



**PRIMARY DRUG RESISTANCE TO RIFAMPICIN IN NEW
TUBERCULAR MENINGITIS PATIENT WITH HIV INFECTION**

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ABSTRACT

Tubercular meningitis (TBM) is the most devastating consequence of infection with Mycobacterium tuberculosis. Rifampicin resistant TBM is the most severe form of Mycobacterium Tubercular infection. The estimated mortality due to TBM in India is 1.5 per 100,000 population. Patients with HIV and active tuberculosis have an increased risk of extra pulmonary tuberculosis, and this risk will also increase with declining CD4+ count. Primary drug resistance is due to infection with

a resistant strain originating from a patient who has acquired resistance as a result of inadequate treatment. Patients of TBM and HIV are swallowing lots of drugs for many opportunistic infections beside TBM ,therefore chances of acquired drug resistance is high. Rifampicin resistant (TBM and Pulmonary) TB is considered as MDR tuberculosis, even though it is not MDR, therefore treatment for these condition, the guidelines have been issued by the Revised National Tuberculosis Control Programme (RNTCP), Guidelines on Programmatic Management of Drug Resistant TB (PMDT) in India.

KEY WORDS: Tubercular meningitis, HIV/AIDS, Mortality, RNTCP, PMDT.

INTRODUCTION

Tuberculosis of the central nervous system (CNS) may present as meningitis, like all forms of tuberculosis, infection is acquired by the inhalation of bacilli within droplet nuclei, followed by early hematogenous dissemination. The estimated mortality due to TBM in India is 1.5 per 100,000 populations. Patients with HIV and active tuberculosis have an increased risk of

extra pulmonary tuberculosis, and this risk will also increase with declining CD4+ count^[1], HIV is associated with increased risk of activation of latent infection. Without HIV infection, individuals with latent infection have a lifetime risk of developing tuberculosis that ranges between 10% and 20%. In contrast, the HIV-infected individual will carry a 10% annual risk of progression to active infection, with increasing risk as the CD4+ count declines.^[2] A critical step in the development of TBM is the deposition of mycobacteria adjacent to the subarachnoid space or ventricles during this dissemination TBM, Rich and McCordock found evidence that, in almost all cases, a subependymal or subpial tuberculoma (“Rich focus”) had ruptured into the subarachnoid space.^[3,4] They postulated that this rupture was the event that precipitated the development of TBM. Rupture of a Rich focus into the cerebrospinal fluid (CSF) induces an immune response and leads to the formation of a tuberculous exudate surrounding the brainstem and cerebellum. Tuberculous meningitis (TBM) is the most devastating consequence of infection with *Mycobacterium tuberculosis*. In case of rifampicin resistant TBM is a most severe form mycobacterial tubercular infection, microbiological confirmation in TBM is very difficult, and due to delayed diagnosis, treatment is often delayed, which increase mortality and morbidity.^[5] Approximately a third of patients die soon after presenting to hospital, and many of those surviving are left with severe neurological sequelae. In patients with HIV co-infection, mortality exceeds 60%. We report a case of primary drug resistance to rifampicin in new tubercular meningitis patient with HIV infection.

CASE REPORT

A 38 year old HIV male referred to the chest OPD for management of Rifampicin resistant *Mycobacterium Tubercular Bacterial meningitis* (TBM) with the complaints of fever, headache with altered sensorium, backache, vomiting, other routine **investigations** were (Hb 8.4gm%, TLC 10,900/cmm), ESR-50/hr, HbA1c-5.8gm%, TSH-2.4Uiu/ml, ECG-Normal, urine-Normal, stool were not remarkable, (CSF) cerebral spinal fluid positive for AFB and it was resistant to Rifampicin by CBNAAT/Gen x-pert (cartridge based nucleic acid amplification test), cytology TLC-180/mm³, DLCp-20%, l-80% and CD4 was 36. His x-ray chest and, CECT Head-No e/o ICSOL/ring enhancement lesion, CECT chest normal, CECT abdomen shows multiple hypo-dense lesion in spleen? Abscess, Cysts, MRI brain Basal enhancement of maninges present, no focal lesion, No e/o PMPE. There is no history of contact to MDR and Rifampicin resistant pulmonary or extra pulmonary TB, other systems are normal. He was non alcoholic, non tobacco chewing and having history of contact to sex

worker. Laboratory parameters included CSF cell count and levels of protein, glucose and adenosine deaminase (ADA). CSF evaluation for Mycobacterium tuberculosis was done by CBNAAT/Gen x-pert (cartridge based nucleic acid amplification test) and (CSF) cerebral spinal fluid positive for AFB and it was resistant to Rifampicin, The radiological details of contrast enhanced CT brain, MRI brain, CT chest.

DISCUSSION

Primary drug resistant is due to infection with a resistant strain originating from a patient who has acquired resistance as a result of inadequate treatment. Thus the patient with primary resistance to a drug has never taken this drug in the past, but the original source of infection must have done so. In clinical practice, it is difficult to determine whether the resistance is primary, since the patients themselves may not know or may deny, that they have had previous treatment for tuberculosis. Overall, among people with newly diagnosed pulmonary tuberculosis, there was resistance to at least one drug in 9.9% of cases, multidrug^[6,7] resistance (resistance to RIF and INH) in 1- 1.4%. Patients of TBM and HIV are swallowing lots of drugs for many opportunistic infections beside TBM, therefore chances of acquired drug resistance is high, The data regarding the Rifampicin resistant TBM and MDR TBM is not much available and the data regarding the prevalence of TBM in HIV is scarce and scattered. Study in children <12 y of age in India, 6.5% TBM patients were reported have HIV coinfection^[8] Tuberculosis has also emerged as a major infection complicating HIV in developing countries. HIV is believed to increase the risk for progression of tubercular infection to disease by depressing the cell mediated immunity. On the other hand, Mycobacterium tuberculosis infection also supports HIV-I replication through its effect on the host's cytokines, chemokines, and their receptors.^[9, 10] Rifampicin resistant TBM and Pulmonary TB is considered as MDR tuberculosis, even though it is not MDR, therefore treatment for these condition, the guidelines have been issued by the Revised National Tuberculosis Control Programme (RNTCP), Guidelines on Programmatic Management of Drug Resistant TB (PMDT) in India. The patients of HIV and neurologically TB (TBM) they must be linked to ART centers, treatment regimen and schedule for EP (Extra pulmonary) Rifampicin resistance MDR cases will remain the same as for pulmonary. Based on guidelines on Antiretroviral therapy for HIV and TB should be started on ART as soon as possible after starting TB treatment. However treatment is more difficult and adverse events more common.^[11, 12]

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