When time is short, and we are late!: A story of chronic meningitis

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ABSTRACT

We often face situations when the exact etiological diagnosis of meningitis is difficult. The reason behind this is that many pathogens have similar clinical, radiological, and laboratory pictures. The low yield of the pathogen in cerebrospinal fluid (CSF), non-availability of detail tests in all corners of the world, delay in availability of reliable results (like cultures), and difficulty in performing confirmatory tests like brain biopsy (in inconclusive cases) make the job of a clinician challenging. We report here a case where a late diagnosis of a disease owing to inconclusive results leads to dissemination. The complications following the introduction of the treatment based on presumption lead to further difficulty. We remained inclined to our diagnosis based on clinical judgement, acknowledged and managed the inflammatory changes secondary to the infection, and finally won the long battle. So, sometimes we need to make decisions based on clinical grounds. We need to depend on the fact that uncommon presentations of common diseases are commoner than a common presentation of uncommon diseases.

Keywords: Chronic meningitis, disseminated tuberculosis, tuberculosis-immune reconstitution inflammatory syndrome

Case Report

An eighteen-year-old woman without known comorbidity was at her baseline till six months before presentation. She had an episode of lower respiratory tract infection when the etiological evaluation was inconclusive. Though improved, she experienced decreased appetite and lost ten kilograms of body weight in the next six months until the second presentation.

A persistent moderate grade fever with holo-cranial headache and neck stiffness for two weeks was her next symptom. They diagnosed tubercular meningitis along with lower respiratory infection (based on clinical presentation only) and started antitubercular drugs with steroids at a local health facility. She improved initially, but after ten days, she presented to our institute with hepatitis (SGOT of 68 IU/L, SGPT of 245 IU/L). During presentation, she was afebrile without meningeal signs or focal neuro-deficit. We changed antitubercular drugs (stopped all and started moxifloxacin and ethambutol), managed hepatitis, and started an extensive search for infective aetiology. Her blood counts and inflammatory markers were normal. Her magnetic resonance imaging MRI of the brain revealed evidence of granulomatous lesion and leptomeningeal enhancement.

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Cerebrospinal fluid (CSF) revealed cells of 150/cubic mm. (65% neutrophils, 35% lymphocytes), protein of 103 mg%, glucose of 68 mg% (corresponding blood glucose of 110 mg%). The comprehensive infection panel, CSF culture, and tubercular Gene X-pert in CSF were negative. Computed tomography (CT) scan of the chest revealed evidence of fibro-atelectatic bands in lung parenchyma with left-sided mild pleural effusion and thickening Figure 1. The pleural fluid examination was exudative but revealed no definite infective aetiology. We ruled out other infective aetiologies, vasculitis, and the possibility of sarcoidosis in this young lady.

She remained asymptomatic except for a mild headache, and within seven days, her hepatic enzymes touched baseline values. We started the gradual reintroduction of isoniazid and rifampicin, followed by pyrazinamide. After five days of symptomatic improvement and biochemical stability, the patient had high-grade intermittent fever with neck and lower back pain. No neuro deficit was clear, but she developed a prominent meningeal sign.

The repeat MRI of the brain Figure 2 revealed tiny enhancing lesions in the right caudate, the right middle frontal cortex, and the left middle cerebellar peduncle. Leptomeningeal enhancement was clearer along the nerve sheath of the trigeminal, seventh, and eighth cranial nerves. MRI of the spine with contrast also revealed mild diffuse leptomeningeal enhancement along the spinal cord and cauda equina nerve roots. CSF study this time revealed an increased cell count of 430 cells/cubic mm. (Neutrophils of 77% and Lymphocytes of 21%), higher protein of 323 mg%, CSF glucose of 54 mg% and CSF TB Gene X-pert was positive this time. We continued antitubercular drugs, hiked up steroids (from dexamethasone four mg orally once daily to thrice daily in injectable form) after ruling out secondary infection.

Her fever subsided, and she improved gradually. We reduced the dose of dexamethasone to twice daily and made an oral form. Her condition deteriorated again just before discharge: temperature hiked up (intermittent fever of up to 103-degree Fahrenheit) with increased headache, neck, and back pain. Repeated blood cultures were non-contributory. We reintroduced steroids to the higher dose and injectable form, and she again improved.

After three more weeks of hospital stay, we finally discharged her home with a full dose of standard antitubercular regimen and oral dexamethasone (tapered off after two months).

**Discussion**

We need tubercular meningitis to be diagnosed as fast as possible (incidence: 193/100,000 population). This is because it is an important prognostic indicator for reduced death and deficit. As the bacillary loads in CSF remain low, the diagnostic tests are mostly insufficient. CSF Ziehl-Neelsen has sensitivity of 10–20%. Mycobacterial culture is more sensitive (approximately 60–70%) but takes more than weeks. Though clinical diagnostic algorithms are there, they are diverse, and their applicability in all populations is untested.

Our patient had probable onset of symptoms at least six months before presentation as lower respiratory tract infection and continued to cause constitutional symptoms (anorexia, loss of weight). The silent destroyer (tuberculosis) had broken through her immunological barrier and later caused the dissemination of the disease.

Her reason for new-onset deterioration may be a progression of the disease process or might be Tuberculosis-immune reconstitution inflammatory syndrome (TB-IRIS).

The fast killing of mycobacteria by anti-TB therapy may release large amounts of mycobacterial antigens, which can precipitate this type of response in some selected patients.

The median time to onset of the tuberculosis-immune reconstitution inflammatory syndrome (TB-IRIS) is 21–56 days after starting anti-tuberculous treatment in non-HIV patients.

The deterioration in our patient was, however, within seven days of the full antitubercular drug initiation. So, it is too early for immune reconstitution inflammatory syndrome (IRIS) though still possible. It may also be because of the progression of...
tuberculosis infection, knowing the fact that we could introduce a full regimen of antitubercular drugs, but it was late. There are no clear guidelines for the management of TB-related IRIS (non-HIV patients). A significant proportion of patients improve spontaneously in few-weeks-time with a continuation of the same antitubercular drug regimen. However, oral steroids (prednisolone 0.5-1 mg/kg/day) may be required in a selected group of patients with marked deterioration accompanied by features of organ malfunction.

Our case highlights the following key points:
1. Early diagnosis of tuberculosis is important to avoid morbidity and mortality.
2. Physicians should be acquainted with a modified treatment regimen in disseminated tuberculosis with organ dysfunction (like hepatitis in our case).
3. Severe inflammation in serious infection is obvious, and steroid is the greatest savior in that context.
4. We should not forget the possibility of IRIS in tuberculosis (non-HIV patients) and give necessary treatment.
5. The dose and duration of anti-tubercular treatment (ATT)/steroid should be individualized and may not follow a definite guideline always.

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Conflicts of interest
There are no conflicts of interest.

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