Coexistence of sarcoidosis and Hashimoto thyroiditis

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SUMMARY

Sarcoidosis is a chronic, inflammatory disease with unknown cause characterized by non-caseating granuloma formations. It can present with bilateral hilar lymphadenopathy, skin lesions, eye involvement and locomotor system findings. Hashimoto thyroiditis is an organ-specific autoimmune disease characterized by increased autoantibody synthesis. Sarcoidosis can involve different endocrine glands. Thyroid gland involvement may lead to increased thyroid function disorders and autoantibodies. Herein, we report an 80-year-old female patient with sarcoidosis and Hashimoto coexistence.

Key words: Sarcoidosis; Hashimoto thyroiditis; Coexistence.

INTRODUCTION

Sarcoidosis is a chronic, inflammatory disease with unknown cause characterized by non-caseating granuloma formation. It can be present with lung, skin, eye, and locomotor system findings, but different organ involvements have also been reported (1). Sarcoid involvement of endocrine glands (e.g., thyroid, adrenal, pituitary) is rare but it is clinically important, because affected glands may show hypofunction (2). Sarcoidosis infiltration was first observed in the autopsy thyroid gland in 1938; and then up to 10% in other studies (3).

In various studies, thyroid autoimmune frequency has been reported in patients with sarcoidosis, but the combination of sarcoid reaction of the thyroid gland and Hashimoto’s disease is uncommon (4, 5). In this article, the rare association between sarcoidosis and Hashimoto in a female patient is described.

CASE REPORT

An 80-year-old female patient presented to the Rheumatology polyclinic with complaints of both ankle arthritis, erythema nodosum, cough and shortness of breath. Her history included coronary artery disease and hypertension. On physical examination, the patient had arthritis of both ankle joints and skin lesions consistent with erythema nodosum in the pretibial region. There were crepitus rales at the pulmonary examination and the other systemic examinations were normal. Laboratory tests was performed; liver function tests including ALT: 23 U/L (normal <33 U/L), AST: 13 U/L (normal <35 U/L), ALP: 34 U/L (normal <58 U/L), GGT: 31 U/L (normal <45 U/L) were in normal limits. Renal function tests; serum creatinine: 0.92 mg/dL (normal <1.0), serum blood urea nitrogen: 43 (normal <45 U/L) were normal. Thyroid function tests was performed; free T3: 0.26 pg/mL (2-4.4 pg/mL), free T4: 0.09 ng/dL (0.93-1.7 ng/dL), thyroid stimulating hormone (TSH): 227 ng/dL (0.27-5.0 IU/mL), antithyroglobulin (anti-Tg): 506 IU/mL (0-115 IU/mL), anti-thyroperoxidase (anti-TPO): 204 IU/mL (0-34 IU/mL). Serum angiotensin converting enzyme (ACE) level was 83 U/L (normal 8-52 U/L), serum calcium and hydroxy D3 levels were normal. Acute phase reactant; C-reactive protein (CRP): 26 mg/dL (normal 0-0.5 mg/dL) and erythrocyte sedimentation...
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rate (ESR): 43 mm/h (normal 0-20 mm/h). In serological tests; antinuclear antibody (ANA): 1/40 homogenous positive, ENA profile, anti-cyclic citrullinated peptide antibodies (anti-CCP) and rheumatoid factor (RF) were negative. The chest X-ray showed hilar and mediastinal enlargement (Figure 1). In thorax computed tomography (CT), mediastinal paratracheal, precardinal, subcardinal, and bilateral hilar masses showed multiple lymph nodes (Figure 2). In thyroid ultrasonography (USG), findings consistent with diffuse thyroiditis (Hashimoto) in chronic phase were seen. She was referred to a chest diseases specialist because of bilateral ankle arthritis, erythema nodosum, bilateral hilar lymphadenopathy (LAP). A diagnosis of acute sarcoidosis (Löfgren syndrome) was made, but biopsy was not recommended. Nevertheless, she was investigated for possible malignancy and/or infection. After tuberculosis, fungal infections, and lymphoma were excluded, the patient was diagnosed with sarcoidosis and Hashimoto thyroiditis according to the clinical, laboratory, and radiologic findings. Levothyroxine 75 mg/day and prednisolone 20 mg/day were started. At the third month control visit, the patient’s complaints were regressed, on laboratory investigation the thyroid function tests and acute phase reactants were normal. The dose of prednisolone was decreased to 16 mg per day. At the sixth month, control thorax CT showed regression of hilar and mediastinal lymphadenopathies, and the dose of corticosteroid was decreased to 4mg per day. Polyclinic follow-up of the patient shows good general condition and remission is continuing.

**DISCUSSION AND CONCLUSIONS**

Herein, we report the coexistence of sarcoidosis and Hashimoto thyroiditis. Sarcoid involvement of endocrine glands is rarely seen. Among the endocrine glands, infiltration of the pituitary, thyroid, and adrenal glands has been reported (6). Sarcoidosis thyroid involvement is rare and has been reported in autopsy cases, fine needle aspiration biopsy and thyroidectomy specimens. Other thyroid disorders that accompany sarcoidosis are goiter, subacute thyroiditis and thyroid cancer. In a Swedish study, significant antithyroglobulin autoantibody elevations (16.7%) were reported in patients with sarcoidosis, but thyroid function tests were reported as normal (7). Nakamura et al. reported the prevalence of sarcoidosis associated with Hashimoto thyroiditis more commonly (3-11%) than other thyroid diseases (8). In another study, thyroid autoantibodies were found to be positive in 17 of 62 middle-aged and el-

![Figure 1](image1.png) - Lung radiography showed bilateral hilar enlargement.

![Figure 2](image2.png) - Thorax CT showed bilateral hilar lymphadenopathy.
derly sarcoidosis patients. Although thyroid autoantibody frequency is normally found to be higher in females than in males, the incidence of thyroid autoantibodies in males is higher in sarcoidosis patients than in females (9). Papadopoulos et al. reported endocrine autoimmune disorders in 20% of 78 sarcoidosis patients in a study (10). Mali et al. reported that autoimmune thyroid disorders were observed in 16% of 68 sarcoidosis patients (11). The prevalence of anti-thyroid autoantibodies (anti-TPO and anti-TG) and Hashimoto’s disease are higher in patients with sarcoidosis than in the age- and sex-matched control group (12). In addition, gland primary hypofunction is frequently reported. However, renal involvement can be concomitant with sarcoidosis and Hashimoto’s thyroiditis and these findings were reported in the literature. Ando et al. described development of minimal-change glomerular disease and Hashimoto’s thyroiditis during the treatment of sarcoidosis with steroid (13). Nishimoto et al. reported the occurrence of sarcoidosis, Hashimoto’s thyroiditis and minimal change glomerular disease in the same patients (14). Our patient was evaluated for probable renal involvement but renal function tests were normal.

Sarcoidosis is a predominantly Th1-cell associated chronic granulomatous disease. There is an increase in the number of T cells in the granulomatous process of the disease. These T cells participate in the production of a large number of cytokines and chemokines, mediators of inflammation and cellular immunological responses (15). There are studies showing the important role of Th17 cells in the pathogenesis of the disease (16). The evidence that Th17 cells are increased in the lung and the peripheral blood of patients with active sarcoidosis supports the multisystem nature

| Table I - Summary of the available case reports in the literature examining the association between sarcoidosis and Hashimoto thyroiditis. |
|---|---|---|---|---|---|---|
| Features/study | Sapkota et al. (20) | Ocak et al. (21) | Kalkan et al. (22) | Ando et al. (13) | Yamamoto et al. (23) | Nishimoto et al. (14) |
| Age/Sex | 49/F | 28/F | 50/F | 66/F | 72/F | 66/M |
| Clinical presentation | Encephalopathy | Pulmonary hypertension | Hepatomegaly | Nephrotic s/m | Skin lesion | Nephrotic s/m |
| Sarcoidosis duration | Newly diagnosed | Newly diagnosed | 4 year | 9 month before HT | Newly diagnosed | Newly diagnosed |
| Occurrence of Hashimoto | Concomitantly | Concomitantly | 1 year after sarcoidosis | 9 month after Sarco | Several years | Concomitantly |
| Stage of sarcoidosis | 1 | 2 | 1 | 2 | 1 | 1 |
| TPO-Ab | Elevated | Elevated | Elevated | Elevated | Elevated | Elevated |
| Tg-Ab | Low | Low | Normal | Normal | Normal | Normal |
| TSH | Normal | Normal | Normal | Normal | Normal | Normal |
| FT3 | Elevated | Elevated | Elevated | Elevated | Elevated | Elevated |
| FT4 | Normal | Normal | Normal | Normal | Normal | Normal |
| Liver Bx- granulomatous hepatitis | Renal bx-MCD | Skin bx- NCG | Renal bx: MCD |
| Bx on lymph nodes bx | NP | Yes | Yes | NP | Yes | Yes |
| Elevated ACE | Yes | NA | NA | No | No | NA |
| Treatment | CS, AZA | CS | L-Thyroxin | CS | NA | CS, CyP |

NCG, non-caseating granuloma; ACE, angiotensin converting enzyme; CS, corticosteroids; AZA, azathioprine; CyP, cyclophosphamide; TPO-Ab, antithyroid peroxidase antibody; Tg-Ab, antithyroglobulin antibody; TSH, thyroid-stimulating hormone; FT3, free triiodothyronine; FT4, free thyroxine; MCD, minimal change disease; NA, not available; NP, not performed; MCD, minimal changed disease; Bx, biopsy.
of the disease. Also sarcoid alveolar macrophages produce elevated levels of IL-17. Downregulation of the immune system’s inadequate proinflammatory process may cause endocrine autoimmune disorders and sarcoidosis coexistence (8). On the other hand, there are data supporting the role of Th17 cells in the pathogenesis of Hashimoto thyroiditis (17). Hashimoto’s thyroiditis is one of the most prevalent autoimmune endocrine disorders, characterized by lymphocytic infiltration and fibrosis of the thyroid gland. CD4+ T-cells play important roles in the pathogenesis of HT and classically this is considered a Th1-mediated disease. 

Figueroa-Vega et al. demonstrate a significant increase in the serum IL-17 levels of Hashimoto thyroiditis patients, suggesting a potential role of this cytokine in disease pathogenesis (18). It must be mentioned that IL-17 is a proinflammatory cytokine and can also induce the expression of diverse proinflammatory cytokines and chemokines. Hashimoto thyroiditis is a local autoimmune disease characterized by increased autoantibody synthesis, involving the thyroid gland. T and B lymphocyte dysregulation plays an important role in the pathogenesis of the disease (19). The association of Hashimoto thyroiditis and sarcoidosis may be the result of exaggerated thyroid-specific T-cell activation due to increased expression of Th1/Th17 cells in both diseases (Table I) (20-23).

In conclusion, the relationship between sarcoidosis and Hashimoto may be a complex immunologic and genetic relationship or an entirely random combination. The rare association of these two diseases should always be considered and more research is needed in this regard.

**REFERENCES**

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