DIAGNOSIS CHALLENGES IN A CASE OF PSYCHOTIC EPISODE IN CONTEXT OF PELLAGRA INDUCED BY ISONIAZID THERAPY - A CASE REPORT

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Abstract:
Pellagra is a nutritional disease caused by niacin (nicotinic acid) deficiency, manifested by the classic triad of 3 D: dermatitis, diarrhea and dementia. This can lead to the fourth D: death (1). Pellagra may be caused by a series of factors that are affecting the requirement for niacin and among those the use of some chemotherapeutic agents, like Isoniazid for the treatment of tuberculosis (2). Isoniazid is known to induce adverse effects such as: dizziness, gastro-intestinal upset, headaches and occasionally psychosis, hepatitis, skin rash, agranulocytosis, purpura and pellagra (3). We present the case of a man with pulmonary tuberculosis treated with Isoniazid and Rhipampicine that developed behavioral changes, confusion, insomnia, delusional thoughts and had skin lesions, all the symptoms suggesting pellagra.

Key words: niacin, nicotinamide, tuberculosis, mental status.

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CASE HISTORY
We present a case of a 42 years old man, diagnosed with pulmonary tuberculosis in February 2010. The patient lives in a rural area, is married and has a poor economic state. The patient has no family history of psychiatric or neurological disorders; he is a smoker but doesn’t drink alcohol. The patient has a history of a depressed episode 2 month before this consult.

In the moment of the psychiatric consult in our clinic, the patient’s treatment for tuberculosis was with Isoniazid and Riphampicine - taken 3 times per week. It was indicated treatment with vitamin B complex but it was not followed.

First psychiatric consult - May 2010: patient was brought from Clinical Pneumoftiziology Hospital for a psychiatric consult; in that moment the diagnosis was depressive episode; it was indicated an antidepressant treatment, but not followed. We don’t have any other information about this episode except the declaration of his wife who said that he was sad all day, he could not sleep and he was lost. She declared that he recovered in approximately 1 month and that he was better since then, except the last week.

Second psychiatric consult - June 2010: the patient was brought by his wife for behavior changes observed in the last week: lost things, confusion, agitation, insomnia and delusional thoughts of persecution.

Psychiatric consult: the patient was agitated, extremely anxious, disoriented in time and space, strange behavior and with auditory hallucinations.

Physical examination: patient with low body mass index (17.7 kg/m²), hyperpigmentation of exposed parts of the body and dry skin, excessive salivation and angular stomatites.

CT cerebral performed at that time - in normal ranges; vital signs in normal ranges.

Blood analysis performed one month ago showed anemia.

Taking into account the skin lesions and rapid evolution of psychiatric symptoms we asked for a medical consult.

In emergency room it was administrated 1 dose of Diazepam, i.m. (10 mg) for agitation. It was indicated one dose of Diazepam 10 mg per day and 1 mg of Risperidone to be followed after the complete medical consult, if it is necessary. The next day the patient remained in the medical department for further investigation. The psychiatric symptomatology persists.

It was suspected a diagnostic of pellagra based on the skin lesions and the mouth lesions in collaboration with treatment with Isoniazid. In collaboration with the department of pneumology it was taken the decision to withdrawn the treatment with Isoniazid and a vitamin B complex with Nicotinamide (in dose of 300mg/ day) treatment was started; the patient remain hospitalized in medical department.

The skin lesions and mental status improved within 2 weeks and the psychiatric treatment was stopped, because it was no longer necessary. Since then the patient remained without any psychiatric symptoms.

DISCUSSION
1. Isoniazid treatment is associated with multiple deficiency states. Patient seems to recover rapidly if Isoniazid is stopped and treatment with Nicotinamide is initiated (4); undiagnosed and untreated pellagra rapidly may cause dementia and death.
2. Pellagra is now a disappearing disease in developed countries, even so still keep attention that “pellagra sine pella agra” (pellagra psychosis without skin lesions) still lies hidden and unsuspected in mortality data of mental hospitals (5). In our case the skin lesions and tardive onset of psychosis raised the question about the underlying condition that may cause psychiatric symptoms and make us to take the best decision: to ask for supplementary consults in such patient.
3. Acute onset of psychosis in an Isoniazid-exposed patient should cause suspicion of this psychiatric side effect of anti-tubercular therapy and lead to consideration of discontinuation of
Isoniazid and a trial of antipsychotic medication. Treatment with pyridoxine and antipsychotic alone, without discontinuation of Isoniazid, may not be effective in all patients.

4. The suggested mechanism for Isoniazid-associated psychosis involves Isoniazid’s altering the levels of catecholamines and serotonin by inhibiting monoamine oxidase or by inducing pyridoxine deficiency, or both (6, 7). Although pyridoxine alone has not been shown to prevent INH-induced psychosis, it may be partially protective.

5. Toxic psychosis due to Isoniazid has occasionally been reported in patients with previous history of psychiatric disturbances. However cases have been reported even in patients without any history of psychiatric symptoms. Prodromal symptoms in the form of anxiety, depression, headache, emotional outbursts, sleep disturbances, tremors usually occur before an acute psychotic attack. Our patient had some of these prodromal symptoms for about a month before he developed frank psychosis. These were somehow ignorated thinking to be a depression. So as a conclusion, every patient on Isoniazid, especially with a history of previous psychiatric symptoms, should be monitored for appearance of any of the prodromal symptoms (6).

6. Isoniazid should be used with caution in patients with convulsive disorders, a history of psychosis, or hepatic or renal impairment. Patients who are at risk of neuropathy or pyridoxine deficiency, including those who are diabetic, alcoholic, malnourished, uraemic, pregnant, or infected with HIV, should be given pyridoxine, usually in a dose of 10 mg daily, although up to 5.0 mg daily may be used.

CONCLUSION

Even it is a disappearing disease, pellagra should be suspected in patients who develop mental and neurological symptoms without any evident cause and who have an increased necessary requirement for niacin, in or in absence of typical pellagra dermatitis.

REFERENCES