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Case Report

An uncommon case of primary biliary cirrhosis and Hashimoto thyroiditis followed by the concurrent onset of multiple sclerosis and Sjögren syndrome

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ABSTRACT

A 51-year-old woman with a diagnosis of primary biliary cirrhosis and Hashimoto thyroiditis followed by concurrent onset of multiple sclerosis and Sjögren syndrome for seven years was admitted. The patient was treated with pulse steroid and cyclophosphamide combined with a physical therapy program. This is a case of four autoimmune diseases coexisting in a single patient, a finding which has not previously been described in the literature. This combination of autoimmune diseases should be kept in mind in patients with the relevant symptoms and signs of each to provide early diagnosis and appropriate treatment.

Keywords: Autoimmune disease, multiple sclerosis, neurological rehabilitation, Sjögren syndrome.

Autoimmune diseases are conditions which are defined by an excessive immune response resulting in tissue damage and organ dysfunction.[1] Although the etiology of autoimmune diseases still remains under debate, studies have shown that the interaction between genetic, environmental, and lifestyle factors contributes to disease development.[2]

Approximately one-quarter of patients with an autoimmune disease develop additional autoimmune diseases.[3] The coexistence of two or three autoimmune disorders in a single patient has been reported in the literature.[4] In 1988, Humbert and Dupond[5] defined multiple autoimmune syndrome (MAS) as the coexistence of three or more autoimmune diseases in a single patient. The MAS classification divides various autoimmune diseases into three separate groups according to the prevalence of their coexistence and their common pathogenic mechanisms.[6] However, according to this classification system, primary biliary cirrhosis (PBC), Hashimoto thyroiditis (HT), Sjögren syndrome (SS), and multiple sclerosis (MS) do not coexist within the same group.

Herein, we, for the first time in the literature, describe the presence of four autoimmune diseases in a single patient.

CASE REPORT

A 51-year-old female patient with previously diagnosed as PBC and HT presented with numbness and weakness in the left upper and lower extremities. Laboratory findings were positive for anti-nuclear antibody (ANA), anti-mitochondrial antibody (AMA), anti-thyroid antibody, and anti SS-A/Ro antibody.

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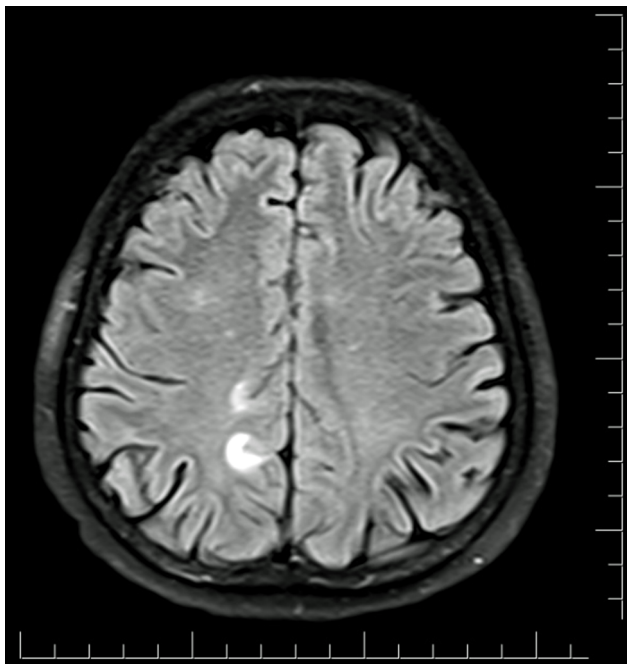

Figure 1. Axial T2-weighted cranial magnetic resonance imaging showing multiple active demyelinating lesions in the supratentorial region.

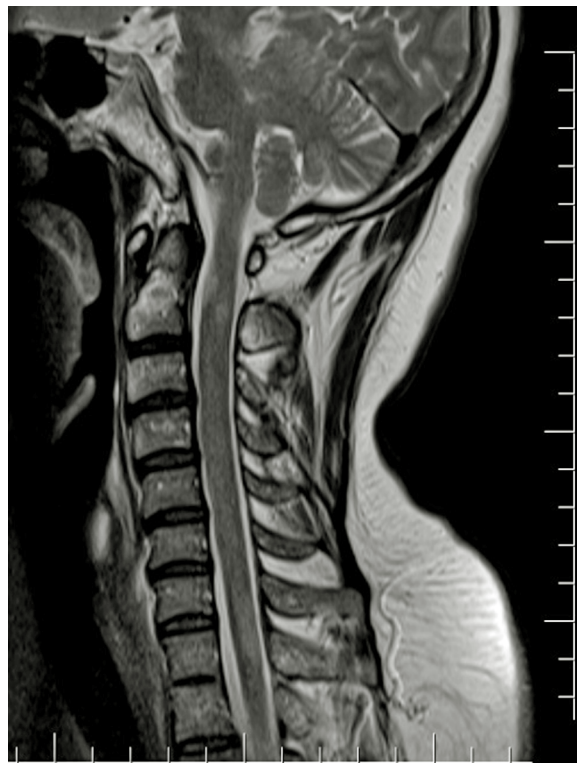

Figure 2. Sagittal T2-weighted MRI of the cervical spine showing chronic demyelinating lesions at the levels of C2 and C7-T1.
MRI: Magnetic resonance imaging.

Cranial magnetic resonance imaging (MRI) showed multiple demyelinating lesions in the supratentorial region with areas of active inflammation (Figure 1). Spinal MRI revealed chronic demyelinating lesions at the levels of C2 and C7-T1 (Figure 2). Laboratory analysis of the cerebrospinal fluid (CSF) revealed a cell count of 8/mm^3, protein 37 mg/dL, two oligoclonal bands, and an elevated immunoglobulin G index. Further questioning revealed symptoms of dryness of the eyes and mouth. Biopsy of the labial minor salivary gland was compatible with an SS score of three. Opthalmologic evaluation revealed a positive Schirmer test result.

The patient was diagnosed with coexistent MS and SS and treated with pulse steroid and cyclophosphamide with a good response to treatment. One year later, following a diagnosis of chronic colitis, cyclophosphamide treatment was discontinued and hydroxychloroquine and azathioprine were initiated. A month later, the patient presented with a flare up of MS symptoms including transient monocular blindness and increased weakness of the extremities. Repeated cranial MRI did not reveal any new lesions; however, repeat cervical MRI revealed a new inflammatory lesion at the C7-T1 spinal segment. The patient was treated with pulse steroid once again.

The patient was consulted to our physical medicine and rehabilitation outpatient clinic due to complaints of muscle weakness and difficulty in mobilization. Neurological examination revealed a left-sided hemiparesis and sensory impairment. The patient was able to ambulate using a walker under supervision. Following a course of physical therapy, including range of motion, strengthening and walking exercises and balance and coordination training the patient was able to walk with a cane and climb stairs. A written informed consent was obtained from the patient.

DISCUSSION

Simultaneous presence of two autoimmune diseases is indicative of a common immunological mechanism in the pathogenesis of both.[7] In this case, we describe a patient who was initially diagnosed with PBC and HT and who developed concurrent SS and MS seven years later.

Primary biliary cirrhosis is a chronic cholestatic liver disease frequently associated with other autoimmune diseases such as thyroid disorders, SS, and systemic sclerosis.[8] Of these, SS is the most common autoimmune comorbidity, diagnosed on average nine years after a diagnosis of PBC.[9,10] In this case, a diagnosis of SS was made seven years after the

diagnosis of PBC. Approximately 10 to 15% of patients with PBC also have thyroid disease, most commonly HT, as was the case in the patient described here.[8]

Sjögren syndrome also frequently occurs alongside thyroid diseases. Embryologically speaking, salivary and thyroid glands are derived from the same cell, implying that cross-immunity may exist between the two of them.[11] The characteristic lymphocytic infiltrates of the lacrimal and salivary glands seen in SS are histopathologically similar to those of the thyroid gland seen in HT. Indeed, the prevalence of concurrent HT and SS ranges from 10 to 54%.[12] Crowe et al.[8] reported a significant relationship between coexisting SS, PBC, and thyroid dysfunction compared to PBC and thyroid dysfunction alone.

The reports of concurrent MS and systemic lupus erythematosus, rheumatoid arthritis, and myasthenia gravis are also available in the literature.[13,14] However, concomitant presence of HT and SS has never been associated with MS. Furthermore, although a few case reports have reported the coexistence of PBC and MS,[15,16] and studies have detected a low prevalence of concomitant SS and MS,[17] to date there have been no reports of PBC and HT being followed by the simultaneous onset of both SS and MS.

The reasons for the concurrence of multiple autoimmune disorders are still widely debated. As well as genetic predisposition, it is believed that environmental triggers in a susceptible person may cause immune dysregulation. Therefore, it is important to accurately describe the relationships between autoimmune diseases to further develop our understanding of common pathophysiological mechanisms and improve patient care.

In conclusion, this case is important in highlighting the possible coexistence of four autoimmune diseases (i.e., PBC, HT, SS, and MS) in a single patient, a clinical picture which has not been reported in the literature to date. This combination of autoimmune diseases should be kept in mind in patients with the relevant symptoms and signs of each to provide early diagnosis and appropriate patient management.

Declaration of conflicting interests

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