CASE REPORT

An Interesting Case of Successful Maternal and Fetal Outcome in a Case of Chronic Liver Disease with Wilson Disease

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Abstract

Aim: To understand a systematic and meticulous approach towards Wilson disease, a genetic disorder of copper metabolism, complicating pregnancy.

Background: Wilson's disease results in increased body retention of copper and its eventual toxicity and related effects on several organ systems, especially neurological and hepatic.

Case description: Here we study a case of a female with neuropsychiatric and hepatic manifestations of Wilson disease, conceiving spontaneously eventuating with a successful maternal and fetal outcome.

Conclusion: With the accurate application of a multidisciplinary team approach with timely investigations, imaging studies, and counseling, successful maternal and fetal outcome in Wilson disease is well within our reach.

Clinical significance: Women of reproductive age-groups with Wilson disease, face recurrent miscarriages and poor obstetric outcomes due to copper deposition in the body with the concomitant chronic liver disease and its sequelae making management challenging.

Keywords: Copper, Cirrhosis, Penicillamine, Teratogenic, Thrombocytopenia, Other, Wilson disease.

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Background

The prevalence of Wilson's disease is around 1:30,000.[1] It is an autosomal recessive disease that results in the loss of the ability of the body to excrete out an adequate amount of copper due to deficiency in protein ATP7B. The accumulation of copper in the body causes oxidative damage to the organs. The deposition of copper in the uterus results in infertility[2] and early gestation spontaneous abortions. The copper chelating agents given as a therapy for the disease also have a teratogenic effect on the fetus. Here, we discuss a case of a patient with Wilson disease with several of its manifestations, who conceived spontaneously and had a successful fetal and maternal perinatal outcome with no congenital anomalies in the baby.

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Case Description

A 21-years-old female, known case of Wilson disease since 8 years, presented to our tertiary care hospital's outpatient department at the 5th month of gestation for antenatal care booking. The patient was earlier followed up in the same institute since the time of diagnosis of Wilson disease in the gastroenterology department. She was diagnosed with the disease when referred to this hospital, 8 years ago, for slurring of speech and thrombocytopenia. The first available blood and urine investigations and imaging scans were suggestive of Wilson's disease with early-stage liver cirrhosis and splenomegaly without portal hypertension or ascites. The patient was started on D-penicillamine and zinc sulfate medications for the same. Magnetic resonance imaging of the brain done on diagnosis showed T2 and FLAIR hyperintense lesions in the bilateral caudate nucleus, putamen, thalamus, and posterior part of tegmentum which also showed patchy restriction of diffusion-weighted imaging. Magnetic resonance cholangiopancreatography showed moderate splenomegaly measuring 18 cm and chronic liver parenchymal disease with signs of regenerative nodules. These findings on MRI were consistent with the manifestations of Wilson's disease.

On booking, the patient gave a history of spontaneous conception and continuation of the teratogenic drugs, penicillamine, and zinc sulfate throughout 1st trimester due to loss of follow-up. Baseline investigations showed thrombocytopenia (80,000 cells/microlitre), raised urine copper levels (134 microgram/24 hours) with a normal laboratory range of 15–60 microgram/24 hours, decreased serum ceruloplasmin levels (2.59 mg/dL) with normal laboratory range of 20–35 mg/dL, and deranged liver function tests (total bilirubin – 1.7 mg/dL). An autoimmune workup was done to rule out other causes of the thrombocytopenia which was within normal limits. Abdomen ultrasound and portosystemic Doppler

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studies showed the presence of cirrhotic nodules with altered echotexture of the liver as shown in Figure 1, dilated splenic vein, moderate splenomegaly with few collateral vessels in the splenic hilum, and no ascites. Ophthalmology consultation was sought which showed the characteristic Kayser–Fleischer (KF) rings as seen in Figure 2 on slit-lamp examination in both the eyes. On neurological examination, mild dysarthria and moderate ataxia could be elicited.

With due counseling of the patient and the relatives, the teratogenic risks of the drugs were explained, and informed consent was taken for the continuation of the pregnancy. With a multidisciplinary team approach, revision of the drug dosage of penicillamine was done to 250 mg/day from the earlier dose of 500 mg/day.[3] Second trimester anomaly scan was done to rule out fetal malformations.

Fortnightly follow-up was maintained until the 8th month of gestation and weekly after that, with regular reporting of serum ceruloplasmin, urine copper, and complete hemogram done alongside fetal ultrasound to check for interval growth. The patient has an uneventful course during the antenatal period and went spontaneously into labor at 37 completed weeks of gestation. The patient was delivered normally and vaginally, and a male baby of 2800 gm was delivered, who cried immediately at birth. Since the baby had a 25% chance of inheritance owing to the autosomal recessive mode of inheritance, investigations were undertaken to rule out the inheritance of the disease and also congenital malformations due to the chelating agents of the neonatology team. Active management of 3rd stage of labor was ensured due to the added risk of postpartum hemorrhage due to the existing thrombocytopenia. Since none of the chelating agents are shown to have expression through breast milk in the literature available, breastfeeding was encouraged.

Esophago-gastroduodenoscopy was undertaken in the postnatal period to check for new varices as advised by the gastroenterology team on a routine annual basis. Contraception counseling was done and the patient was willing for an injectable form of depot medroxyprogesterone acetate to avoid subsequent pregnancies. She was eventually discharged and advised regular follow-up with the obstetrics and gastroenterology department.

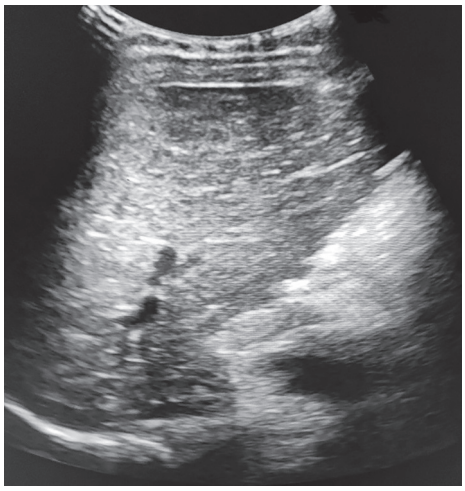

Fig. 1: Altered liver echotexture with nodularity

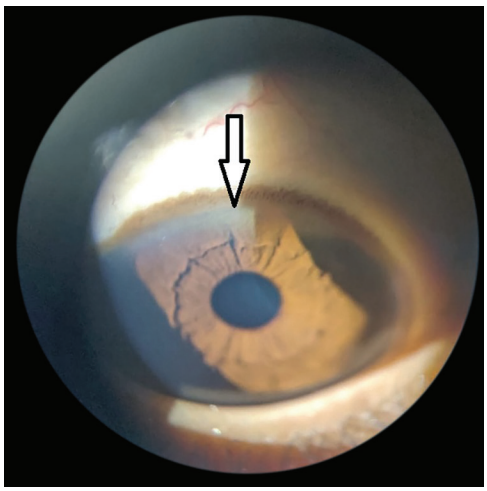

Fig. 2: KF ring (arrow) on slit-lamp examination

Discussion

Liver diseases in pregnancy can be categorized into ones caused during pregnancy and due to pregnancy, or ones existing preconceptionally. The former consists of acute fatty liver of pregnancy, HELLP syndrome, intrahepatic cholestasis of pregnancy, or hyperemesis gravidarum.[4] Wilson disease falls under the latter category. It is a disease characterized by inefficient copper metabolism. It is caused due to ATP7B enzyme deficiency in the liver that results in the impaired pairing of free copper in the body with its transporter ceruloplasmin and inadequate excretion of excess copper into bile. As a result, a non-copper bound form of ceruloplasmin called apoceruloplasmin is released into the bloodstream which is immediately degraded. As a result, serum ceruloplasmin levels are below the normal range, and copper, due to its increased excretion through urine, has urine levels of copper above normal.

Increased copper levels in the body lead to its deposition in organs like the liver, brain, eyes, and the uterus.[5] In the brain, its deposition in the lenticular nucleus and cerebellum led to dystonic dysarthria and ataxia in the patient. Dysarthria is said to be one of the cardinal neurological signs of Wilson's disease. Occupational therapy and rehabilitation sessions aid the patient in coping with these disabilities and improving the quality of life. Deposition of copper in the Descemet membrane in the eyes leads to the characteristic Kayser–Fleischer ring on slit-lamp examination. Deposition in the uterus has toxic effects on the fertilization process and subsequent maturation of the conceptus, causing either infertility or multiple 1st trimester miscarriages. In the liver, cirrhosis and its sequelae in the form of portal hypertension and splenomegaly were detected on ultrasound, which would cause splenic sequestration of platelets, resulting in thrombocytopenia. Increased values on immature platelet fraction tests confirmed the increased destruction of platelets as a cause of thrombocytopenia, rather than decreased production. Keeping blood and blood products cross-matched and ready if required intrapartum along with immaculate use of uterotonics went a long way in insuring against the ensuing thrombocytopenia, which might have caused a catastrophic postpartum hemorrhage in the 3rd stage of labor and beyond.

The other point of discussion here is the focus on the chelating agents. Zinc salts and D-penicillamine were used for several years in this patient to reduce the effective serum copper concentration. But given the teratogenicity of D-penicillamine seen in studies done

on rats, like fetal skeletal defects, cleft lips, and fetal resorption of the drug, a strict ultrasound monitoring for malformations and interval growth monitoring is essential. Regulating the dosage of D-penicillamine to 250 mg/day in the antenatal period from the erstwhile dose or 500 mg/day in the pre-conceptional period helps avoid the risks of fetal malformations.

Conclusion

Thereby, a multidisciplinary team approach through the pre-conceptional, antenatal, intrapartum, and postnatal periods is necessary for the appropriate management of a case of Wilson disease for a successful fetal and maternal outcome.

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