CASE REPORT

Antitubercular drug-induced violent suicide of a hospitalised patient

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SUMMARY

We present a case where a young adult male, on treatment for multidrug-resistance tuberculosis (MDR-TB), developed drug-induced psychosis. The psychiatric symptoms were ascribed to the anti-TB drug and were duly withdrawn by the treating doctors and supplemented with other drugs. However, the victim continued to have psychiatric symptoms and committed suicide in the hospital. He ended his life in a violent manner by stabbing and cutting himself with a kitchen knife. The case is briefly reported in this paper with a discussion on anti-TB drug-induced psychiatric effects leading to suicide.

BACKGROUND

Tuberculosis (TB) is one of the infectious diseases that has created health and social problems especially in developing countries like India. The prevalence of all cases of TB in India as per 2009 WHO report is two million. The report also shows India at the top of the list of countries in the total number of multidrug-resistance TB (MDR-TB) cases (1, 31 000).¹ The Revised National Tuberculosis Control Programme (RNTCP) in India advocates category IV treatment for MDR-TB.² This regimen comprises of six drugs—kanamycin (K), levofloxacin, ethionamide, pyrazinamide (Z), ethambutol (E) and cycloserine (Cs)—during 6–9 months of the intensive phase and four drugs—ofloxacin (levofloxacin), ethionamide (Eto), ethambutol and cycloserine—during 18 months of the continuation phase. *p*-Aminosalicylic acid (PAS) is included in the regimen as a substitute drug if any bactericidal drug (K, Z and Eto) or two bacteriostatic (E and Cs) drugs are not tolerated.² The extensive therapies of these drugs are not without their side effects. Various known complications of these anti-TB are hepatotoxicity (Z), convulsions (Eto), gastrointestinal such as anorexia, nausea, diarrhoea (Z, R, INH), headache, dizziness (Levofloxacin), generalised hypersensitivity, psychosis (E, Cs), etc.^{3, 4} but neuropsychiatric side effects arising out of long-term therapies leading to self-harm or violent behaviour are rarely discussed. We present a case of violent and bizarre suicidal death of a hospitalised patient who was diagnosed with MDR-TB and drug-induced psychosis.

CASE PRESENTATION

A 25-year-old man, thin build, weighing 45 kgs, a known patient of MDR-TB undergoing antitubercular therapy, got admitted to a specialty hospital dealing with TB and respiratory diseases. He

presented with the symptoms of cough with expectoration, low-grade fever, breathlessness and decreased sleep since a week. On the second day of admission, he developed incoherent speech and also reported of a sense of 'machines moving and talking inside his brain'. In the early morning hours, the patient expressed his wish to go to the bathroom. However, when he did not return even after half an hour, his mother and attendants started looking for him. The bathroom door was found closed from inside and there was no response from the patient even to multiple loud calls by the bystanders. On peeping through the ventilator of an adjacent room, the patient was found lying on the bathroom floor in a pool of blood (figure 1). The door was broken open by the attenders and was shifted immediately to the casualty where he was declared dead on arrival. The deceased was unmarried and belonged to a family with low socioeconomic status. He had a history of two suicidal attempts including hanging and jumping from the first floor of a building during the anti-TB regimen. There was no history suggestive of mania/psychosis/delirium prior to the drug regimen and there was no history of addiction to any drug of abuse. The scene of occurrence was visited by the police investigating team, where they found a single-edged kitchen knife inside the bathroom. The knife was readily available to the victim, as it was used in the hospital by the patient's attendants for cutting fruits served to the patients.

The patient was first diagnosed with pulmonary TB in 2007 and was treated for 8 months with drugs isoniazid, rifampicin, pyrazinamide and ethambutol (category I). However, the disease relapsed in 2008 and he was put on isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin (category 2) for 8 months. He was cured of pulmonary TB, but in 2010, he developed abdominal tuberculosis for which the treatments with category 2 drugs were continued for 10 months, but he was not cured. In 2011, it was found that he was resistant to isoniazid and rifampicin and was declared to be MDR-TB. Hence, the patient was put on treatment with the category IV drugs (ethionamide 750 mg, ethambutol 1200 mg, levofloxacin 1000 mg, pyrazinamide 100 mg, pyridoxine 100 mg, all once daily) for 15 months.

The patient had presented to the outpatient department, a month earlier, with symptoms of decreased sleep, symptoms of anxiety, acne, abnormal whistling sounds in the ears and abnormal talk accompanied with visual hallucination

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Figure 1 Scene of occurrence with blood stains inside the bathroom.

(seeing persons/objects which were not present in real) since 1 month. He was suspected of cycloserine-induced toxicity and was advised to stop the drug. The remaining drugs of category IV regimen were continued along with PAS and supplemented with alprazolam tablet 0.5 mg once daily. He was referred for psychiatry evaluation where he was prescribed risperidone and clonazepam. Otolaryngorhinology evaluation revealed bilateral mild sensorineural hearing loss associated with tinnitus.

Autopsy findings

The body was that of a young adult male of age 25 years, thin build, with no cuts or tears on his clothings. Multiple incised wounds were present on the forehead, chin and anterior abdominal wall regions. Multiple stab wounds were present on the anterior chest wall perforating the pericardium and the right ventricle (figure 2). Peritoneal cavity contained about 1 L of clotted and fluid blood. Toxicological screening of blood was negative for alcohol. The cause of death was haemorrhagic shock as a result of multiple injuries over the body caused by a sharp-edged weapon.

Figure 2 Multiple stab and incised wounds on the chest and the abdominal region.

OUTCOME AND FOLLOW-UP

Death.

DISCUSSION

Death by a sharp-edged weapon is an uncommon method of suicide. In India, hanging and poisoning are common methods of suicide. The reported cases of self-stabbing on various sites of the body included the cranium, neck, abdomen and chest, in varying combinations.^{5–9} Usually, such acts are commonly seen in victims with underlying neuropsychiatric conditions or under the influence of drugs or alcohol.

Drugs such as isoniazid, cycloserine, ethambutol and fluoroquinolones used in the treatment of tuberculosis have been reported to produce drug-induced psychosis.^{10–16} Madan *et al*¹⁷ have reported a case of suicidal attempt in a patient on isoniazid treatment, who had attempted 4 days after the onset of psychosis. Schumann *et al* reported a case of unmotivated suicide in a patient with pulmonary TB treated with D-cycloserine.¹⁸

In our case, the patient was diagnosed with a case of multidrug-resistant pulmonary tuberculosis who was on treatment for the past 15 months. He was prescribed category IV drugs which included cycloserine, ethambutol and levofloxacin (fluoroquinolones). During the treatment, he developed various clinical symptoms such as acne, tinnitus and lack of sleep with abnormal talking. He was also referred to skin specialist, otolaryngorhinologist and psychiatric specialist for the symptoms of hallucinations. The Diagnostic and Statistical Manual of Mental disorders (DSM IV-TR) notes that a diagnosis of drug-induced psychosis is made only when the psychotic symptoms are above and beyond what would be expected during intoxication or withdrawal and when the psychotic symptoms are severe.¹⁹ He was diagnosed to have all the above symptoms after starting the anti-TB regimen. There was no history suggestive of psychotic disorder or substance abuse in the past. Cycloserine was withdrawn in view of his psychiatric symptoms and it was replaced with PAS. The rest of the drugs were continued. In spite of cessation of cycloserine and supplementation of anxiolytic drugs, the patient continued to have a lack of sleep and was admitted to the hospital. On the second day of admission, the patient locked himself in the bathroom of the hospital and stabbed multiple times on his abdomen and chest and cut his forehead with a kitchen knife. On non-returning of the patient to the bed, the bystanders searched for him in the bathroom, where he was found in an unresponsive state in a pool of blood. The bathroom door was broken open and he was rushed to the casualty where he was declared dead on arrival. Autopsy revealed fatal stab injuries to the chest and abdomen caused by a sharp-edged weapon. The chest wound had penetrated the heart causing cardiac tamponade, whereas the abdominal stab wound had caused haemoperitoneum, which was individually sufficient by itself to cause death. Although the patient was diagnosed of cycloserine-induced psychosis, other drugs such as ethambutol and fluoroquinolones that had the potential to cause psychosis were not stopped. Psychosis is also reported to have a strong association with potentially lethal suicide attempts using sharp objects and the risk is higher in those patients, who have never received treatment for psychosis.²⁰ This paper thus highlights the violent suicide as an outcome of a psychotic symptom, arising as an adverse effect of antitubercular medication. There is a need for close monitoring of high-risk patients during the treatment, with counselling and appropriate tailoring of drugs to prevent adverse effects.

Learning points

- ▶ Patients undergoing antituberculosis treatment can present with a range of symptoms including tinnitus, acne and severe psychosis even in prescribed dosages.
- ▶ Antituberculosis drugs such as cycloserine, ethambutol and fluoroquinolones can lead to severe psychosis associated with suicidal tendencies.
- ▶ Bizarre and fatal self-stabbing and cutting, in our case, is ascribed to the drug-induced psychotic manifestation.
- ▶ Preventive strategies must be undertaken by the hospital authorities in such patients admitted for psychiatric or other symptoms.

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