



An anxious 17 year old school student from a small town presented to the Psychiatry OPD with complaints of being followed by the CBI, and suspicions of being followed through a satellite. Physical examination revealed mild pallor and slightly exaggerated knee jerk.

She was provisionally diagnosed with paranoid schizophrenia and prescribed Haloperidol tablets.

However, she did not improve. Instead, her delusions persisted and over 3 weeks, the knee jerk became more exaggerated. This was followed by an involuntary dance like movement of the body.

An MRI scan of brain revealed high intensity signals in cerebral cortex and basal ganglia.

A slit-lamp examination revealed a brown ring around the limbus.

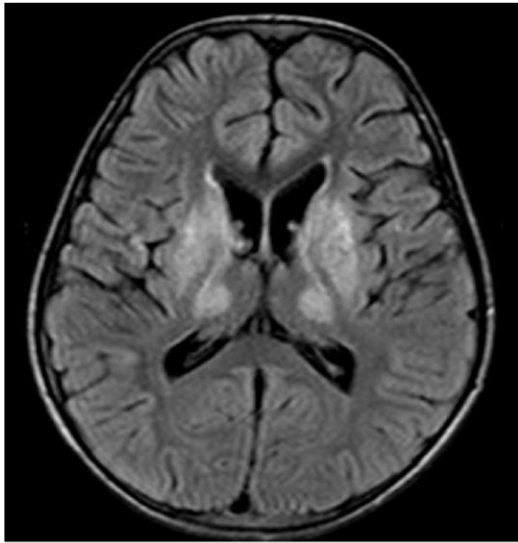


Image-1



Image-2

Questions:

1) **What is your provisional diagnosis?**

Answer-Wilson's disease with neuropsychiatric manifestation.

- Wilson's disease is an autosomal recessive disorder caused by mutations in the ATP7B gene, which encodes a membrane-bound, copper-transporting ATPase.
- Two main defects in Wilson's are inability to excrete copper in bile and inability to excrete copper into apoceruloplasmin (Apo ceruloplasmin binds to copper to form ceruloplasmin which acts as a copper transporter and transfers copper to various sites of the body for utilization).
- Due to the above defects copper accumulates in the liver and after reaching a threshold, free copper leaks out into the blood.
- Copper accumulation causes liver damage via the Fenton reaction as it generates free radicals. The leaked copper in blood deposits in various tissues and also causes free radical damage.
- Pallor is due to haemolytic anemia (free radical damage by copper in the blood)
- T2 Flair image shows hyperintensity signals in the basal ganglia due to free copper deposition.
- Slit lamp exam shows Kayser-Fleischer rings which is again due to copper deposition at the limbus.

2.How do you explain the psychiatric and motor manifestation?

- Initially the patient presented to the psychiatry OPD with complains of anxiety, and delusions of persecution (followed by the CBI, and suspicions of being followed through a satellite)
- Wilson's disease patients are often misdiagnosed initially as psychiatric diseases and interestingly they have similar pathogenesis.
- Schizophrenia occurs due to increase in dopamine in the mesolimbic pathway.
- Rise of Dopamine levels has been shown to result in psychosis.
- In Wilson's disease copper deposits in the mesolimbic pathway and causes excitotoxicity leading to increased dopamine secretion and hence psychosis.
- Patient after being misdiagnosed as paranoid schizophrenia was prescribed Haloperidol (Typical antipsychotic, MOA-Blocks D2 receptor both in mesolimbic and nigrostriatal pathway hence leads to extra pyramidal side effects)
- The case further states that the patient does not improve on haloperidol as it does not target the etiology of the disease i.e. copper accumulation.
- Knee jerk becomes exaggerated due to upper motor neuron lesion (case states MRI shows hyperintensity at the cerebral cortex due to copper deposition)
- Appearance of dance like movements occur due to damage of the indirect pathway of basal ganglia again as a result of copper deposition.

3.How will you confirm your diagnosis?

- Investigation of Choice for screening- Urinary Free Copper measurement (increased)
- Investigation of Choice for confirmation- Liver Biopsy for quantitative estimation of copper in dry weight of liver >250 Microgram/Dry weight of liver.

4.What are the treatment options?

- Drug of choice for hepatitis- Zinc (inhibits copper absorption from the gut)
- If cirrhosis present-
 - Rx as per Nazer Score (PT + Serum Bilirubin + SGOT)
 - Score <7 – Zinc + Trientine
 - Score 7-9 - +/- Liver transplant
 - Score >9 – Liver transplant

