Multiple Side Effects Of Second Line Antitubercular Therapy In A Single Patient

S Verma, V Mahajan

Citation

S Verma, V Mahajan. *Multiple Side Effects Of Second Line Antitubercular Therapy In A Single Patient*. The Internet Journal of Pulmonary Medicine. 2007 Volume 9 Number 2.

Abstract

Treatment of Multi-Drug Resistant Tuberculosis (MDR-TB) with second line anti tubercular drugs is associated with lot of side effects which can be dangerous. Here we are reporting a case of MDR-TB having multiple side effects from second line chemotherapy in the same patient which is a rare presentation.

INTRODUCTION

MDR-TB is a growing hazard to human health world wide and threat to control of tuberculosis[1]. Treatment of MDR-TB is difficult, complicated, much costlier, challenging and needs experience and skills. Reserve drugs are frequently associated with very high rates of unacceptable adverse drug reactions, needing frequent interruption and change of regimen[2]. All measures should be taken to persuade and encourage patients not to stop treatment despite all its discomforts to prevent morbidity, mortality and transmission of MDR-TB.

CASE REPORT

A 45 years old male, nonsmoker patient was admitted in emergency department with the chief complaint of haemoptysis. He was known as a case of pulmonary tuberculosis for the last two years and had taken adequate anti tubercular therapy twice before coming to our department. Initially he was declared cured after category I but was again given category II due to relapse. He was improving on category II initially but again deteriorated. He was non diabetic. There was history of contact of pulmonary tuberculosis in the family who was on second line drugs from last one year.

On physical examination, the patient was febrile with a pulse rate of 92/min, respiratory rate of 20/min and a right arm supine blood pressure of 126/70 mmHg. There was no pallor, cyanosis or clubbing. Chest examination was unremarkable on inspection, palpation and percussion. On auscultation bilateral course crepts were audible. Examination of other systems was unremarkable. Routine investigation showed; hemoglobin: 11 gm%, total leukocyte count: 10700/mm^3, differential count: neutophils 68%, lymphocyte 30%, eosinophil 2%. Sputum samples for acid-fast bacilli were found to be positive on three consecutive days.

Chest X-ray PA view revealed bilateral fibrocavitory lesions confined mainly to upper lobes. Thinking of the diagnosis of multi drug resistant tuberculosis, sputum culture and sensitivity for mycobacterium tuberculosis was sent. He was started on empirical second line chemotherapy regimen comprising of Kanamycin, Isoniazid, Para amino salicylic acid, Ethionamide, Cycloserine and Ofloxacin according to weight.

15 days after starting the treatment, he got two episodes of seizures. He had no past history of any similar episode. Computed Tomograph head and cerebro spinal fluid(CSF) was within normal limits. So thinking cycloserine or ofloxacin to be the culprit, both drugs were stopped and prophylactic phenytoin was started. 20 days after the treatment with the remaining drugs, he was complaining of hearing impairment which was increasing slowly. Audiometry was suggestive of bilateral sensori-neural hearing loss. So kanamycin was stopped immediately thinking the side effect to be irreversible. The regimen was reduced to only three drugs to make the patient tolerate these drugs. But to make the condition worse, he was complaining of severe burning sensation in both hands and feet. Isoniazid, cycloserin and ethionamide were thought to be the culprits. He was referred to a neurologist and pyridoxine was given for relief. A trial of cycloserin and ofloxacin was given

successively and he tolerated now without any seizure episode. So he was given a five drug regimen and he is still in follow up with clinical improvement.

DISCUSSION

Multi drug resistant tuberculosis (MDR-TB) is a growing hazard to human health world wide. MDR-TB is suspected if sputum is persistently positive for acid fast bacilli with clinical and radiological deterioration after multiple courses of irregular/regular treatment. MDR tuberculosis is defined as disease due to M tuberculosis that is resistant to Isoniazid (H) and Rifampicin (R), with or without resistance to other drugs[3]. Primary drug resistance is defined as drug resistance in a patient who has not received any anti-tubercular treatment in the past, while acquired drug resistance is defined as resistance that develops in a patient who has received prior chemotherapy[4].

Second line drugs are frequently associated with very high rates of unacceptable adverse drug reactions, needing frequent interruption and change of regimen. Some authors reported that 41% patients, experienced some side effects and only 21.1% patients required stoppage or change of drug in their study of 39 patients of MDR-TB[5].

Close monitoring of the patient is necessary to ensure that the adverse effects of second line drugs are recognized quickly. The ability to monitor patients for adverse effects daily is one of the major advantage of Directly Observed Treatment as in category IV treatment running as a pilot project in some states of India. The majority of adverse effects are easy to recognize. Commonly, patients will volunteer that they are experiencing adverse effects. However, it is important to have a systematic method of patient interviewing since some patients may be reticent about reporting even severe adverse effects. Other patients may be distracted by one adverse effect and forget to tell the physician about others. The physician should be trained to screen patients regularly for symptoms of common adverse effects : rashes, gastrointestinal symptoms(nausea, vomiting, diarrhea), psychiatric symptoms(psychosis, anxiety, depression, suicidal ideation), jaundice, ototoxicity and peripheral neuropathy[6].

Prompt evaluation, diagnosis and treatment of adverse effects are extremely important, even if the adverse effect is not particularly dangerous. If the adverse effect is mild and not dangerous like peripheral neuropathy in our patient, continuing the treatment regimen, with the help of ancillary drugs if needed, is often the best option[7]. In patients with highly resistant tuberculosis, a satisfactory replacement drug may not be available, so that substituting a drug will make the treatment regimen less potent. Some adverse effects may disappear or diminish with time, and patients may be able to continue receiving the drug if sufficiently motivated like cycloserine of ofloxacin induced seizures in our patient. Reducing the dosage of the offending drug is another method of managing adverse effects.

Some adverse effects are irreversible like ototoxicity and the offending drug like kanamycin should not be given again to the patient for ever. So, again we can say that treatment of MDR-TB with second line drugs is less efficacious and is associated with potential side effects which can be irreversible. It is better to treat drug sensitive TB effectively with right combination of drugs to prevent the emergence of MDR-TB.

CORRESPONDENCE TO

Dr. S.K.Verma Associate Professor Department of Pulmonary Medicine Chhatrpati Shahuji Maharaj Medical University,UP Lucknow (India)-226003. Phone – 0522 – 2254346 Email – drskverma@rediffmail.com

References

1. Cohn DL, Bustreo F, Raviglione MC. Drug resistant tuberculosis. Review of the world wide situation and the WHO / IUATLD Global Surveillance Project. International Union Against Tuberculosis and Lung Diseases. Clin Infect Dis 1997; 24:S121-S130.
2. Furin JJ, Mitnick CD, Shin SS, Bayona J, Becerra MC, Singler JM et al. Occurrence of serious adverse effects in patients receiving community-based therapy for multidrug-resistant tuberculosis. Int J Tuberc Lung Dis 2001;5:648-55.
3. Treatment of tuberculosis:guidelines for national programmes, 3rd ed. Geneva, World Health Organization, 2003 (WHO/CDS/TB/2003.313).
4. Prasad R. Management of multi drug resistant tuberculosis : practitioner's view point. Indian J Tuberc 2007; 54:3-11.
5. Prasad R, Verma SK, Sahai S, Kumar S, Jain A. Efficacy and safety of Kanamycin, Ethionamide, PAS and Cycloserine in multi-drug resistant pulmonary tuberculosis patients. Indian J Chest Dis Allied Sci 2006; 48:183-186.
6. Nathanson E. Adverse events in the treatment of multidrug resistant tuberculosis : results from the DOTS-Plus initiative. . Int J Tuberc Lung Dis 2004;8:1382-1384.
7. Shin SS, Hyson AM, Castaneda C, Sanchez E, Alcantara F, Mitnick CD et al. Peripheral neuropathy associated with treatment for multidrug-resistant tuberculosis. Int J Tuberc Lung Dis 2003;7:347-53.

Author Information

S.K. Verma
Associate Professor, Department of Pulmonary Medicine, Chhatrpati Shahuji Maharaj Medical University

Vineet Mahajan
Resident, Department of Pulmonary Medicine, Chhatrpati Shahuji Maharaj Medical University