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The liver and thyroid gland: What's the connection?

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Abstract

Thyroid hormones are essential for the normal growth, development, and function of body organs. These hormones regulate the basal metabolic rate of all cells, including hepatocytes. A complex interplay exists between the thyroid and the liver. Thyroid dysfunction can cause liver function test abnormalities, usually reverted by normalizing thyroid status. On the other hand, liver disorders may cause thyroid function abnormalities that may or may not need to be treated. Nevertheless, the relationship between liver and thyroid is often overlooked, and thyroid function is not commonly investigated in patients with liver diseases and vice versa.

Keywords: Hyperthyroidism; liver cirrhosis; hypothyroidism; hepatitis.

Hepatic abnormalities in thyroid diseases

Hypothyroidism

Hypothyroidism may share common symptoms that may be seen in liver diseases for example: Fatigue, weakness, myalgias, muscle cramps, changes in the mental status, dyspnea on exertion, edema, and pericardial effusion are observed both in hypothyroidism and hepatic failure [1]. Moreover, untreated hypothyroidism may be associated with slightly increased serum Alanine Amino-Transferase (ALT) and Gamma Glutamyl Transferase (GGT) concentrations, which may be attributed to diminished lipid metabolism and hepatic steatosis that can occurs in hypothyroidism [2]. In addition, an increase in the Aspartate Amino-Transferase (AST) and Lactate Dehydrogenase (LDH) might be related to hypothyroidism-induced myopathy [3].

Hypothyroidism may play pathogenic factor is gallstone formation via decrease in bilirubin excretion rate due to the decreased activity of bilirubin UDP-glucuronyltransferase, hypercholesterolemia and hypotonia of the gallbladder causing delayed emptying of the biliary tract [4]. It is advisable that all patients with common bile duct stones be screened for thyroid dysfunction [5].

Thyroid hormone medication

Levothyroxine is the treatment of choice for hypothyroidism and a safe medication if the dose is appropriate [6]. Hypersensitivity reactions to levothyroxine associated with increase in the liver enzymes and mild jaundice have been reported [7].

Hyperthyroidism

Hyperthyroidism, particularly Graves Disease (GD), can associated with liver diseases. Up to 10% of patients with GD have a coexisting autoimmune disorder [8]. The association between GD and primary biliary cirrhosis or autoimmune hepatitis is well described in the literature [8]. On the other hand, GD is a common concurrent autoimmune disease associated with different chronic liver diseases [9]. Liver function tests are frequently abnormal in patients with newly diagnosed thyrotoxicosis/hyperthyroidism with a prevalence ranging about 15 and 76% which

may be attributed to the increased oxygen consumption consequent to the enhanced metabolic rate with relative hypoxia in the perivenular region [10]. Serum alkaline phosphatase elevation is the most frequent abnormality in hyperthyroidism, being observed in about 64% of thyrotoxic patients [11]. However this is not necessarily liver-specific, as it can originate from bone and/or liver [12].

Hepatic involvement in overt thyrotoxicosis/hyperthyroidism is usually self-limited, but there are a few case reports of thyrotoxic patients with fulminant hepatic failure especially in patients with coexisting heart failure [13].

Anti-thyroid drugs (ATD)

The overall incidence of ATD-associated hepatotoxicity is estimated to be less than 0.5%, although the exact figures are unknown [14]. The risk of severe liver injury appears to be more frequent by using propylthiouracil, especially in children [15]. Therefore, methimazole, currently is the preferred ATD, except for particular conditions, such as in the first trimester of pregnancy because of the higher risk of malformations associated with methimazole [16].

Thyroid abnormalities in liver disease

Acute hepatitis

In acute hepatitis of mild or moderate severity, patients have elevated serum levels of total T4, due to increased thyroid-binding globulin, which is synthesized as an acute-phase reactant, but normal levels of free T4 [17].

Acute liver failure

In acute hepatic failure, low total T4 levels may reflect reduced hepatocellular synthesis of thyroid-binding globulin. Serum T3 levels are extremely variable, but the free T3:T4 ratio correlates negatively with the severity of the liver disease and has prognostic value [18].

Chronic hepatitis C

Hashimoto's thyroiditis is the most common thyroid disorder reported in patients with chronic hepatitis C and near to 10–15% of the patients had positive thyroid antibodies before starting Interferon (IFN) treatment [19]. Pathogenesis of HCV-related thyroid dysfunction might be mediated by stimulation of the immune system by HCV, rather than by HCV infection itself. A potential oncogenic role of HCV through the direct infection of thyroid cells has been postulated to explain the relationship between HCV infection and the risk of papillary thyroid cancer [20].

Liver cirrhosis

The most common finding is a decrease in serum total T3 and free T3, an increase in reverse T3, in the presence of normal serum TSH levels [21]. Serum T3 concentration is negatively correlated with the Child–Turcotte– Pugh score, a measure of severity of liver dysfunction indicating a direct relationship between severity of liver dysfunction and changes in circulating thyroid hormones [22].

An increase in serum TSH concentrations has also been reported in cirrhotic patients, suggesting primary hypothyroidism [23]. Hyperthyroidism has been also reported in patients with cirrhosis, although less frequently than hypothyroidism [24]. Based on these observations, it is reasonable to suggest that thyroid function tests should be regularly checked in patients with liver cirrhosis and prompt treatment initiated in case of overt or subclinical hypothyroidism (elevated TSH and normal-to-low FT4 and FT3), whereas it is not indicated to treat isolated low FT3 [25]. Furthermore, liver cirrhosis is a cause of mal-absorption, thus hypothyroid patients with severe cirrhosis may require higher doses of levothyroxine [26].

Conclusions

A complex interplay exists between the thyroid and the liver. Thyroid dysfunction can cause liver function test abnormalities, usually reverted by normalizing thyroid status. On the other hand, liver disorders may cause thyroid function abnormalities that may or may not need to be treated.

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