

## SARCOIDOSIS OF THE THYROID GLAND AND CONCOMITANT HÜRTHLE CELL ADENOMA: CASE REPORT

### SARKOIDOZA TIREOIDNE ŽLEZDE I KONKOMITANTNI HÜRTHLE CELL ADENOM: PRIKAZ SLUČAJA

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**Summary:** Sarcoidosis is a multisystem disorder, characterized by the presence of noncaseating epithelioid-cell granulomas. The etiology remains unclear, although it is recognized as a disease of activated T lymphocytes. There is a diverse range of possible presentations with respiratory, gastrointestinal, reproductive, endocrine and other complications. The thyroid is an uncommon site of the disease with only 4% incidence according to some autopsy series. We present a case of a 55-year-old female patient with sarcoidosis of the thyroid gland and concomitant Hürthle cell adenoma. Upon performing a routine thyroid scintigraphy, a cold nodule has been observed. The diagnosis of the underlying disease was established by correlating the anamnesis data, patient's clinical history, fine needle aspiration biopsy and pathological examination of the thyroidectomy specimen. To our knowledge, the association has rarely been previously reported, indicating that thyroid involvement should be suspected in sarcoidosis patients who present with cold nodules.

**Keywords:** sarcoidosis, thyroid gland, Hürthle cell adenoma

### Introduction

Sarcoidosis of the thyroid gland is a rare disorder reported for the first time in 1938 (1). The thyroid is an uncommon site of the disease, with clinically evident involvement uncommonly reported in the literature. The incidence is approximately 4% in some

**Kratak sadržaj:** Sarkoidoza je generalizovana bolest koju karakteriše prisustvo nekazeantnih granuloma epitelioidnih ćelija. Etiologija ostaje enigma i pored toga što se svrstava u grupu bolesti aktiviranih T limfocita. Bolest ima veliki dijapazon prezentacija, kako respiratornog, tako i gastrointestinalnog, reproduktivnog i endokrinog oblika. Tireoidna žlezda je veoma retka lokalizacija sa incidencom od samo 4%. Predstavljen je slučaj 55-godišnje ženske osobe sa sarkoidozom tireoidne žlezde i pratećim Hürthle cell adenomom. Nakon rutinske tireoidne scintigrafije, otkriven je »hladni« nodus u levom lobusu žlezde. Konačna dijagnoza je postavljena korelacijom anamneze, kliničkih i laboratorijskih pokazatelja, aspiracione biopsije i patohistološke analize operativnog materijala. Ovo je veoma retka prateća prezentacija i ukazuje na potrebu svrstavanja sarkoidoze u diferencijalno-dijagnostički moguće etiološke činioce »hladnih« tireoidnih nodusa.

**Ključne reči:** sarkoidoza, tireoidna žlezda, Hürthle cell adenom

autopsy series (2). Middle-aged females are primarily affected, although it is incidently observed in children and in the elderly. Sarcoidosis of the thyroid gland usually results in hypothyroidism because of fibrosis interfering with thyroid function (3). However, it may also cause a euthyroid form of thyroiditis and goiter with peripheral or intrathoracic lymphadenopathy. Occasionally, sarcoidosis of the thyroid gland occurs in association with Graves' disease and less commonly in patients with toxic multinodular goiter (3). In addition, sarcoid lesions can present as cold thyroid nodules and be mistaken for thyroid cancer (4). In this article, we outline a case of concomitant Hürthle cell adenoma and sarcoidosis of the thyroid gland.

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## Case report

A 55-year-old female patient, with incoming diagnosis: Sarcoidosis pulmonum, Hepatitis granulomatosa; from the Clinic for Respiratory Diseases, University Clinical Center – Medical Faculty, Skopje, was admitted and routine thyroid gland examination (FT4, TSH, ultrasonography) and radionuclide scintigraphy with  $^{99m}\text{Tc}$  were performed.

The disease was diagnosed taking into consideration the previous laboratory findings: increased PTH levels (168 pg/mL; normal values 9.5–78 pg/mL), SR 30/55, increased levels of ionized calcium up to 3.20 mmol/L (2.1–2.8 mmol/L), AST 36 U/L (10–34), ALT 54 U/L (10–45), ALP 264 U/L (38–126), bilateral lymphadenopathy presented on the lung X-ray images and the bronchoscopy findings. Although the anamnesis data did not indicate the presence of concomitant thyroid disorder, the laboratory findings presented borderline values of the FT4 (FIA) – 15 pmol/L (8.5–16 pmol/L) and normal values of the serum TSH – 0.9  $\mu\text{mol/L}$  (0.4–4.5  $\mu\text{mol/L}$ ) with an ultrasonographic presentation of a slightly enlarged thyroid gland and a nodule of 17 mm in diameter located in the left thyroid lobe. The thyroid autoantibodies were negative:  $\alpha\text{-hTG}$  <20 U/mL (<60 U/mL),  $\alpha\text{-TPO}$  <10U/mL (<60 U/mL).

The radionuclide scintigram, performed 20 minutes after the application of  $^{99m}\text{Tc}$ , using the standard positions (AP), revealed a cold nodule in the left lobe of the gland (*Figure 1*). Fine needle aspiration biopsy (FNAB) was performed and the result was classified as a III-group with cells presenting partial characteristics for malignancy.

The surgical procedure, thyroidectomy totalis, was performed 1 week after the FNAB and the pathological examination of the thyroidectomy specimens revealed interstitial sarcoid noncaseating epithelioid-

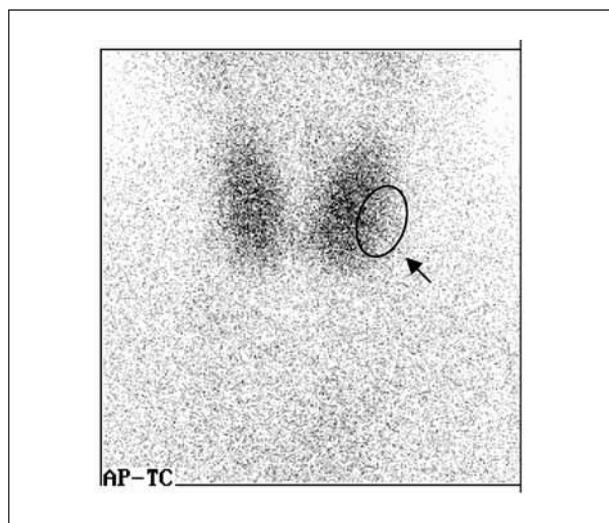
cell granulomas in both the left and the right thyroid lobe with four concomitant Hürthle cell adenomas as an incidental finding. The Hürthle cell adenomas were well encapsulated and composed of benign cells. They were all part of the nodule seen in the left thyroid lobe on ultrasonography, presenting itself as cold on  $^{99m}\text{Tc}$  scintigraphy.

## Discussion

Sarcoidosis of the thyroid gland, as an uncommon site of the disease, usually causes hypothyroidism although it may also cause euthyroid thyroiditis, and it may occur in patients with hyperthyroidism. Hypothyroidism is due to fibrosis of thyroid tissue or interference with the function of normal thyroid cells. However, when sarcoidosis occurs in patients with hyperthyroidism caused by Graves' disease or toxic multinodular goiter, the hyperthyroidism is often resistant to treatment with I131 ablation or anti-thyroid drugs. Patients with hyperthyroidism who show a poor response to these kind of treatments should be evaluated for thyroid sarcoidosis. In cases where thyroidectomy surgery was used to treat hyperthyroidism resistant to other treatments, sarcoidosis of the thyroid gland has been reported as an incidental finding (5). Unilateral or bilateral proptosis, as seen in patients with hyperthyroidism/Graves' disease, may occur in patients with sarcoidosis who do not have endocrine exophthalmos, retro-orbital infiltration by sarcoid tissue being the probable pathogenesis (6).

In cases of chronic sarcoidosis, skin lesions, enlarged lymph nodes (especially in the chest cavity), enlarged spleen, enlarged liver, uveitis, cardiac symptoms, and arthritis may occur. Our patient had bilateral lymphadenopathy in the chest cavity and also the liver was affected with sarcoid granulomas–hepatitis granulomatosa. This correlates with the fact that the diagnosis of pulmonary sarcoidosis was initially made in the year of 2002.

Sarcoidosis frequently causes an elevation of calcium levels in the blood. The association between sarcoidosis and hypercalcaemia is seen in 5–10% of cases (7). Hypercalcaemia is usually transient in subacute sarcoidosis, but may fluctuate in chronic sarcoidosis, depending on disease activity. The underlying mechanism is thought to involve high circulating concentrations of 1,25-dihydroxyvitamin D3 [ $1,25(\text{OH})_2\text{-D}_3$ ], produced by extrarenal 1 $\alpha$ -hydroxylation of vitamin D in alveolar macrophages and sarcoid granulomas (8). Granulomatous production of parathyroid-hormone related protein (PTH-rP) may also play a role in abnormal calcium metabolism, where tissue necrosis factor-alpha (TNF- $\alpha$ ) and interleukin-6, produced by macrophages, increase PTH-rP gene expression. PTH-rP, the usual etiological agent of humoral hypercalcaemia of malignancy, was reported in one series to be present in 85% of biopsies of granulomatous tissue from patients with sarcoidosis (9).



**Figure 1**  $^{99m}\text{Tc}$  scintigraphy in AP position reveals a cold nodule in the left lobe of the gland.

Our patient had an increased value of PTH and also elevated levels of ionised calcium that correlate with the literature data.

Based on clinical and biochemical data, our patient was euthyroid, with near-normal ultrasonographic morphology of the surrounding tissue, which was capable to maintain thyroid function the normal range, and a nodule of 17 mm in diameter located in the left thyroid lobe. Although some scientific papers (10) suggest elevated levels of  $\alpha$ -hTG autoantibodies in sarcoid patients, we found normal values of both  $\alpha$ -TPO and  $\alpha$ -hTG autoantibodies. Thus, the pathophysiologic significance of antithyroglobulin autoantibodies in the serum of patients with sarcoidosis has yet to be evaluated and, at the present time, it should be interpreted as another non-specific characteristic of a generalized immune dysfunction.

Sarcoid granulomas in the thyroid gland may be mistakenly identified as thyroid neoplasms especially when they are identified as cold nodules. This case is an example of four concomitant Hürthle cell adenomas and sarcoid affection of the thyroid gland in the form of interstitial noncaseating epithelioid-cell granulomas. To our knowledge, it is a very rare association and has previously been reported very few times in the literature (11). Up to date, no strong evidence of common pathways in the pathogenesis of these two conditions has been established.

Had there been no indication on the FNAB of a III-group classification with cells presenting partial characteristics for malignancy, there would have been a strong possibility that we would not have diagnosed the sarcoid affection of the thyroid gland. The cold nodule in the left thyroid lobe, the main reason for further investigations in our patient, turned out to be caused not by sarcoid granulomas, but by four Hürthle cell adenomas.

### Conclusion

In conclusion, thyroid involvement should be suspected in sarcoidosis patients who present with cold nodules in the thyroid. Furthermore, if noncaseating granulomas are observed in thyroid specimens after a thyroidectomy in an otherwise healthy person, the patient should be evaluated further for multisystem sarcoidosis. Patients with hyperthyroidism who show a poor response to  $I^{131}$  ablation or anti-thyroid drugs treatment should be evaluated for thyroid sarcoidosis. The concomitant presentation of Hürthle cell adenoma and sarcoid affection of the thyroid gland should also be taken into consideration, especially when cold nodules are present on imaging tests.

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