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Pleuropericardial compromise associated with Graves' disease — a diagnostic challenge

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When a hyperthyroid patient presents a pleuropericardial compromise (PPC), we must develop a diagnostic and therapeutic approach because the aetiology can be varied. We report the case of a woman with pleuropericardial effusion associated with Graves' disease (GD), emphasizing the importance that pleuropericardial compromise associated with this disease should be diagnosed, discarding other differential diagnoses, and that the treatment of GD is the cornerstone.

A 57-year-old Peruvian woman came to our hospital emergency room due to palpitations and moderate exertional dyspnoea. Three months previously, she had been diagnosed with hyperthyroidism [thyroid-stimulating hormone (TSH): 0.005 uUI/mL; free triiodothyronine (FT3): 32.55 pg/dL; free thyroxine (FT4): 7.77 mg/dL] and prescribed propranolol 40 mg/day and thiamazole 30 mg/day in other hospitals. Examination revealed blood pressure of 100/60 mm Hg, heart rate of 90 bpm, lower extremity oedema, decreased vesicular breath sounds at the base of both hemithorax, and muffled heart sounds. Electrocardiogram and echocardiography indicated pericardial effusion, without signs of cardiac tamponade or ventricular involvement; in addition, her left ventricular ejection fraction was 60%. Pericardial diagnosis aspiration obtained 240 mL of serohematic exudative fluid with polymorphonuclear predominance. A computed tomography (CT) scan revealed pericardial effusion with a thickness of 47 mm, accompanied by moderate bilateral pleural effusion and passive atelectasis (Fig. 1).

The patient persisted with dyspnoea, whitish sputum, palpitations, oxygen saturation of 95%, and blood pressure of 100/60 mm Hg. Biochemical analysis revealed reduced thyroid hormone concentrations, so we decreased the thiamazole dose to 10 mg/day. The antibody results were as follows: antithyroid peroxidase (anti-TPO) antibodies (456 IU/L, average values < 35

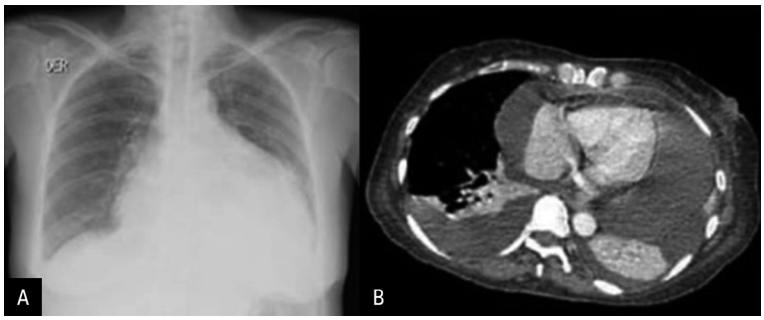

Figure 1. A. *Chest X-ray showing an increase in the cardiac silhouette as well as the presence of a slight pleural effusion, observed by the venography of the costodiaphragmatic sinus.* **B.** *Computed tomography showing a hypodense material that surrounds the heart and is present in the pleural cavity, which corresponds to the pericardial and pleural fluid, respectively*

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Table 1. *Thyroid hormone levels according to calendar*

Date	12/2017	02/2018	27/2018	29/2019	RV
Context	Debut – thiamazole 30 mg/d	Thiamazole 20 mg/d	Without thiamazole	One year after	
TSH [μUI/mL]	0.005	0.129	0.085	2.1	0.4–4
FT3 [pg/dL]	32.55	NR	16.3	3.7	1.8–4.2
FT4 [mg/dL]	7.77	0.73	3.46	1.17	0.8–1.9

TSH — thyroid-stimulating hormone; FT3 — free triiodothyronine; FT4 — free thyroxine; NR — does not refer; RV — reference value

IU/L) and positive for antinuclear antibodies (ANA), with a mottled pattern.

The cytochemical analysis of the pleural fluid revealed a predominance of lymphocytic cells plus mesothelial cells with mild atypia. Pap stain, bacterial cultures, adenosine deaminase test at 2.3 U/L, and acid-fast bacilli stain (in three separate sputum samples) were all negative.

She underwent surgical pericardial window, and 400 and 200 mL of pericardial fluid and pleural fluid were extracted, respectively. The pericardial biopsy reported chronic inflammation without evidence suggestive of tuberculosis.

Thyroid ultrasonography and a thyroid scintigraphy with iodine uptake after suspension of antithyroid drugs (ATD) revealed a toxic diffuse goitre, leading to diagnosis of GD. A reduction in the thyroid hormones was observed. However, the TSH levels did not increase, which indicated that the patient did not reach a euthyroid state. Consequently, after thiamazole suspension, she received radioactive iodine (RAI) therapy (12 mCi of I^{131}) as definitive therapy for hyperthyroidism and was discharged on thiamazole 15 mg/day plus bisoprolol 5 mg/day.

One month after discharge, additional analyses revealed negative ANA control, anti-double-stranded DNA (anti-ds-DNA) antibody, and anticardiolipin. In addition, physical examination and imaging studies demonstrated no signs of pleural or pericardial effusion. Six months after the RAI therapy, the patient developed hypothyroidism. Consequently, she received levothyroxine 0.1 mg/day. She is currently asymptomatic from a thyroidal, respiratory, and cardiac standpoint. Thyroid levels throughout the natural history of the disease are shown in Table 1.

The team discarded various aetiologies that may cause pericardial and pleural effusion; namely, neoplasms, tuberculosis, and rheumatologic and autoimmune diseases [1]. Then, because the patient was previously diagnosed with hyperthyroidism, we conducted an RAI uptake test, due to the need to identify the cause of hyperthyroidism, which was not totally clear because of the lack of orbitopathy (which occurs in 25% of patients with GD) or diffuse goitre, a characteristic finding [2]. The presence of antithyroperoxidase antibodies and a diffuse goitre in thyroid scintigraphy enabled us to confirm GD. Therefore, the diagnosis of PPC associated with GD was established.

Pleural and pericardial inflammation accompanied by effusion in patients with hyperthyroidism is rare. It is postulated that the pathophysiology may involve an interaction between antithyroid antibodies and pericardium, similarly to orbitopathy and dermopathy [3].

Even though the patient had symptoms related to hyperthyroidism, she did not have typical signs of pericarditis. It differs from most cases, which reported signs of pericarditis, such as sharp chest pain [4].

Treatment was started with thiamazole due to the symptoms, age, and high thyroid hormone concentrations. Then, we selected adjuvant therapy with bisoprolol due to thyrotoxicosis and cardiovascular compromise. We administered RAI as the definitive therapy because of the disease severity, according to the ATA and AACE guidelines [5].

In conclusion, patients with GD can present cardiovascular complications, accompanied by pleuropericardial compromise as initial clinical manifestations. Because of that GD may have a delayed diagnosis. Imaging methods are useful tools to the diagnosis of PPC. The main treatment is the control of GD.

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