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Case Report

Psychiatry Section

Acute Psychosis after Recent Isoniazid Initiation

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ABSTRACT

Isoniazid as part of Directly Observed Treatment-Short course (DOTS) regimen is universally used. Although, associated psychosis in certain cases is documented earlier, type of symptoms and onset of symptoms remains highly variable. We describe a case of 54-year-old female on anti-tubercular therapy with onset of psychosis within three days of Isoniazid initiation characterised by agitation, loosening of association, echolalia with spontaneous remission after drug stoppage. This case highlights the importance of remaining vigilant and considering isoniazid as possible causative agent for psychosis even within days of its intiation and avoiding delay in management.

Keywords: Secondary psychosis, Tuberculosis

CASE REPORT

A 54-year-old married female, smoker, presented to Department of Emergency Medicine at Pt. BDS PGIMS Rohtak, (tertiary care hospital), with the complaints of chronic cough and weight loss for two months and abnormal behaviour characterised by agitation, disturbed sleep, and irrelevant talks for past two days. The patient had been diagnosed as a case of sputum positive tuberculosis five days back at a public health centre with positive radiological findings on chest x-ray and was started on anti-tubercular therapy (Isoniazid 300mg/day, Rifampicin 600mg/day, Pyrazinamide 1.5gm/day, Ethambutol 800mg/day and Pyridoxine 20mg/day). Her past record was significant for viral encephalitis two years ago from which the patient had no residual neurological deficits. The diagnosis of encephalitis was considered at that time in view of suggestive CSF findings and the patient was treated with acyclovir (but no proper records of the same were available with the patient).

There was no past or family history of any psychiatric illness. Her clinical examination revealed respiratory rate of 26/min while hemodynamic parameters and general examination were within normal limits. Her respiratory system examination revealed bilateral coarse crepitations with bronchial breath sounds in bilateral upper chest. A psychiatric opinion was sought in which she was found to be oriented to time place and person, but was markedly restless, unable to sit at one place for long and exhibited severe psychomotor agitation. Her rate of speech was increased and her thought process was characterised by loosening of association along with echolalia, while no kind of hallucinations were reported. There was no neurological deficit (focal weakness, cranial nerve involvement, sign of meningeal irritation) and fundus examination was normal.

Her radiological investigation did not reveal any significant findings except the chest x-ray showing bilateral upper lobe infiltrates suggestive of tuberculosis, the NCCT head was essentially normal except for some age related changes. Her biochemical evaluation revealed a normal blood gas analysis (BGA), a normal blood count, electrolyte levels, liver and kidney functions. The Cerebrospinal fluid (CSF) examination was also found to be within normal limits (CSF proteins=46 mg/dl, sugar=87 mg/dl and TLC= 5 lymphocytes/mm^3). An initial diagnosis of drug-induced psychosis was made after a thorough screening for organincity and a psychiatric consultation, with Isoniazid being identified as the likely culprit.

The patient's acute agitation was managed by 10mg of diazepam given IV and Isoniazid was withdrawn. The patient completely became free of psychotic symptoms over the next two days while being on 5 mg diazepam twice daily which was tapered off over next three days. Considering the efficacy of Isoniazid and its role as a firstline treatment in tuberculosis, an attempt was made to restart it one week later with a low 'test' dose after explaining to the patient and taking a consent. Agitation was seen on 3rd day of restarting isoniazid and so it was promptly stopped after patient expressed reservations against its further use. The patient was continued on a modified antitubercular therapy. After three months the patient become sputum negative and is recovering. She has not reported any psychiatric manifestation over this period. The case highlights that psychosis onset can occur within a very short span after isoniazid initiation and the presence of previous neurological involvement (encephalitis in our case) may have a bearing on early appearance of such symptoms.

DISCUSSION

Tuberculosis continues to be a challenge, infecting more than one-third of the population worldwide [1]. Major drugs used in treating tuberculosis include isoniazid, rifampicin etambutol and pyrazinamide. Isoniazid, as part of DOTS regimen, is the first line of drug and very commonly used. Adverse effects include hepatitis, peripheral neurotoxicity, lupus like syndrome, and central nervous system effects including dysarthria, seizures, irritability and even psychosis [2].

Studies have found higher prevailing rates of mental illness, including psychosis in tuberculosis. Psychosis in tuberculosis may result as adverse effects of anti-tuberacular drugs including isoniazid, ciprofloxacin, etambutol and rifampicin [2,3] or maybe a presenting complaints in cases of intracranial tuberculoma [3].The association of Isoniazid and psychosis was first highlighted by Jackson in 1957 [4]. Since then, there has been growing literature linking Isoniazid to psychotic episodes [5-7]. Various mechanisms of action has been suggested for this interaction, of which two have been most important, i) depletion of pyridoxine (also responsible for neuropathy) and ii) inhibition of monoamine oxidase leading to alteration in level of cathecholamines and serotonin [8].

The onset of psychosis in index case was after 3 days of isoniazid initiation, which has been an unusual finding in literature. Usually the onset of psychotic symptoms varies from days to months, with few weeks being the most common time period cited in literature. A number of psychiatric symptoms have been previously described including paranoid delusions [4,9], auditory, visual as well as tactile hallucinations [5,6], suicidality [7], mood symptoms

and disorientation [8,10]. Certain prodromal symptoms like anxiety, headaches, sleep disturbance, twitchings have also been described [10,11], but there is no mention of loosening of associations and echolalia in existing literature. Role of previous psychiatric episodes is not clear as psychosis has been seen in those with [6] or without a past psychiatry history [9-11]. In one of the similar cases highlighted in literature a 57-year-old woman developed irritability, delusions, auditory and visual hallucinations on third day of isoniazid initiation. She was managed by stopping isoniazid and high dose of typical antipsychotic and became symptom free within two days. The picture in this patient resembled delirium and was complicated by co-morbid lung effusion, making temporal association unlikely [9]. Similarly in another instance in a 22-year-old patient highlighting the development of psychosis on 4th day of isoniazid initiation, presenting picture was confused with co-existing diabetes and milliary tuberculosis [10].

Our patient belonged to Category 1 of DOTS therapy and suffered from no existing comorbidities (except for a past history of encephalitis), minimizing the possible confounding factors as seen in past reports. There was no history of any psychiatric illness. However, past history of an episode of encephalitis was reported which had subsided without any neurological deficits. This may possibly be a risk factor, with previous neurological insult making patient susceptible to Isoniazid induced psychosis. Few risk factors already highlighted in literature includes slow acetylators, malnourishment, diabeties, hepatocellular dysfunction and neuropsychological disorders. Another possible reason for such acute onset of psychosis may be the pharmacokinetic properties of the drug including hepatic metabolism and protein binding. It has been described that about 40% of Indian population is slow acetylators [11], thus causing slow metabolism leading to drug accumulation and thus more side effects.

CONCLUSION

Isoniazid, being the cheapest and most potent drug, continues to be a part of first line management of tuberculosis. Physicians, especially in developing countries must be aware and pay special attention to confusing clinical presentation after recent isoniazid initiation. The fact that the psychosis onset can even occur within few days of treatment initiation should be kept in mind. This case report adds to further literature on isoniazid induced psychosis along with describing new cluster of symptoms (onset after very recent initiation, loosening of association, echolalia) and proposing previous neurological insult as risk factor .

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