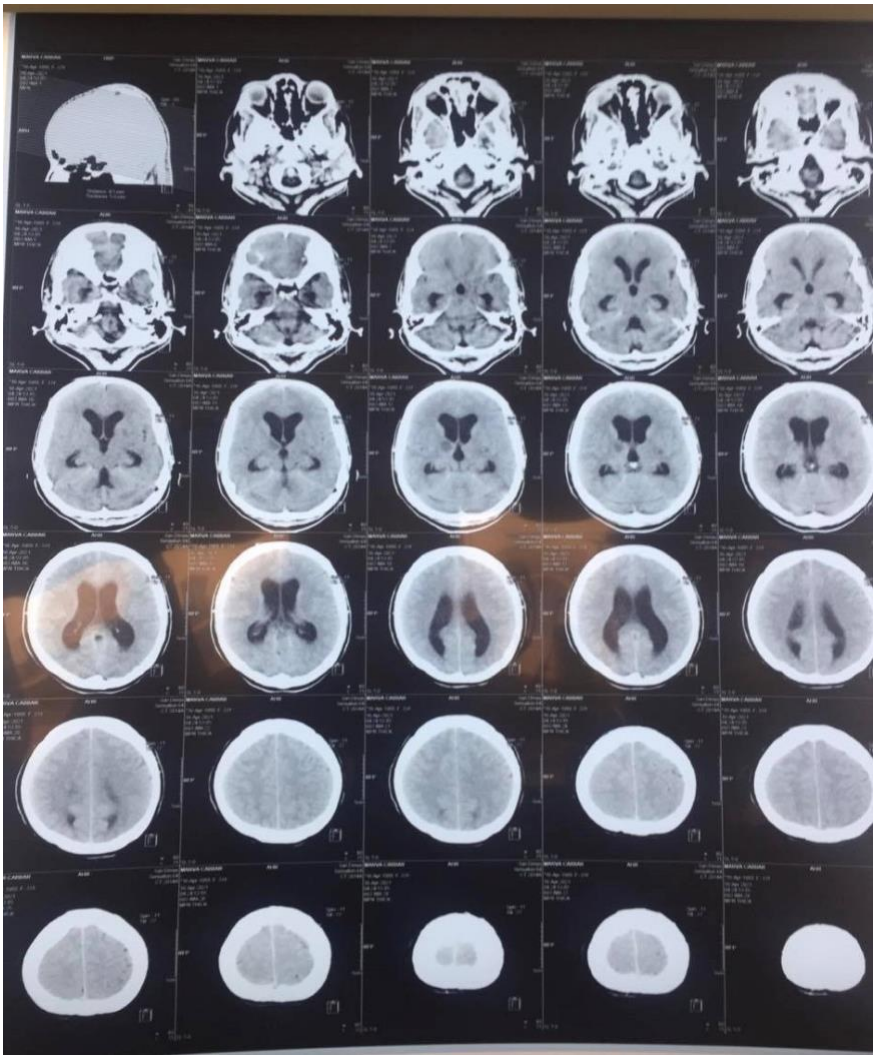

**Figure (1):** Axial section of the CT- Scan of brain showing dilated ventricles (hydrocephalus) with right thalamic infarction.



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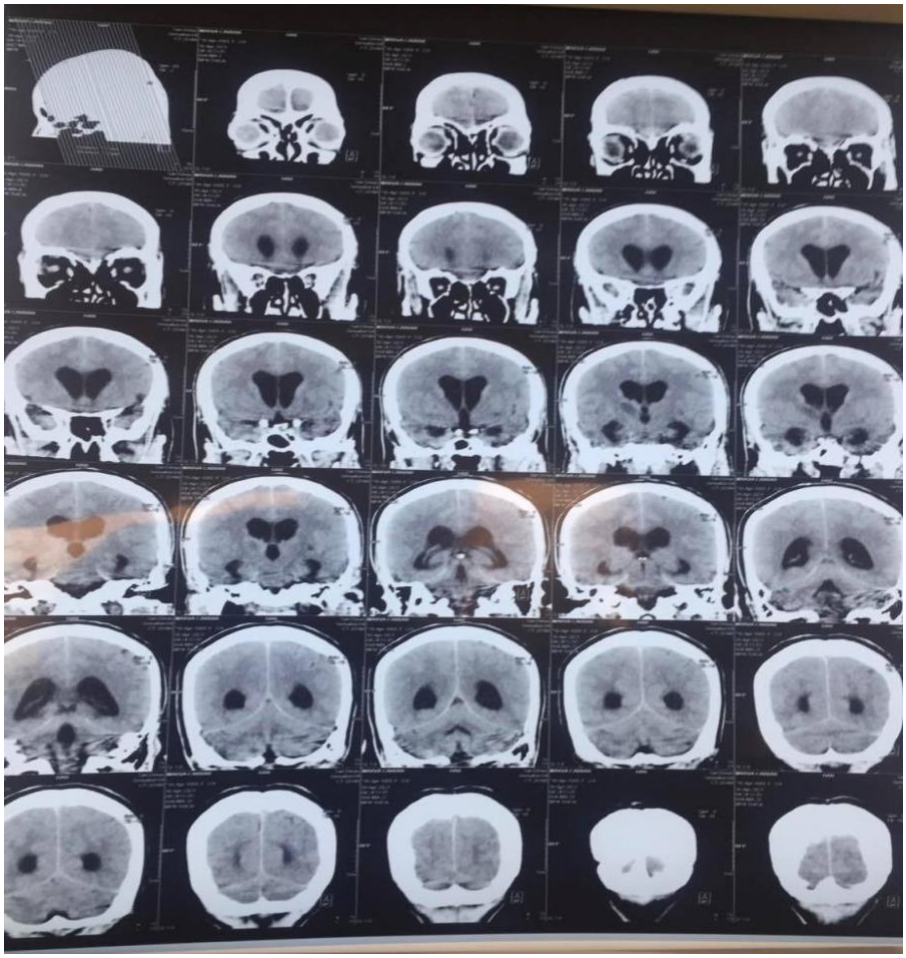
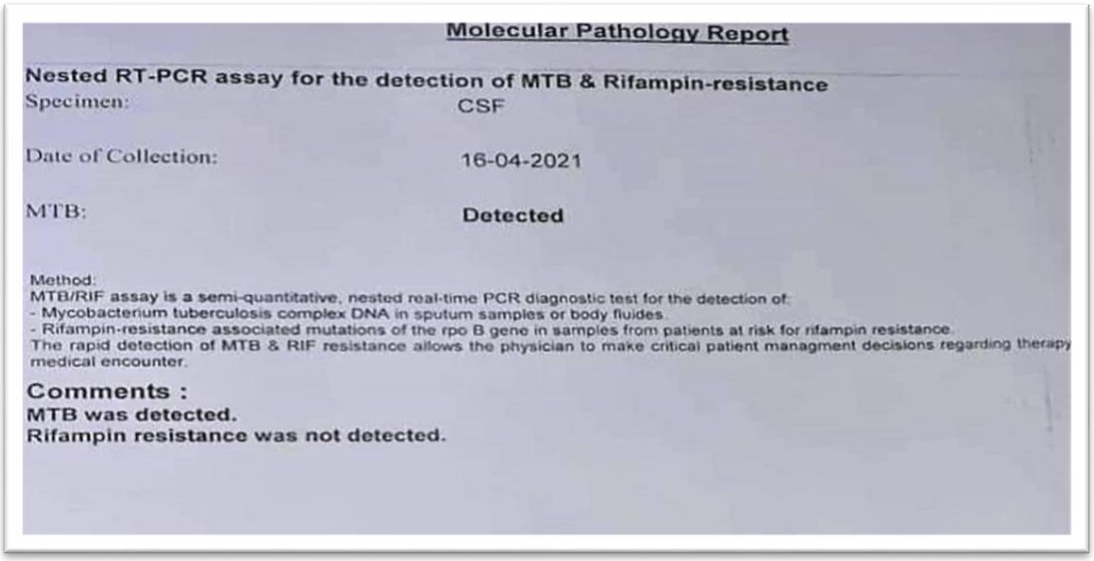


**Figure (2):** Coronal section of the CT- Scan of brain showing dilated ventricles (hydrocephalus) with right thalamic infarction.



**Molecular Pathology Report**

**Nested RT-PCR assay for the detection of MTB & Rifampin-resistance**

Specimen: CSF

Date of Collection: 16-04-2021

MTB: **Detected**

Method:
MTB/RIF assay is a semi-quantitative, nested real-time PCR diagnostic test for the detection of:
- Mycobacterium tuberculosis complex DNA in sputum samples or body fluides.
- Rifampin-resistance associated mutations of the rpo B gene in samples from patients at risk for rifampin resistance.
The rapid detection of MTB & RIF resistance allows the physician to make critical patient managment decisions regarding therapy medical encounter.

**Comments :**
**MTB was detected.**
**Rifampin resistance was not detected.**

**Figure(3):** displays the result of the CSF PCR which was positive



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

| Date | Cell count (/μL) | Polymorphs (%) | Lymphocytes (%) | Protein (mg/dL) | CSF Sugar (mg/dL) | Blood sugar[a] (mg/dL) |
|---|---|---|---|---|---|---|
| 5.4.21 | 140 | (All) | zero | 187 | 31 | 85 |
| 13.4.21 | 1280 | 70 | 30 | 102 | 28 | 85 |
| 18.4.21 | 60 | 72 | 30 | 65 | 28 | 93 |
| 21.4.21 | 40 | 80 | 20 | 62 | 30 | 87 |

[a] Corresponding Blood sugar at the time of CSF analysis

## Discussion

Tuberculosis (TB) is one of the most progressive infectious diseases caused by Mycobacterium tuberculosis. This pathogen is the first cause of mortality linked to a single pathogen worldwide, especially in poor and developing countries. Although there has been a decline in the incidence of TB in Iraq recently, it is still out of control in our country.[4, 5] The process of diagnosis of TBM is usually done by combining clinical features along with CSF finding of predominant lymphocytes, low sugar, high protein, CSF culture, and acid fast bacilli (AFB), which offer low yield for organism detection ,the pooled sensitivity and specificity of CSF AFB is about 8% and 100% respectively , but PCR or nucleic acid amplification (NAAT) has higher sensitivity rate about 70%.[6] During the early phase of tuberculous meningitis, there may be neutrophilic pleocytosis, which may mask the early diagnosis of TB meningitis, but after a week, it usually starts to transform into lymphocytes in the CSF.[7] According to several authors, a huge variability in CSF cell counts and the increment of cells during the early phase of the meningitis support the diagnosis of tuberculous meningitis.[8] Neurologists find it puzzling when cases of pyogenic meningitis or persistent neutrophils in the CSF don't improve because cultures may not be helpful due to antibiotics use, which should raise doubt about the diagnosis and cause them to consider other causes like tuberculosis or nocardia as additional causes for antibiotic resistance, Ineffective treatment (inadequate medication action, dose, or CSF penetration; resistant organisms) or the emergence of a neurologic consequence (hydrocephalus) .[2] Here, the patient was pregnant in her first trimester and had undergone in vitro fertilization (IVF). According to Yao et al., the incidence of tuberculosis in pregnant IVF embryo transfer patients is serious and needs early recognition and management to prevent complications for both mother and fetus.[8]

## Conclusion:

To conclude, tuberculous meningitis runs a fatal course if left untreated, and persistent neutrophilic pleocytosis is a poorly described variant of TB meningitis; therefore, its earlier detection is of paramount importance. The presence of neutrophils in CSF in tuberculous meningitis beyond 2 weeks indicates aggressive disease. Clues that helped us to review the diagnosis were the subacute rather than acute course, the non-responsiveness to broad spectrum antibiotics and increment of CSF cell count over subsequent exams as well as radiological features. Further research is needed to elaborate on this entity more clearly.

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