Case Report *doi: 10.5455/medscience.2015.04.8302*

Postpartum Diagnosed Wilson's Disease

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Abstract
Wilson's disease is an autosomal recessive genetic disorder in which defective biliary excretion of copper leads to its accumulation, especially in liver, brain and cornea. Clinical manifestations can vary widely. Untreated Wilson's disease may lead to subfertility and pregnancy complications such as; recurrent miscarriages, induced hypertension, preeclampsia, placental abruption and intrauterine growth restriction. Here we present a case with Wilson's disease (WD) diagnosed postpartum, underwent urgent cesarean section with a presumptive diagnosis of HELLP (Hemolysis, Elevated Liver Enzymes, Low Platelet Count) syndrome. Acute intravascular hemolytic anemia and thrombocytopenia in WD can be interpreted as a feature of HELLP syndrome besides acute liver failure. It should be considered in the diferrantial diagnosis.

Keywords: Wilson's disease, pregnancy, HELLP syndrome, postpartum, diferrantial diagnosis

(Rec.Date: Apr 28, 2015 Accept Date: May 11, 2015)

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Introduction

Wilson's disease (WD) is an autosomal recessive genetic disorder in which defective biliary excretion of copper leads to its accumulation, especially in liver, brain and cornea [1]). It is found world-wide, with a prevelance of 1:30.000- 1:100.000 live births [2]. Clinical manifestations can vary widely, but the key features of the disease are hepatic, neurophychiatric disturbances and Kayser-Fleischer rings in Descement membrane of the cornea. Hemolysis associated with acute liver failure is also a common finding [1-3]. Untreated Wilson's disease may lead to subfertility and pregnancy complications such as; recurrent miscarriages, induced hypertension, preeclampsia, placental abruption and intrauterine growth restriction [4].

Here we present a case with Wilson's disease diagnosed postpartum, underwent urgent cesarean section with a presumptive diagnosis of HELLP syndrome.

Case

A 38 year-old, gravida 2 para 1, woman with 35 weeks of gestation was admitted to our emergency room with labour pain and vomiting. She had a blood pressure between 140/80-150/100 on admission and had 3+proteinuria on urinalysis.

Baseline investigations showed haemoglobin 10.3 g/dL, platelets 60.000/mm3, blood urea 6 mg/dL, creatinine 0.73 mg/dL, total bilirubine 3.53 mg/dL, AST:97 u/L,ALT:88 u/L, INR 2.3, fibrinogen level 126 mg/dL.

Ultrasound examination revealed alive fetus with biometric measures of 34 weeks and oligohydramnios. The emergency cesarean section was performed under general anesthesia based upon the diagnosis of HELLP (Hemolysis, Elevated Liver Enzymes, Low Platelet Count) syndrome.

On postpartum day 5, despite being normotensive and appropriate supportive treatment, her laboratory parameters such as AST,ALT, bilirubin and INR levels showed an increase and ecchymoses appeared widely in her body.

Abdominal ultrasonography revealed hepatomegaly with echo poor echo pattern and marked periportal echogenicities consistent with chronic liver parenchymal disease, normal blood flow through the portal vein, an enlarged spleen and ascites.

She had no history of intake of any drug with known hepatotoxicity. Her medical and obstetric history was normal. Her grandfather had a history of cirrhosis. She tested negative for all hepatitis viruses. She also tested negative for ANA, ASMA, anti LKM1, AMA antibodies by ELISA.

Her neurological examination and cranial MRI was normal, however ophtalmoscopic examination by slit lamp showed Kayser-Fleischer rings in both eyes. On further examination her serum ceruloplasmin level was 10.9 mg/dL, serum copper was 72.6 mcg/dL and 24 hours urinary copper was 750 mcg/24hrs.

Patient was diagnosed as Wilson's disease and put on copper chelation therapy.

Discussion

WD is a rare autosomal recessive disorder resulting in copper overload. It was first described in 1912 by Kinnear Wilson as progressive lenticular degeneration [5]. In 1993 the gene that is abnormal in WD was identified as ATP7B which is located on the 13 th chromosome. Responsible for the transport of copper from the hepatocytes to bile is the protein ATP7B. The Wilson's disease gene mutation leads to absence or diminished function of ATP7B, resulting in a decrease in biliary copper excretion [6].

The clinical presentations of WD are liver and neuropsychiatric problems. Chronic active hepatitis, culminating in cirrhosis is the most common hepatic presentation, but some patients present with fulminant liver failure. Typical neurological sign include tremor, rigidity, drooling, incoordination, tremor, difficulty with fine motor tasks, and gait difficulties. Psychiatric manifestations include compulsive behavior, aggression, depression, impulsive behavior, and phobias [4,7].

The clinical hallmark of Wilson's disease is the Kayser–Fleischer ring caused by deposition of copper in Descement's membrane of the cornea which is present in 95% of patients with neurologic symptoms and somewhat over half of those without neurologic symptoms [8]. It

can be identified with a slit-lamp examination as we did in our patient. But it should be kept in mind that Kayser–Fleischer rings may be absent in up to 50% of patients with Wilson's disease affecting the liver [8].

The majority of patients with Wilson disease are diagnosed between the ages of 5 and 35 years. Diagnosis is based on clinical evaluation along with biochemical and neuroimaging confirmation. Biochemical studies reveal a low serum ceruloplasmin level (<20 mg/ dl) and increased urinary copper excretion (more than >100 ìg copper per 24 hours). Hepatic copper estimation, of more than 250 g/g of dry tissue (Normal 15-55 ìg/g) is the most definitive method of diagnosis [9]. Magnetic resonance imaging (MRI) or computerized tomography of the brain may detect structural abnormalities in the basal ganglia [10]. The most frequent findings are an increased density on computerized tomography or hyperintensity on T2 MRI in the region of the basal ganglia. MRI may be more sensitive in detecting these lesions. Abnormal findings are not limited to this region, and other abnormalities have been described. A characteristic finding in Wilson's disease is the ''face of the giant panda'' sign but is found only in a minority of patients. We couldn't detect abnormalities in our patients' cranial MRI.

In the reproductive period of women with Wilson's disease; infertility due to menstrual irregularities result of hormonal changes caused by hepatic failure and recurrent miscarriages at the first trimester because of increased copper deposition in the uterus are two major issues. But spontaneous conceiving, successful pregnancies and uneventful full term delivery may occur in treated patient [1-4].

Pregnancy does not seem to have adverse effect on the clinical course of Wilson's disease but the patient's copper status should be optimized prior to pregnancy. Otherwise the increased copper levels can bring out the development of preeclampsia caused by copper accumulation in the liver as in our case. It may also cause intrauterine growth restriction. Copper deposition in uterus may be cause the abruption of the placenta. The fetus may also suffer neurologic damages, which are often a result of hypoxia caused by the accumulation of copper in the placenta and fetal tissue [4].

Prepregnancy counselling and antenatal monitoring of these women might avert feto-maternal complications to a certain considerable extent. However while women remained undiagnosed as in our case, Wilson's disease should be considered in the differential diagnosis of HELLP

syndrome. The presence of hemolytic anemia, thrombocytopenia and elevated liver enzymes may lead to confusion in diagnosis, hepatosplenomegaly, and ascites, acute liver failure on postpartum period should suggest the reviewing of presumptive diagnosis [11].

Women with Wilson's disease who become pregnant are recommended to have their treatment continued throughout pregnancy. Interruption of treatment during pregnancy has resulted in acute liver failure.Treatment with chelating agents (both D-penicillamine and trientine) and zinc salts have been associated with satisfactory outcomes for both the mother and fetus [4]. Although considered to be a safe choice in pregnancy, in a small number of cases d-penicillamine has been reported to cause congenital malformations of the fetus, including fragile blood vessels, low positioned ears, micrognathia, and hyperflexy hips and joints [12].

Conclusion:

Wilson's disease is a rare congenital disease. Acute intravascular hemolytic anemia and thrombocytopenia in WD can be interpreted as a feature of HELLP syndrome besides acute liver failure. It should be considered in the diferrantial diagnosis. These pregnancies demand intense monitoring and team work in order to achieve a successful outcome for both the mother and the child.

Conflict of interest: We have no financial or commercial conflicts of interest.

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