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Case of Successful Pregnancy in Wilson's Disease

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ABSTRACT

Wilson's disease or Hepatolenticular degeneration is an inherited condition of autosomal recessive type wherein the copper transporting gene ATP7B is variably affected leading to copper overload in the body. Two main manifestations are seen. The hepatic, which generally presents earlier,and the neuropsychiatric form. The incidence ranges between 1 in 5000 to 1 in 30000. Untreated female patients additionally suffer from subfertility, the reason for which is not very clear. However, treatment of the disease usually corrects the problem and successful pregnancy may ensue. Here, we present a rare case of successful pregnancy in Wilson's disease on treatment with zinc.

Keywords: *Wilson's disease, Hepatolenticular degeneration, Pregnancy.*

INTRODUCTION

Wilson's disease is a manifestation of excess copper deposition in various parts of the body. Amongst these, the liver and brain bear most of the brunt of the disease. Its incidence is 1in 5000 to 1 in 30000 while the heterozygous carrier rate is 1 in 90. It is an autosomal recessive, inherited condition wherein the copper transporting gene ATP7B suffers mutations, insertions or deletions anywhere along its long length of 21 exons [1]. Most of the female patients suffer from subfertility or repeated miscarriages [2]. However, treatment may result in a normal pregnancy [3]. Here we present a rare case of successful pregnancy in Wilson's disease on treatment with zinc.

CASE

A 28 year old third gravida with previous 1 live issue reported to us at 5 weeks gestation for antenatal booking. Her index pregnancy, 4 years back, had been normal with regard to her personal history and course of pregnancy. But during her second pregnancy, 2 years back, she developed sudden unexplained jaundice in the late first trimester. Thereafter, in her second trimester, the patient had a psychotic breakdown. Subsequently she went into preterm labour at 7 months of gestation and was referred to our hospital where she delivered a premature male baby. He was admitted to the neonatal intensive care unit but died at 1 month of extra uterine life.

At the time of the second pregnancy, following delivery, patient was referred to the Gastroenterology wing of the same hospital where she was investigated on the lines of Wilson's disease based on high degree of suspicion regarding her condition (unexplained haemolytic jaundice with low liver enzymes in a young patient with neuropsychiatric symptoms). Based on her serum ceruloplasmin of 15 mg/dL, 24 hours urinary copper 227.75µg, positive Kayser-Fleischer rings and liver biopsy, copper >320 µg/ gm of dry weight of liver tissue she was positively diagnosed as a case of symptomatic Wilson's disease and started on Zinc therapy (50 mg twice daily).

During her present (third) pregnancy patient was booked and all her routine investigations were normal. She was under constant supervision of a team of obstetrician and gastroenterologists. Zinc therapy continued throughout with iron, calcium and the entire course of pregnancy remained uneventful. At 37 weeks of gestation, patient reported to the labour room with 6 cm dilatation and she delivered a female baby of 2.7 kg. Both mother, child remained healthy and at the time of her discharge 24 hours urinary copper was 60.23µg and serum ceruloplasmin 21.5mg/dL.

DISCUSSION

As has been previously stated, the symptomatology of Wilson's disease depends on copper deposition in various organs like the brain and liver which is why it is also called hepato-lenticular degeneration. The hepatic presentation has an earlier manifestation almost by a decade, in comparison to its neuropsychiatric form. In India, the disorder presents even earlier possibly due to the traditional practice of eating in copper utensils Symptoms start appearing once copper causes oxidative damage to the hepatocytes and as a result is released into circulation, again causing damage to the erythrocytes. This results in haemolysis and jaundice as was present in our patient. Excess copper in the blood gets deposited in the lenticular nucleus of the brain causing necrosis, gliosis and cystic changes. About one third of these patients present primarily with psychiatric manifestations, similar to our patient. Kayser-Fleischer rings are deposition of copper in the descemet's membrane in the limbus of the cornea, seen on slit lamp examination. These reflect copper deposition in the brain and are present in 90% of patients of Wilson's disease with neuropsychiatric manifestation. However, they disappear upon treatment [1].

Untreated Wilson's disease may cause subfertility in female patients [2,4]. The reason is not clear, but this

may be a direct effect of the hormonal changes associated with liver disorders [4]. In liver failure there is inability to metabolize oestrogen & progesterone and levels of sex hormone binding globulins remain low. As a consequence the excess hormones exert an inhibitory effect on the pituitary, decreasing follicle stimulating hormone (FSH) and thereby inhibiting follicular growth in the ovary. Excess oestrogen also causes endometrial hyperplasia in the uterus thus causing menstrual irregularity (Guyton & Hall Text book of Medical Physiology, 12th Edition). However, these changes may be seen with liver failure of any aetiology.

Evidence of association of copper with subfertility comes indirectly from old studies related to intrauterine copper devices. Although copper appears to have some effect on the blastocyst, its main effect is on the inability of the endometrium to participate in the implantation process as a result of decreased metabolism of prostaglandins in the uterus [5]. Another novel mechanism attributed to copper intrauterine devices is decrease in HOXA10 expression in the uterus by suppressing the gene. This leads to decreased endometrial receptivity [6]. Possibly, the same mechanisms work in Wilson's disease. More recently, in a study conducted by Torgut A. et al, they found significantly higher levels of copper in serum of patients of endometriosis. However, it is encouraging to see that treatment of Wilson's disease by copper chelation or decreasing intestinal absorption seems to reverse the mechanism causing subfertility and successful pregnancies may ensue as a result as evidenced by our case. A point to note in our case is that the index pregnancy had also been uneventful at which time the patient showed no symptoms of the disease. This may have been possibly due to less damage caused in the pre-symptomatic stage or the patient may not have had a severe mutation. Also, she may have been heterozygous for the condition. However, confirmation by mutation analysis is a very difficult, tedious process and not always feasible.

In conclusion, early detection and treatment of the disease leads to satisfactory quality of life for the female patient although the treatment may have to be taken lifelong.

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