Tuberculosis-immune reconstitution inflammatory syndrome in an immunocompetent patient

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Abstract

Tuberculosis-immune reconstitution inflammatory syndrome is commonly seen among patients with acquired immunodeficiency syndrome either as a paradoxical worsening of an already diagnosed disease or as an unrevealing of a dormant infection. There is evidence of paradoxical worsening of central nervous system tuberculosis (CNS-TB) once the treatment is instituted even among immunocompetent patients leading to significant morbidity. We report a case of a previously well young woman with paradoxical worsening of CNS-TB after commencement of treatment. This case highlights an important possible clinical sequelae of CNS-TB, a practicing physician should be aware of.

Key words: Tuberculosis-immune reconstitution inflammatory syndrome, central nervous system tuberculosis

Introduction

Tuberculosis (TB) is an intracellular bacterium manifesting commonly as a chronic pulmonary infection in the tropics with poor socio-economic backgrounds. TB has contributed immensely to the healthcare burden of Sri Lanka with around 8000 cases reported every year.(1) Tuberculosis-immune reconstitution syndrome (TB-IRIS) is a paradoxical worsening of an already diagnosed TB or unravelling of a dormant TB infection upon restoration of a previously obtund immune system. This usually occurs in the setting of treating an acquired immunodeficiency syndrome (AIDS) or stopping an immunomodulating drug like Infliximab.(2-5) Even among immunocompetent patients paradoxical worsening of central nervous system tuberculosis (CNS TB) once the treatment is instituted has been reported.(6-10)

Case presentation

We discuss a 22-year-old woman, who presented with an insidious onset dry cough, shortness of breath and constitutional symptoms for three months. The patient lived in a congested home with her extended family. However, there was no contact history of tuberculosis (TB). The patient was diagnosed with miliary TB with a positive sputum GeneXpert study and a chest x-ray demonstrating miliary mottling. The bacterial cultures were negative. She was started on anti-TB therapy. A week into the treatment she complained of a severe headache with neck stiffness. The cerebrospinal fluid (CSF) analysis revealed 121.8 mg/dL of proteins, 60 lymphocytes / mm³, with a significant CSF sugar drop and a positive CSF TB PCR. MRI scan of her brain revealed multiple rim

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enhancing tuberculomas in both cerebral hemispheres and cerebellum.

For management of CNS-TB intravenous dexamethasone regimen was commenced and continued for four weeks. It was subsequently converted to oral prednisolone. The patient was stable and was discharged.

Two weeks later she presented to us again with a worsening headache and early morning vomiting without focal neurological signs. Further imaging revealed multiple new tuberculomas and enlargement of the existing lesions.

Repeat CSF analysis showed 206 mg/dL of proteins, 32 polymorphs and 09 lymphocytes per mm3 and an ADA of 5.1 U/L. The CSF TB PCR, TB culture and pyogenic culture were negative. The sputum TB culture which was done during the last admission was traced and it did not show antibiotic resistance. The erythrocyte sedimentation rate was 55 mm and the c- reactive protein was only 9 mg /dL. However, the patient had ongoing fever spikes. Blood and sputum cultures were repeatedly sterile.

Paradoxical worsening of her clinical condition made us consider TB-IRIS. Thus, the patient underwent further evaluation to look for an immunocompromised status. The HIV status was negative. The full blood count, immunoglobulin and complement levels, neutrophil function tests and flow cytometric assessment of lymphocytic sub-types revealed an adequately functioning immune system. TB-immune reconstitution inflammatory syndrome occurring in an immunocompetent patient was considered as the working diagnosis after a multi-disciplinary discussion. The patient was started on an IV dexamethasone regimen with 0.4 mg /kg for 2 weeks, 0.2mg/kg during the third week and 0.1mg/kg in the fourth week. After a course of IV steroids, she showed a considerable response and was started on oral prednisolone 1mg/kg upon discharge. Patient had an uneventful recovery.

Discussion

Disseminated TB in an immunocompetent young girl is uncommon. Furthermore, the development of TB-IRIS is even rarer among immunocompetent individuals. In this case, an alternative explanation for the deterioration of central nervous system tuberculosis (CNS-TB) such as non-compliance to drugs, sub-optimal quality of the drugs, drug resistance in the given epidemiological background or poor delivery of the anti-TB therapy into the deep brain matter should be thought of.

There is evidence of resolution of infection in the lungs of this patient with treatment. Therefore, a
drug resistant variant or non-compliance is less likely despite a selective non-penetration of the brain parenchyma could be an issue. Isoniazid is said to have good CNS penetrance as opposed to rifampicin whose CNS bioavailability is roughly around 20% that of plasma. It is also postulated that even though rifampicin has poor CNS penetrance the amount of active drug in CSF is comparable to that of plasma. (11,12) The negative culture and PCR in subsequent cerebrospinal fluid could be considered as evidence of resolving parenchymal infection in this patient.

Sri Lanka where tuberculosis is endemic. Unfortunately, there is a lack of data on treatment options of this condition with high morbidity.

**Conclusion**

The paradoxically worsening CNS-TB in an immunocompetent individual is increasingly identified. This case highlights an important entity that internists in our region should be aware of as South East Asia carries a high disease burden of TB. We would like to emphasize the importance of adherence to glucocorticoid regimen when treating CNS-TB.

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