Case Report

Alpha-Methyldopa-induced hepatitis during pregnancy

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Summary

Alpha-methyldopa is one of the most widely used antihypertensive drugs during pregnancy. In spite of its known potential hepatotoxicity, there have been only a few reports describing hepatotoxicity with the use of this drug during pregnancy. We report here a new case of a 36-year-old pregnant hypertensive woman presented with acute hepatitis related to the use of alpha-methyldopa.

Keywords: *Alpha-Methyldopa; Acute; hepatitis; pregnancy*

Introduction

Although it is difficult to diagnose the liver diseases in pregnancy, the diagnosis is very important as it has clinical and prognostic implications for both the mother and the fetus. Medications can often be unnoticed as a cause of liver diseases in this situation. We present a case of acute toxic hepatitis in a pregnant woman secondary to α-methyldopa.

Case presentation

A 36 years old, pregnant female at the beginning of the third trimester of pregnancy (gravida 2, para 2) presented with deep jaundice, pruritis and persistent elevation of liver enzymes for more than 2 months ago. Her previous two pregnancies were normal. She had a history of arterial hypertension diagnosed two years ago. She was treated during the pregnancy with α-methyldopa (500 mg once a day). Medical examination and laboratory tests were performed. Upon examination, she was obese with body mass index more than 35 and with jaundice, normal fetal monitoring, and an abdominal pain in right upper quadrant. Laboratory investigations revealed a total serum bilirubin of 4.2 mg/dl (indirect 3.9 mg/dl and direct 0.3 mg/dl), albumin was 4.2 g/dl, alkaline phosphatase 275 U/L (20-105), γ-glutamyl transpeptidase 123 U/L (5-35), aspartate aminotransferase 1440 U/L (5-35), alanine aminotransferase 1115 U/L (10-35) and International Normalized Ratio (1.3). Hemoglobin, platelets, white cell count and serum creatinine were all within normal limits. The patient was negative for anti-HCV (3rd generation), HBV (negative HBsAg, anti HBc IgM,), anti HEV, anti HAV IgM. Autoimmune hepatitis was excluded by negative anti smooth muscle antibody, antimitochondrial antibody and anti-liver kidney microsomal (LKM). The patient had been diagnosed as acute hepatitis induced by α-methyldopa. The α-methyldopa has been withdrawn on the first day of diagnosis and replaced by calcium channel blocker. Three weeks later, the patient showed an improvement in hepatocellular function characterized by a rapid decrease in the serum bilirubin to normal level and a normalization of serum transaminase.

Discussion

Alpha-methyldopa is commonly used for the treatment of arterial hypertension during pregnancy because the drug produces less of a direct effect on the vascular system in the fetus than other antihypertensive drugs. The

pathogenesis of the associated hepatotoxicity could be linked to an abnormal transformation of the drug by cytochrome P450 and/or an autoimmune reaction to that metabolite. Methyldopa is a pro-drug that is metabolized to alpha-methylnorepinephrine (its active component) when the transformation of the pro-drug via CYP 450 enzymes is disrupted and an immune reaction to the resulting metabolite occurs[1]. The risk of hepatotoxicity from methyldopa in pregnant patients is approximately 1% and can occur between 1 and 20 weeks within starting the drug. The clinical spectrum ranges from minor elevation of liver enzymes to fulminant hepatitis and the severity of liver injury does not appear to be related to the dose of methyldopa[2]. The literature reviewed on pubmed until 2014 reveled nine cases of hepatotoxicity from α-methyldopa[1,3-8]. The onset in most of the cases was characterized by asthenia, nausea, vomiting, jaundice, and coluria. In addition to those symptoms, three patients had experienced pruritus and two had presented with fever[9]. In our case the serum bilirubin and liver enzymes dramatically decreased after three weeks from stoppage of α-methyldopa and the general condition of the patient improved.

Conclusion

Alpha-Methyldopa is a frequent antihypertensive drug that is used in pregnancy. This case report of acute hepatitis in pregnant women, draws attention to these drug and consideration of monitoring of liver enzymes and serum bilirubin during pregnancy in women treated by α-methyldopa and immediate withdrawal of that medication when hepatitis developed.

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