Magnetic resonance cholangiopancreatography (MRCP) showed irregularly dilated intrahepatic biliary tree suggestive of PSC. The present case aims to shed light in this gap. Further studies are needed to investigate this association.

Keywords: Grave's disease; Primary sclerosing cholangitis (PSC); Immunogenetic mechanism; Association between Grave’s and PSC

Abstract

Grave’s disease is an autoimmune thyroid disease with multi-system involvement. It’s manifestations are diverse, including liver function abnormalities and association with other autoimmune disease. The objective of this report is to present an unusual case of Grave’s disease with PSC. This is a 28-year-old woman that present with cholestatic jaundice along with signs and symptoms of thyrotoxicosis. She diagnosed to have Grave’s disease with PSC. Despite an initial high bilirubin, treatment with antithyroid agents in addition to Ursodeoxycholic acid led to marked improvement in her clinical status and bilirubin level. The proposed mechanisms underlying the association of Grave’s disease with PSC are discussed and the literature on similar cases is highlighted. Both Grave’s disease and PSC have been shown to be associated with other autoimmune mediated diseases. This case report shows an association between Grave’s disease and PSC whether due to an underlying immune-genetic predisposition or coincidence. Further studies are needed to investigate this association.

Table 1: Laboratory data on admission.

| Parameter                  | Result |
|----------------------------|--------|
| Liver function test        |        |
| AST (IU/L)                 | 78     |
| ALT (IU/L)                 | 128    |
| Total bilirubin (mg/dL)    | 110.4  |
| Direct bilirubin (mg/dL)   | 95.9   |
| GGT (IU/L)                 | 251    |
| ALP (IU/L)                 | 364    |
| Albumin (g/L)              | 37     |
| INR                        | 1.8    |
| Viral markers              |        |
| IgM anti-HAV               | Negative|
| HBsAg                      | Negative|
| Anti-HBc                    | Negative|
| Anti-HBs                    | Negative|
| Anti-HCV                    | Negative|
| Thyroid function test      |        |
| TSH (mIU/L)                | <0.005 |
| Free T4 (pmol/l)           | 88.4   |
| Free T3 (pmol/l)           | 36.4   |
| Autoantibodies             |        |
| Thyroid stimulating antibody| Positive|
| Anti-TPO                   | 225.6  |
| TG                         | 5.35   |
| Anti-LKM                   | Negative|
| ANA                        | 1 : 40 |
| Anti-smooth muscle antibody| Negative|
| AMA                        |        |

Case Report

A 28-year-old Saudi female was presented in the emergency department of King Fahad Medical City (KFMC), Riyadh, Saudi Arabia, with a history of chronic pruritus (4 months) with undocumented weight loss, diarrhea, palpitations and heat intolerance in the last month. Five days prior to presentation she developed jaundice. Grave’s disease was present in the family history (maternal).

On examination, the patient had icteric sclera with a pulse rate of 100 beats/min. Physical examination showed signs of thyrotoxicosis. She had a diffusely enlarged thyroid gland with positive bruit, hand tremors, warmth, and sweating. Eyes signs: lid lag, lid retraction and exophthalmos with evidence of proximal myopathy. Laboratory showed elevated liver function: ALT: 128 IU/L, AST: 78 IU/L, ALP: 364 IU/L, GGT: 251 mg/dL, Total bilirubin 110.4 mg/dL and direct bilirubin: 95.9 mg/dL. Thyroid function test was consistent for hyperthyroidism (TSH<0.005 mIU/L, Free T4: 88.4 pmol/l, Free T3: 36.4 pmol/l, positive TSH receptor antibodies, Anti-TPO 225.6 and TG 5.35) (Tables 1 and 2). Thyroid ultrasound showed diffusely enlarged thyroid gland (The right lobe is measuring 1.8 cm x 2.1 cm x 5.3 cm and the left 1.9 cm x 1.7 cm x 4.9 cm) with heterogeneous echotexture and increased vascularity. Thyroid scintigraphy showed enlarged thyroid with diffusely inhomogeneous increased uptake consistent with the diagnosis of Grave’s disease (Figures 1 and 2). Computerized tomography (CT) of the abdomen and pelvis with IV contrast in the porto-venous phase showed irregularly dilated intrahepatic biliary tree suggestive of PSC. Magnetic resonance cholangiopancreatography (MRCP) showed extreme dilatation of intrahepatic biliary tree with multiple focal nodules suspicious for PSC. The patient was treated with propylthiouracil and Ursodeoxycholic acid.

Discussion

Grave’s disease is an autoimmune thyroid disease defined by the presence of thyroid stimulating antibodies. The incidence of vitamin D deficiency is high among patients with autoimmune thyroid disease. The association of Grave’s disease with liver disorders is common and primary sclerosing cholangitis is one of these. Other autoimmune diseases have been associated with primary sclerosing cholangitis. This is a case report of a patient with Grave’s disease and primary sclerosing cholangitis. Further research is needed to investigate this association.
biliary abnormalities consistent with PSC (Figure 3). Liver biopsy confirmed PSC diagnosis (Figure 2). The patient was initially started on propranolol 40 mg orally TID to control thyrotoxic symptoms, after which she was given Carbimazole 10 mg orally daily. Also, she was started on ursodeoxycholic acid 500 mg orally BID. After improvement of thyroid function with anti-thyroid medications, she underwent radioactive iodine treatment of the thyroid gland which subsequently led to marked improvement in her follow-up liver function tests. With

| Laboratory data       | Sep 2012 | Jan 2013 | May 2013 |
|-----------------------|----------|----------|----------|
| ALT (IU/L)             | 128      | 51       | 69       |
| Total bilirubin (mg/dL)| 110.4    | 298.2    | 44.3     |
| Direct bilirubin (mg/dL)| 95.9    | 272      | 35.5     |
| GGT (IU/L)             | 251      | -        | 522      |
| ALP (IU/L)             | 364      | 203      | 313      |
| Liver function test    |          |          |          |
| Thyroid function test  |          |          |          |
| TSH (mIU/l)            | 0.005    | 0.005    | 0.005    |
| Free T4 (pmol/l)       | 88.4     | 31.2     | 14.6     |
| Free T3 (pmol/l)       | 36.4     | 9        | 4        |

**Table 2:** Follow up liver and thyroid function tests.

**Figure 1:** Thyroid scintigraphy showed enlarged thyroid with diffusely inhomogeneous increased uptake.

**Figure 2:** Bile duct disease consistent with sclerosing cholangitis with early cirrhosis.
time her liver function worsened again with impairment of synthetic function, so she is referred to a liver transplant center and currently she is waiting to undergo liver transplantation.

Discussion

The exact etiology of PSC remains unknown, but several proposed mechanisms include immunologic, infectious, toxic and genetic mechanisms [2]. Majority of existing studies agree that immunogenetic process is the most acceptable pathologic mechanism for PSC based on its association with HLA-B8, DR [3], DR2, DR [4,5-8] and DRw52a [9] as well as increased risk of PSC and ulcerative colitis in first-degree relatives of patients with PSC [10] common association with ulcerative colitis and less commonly with other autoimmune diseases like rheumatoid arthritis, SLE, systemic sclerosis and autoimmune hepatitis [11,12] HLA-B8 and DR3 are associated with autoimmune diseases such as Graves’ disease, systemic lupus erythematosus, and myasthenia gravis [13]. The clinical manifestations of hyperthyroidism are largely diverse, including liver function abnormalities [14-16]. The liver has a central role in de-iodination and also performs specific functions related to thyroid hormone transport and metabolism [17-20]. Normal functioning thyroid and liver axis are essential for normal growth and metabolism [21]. PSC in comparison with inflammatory bowel disease (IBD) was found to be common with other autoimmune diseases like Hashimoto’s thyroiditis, Graves’s disease and Riedel’s thyroiditis [2]. Furthermore, hyperthyroidism is associated with liver function abnormalities, including elevations in transaminases, alkaline phosphatase, prothrombin activity, bilirubin and low serum albumin, although the mechanism of liver dysfunction is unclear [15]. The incidence of thyroid disease with PSC is 2.1 per 100 person-years [16]. In another study looked for associated immune-mediated diseases in 241 patients with primary sclerosing cholangitis, 4% of patients have an association with thyroid disease [22]. Improvement in bilirubin and thyroid function tests seems to be parallel with hyperthyroidism being the crucial contributing factor to cholestasis [15].

Conclusion

This case report showed an association between Grave’s disease and PSC whether due to an underlying immune-genetic predisposition or coincidence. Further studies are needed to investigate this association.

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