

## Letters to the Editor

### Comorbidity of sarcoidosis and Graves' disease



### Comorbilidad de la sarcoidosis y la enfermedad de Graves-*Basedow*

Dear Editor,

Sarcoidosis is a chronic inflammatory disease with unknown etiology, characterized by non-caseating granuloma formation. Extrapulmonary involvement is usually seen in locomotor system, skin, lymph nodes, eyes and liver, but could be in any organ.<sup>1</sup> Sarcoid involvement of the endocrine glands has rarely been observed.<sup>2</sup> The incidence of thyroid autoimmune disease has been reported in patients with sarcoidosis in various studies, but comorbidity of Graves' disease (GD) is not common. Comorbidity of sarcoidosis and GD has been described in this paper.

### Case presentation

A 35-year-old female patient was admitted to our Rheumatology clinic with complaints of pain and swelling in the ankle joint, morning stiffness, fatigue, dry cough, and palpitations. Physical examination revealed findings related with right ankle arthritis, growth and tenderness of the thyroid gland in palpation and tachycardia in cardiac auscultation. As for thyroid function tests; we determined FT3: 14.27 pg/ml (normal 2.0–4.4 pg/ml), FT4: 5.25 ng/dl (normal 0.93–1.7 ng/dl), TSH: 0.01 ng/dl (normal 0.27–4.2 ng/dl), anti-thyroglobulin: 164.7 IU/ml (normal 0–115 IU/ml), anti-TPO: 7.10 IU/ml (normal 0–34 IU/ml), TSH receptor antibody: 12.77 IU/L (normal < 1.22 IU/L). Serum ACE level was found as 89 (normal < 35). In the serological tests; ANA, ANCA, anti-CCP, RF were found to be negative. Thoracic CT revealed mediastinal and bilateral hilar lymphadenopathy (Fig. 1). The chest disease specialist was contacted, endobronchial ultrasound (EBUS) guided biopsy was performed. Histopathological evaluation showed non-caseating granulomas, thus sarcoidosis was considered in the patient. Thyroid ultrasonography showed the increased size of the thyroid gland, with heterogeneous and coarse parenchyma, which appeared to be related with Graves' disease. Diffusely increased uptake of radioactive iodine was found in thyroid scintigraphy. The patient was diagnosed with sarcoidosis and Graves' disease based on clinical, laboratory, radiological and histological data. Moderate dose of a corticosteroid (40 mg/day) and propylthiouracil 3 × 1/day were initiated to the patient. At the 6th month of clinical follow-up, thyroid function tests were observed to be normalized, palpitations and complaints of locomotor system were found to be decreased. Control thorax CT showed significant regression in terms of mediastinal and hilar lymphadenopathy.

### Discussion

Sarcoidosis is a multisystemic, chronic granulomatous disease with unknown etiology, characterized by non-caseating granuloma formation. Sarcoid involvement

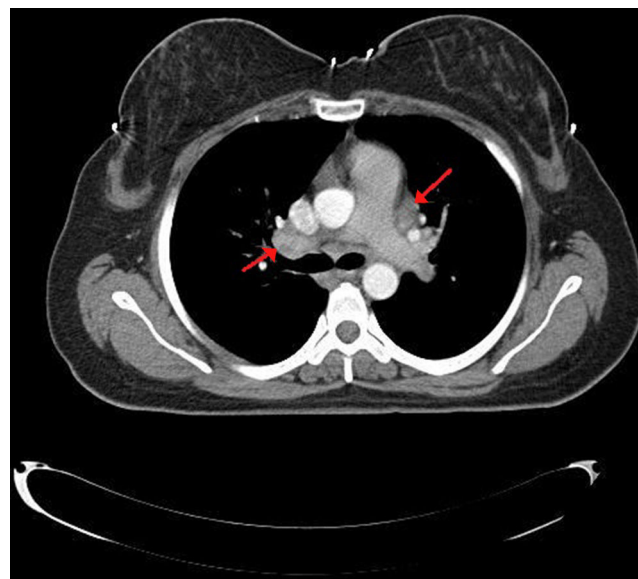


Fig. 1. Torax CT showed bilateral hilar and mediastinal lymphadenopathy.

of the thyroid gland has been detected upon autopsy or fine needle aspiration biopsy and thyroidectomy.<sup>3</sup> Graves' disease is an autoimmune disease in which activated T and B cells can cause intrathyroidal lymphocytic infiltrations.<sup>4</sup> Graves' disease was shown in a case of sarcoidosis, although hyperthyroidism is considered rare.<sup>5</sup> On the other hand, Graves' disease in patients with sarcoidosis may be simply coincidental. Goiter, subacute thyroiditis and thyroid cancer have been reported among other thyroid disorders accompanying sarcoidosis.<sup>6</sup> In a Swedish study, significantly elevated levels of antithyroglobulin autoantibodies have been reported in patients with sarcoidosis.<sup>7</sup> Nakamura et al. have reported that the prevalence of sarcoidosis related with Hashimoto's thyroiditis was 3–11%, much more common than other thyroid diseases.<sup>8</sup> In another study, antithyroglobulin autoantibodies were significantly higher in patients with sarcoidosis, but the basic thyroid function tests were in the normal range.<sup>9</sup> However, comorbidity of sarcoidosis of the thyroid gland and Graves' disease has rarely been reported.<sup>10,11</sup> Karlish and McGregor have reported that hyperthyroidism developed in 6 patients with sarcoidosis but long-acting thyroid stimulating antibodies could not be detected.<sup>12</sup>

As a result, based on clinical, radiological and histopathological examinations, we hereby report the comorbidity of Graves' disease and sarcoidosis in our patient. Since both are chronic and inflammatory diseases, this suggests that they may have a common etiopathogenesis and/or it may be just a coincidence. Further studies on this topic are required.

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## Immunoglobulin A Nephropathy in Rheumatic Diseases<sup>☆</sup>



### Nefropatía IgA en las enfermedades reumáticas

To the Editor,

Immunoglobulin A nephropathy (IgAN) is a glomerulopathy characterized by the presence of mesangial deposits of IgA, either alone or showing predominance over other immunoglobulins.<sup>1</sup> The pathological study enables the diagnosis and evaluation of the disease activity. Its association with rheumatic diseases has been reported<sup>2,3</sup>; however, the pathophysiological relationship is still not clear.<sup>1,4</sup> For the purpose of establishing the prevalence, clinical features, analytical findings, treatment and outcome of IgAN in a cohort of patients with rheumatic disease, we conducted a retrospective study (1984–2014) in a university hospital serving a population of 850 000. We reviewed the pathological diagnoses of 27,215 patients being treated in the rheumatology department and selected those with a histological diagnosis of IgAN. We excluded the patients in whom the only rheumatic disease diagnosed was gout, osteoporosis or noninflammatory disease. We identified 6 patients (0.025%), all men. Of 1110 patients with rheumatoid arthritis, 2 (0.009%) had been diagnosed with IgAN. Of 287 patients with ankylosing spondylitis, 2 (0.69%) had IgAN. Only 1 (0.17%) of the 558 patients with psoriatic arthritis had received a diagnosis of IgAN, as was the case of 1 of the 13 patients (0.7%) with undifferentiated connective tissue disease. The mean age at the diagnosis of IgAN and of the rheumatic disease was 46.7 and 37 years, respectively (range: 34–54 and 18–67 years). The mean duration of the rheumatic disease prior to the diagnosis of IgAN was 15.4 years. Hematuria (100%), renal failure (100%) and nephrotic syndrome (8.6%) were the signs that led to the suspicion of the presence of IgAN. All 6 patients had hypertension and 8.6% had nephrotic-range proteinuria. The mean values of serum creatinine and 24-h proteinuria at the time of the diagnosis of IgAN were 1.85 mg/dL (range: 1.5–2.5) and 1.94 g (range: 0.8–4.12), respectively. Over the course of the disease, 3 patients (50%) required hemodialysis after a mean period of 5.6 years since the diagnosis (range: 2–11); all 3 underwent renal transplantation within an interval of 9–25 months after starting hemodialysis. One patient (16.6%) died at the

age of 60 years (7 years after the diagnosis of IgAN) due to sepsis of pulmonary origin. During follow-up, the mean creatinine levels of the patients who did not receive dialysis was 1.4 mg/dL (range: 1.1–1.6); they were treated medically (angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers).

The prevalence of IgAN in the general population is 25–50 cases per 100 000 population<sup>5</sup> and, although in the majority of the patients with chronic inflammatory arthropathy, renal involvement is secondary to amyloidosis or an adverse drug reaction,<sup>2,3</sup> there are reports that indicate the possible relationship between rheumatic diseases and IgAN.<sup>6,7</sup> Given the prevalence of IgAN in the general population, in some cases, its coexistence with a rheumatic disease may be coincidental. In patients with spondyloarthropathies, the relationship would be explained by the reported change in the catabolism of glycoprotein receptors and IgA-specific receptors (FcαR or CD89) found in tissue and peripheral blood.<sup>6,7</sup>

The results of the present study do not differ from previous findings reported in the literature.<sup>5</sup> The prevalence is higher in men and the clinical presentation is characterized by proteinuria, hypertension and hematuria. The cohort of patients of Azevedo et al.<sup>5</sup> showed a higher frequency of calcaneal enthesitis and anterior uveitis. In accordance with our observations, in clinical practice, the diagnosis of IgAN should be considered in patients with a rheumatic disease who develop hematuria, proteinuria, renal failure and hypertension during the course of their disease.

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