Clinical Characteristics of Concomitant Primary Biliary Cirrhosis and Graves' Disease: A Literature Review

Toru Shizuma

Department of Physiology, School of Medicine, Tokai University, 143, Shimokasuya, Isehara, Kanagawa, Japan

Corresponding author:

shizuma@is.icc.u-tokai.ac.jp

Received date: **Accepted date:** **Published date:**

Abstract

Keywords: Primary biliary cirrhosis; Graves' disease; Hyperthyroidism; Thyrotoxicosis; Hashimoto's thyroiditis

Introduction

Primary biliary cirrhosis (PBC) is an autoimmune liver disease of unknown etiology, although the causes appear to involve both environmental and genetic factors [1,2]. PBC is characterized by chronic progressive cholestasis with destruction of the small intrahepatic bile ducts, particularly the interlobular bile ducts [3-7].

Autoimmune thyroid diseases include Graves' disease (GD) and Hashimoto's thyroiditis (HT). HT is one of the most common autoimmune endocrine diseases and is characterized by autoimmune-mediated destruction of the thyroid gland [8]. Moreover, HT is a relatively common extrahepatic manifestation of PBC. However, the coexistence of PBC and GD is comparatively uncommon. Moreover, it

GD is caused by circulating anti-thyroid stimulating hormone (TSH) receptor autoantibodies that mimic the action of TSH, thereby resulting in increased synthesis and release of thyroid hormones [13,14]. GD is associated with extrathyroidal manifestations, including orbital disease (ophthalmopathy), skin changes, and rarely, fingertip and nail abnormalities [14]. However, its coexistence with other autoimmune liver diseases, such as PBC, is uncommon.

GD Complicated With PBC

Sjögren's syndrome (SjS) appears to be the most common autoimmune disorder concomitantly present with PBC [15-18]. Similarly, HT, rheumatoid arthritis, systemic sclerosis, and Raynaud syndrome may coexist with PBC [17-19]. Silveria et al. [20] reported that among 67 patients with PBC, 32 (48%) had at least one extrahepatic autoimmune diseases and nine (13.4%) had thyroid dysfunction. However, the incidence of GD in PBC patients was not reported in this study [20].

There have been few reports regarding the incidence of GD or hyperthyroidism in patients with PBC. However, Floreani et al. [19] recently reported that among 361 patients with PBC who were followed-up for a mean period of 8 ± 6.9 years, 221 (61.2%) had at least one extrahepatic autoimmune disease. Further, they only found a significant positive association between female sex and extrahepatic manifestation of autoimmune conditions in PBC, while there were no significant correlations between AMA positivity, histological stage, mean age at diagnosis of PBC, and the presence of extrahepatic autoimmune disease [19]. They also reported that among 361 patients with PBC, seven (3.2%) had GD and 45 (20.4%) had HT [19].

Characteristics of Patients with Concomitant PBC and GD

The characteristics of the 24 reported patients of concomitant PBC and GD, including one English and nine Japanese proceedings, are summarized in Table 1 [21-35]. All 24 patients involved females and, notably, both PBC and GD particularly occurred in middle-aged women. Of 10 patients simultaneously diagnosed with PBC and GD, PBC was diagnosed before GD in seven and GD was diagnosed first in seven of the remaining 14 patients. Hence, there was no clear tendency for one disease to precede the other. Concomitant disease was diagnosed in all patients between the ages of 35 and 64 years. The interval between diagnosis of primary and concomitant disease was 0–10 years and within five years in 19 (82.6%) of 23 patients, while the interval was unclear in one case. Therefore, the interval between the diagnoses of primary and concomitant diseases was relatively short. Among all 24 patients, one was familial GD [28]. The most common complicated disease was SjS, which occurred in four (17%) of 24 patients of concomitant PBC and GD [23,28,30].

Case	Year	Sex	Age at diagnosis at PBC (Years)	Age at diagnosis at GD (years)	PBC prior to GD

20. Silveira MG, Mendes FD, Diehl NN, Enders FT, Lindor KD (2009) Thyroid dysfunction in primary biliary cirrhosis, primary sclerosing cholangitis and non-alcoholic fatty liver disease. Liver Int 29: 1094-1100.
21. Nieri S, Riccardo GG, Salvadori G, Surrenti C (1985) Primary biliary cirrhosis and Graves' disease. J Clin Gastroenterol 7: 434-437.
22. Floreani A, Caroli A, Chiaramonte M, Gasparoni P, Naccarato R (1989)