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(CASE REPORT)

Cycloserine (anti-tuberculous drug) and psychiatric disorders: A case report

Anouar KADDAF [1,*], Adil Zegmout [2] and Mohamed KADIRI [1]

[1] *Department of Psychiatry, Military Hospital of Instruction Mohamed V, Rabat, Morocco.*
[2] *Department of Pneumology, Military Hospital of Instruction Mohamed V, Rabat, Morocco.*

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Abstract

Background: Tuberculosis continues to pose a significant global public health challenge, especially with the rise of multidrug-resistant tuberculosis (MDR-TB), necessitating second-line treatment regimens that entail considerable adverse effects. cycloserine, an important second-line anti-tubercular drug, is well-known for its neuropsychiatric side effects, which include depression, anxiety, psychosis, and obsessive-compulsive symptoms.

Case Presentation: We present the case of a 30-year-old male patient with a history of insulin-dependent diabetes mellitus and no previous psychiatric disorders, undergoing treatment for pulmonary tuberculosis. After treatment failure and confirmation of MDR-TB, the patient began a second-line regimen that included cycloserine. After three months of treatment, he started to have depressive symptoms, trouble sleeping, ringing in his ears, headaches, and obsessive-compulsive thoughts that were religious in nature. A psychiatric evaluation resulted in a diagnosis of depressive disorder with obsessive-compulsive characteristics, presumably associated with antitubercular treatment. Fluoxetine and alprazolam were given to treat the symptoms, and this helped a little.

Conclusion: This case underscores the necessity of identifying and swiftly addressing psychiatric adverse effects linked to cycloserine and other second-line antitubercular medications. To make sure that patients with MDR-TB are safe and get the best treatment possible, pulmonologists and psychiatrists need to work closely together.

Keywords: Multidrug-Resistant Tuberculosis; cycloserine; Psychiatric Side Effects; Depression; Obsessive-Compulsive Disorder; Adverse Drug Reaction; Neurotoxicity

1. Introduction

Tuberculosis is an infectious disease that constitutes a global public health problem. However, it remains curable with standardized and well-administered antibiotic treatment.

The occurrence of psychiatric disorders during the antituberculosis treatment phase has been reported by several authors. In cases of resistance to first-line antituberculosis drugs, second-line drugs are used, which are more effective but have more adverse effects. Among these, cycloserine, a broad-spectrum antibiotic, has adverse effects, particularly psychiatric ones, that are likely to occur during the first months of treatment. These effects, such as anxiety, hallucinations, depression, euphoria, behavioral changes, and suicidal tendencies, have been well described in the literature.

Using a clinical case, we will highlight the psychiatric side effects in patients receiving treatment for multi-resistant tuberculosis, and the need for close collaboration between pulmonologists and psychiatrists in order to quickly detect adverse events that may be life-threatening.

* Corresponding author: Anouar KADDAF

2. Clinical Case

A 30-year-old patient, known to have diabetes treated with insulin, and with no psychiatric history, had been followed for pulmonary tuberculosis for two and a half years.

After six months of well-managed treatment (first-line antituberculosis drugs), the patient was readmitted to the pulmonology department due to the recurrence of hemoptysis, suggesting treatment failure. A retreatment protocol (3RHZE/5RH) was initiated while awaiting the results of the drug susceptibility testing, which confirmed multidrug resistance to rifampicin and isoniazid (INH).

The diagnosis of multidrug-resistant tuberculosis (MDR-TB) was made, and the patient was transferred to another pulmonology department specializing in the management of such cases.

The short-term course, after two months of hospitalization and under second-line antituberculosis treatment (kanamycin, levofloxacin, cycloserine, pyrazinamide, ethionamide, and ethambutol), was marked by a significant improvement.

Paradoxically, after three months of follow-up visits, the patient developed symptoms including sadness, a tendency toward isolation, insomnia, tinnitus, headaches, and obsessive-compulsive thoughts with religious themes.

Given the uncertain etiology of these symptoms, the patient was referred for psychiatric consultation, where a depressive state with obsessive-compulsive disorder was diagnosed, with no pre-existing personality disorder. This could be related to the antituberculosis medication. The patient was initially prescribed fluoxetine 20 mg/day and alprazolam 1 mg/day while continuing the same antituberculosis treatment. At the same time, an otolaryngological examination revealed no organic lesions. The tinnitus was most likely secondary to the auditory toxicity of the antituberculosis drugs.

Subsequent follow-up visits showed an improvement in mood and headaches, with persistent obsessive thoughts.

3. Discussion

The regimens used for treating MDR-TB cause more adverse effects than those used in first-line therapy and are associated with increased mortality and a treatment discontinuation rate of 19–55%. [1]

These adverse effects present additional challenges for patient management because they influence treatment outcomes and adherence. [2]

Our patient had no personal or family history of psychiatric disorders but was taking several antituberculosis drugs known for their psychiatric side effects. The onset of psychiatric disorders only with the introduction of second-line agents suggests that these drugs may be responsible for triggering these disorders.

Among the most implicated molecules is cycloserine, a broad-spectrum antibiotic introduced in 1954 [2] and classified by the WHO as a second-line agent used for MDR-TB. [1]

Several predisposing factors for neuropsychiatric adverse events are associated with cycloserine: premorbid personality disorder, female sex (the incidence of psychiatric adverse effects is twice as high in women as in men), and alcoholism. [2]

The adverse effects of cycloserine primarily affect the central nervous system and are mainly dose-related. Psychiatric disorders such as anxiety, confusion, hallucinations, depression, psychomotor agitation, euphoria, behavioral changes, and suicidal tendencies have been reported in 9.7% to 50% of people taking cycloserine. These side effects are most likely to occur during the first 3 months of treatment. [1][3]

The hypothesis that cycloserine can trigger delirium was based on its mechanism of action centered on the GABA system and glutamate. Cycloserine does indeed cause an increase in GABA by inhibiting GABA-transferase, as well as effects on glutamatergic transmission through actions on NMDA receptors. [1]

The seriousness of the prognosis lies in the occurrence of adverse effects that can be life-threatening. Indeed, several authors have linked increased mortality to the onset of mania, psychosis, or suicide attempts while taking cycloserine. [4] [5]

Alcohol consumption is an aggravating factor. Prescribing sedative neuroleptics and vitamin B6 at a dose of 100–300 mg/day is standard practice in patients with a history of epilepsy or psychiatric illness. [5]

The relationship between obsessive-compulsive disorder and antituberculosis drugs has been well described in the literature, especially for INH. The appearance of obsessive-compulsive thoughts in our patient after starting second-line antituberculosis drugs suggests that these drugs, and especially cycloserine, may be implicated. [3]

Individual counseling or group therapy may be necessary in the management of patients with a psychiatric condition or a psychiatric adverse effect of medication. Group therapy has proven effective in providing a supportive environment for people with MDR-TB. [5]

The use of cycloserine is not absolutely contraindicated in psychiatric patients, but close monitoring is essential. All healthcare providers involved in the management of MDR-TB should work closely with psychiatrists. [5]

Finally, Individuals with tuberculosis are approximately four times more susceptible to exhibiting symptoms of depression [6]. A study found that tuberculosis patients experiencing high levels of stress had a greater likelihood of mortality during treatment compared to those with lower stress levels [7], so it is advisable to have patients with mental health disorders assessed by psychiatrists before initiating MDR-TB treatment. This initial assessment records any pre-existing psychiatric conditions and provides a baseline for comparison should new psychiatric symptoms develop during treatment [5]. In addition, it's necessary to include mental health issues in tuberculosis (TB) programs. It asks for person-centered care that involves complete psychoeducation for patients and their families. This is because better management of illnesses like depression has been demonstrated to help people stick to their treatment plans. [8,9]

4. Conclusion

All healthcare providers involved in the care of tuberculosis patients should be made aware of the psychiatric side effects of antituberculosis drugs and the importance of close collaboration with psychiatrists to identify those that may be life-threatening.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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