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Case Report

A case report on anti-tubercular agent induced hepatotoxicity

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ABSTRACT

Hepatotoxicity is the serious adverse effect of tuberculosis treatment and it leads to the discontinuation of Anti-tubercular agent (ATT) causing increased drug resistance, morbidity and mortality. We report a 69 years old male patient with ATT induced hepatotoxicity.

Keywords: Anti-tubercular agent, Hepatotoxicity, ALT, AST

INTRODUCTION

Tuberculosis is a serious contagious bacterial infection caused by Mycobacterium Tuberculosis and it mainly affects the lungs but also other organs may be involved such as kidney, spine, brain and skin etc. It spreads by airborne respiratory droplets (coughs or sneezes) and by saliva.[1,2] Thecurrently approved first line agents for TB is a regimen of isoniazid (INH), rifampicin (RMP), pyrazinamide (PZA), and ethambutol (EMB) for 2 months, followed by 4 months of INH and RMP and / or EMB.[3]

The main adverse effect of anti-tuberculosis treatment is hepatotoxicity, skin reactions, gastrointestinal and neurological disorders. Among that hepatotoxicity is the most consequential adverse effect and also treatment effectiveness will be declined, leading to treatment failure, relapse or emergence of drug resistance.[4] Due to interruption of first line anti-tubercular drugs management continues with second line agents such as levofloxacin, moxifloxacin, streptomycin, kanamycin, amikacin etc. Isoniazid, rifampicin and pyrazinamide are most probably hepatotoxicity drugs because these drugs are metabolised by liver.[5]

CASE REPORT

A 69 years old male patient was admitted in neurology department with complaints of fever, cough, constipation since 4 days, loss of balance while walking since 4 days, 1 episode of vomiting since 1 day with altered sensorium and was outside intubated due to GCS-4. Patient had a medical history of systemic hypertension, type 2 diabetes mellitus, hypothyroidismand medications include T. Metformin 500 mg twice daily and T. Thyronorm 150 mcg once daily.

On laboratory investigation, the patient AST (40 U/l), ALT (50 U/l) and ALP (78 U/l) was found to be normal at the time of the admission, on the further days of treatment with first line anti-tubercular drugs (isoniazid, rifampicin, ethambutol, pyrazinamide) the AST and ALT are significantly elevated and normalised when drugs stopped. TSH was 15.20 µIU/ml. Blood C/S indicate the presence of Burkholderiacepacia (MDR) and urine C/S shows *Candida tropicalis*, sputum C/S and throat swab C/S shows *Pseudomonas aeruginosa*.

His cytology- CSF indicate paucicellular smears show occasional scatterd matures lymphocytes, Background is clear, no malignant cells are noted in smears studied.

His EEG findings suggestive of interictal record intermittent sharp ways seen that describes epileptiform discharge.

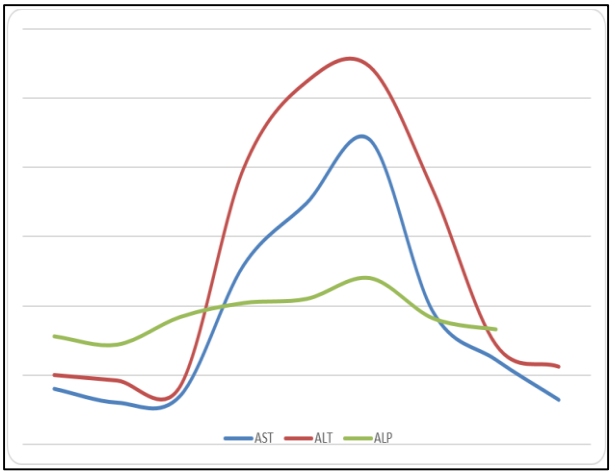

Figure 1: Graphic representation of fluctuations in liver function indicators.

CT abdomen and pelvis indicate sludge in gall bladder, bilateral diffuse perinephric and peri-ureteric, fat stranding, umbilical and left inguinal hernia. His MRI showed patchy meningitis and suspected to have meningoencephalitis. His lumbar puncture showed TC- 6 cells, lymphocyte- 4, protein- 60 and started on meningitis antibiotic and antiviral regimen such as Inj. Meropenem 1 g IV three times daily, Inj. Ceftriaxone 2 g IV two times daily, Inj. Doxycycline 100 mg IV two times daily, Inj. Vancomycin 1 g IV two times daily, Inj. Acyclovir 500 mg IV three times daily and other medications administered are Inj. Levipil 500 mg IV three times daily and Inj. Dexamethasone 8 mg IV three times daily. His sensorium does not improve much after 10 days of treatment.

After 10 days of treatment his CT brain shows right temporal infarct and repeat lumbar puncture suggestive of lymphocytes, protein-79. Tracheostomy done after prolonged ventilation. TB Meningitis was suspected and empirical ATT startedwith Akt 4 kit (Isoniazid 300 mg, Rifampicin 450 mg, Ethambutol 800 mg, Pyrazinamide 750 mg). He had ventilator-associated pneumonia, treated and improved. He was weaned off ventilation and sensorium improved. After the administration of ATT patient had developed hepatotoxicity. So second line anti-TB agents started such as Inj. Streptomycin 0.75 mg IM once daily and T. Levofloxacin 500 mg p/o once daily and other medications administered are T. Baclofen 10 mg p/o once daily, T. Pyridoxine once daily, Neb Levolin four times daily, Inj. Pantop 40 mg once daily, T. Modafinil 200 mg once daily, T.T. Thyronorm 150 mcg once daily, T. Metformin 500 mg twice daily.

After discontinuing first line anti-TB agents patient transaminases levels gradually becomes normal (AST: 220 U/L→32 U/L, ALT: 273 U/L→56 U/L, ALP: 120 U/L→83 U/L) and other conditions improved and the patient discharged with the advice of Hinex HP protein powder 2 tsp twice daily for 2 weeks, T. Pyridoxine once daily for 2 weeks, Inj. Streptomycin 0.75 mg IM once daily for 2 weeks, T. Levofloxacin 500 mg once daily for 2 weeks, T. Thyronorm 150 mcg once daily for 2 weeks, T. Modafinil 100 mg once daily for 2 weeks, T. Dexa 4 mg once daily for 1 week then 3 mg once daily for the next one week and 2 mg once daily for the last week and T. Metformin 500 mg two times daily for 2 weeks.

DISCUSSION

Hepatotoxicity is a serious adverse effect of anti-TB drugs. The serum aspartate aminotransferase and / or alanine amino transferase levels greater than 5 times the upper limit of normal in ATT induced hepatotoxicity. The drugs such as isoniazid, rifampicin and pyrazinamide carry a high risk of causing hepatotoxicity, with clinical signs including nausea, vomiting, weakness, fatigue and yellowing of the eyes. These adverse effects may be attributed to one, two or all three of these medications leading some patients to discontinue anti-tubercular treatment, thereby compromising efficacy. Risk factors for hepatotoxicity with anti-tubercular drugs include concurrent use of other hepatotoxic agents, advanced age, alcohol consumption, and pre-existing liver conditions.[6] Isoniazid can lead to peripheral neuropathy and liver issues marked by increased levels of serum transaminases and bilirubin. Rifampicin may trigger immune-allergic responses and liver problems, characterized by elevated serum transaminases, alkaline phosphatase and bilirubin. Pyrazinamide can cause joint pain due to heightened serum uric acid levels and liver issues reflected in increased serum transaminases and bilirubin. Our patient AST and ALT was elevated after the treatment with first line agents.

Treatment for ATT induced hepatotoxicity is to stop the drugs and start with an alternative agent. In our patient first line anti-TB drugs cause hepatotoxicity hence withheld it and continues with second line anti-TB agents.

CONCLUSION

Hepatotoxicity emerges as a serious adverse drug reaction in individuals undergoing treatment with anti-tubercular drugs like isoniazid, rifampicin and pyrazinamide. Various studies indicate that ATT-induced hepatotoxicity is reported in 5-28% of patients receiving these drugs, with liver function tests revealing a substantial fivefold elevation in ALT and AST enzymes. Clinical manifestations encompass abdominal pain, nausea, vomiting and jaundice. In essence, this entails a patient experiencing hepatotoxicity after taking anti-tubercular drugs, necessitating supportive care. Educating patients on potential adverse drug reactions (ADR) is crucial and physicians should advise them on recognising and promptly reporting signs and symptoms of hepatotoxicity. Hence the liver function of patients should be regularly monitored mainly serum aspartate aminotransferase and / or alanine amino transferase levels.

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