Hyperthyroidism in a Patient with Bartter Syndrome

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A 27-year-old female presented with a history of weight loss, insomnia, and palpitations. She had been diagnosed with Bartter Syndrome since childhood and was on hemodialysis due to renal failure secondary to nephrocalcinosis. Her thyroid function test showed hyperthyroidism with a thyroid stimulating hormone (TSH) level of 0.01 uIU/ml (normal range: 0.27-4.2 uIU/ml), FT4 level of 60.27 ppmol/L (normal range: 12-22 pmol/L), and FT3 level of 29.11 pmol/L (normal range: 3.1-6.8 pmol/L). The patient was also found to have a high alkaline phosphatase level of 781 IU/L (normal range 35-105 IU/L). She was started on carbimazole and propranolol, and her TSH was 0.01, her FT4 level was 26.2 pmol/L, and her FT3 level was 7.4 pmol/L. However, her alkaline phosphatase level increased to 1176 IU/L. Carbimazole was then discontinued, and the patient was started on radioiodine therapy. Three months following radiodine therapy the thyroid function test was repeated, and her TSH was 21.64 uIU/ml, her FT4 level was 1.61 pmol/L, and her FT3 level was 1.09 pmol/L. The patient was then started on levothyroxine (25 mcg).

INTRODUCTION

Hyperthyroidism is a condition where the thyroid gland produces excess levels of thyroid hormone. Many hypotheses have been proposed to explain the abnormalities in liver function tests in patients with thyrotoxicosis, including liver hypoxia, cardiac insufficiency with liver venous congestion, direct damage induced by excess triiodothyronine (T3) or anti-TSH receptor antibodies (TRAb), co-existence of autoimmune liver disease, and antithyroid drug-induced hepatotoxicity. Patients with thyrotoxicosis were found to have higher levels of alkaline phosphatase, which indicates an increased bone-turnover activity[1,2].

Antithyroid drugs have been used in the management of hyperthyroidism, including propylthiouracil, methimazole, and carbimazole. Their primary effect is to inhibit thyroid-hormone synthesis by interfering with the thyroid peroxidase-mediated iodination of tyrosine residues in thyroglobulin, which is an important step in thyroxine synthesis. The side effects of methimazole and carbimazole are dose related, while propylthiouracil's side effects are less related to the dose.

Hepatotoxicity is a major side effect of anti-thyroid drugs. Propylthiouracil-related hepatotoxicity is an allergic hepatitis with laboratory evidence of hepatocellular injury. This condition is marked by elevated aminotransferase levels and submassive or massive hepatic necrosis in the biopsy. The rare hepatic abnormalities associated with methimazole and carbimazole are typical of a cholestatic process.

Biopsy specimens show preserved hepatocellular architecture along with intracanalicular cholestasis and mild periportal inflammation. Complete but slow recovery is seen after drug discontinuation. This study presents a case of a patient with Bartter syndrome and hyperthyroidism in which carbimazole was started causing cholestatic liver impairment. Carbimazole was discontinued, and the patient was then treated with radioiodine therapy.

THE CASE

A 27-year-old female presented with a known case of Bartter syndrome with nephrocalcinosis and was on hemodialysis. She had initially been diagnosed with Hashimoto's thyroiditis during childhood and was started on thyroxine replacement therapy. Thyroxine replacement was then stopped as her laboratory results were showing hyperthyroidism. She had a history of palpitations and insomnia (Figure 1). Her laboratory investigations showed a TSH level of 0.01 uIU/ml (normal range: 0.27-4.2 uIU/ml), FT4 level of 60.27 pmol/L (normal range: 12-22 pmol/L), and FT3 level of 29.11 pmol/L (normal range: 3.1-6.8 pmol/L)). The patient was also found to have a high alkaline phosphatase level of 781 IU/L (normal range 35-105 IU/L). Other liver function test results were within normal limits.

A thyroid scan was done, which showed an increase in total thyroid uptake of 8.9% (5.4% on the left side and 3.6% on the right side; Figure 2). She was started on propranolol and carbimazole at 10 mg twice daily. Her liver function test showed cholestatic derangement with an increased alkaline phosphatase level of 1176 IU/L. Carbimazole was then discontinued.

The patient was then started on radioiodine therapy. Three months following radioiodine therapy the symptoms improved with resolution of the hyperthyroid symptoms. Further investigations for the high alkaline phosphatase level were done. An abdomen ultrasound showed mild hepatomegaly suggestive of chronic liver parenchymal disease and chronic non-calcular cholecystitis. Serology testing was negative for hepatitis B and C, and the ANA screening result was negative. The thyroid function test was repeated, which showed a TSH of 21.64 uIU/ml, FT4 level of 1.61 pmol/L, and FT3 level of 1.09 pmol/L. The patient was started on levothyroxine at 25 mcg.

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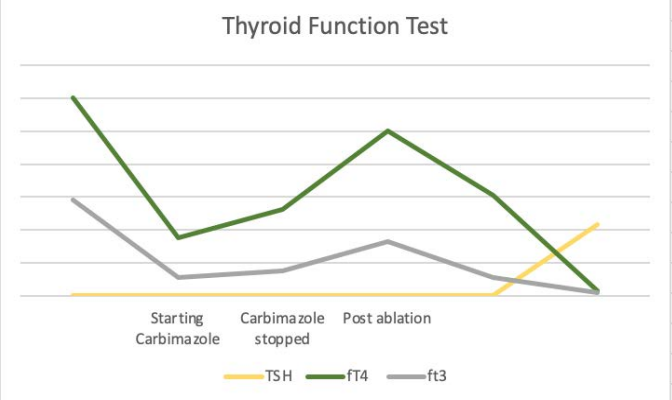

Figure 1: Thyroid function test

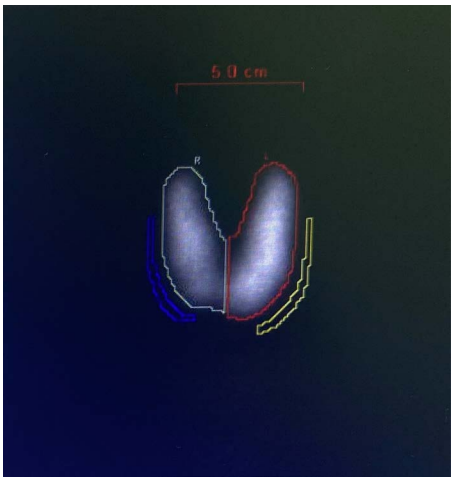

Figure 2: Ant 99m Technetium scan

DISCUSSION

In a cohort study done on 1514 subjects with thyrotoxicosis, the incidence of abnormal liver function within six months of thyrotoxicosis was 39%[1]. Acute symptomatic cases in patients with thyrotoxicosis are very uncommon, including hepatitis, cholestasis, and fulminant hepatic failure[1]. The mechanisms involved in an abnormal liver function test in a patient with hyperthyroidism include the development of ischemia and tissue necrosis due to increased liver oxygen consumption caused by thyrotoxicosis without a concomitant increase in hepatic blood flow[3,4,5].

Another mechanism of abnormal liver function tests in patients with thyrotoxicosis is right-sided heart failure with venous congestion[6]. A third hypothesis involves a direct hepatotoxic effect of excess thyroid hormones. Cellular lines in animal models have shown disruption of the outer mitochondrial membrane after exposure to high concentrations of T3[7,8]. Anti-thyroid medications are also found to cause abnormal liver function tests in patients with thyrotoxicosis.

In a recorded case, it was shown that treatment with carbimazole in a patient with thyrotoxicosis caused him to develop jaundice and pruritus. His liver function test showed cholestasis with hyperbilirubinemia secondary to cholestatic drug reaction. In that patient, carbimazole was discontinued, and the patient was started on prednisolone at 25 mg and propranolol. Thereafter, his liver function improved and normalized. After three months of carbimazole cessation, he was then treated with radioactive iodine, which led to normalization of his thyroid function test within 2 months[1].

Radioactive iodine therapy has been used in patients with hyperthyroidism. It improves symptoms of hyperthyroidism within weeks of initiation. Post-ablation thyroid function should be monitored throughout life, and if hypothyroidism develops, it should be treated immediately[2].

CONCLUSION

We have presented a case of a patient with Bartter's syndrome with nephrocalcinosis on hemodialysis who was diagnosed with Graves' disease and also found to have a mildly elevated alkaline phosphtase level. She was initially started on cabrimazole and propranolol, after which her alkaline phosphatase level increased, and carbimazole was discontinued. It is important to recognize the side effects of anti-thyroid medications as well as the causes of impaired liver function in patients with hyperthyroidism.

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