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An Unusual Case of Grave's Disease with Primary Sclerosing Cholangitis (PSC)

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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.

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

Introduction

Primary sclerosing cholangitis (PSC) is a cholestatic liver disease of unknown etiology characterized by inflammation and destruction of both the intra- and extrahepatic bile ducts progressing to fibrosis and ultimately cirrhosis [1]. Acceptable mechanisms include immunological and genetics factors [2]. Grave's disease is an autoimmune disease of the thyroid gland which affects approximately 0.5% of the population and is the underlying cause of 50% to 80% of hyperthyroidism cases [3]. While rare, Grave's disease may be associated with other liver conditions and autoimmune disorders [4]. Few cases have reported Grave's disease with PSC. The present case aims to shed light in this gap.

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 ml U/L, Free T4: 88.4 pmol/l, Free T3: 36.4 pmol/l, positive TSH receptors 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 × 2.1 cm × 5.3 cm and the left 1.9 cm × 1.7 cm × 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

Laboratory data	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	
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	

Table 1: Laboratory data on admission.

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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
Liver function test			
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
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.

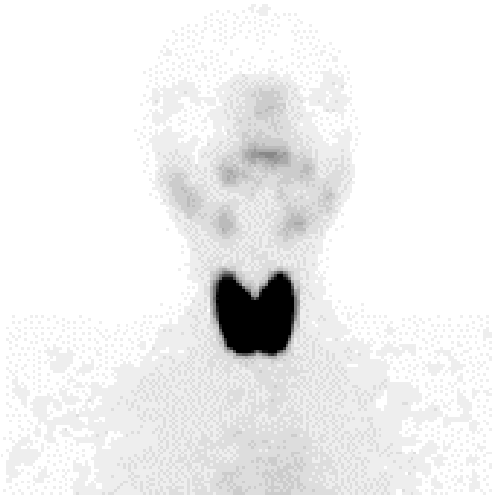

Figure 1: Thyroid scintigraphy showed enlarged thyroid with diffusely inhomogeneous increased uptake.

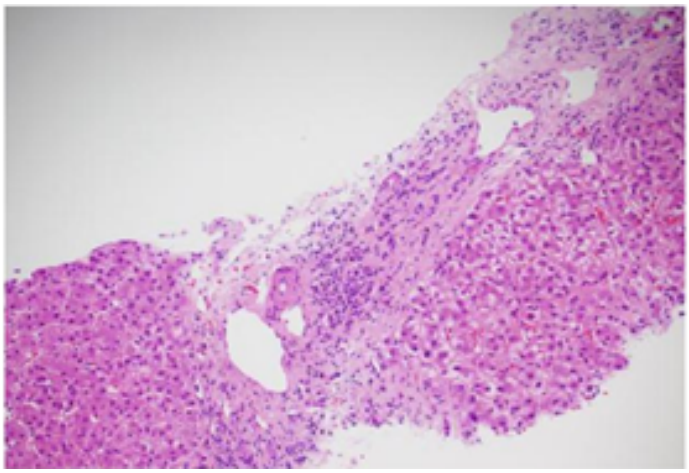

Figure 2: Bile duct disease consistent with sclerosing cholangitis with early cirrhosis.

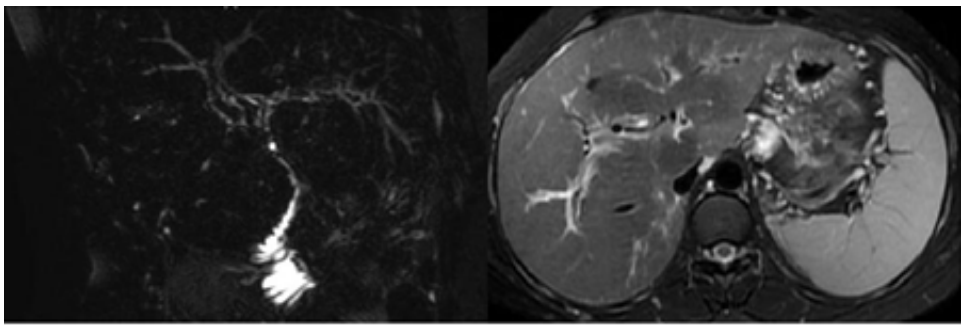

Figure 3: MRCP and liver showed irregularity of the intra and extrahepatic biliary channels consistent with PSC.

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 more 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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