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AKT 4 INDUCED DELIRIUM: CASE REPORT

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ABSTRACT

Tuberculosis (TB) is the major problem in countries like India or developing countries. Anti- tubercular drugs prescribed for TB can cause certain side effects in patients, these can be dose related, due to genetics or resistance to anti TB drugs. Delirium or psychosis caused by AKT-4 is reported in many patients taking AKT- 4 therapy for TB. Especially Isoniazide and Ethambutol can cause psychosis. A 21 years old male patient came with the complaints of high- grade fever with chills and altered sensorium since 3- 4 days. He had 1 episode of vomiting. He had seizure attack 3 days back (3 episodes for 1-2 mins) associated with involuntary movements of bilateral upper limb and lower limb with up rolling of eyes, post ictal confusion. Patients had TB 6 months back for which he had taken AKT-4 and he completed his regimen 1 month back. His X- Ray and CBNAAT (Cartridge- based nucleic acid amplification test) confirming of TB. MRI (Magnetic Resonance Imaging) brain suggests flair and hyperintense lesion with low ADC is seen in left superior temporal cortex that appeared a tiny acute infarct. Patient took discharge against medical advice, so treatment is discontinued. Proper identification of delirium causing drug in anti TB therapy can prevent delirium in patient by discontinuing the particular drug or by changing the dose.

KEYWORDS: tuberculosis, meningitis, Anti TB therapy, delirium, Isoniazide, ethambutol.

INTRODUCTION

TB is an infectious disease and it is the one of the leading causes of death worldwide. The Bacillus Mycobacterium Tuberculosis can cause TB. TB is mostly spread through air, when

people who are infected with TB expel bacteria while coughing or sneezing. The disease usually affects the lungs (pulmonary tuberculosis), but it can also affect other parts of the body (extra pulmonary tuberculosis). Tuberculosis is both curable and preventive. A 6-month treatment regimen can successfully treat 85 percent of persons who get tuberculosis, and 1–6-month drug regimens can also be effective.[1]

M. tuberculosis infects around a quarter of the world's population, or approximately 2 billion individuals. Higher incidence of TB can be seen in patients with HIV, Diabetes, malnourished patients or who are addicted to smoking and alcohol. Men are more infected than female.[1]

Diagnosis can be done by Sputum smear microscopy or rapid molecular tests. MDR TB can be diagnosed by rapid testing, sequencing technologies, or culture methods.[1]

Treatment for TB include AKT- 4 as first line agents, AKT-4 includes Isoniazide, Pyrazinamide, Ethambutol and Rifampicin. BCG vaccine is the only vaccine used for the prevention of TB.[1]

Isoniazid (150mg), rifampicin (250mg), pyrazinamide (400mg), and ethambutol (250mg) are currently approved as first choice of medication for tuberculosis, followed by 4 months of INH, RMP, and/or EMB, while second-line agent drugs include streptomycin, para-amino salicylic acid, Isoniazid should be taken with or without food, and antacids should be avoided for at least 2 hours after taking it.[2]

Extrapulmonary tuberculosis has a variety of clinical symptoms that varies based on the organ system(s) implicated, but they usually include a steady deterioration in organ function, low-grade temperature, and other clinical signs.

Extra pulmonary TB (especially involving CNS) has high rate of mortality than pulmonary TB. Clinical features that present in adults are meningitis like symptoms such as fever, stiff neck, altered consciousness, focal neurological deficits, or behavioral changes and headache. There may be confusion, lethargy, inattention or paralysis in patients with TB involvement. Children may have symptoms like fever, nausea, vomiting, stiff neck and seizures. TB patients with CNS involvement are typically treated for 9–12 months.[3]

Mechanism of action

Although the specific cause of isoniazid-related psychiatric diseases is unclear, it is known that the drug disrupts several metabolic pathways that are required for brain activation. Isoniazid causes vitamin B6 deficiency by causing an increase in vitamin excretion and disrupting normal tryptophan metabolism. Isoniazid also reduces the activity of brain pyridoxal-5-phosphate (which the body produces from pyridoxine), producing a drop in brain gamma-aminobutyric acid and other synaptic transmitters, resulting in neurologic disorders. Diabetes, hepatic insufficiency, advanced age, intoxication, and a family or personal history of mental illness are all risk factors for psychosis.[4]

One of the most often used medications in the treatment of tuberculosis is ethambutol. Retrobulbar neuritis is the most common side effect. Toxicology of the central nervous system is rarely recorded, and psychosis as a result of it is extremely unusual. The mechanism behind ethambutol-induced psychosis is unknown. Ethambutol-induced delirium or psychosis shares many of the same symptoms as isoniazid-induced psychosis.[4]

CASE Description AKT4 Induced Delirium

A 21year old male patient came to the tertiary care hospital with the complaints of high-grade fever with chills since 4 days, altered sensorium since 3-4 days, he also had seizure 3 days back before hospitalization which was 3 episodes of 1-2 mins and it was associated with involuntary movement of bilateral upper limb and lower limb, up rolling of eyeball and postictal confusion with no loss of consciousness. he also had complaint of 1 episode of vomiting and cough with expectoration. Patient had a history of TB 6 months back. He had also taken AKT 4 treatment for 6 month and the dose was completed 1 month back since the admission. Patient had no significant family history and no other social history present.

He was provisionally diagnosed with acute febrile illness with meningitis. His lab test showed hemoglobin level of 15.5gm/dl. The chest X-ray AP view showed prominent bronchovascular markings which are noted bilaterally. The Cartridge- based nucleic acid amplification test test was also positive in this patient, which shows extrapulmonary effect of TB. His MRI brain reports showed small flair and diffusion hyperintense lesion with low Apparent diffusion coefficient (ADC), is seen in left superior temporal cortex that appeared a tiny acute infarct. After the ophthalmology opinion it showed that patient had an early sign of papillo edema.

Here patient was semi-conscious but orientation was impaired so MSE could not been evaluated. As there was temporal relationship was present between AKT 4 treatment and occurrence of delirium, here it is suspected that AKT 4 may be a main factor inducing this condition. Patient took discharged against medical advice, so further changes in the drug therapy could not been done. After that also patient was advised for AKT 4 in frequency of 4-0-0, tablet B LONG -F in 0-1-0 frequency, and tablet TRANCODOL dt (1.1 mg) in frequency 1-0-1.

Medication Chart

Table-1

Brand Name	Generic Name	ROA	Dose	Frequency
Inj. Falcigo	Artesunate	IV	120 mg	12 hourly
Inj. Ceftriaxone	Ceftriaxone	IV	2 gm	12 hourly
Inj. Vancomycin	Vancomycin	IV	1 gm	12 hourly
Inj. PAN	Pantoprazole	IV	40 mg	12 hourly
Inj. Emset	Ondensetron	IV	4 mg	8 hourly
IVF NS /RL + Optineuron	Normal saline/ Ringer Lactate +Optineuron	IV	5 amp	80cc/hr
Inj. Lorazepam	Lorazepam	IV	4 mg	SOS
Inj. Seranace	Haloperidol Decanoate	IV	1 amp	SOS
Inj. Mannitol	Mannitol	IV	1 pint	8 hourly
Inj. Febrinyl	Paracetamol	IV	1 amp	SOS
Inj. Dexona	Dexamethasone	IV	4 mg	8 hourly in 10ml NS
T. AKT 4	Isoniazide + Rifampicin + Ethambutol + Pyrazinamide	PO	300mg+ 450mg+ 800mg+ 750mg	4-0-0
T. BLONG- F	Pyridoxine + Folic acid	PO	1mg	0-1-0
Syp. Duphalac	Lactulose	PO	15 cc	0-0-1
Thrombophob ointment	Heparin sodium+ benzyl nicotinate		50IU+2mg	1-1-1-1

CAUSALITY ASSESSMENT

Causality and severity assessment have done with the help of three different scales and results are following.

Table 2.

Scale's Name	Result
Naranjo's algorithm	Possible
Who probability	Unclassifiable
Shumock and thornton	Probably preventable

DISCUSSION

AKT-4 is the standard 1st line treatment given for TB. It stops the infection-causing bacteria from multiplying. Dermatological, gastrointestinal, hypersensitivity, neurological, haematological, and renal responses are all significant side effects of antitubercular effect. Antituberculosis therapy has effects on both the central and peripheral nerve systems. Isoniazid is the most commonly related nervous system effects among the traditional forms of first-line antituberculosis therapy, with peripheral neuropathy, psychosis, and seizures being the most common. Other antituberculosis drugs have been linked to side effects, the most common of which are visual neuropathy from ethambutol and ototoxicity and neuromuscular inhibition from aminoglycosides.[5,6] Sudden confusion, often known as delirium, might indicate a variety of health issues. It appears suddenly, sometimes within hours or days. Major sign and symptoms which can be seen mostly are muttering to self, hallucination, tremor, dysphasia, dysarthria, motor abnormalities, clouding of consciousness, illusions, difficulty in focusing.

DSM V criteria

A. severe hallucinations or delusions

B. There is evidence from the patient's medical history, physical examination, or test findings or

(1) or (2):

(1) The symptoms in criterion A develop during, or within a month after intoxication or abstinence from a substance.

(2) Medication use is linked to the disturbance on an etiological level.

C. The symptoms appear before onset of the substance use (or medication use); the symptoms last for a long period of time (e.g., a month) after the cessation of acute withdrawal or severe intoxication or are significantly more severe than what would be expected given the type or amount of the substance used or the duration of use; or there is other evidence that suggests the existence of an independent non-substance-induced psychotic disorder (e.g., a history of recurrent non-substance-related episodes).

From above DSM criteria, we have done assessment of patient and the patient fulfills all the criteria.[4]

CONCLUSION

Isoniazide and ethambutol are commonly prescribed drugs for tuberculosis. And they are also considered as first line agents. Different studies show isoniazide and ethambutol can cause delirium or psychosis irrespective of early initiation or long term therapy. Here we discussed a case of AKT-4 induced delirium which suggests that it can be done by any of the four first line agents.

Strength of the study

The present study explains about giving alternative anti tubercular drugs in different dosage alteration can be done to prevent delirium and other side effect.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBRIVIATIONS

ADC: Apparent diffusion coefficient**, BP:** Blood Pressure, **BCG:** Bacille Calmette- Guerin, **CBNAAT:** Cartridge- based nucleic acid amplification test, **CNS:** Central Nervous System, **DSM V:** Diagnostic and Statistical Manual of Mental Disorders, **EMB:** Ethambutol, **INH:** Isoniazide, **IV:** Intravenous, **MSE:** Mental Status Examination, **MRI**: Magnetic Resonance Imaging, **PO:** Per Oral, **PZA:** Pyrazinamide, **RMP:** Rifampicin, **SOS:** As and when needed**, TB:** Tuberculosis, **WBC:** White Blood Cells.

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