WILSON DISEASE- A RARE CASE REPORT

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Abstract

Ten years old female child presented with clumsy gait, drooling of saliva, difficulty in speech, and behavioral changes. Patient also had poor performance in school. Ocular examination showed positive Kayser-Fleischer ring (K.F.ring) with torch, which was confirmed by slit lamp examination of cornea. Her biochemical and radiological parameters supported the diagnosis of Wilson Disease. Medical line of treatment was started and regular follow up advised to evaluate the outcome.

Key words: *Wilson disease, Kayser-Fleischer ring, Serum ceruloplasmin, Urinary copper*

Introduction:

Wilson disease is a rare (1/40000- 1/100000) an autosomal recessive disorder, characterized by degenerative changes mainly in liver and brain. The incidence is some what more common in Indian children. [1] The involvement may be unisystemic or multisystemic. It affects different systems at different ages. Hepatic and hematological manifestations appear early and neurological follow later. Wilson disease is progressive and fatal if untreated. However effective treatment is available and early initiation of therapy is gratifying.

Case report

Ten years old female child reported to Pravara rural hospital, Loni with complaints of clumsy gait, drooling of saliva, difficulty in speech since 5months.She also had behavioral changes, poor school performance and lack of coordination. Family history was insignificant. CNS examination showed subnormal Intelligence. Patient had dysarrthria. Cranial nerves were normal. Patient had shuffling gait with short steps. There were no associated hand movements while walking. Other systems were normal. Ophthalmic examination with torch showed greenish brown ring at limbus in both eyes which was confirmed on slit lamp (Fig 1,2.) Provisional diagnosis of Wilson disease was made and the case was investigated accordingly.

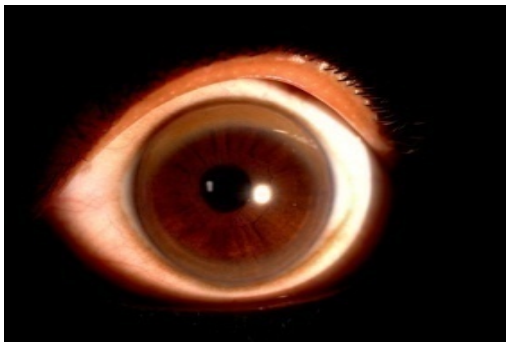

Fig1: Torch exam-K.F. ring

Fig 2: Slit lamp K.F. ring confirmation

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Investigations

1) Haemogram showed normal hemoglobin and count. Routine urine examination was normal. Liver function tests and renal function tests were normal.
2) Serum ceruloplasmin levels - 3.95mg/ dl. (N-19-57mg/dl)
3) 24 hrs urinary copper estimation - 123 µg / day. (N<40 µg /day)
4) CT scan showed mild lateral ventricular dilatation.

Diagnosis

Based on the clinical findings and the investigations the diagnosis of Wilson disease was confirmed.

Management

The patient was put on low copper diet and oral zinc supplements 75 mg daily. D-penicillamine was started on low dose of 10 mg/kg body weight, gradually increased to 20mg /kg bodyweight. Regular follow up visits were explained to parents to see clinical improvement and potential side effects of D-penicillamine. Family screening of parents and siblings for K.F. ring was done. However it was negative.

Discussion

The disease is also known as hepatolenticular degeneration as it mainly involves liver and brain. The precise cause of Wilson disease is not known. But basic mechanism relates to decrease in excretion of billiary copper due to lysosomal defect in liver cells. There is diffuse accumulation of copper in cytosal of hepatocytes. When liver cells become over loaded, copper is redistributed to other tissues like brain, cornea and kidneys. The gene for Wilson disease has been mapped to chromosome 13q-14.3. Due to multiple mutations in the gene of Wilson disease presentations are variable. More than 250 mutations have been identified. Milder mutation leads to late manifestation of the Wilson disease. [4]

Various clinical presentations

1) Hepatic form- This form present as asymptomatic hepatomegaly, subacute to chronic hepatitis or fulminent hepatic failure or cirrhosis of liver. Hepatic form is seen in young patients. K.F. ring present in 30-50% of patients.[1]
2) Neurogenic form- This usually occurs after second decade but earlier in Indian children.[1] It has insidious onset with intention tremors, dystonia, poor school performance, behavioral changes, dysarthria, incoordination and neuropsychiatric manifestations. KF ring is present in 99% of patients.[1] K.F. ring is due to copper deposit in descemet layer of cornea and is best seen with slit lamp. This ring may disappear with treatment. [5]
3) Psychomotor disturbances –This type manifests in the form of anxiety, depression, and psychosis.
4) Hemolytic anemia- This is possibly due to excretion of large amount of copper by damaged hepatocytes in circulation.
5) Renal involvement may lead to progressive renal failure.
6) Unusual presentations include arthritis, cardiomyopathy, endocrinopathy especially hypoparathyroidism.

Diagnostic features of wilson disease

1) Best screening test is Serum cerulospasmin. Most patients of Wilson disease have decreased levels of Serum cerulospasmin <20 mg/dl. Urinary copper excretion is increased. It may be upto >100µg/day. (N <40µg/day).
2) K.F. ring on slit lamp is pathognomonic.
3) Liver biopsy to estimate hepatic copper contents which exceeds 250µg/gm of dry weight. (N < 10 µg / gm).

Management strategies

1) Restriction of copper intake (avoid fish, nuts, chocolates, liver).
2) D-penicillamine an oral chelating agent 20 mg/kg body weight. Begin therapy with 50% of the desired dose and then increase over 1-2 weeks. The drug has to be continued for life. Side effects include fever, skin rash, arthralgia, pancytopenia and nephrotic syndrome. Tetra-amine dihydrochloride is useful alternative, if child doesn't tolerate D-penicillamine due to its side effects.
3) Zinc suppliments 25 mg thrice a day reduces copper absorption from gut.
4) Vitamin B6 is recommended to be given to counteract the antifolate effect of D-penicillamine.

Prognosis of the disease

Untreated patients die due to hepatic complications like acute fulminant hepatitis, chronic active hepatitis leading to cirrhosis of liver. Neurological complications are progressive in nature ultimately lead to coma and death. Results of chelation therapy are variable, which depend upon prompt & early initiation of therapy. Liver transplant is curative with success rate of 85-90%.

Future prospects

Ammonium tetrathiomolybdate acts by preventing absorption of copper by gut is under trial for patients with neurological disease but experience in children is limited. Gene therapy is an ultimate answer. [4]

Conclusion

Wilson disease must be suspected in any child & teenager, who presents with unexplained acute or chronic liver disease, or abnormal neurological symptoms of unknown cause. In this patient we suspected the diagnosis mainly due to abnormal neurological symptoms, extra pyramidal manifestations and classical K.F. ring. Though neurological manifestations are rare before 20 years of age, this patient had early manifestations.

References

1. Ganguli S, Samanta T; Wilson disease,IAP teaching module 2005.

2. Pandit A, Bhave S, BawadekarA. Wilson disease. Indian j. of pediatrics2002; 69:758-9.

3. Ghai O.P; Essential of pediatrics, 7th edition, CBS publishers, 2009: 291-92.

4. Nelson text book of pediatrics-volume 2, 18th edition. Elsevier2009:1677-79.

5. Kalra Veena; Practical pediatric neurology 2nd edition Arya publications, 2008:205-206.