SARCOIDOSIS VASCULITIS AND DIFFUSE LUNG DISEASES 2014; 31; 239-243

Thyroid Cancer & Sarcoidosis

Ahmet Bahadir Ergin, Christian E Nasr
Endocrinology & Metabolism Institute. Cleveland Clinic, Cleveland, Ohio

Abstract. *Introduction:*
The association of thyroid cancer and Sarcoidosis (SA) has been previously described in individual case reports. We are describing 4 patients with co-existence of papillary thyroid cancer (PTC) and SA who presented a diagnostic and management challenge. *Patients:* One patient (Patient 1) with known history of SA was referred for thyroid nodules and cervical adenopathies; Fine needle aspiration (FNA) showed PTC. At surgery, he was found to have non-necrotizing granulomatous inflammation (NNGI) in lymph nodes (LN) in addition to PTC. Another patient (Patient 2) with known history of PTC presented with a palpable LN. FNA showed NNGI. She was subsequently found to have diffuse lymphadenopathies from SA. A third patient (Patient 3) who was totally asymptomatic, without history of PTC or SA, presented with a right thyroid nodule and a right lateral neck adenopathy both of which were positive for PTC. Pathology showed extensive NNGI and PTC in 4 LNs. Subsequent work up revealed diffuse lymphadenopahies throughout the body on positron-emitting tomography/computed tomography with elevated serum angiotensin converting enzyme level. The last patient (Patient 4) who did not have any history of SA or PTC presented with systemic symptoms. Work up revealed a large goiter with substernal extension that required a thyroidectomy. At surgery, suspicious adenopathies were resected and were found to contain NNGI. The thyroid specimen contained PTC. *Conclusion:* Clinicians should be wary of this association/co-existence of SA and PTC to avoid mismanagement of neck lymphadenopathies in patients with current or history of SA. Although 4% of thyroid cancers may induce a sarcoid reaction in the thyroid gland, SA as a disease may coexist with PTC although causality remains uncertain. Being aware of this association is important in the differential diagnosis of a thyroid mass and/or a LN in a patient with SA. Therefore, patients with known SA who are found to have cervical adenopathies or thyroid nodules should have a thorough work up. *(Sarcoidosis Vasc Diffuse Lung Dis 2014; 31: 239-243)*

Key words: Thyroid cancer, Sarcoidosis, Lymph Nodes

Introduction

The development of cervical lymphadenopathy in a patient with both sarcoidosis (SA) and papillary thyroid carcinoma (PTC) can create a diagnostic dilemma. Occasionally, lymph nodes with PTC metastasis and SA may coexist in the neck. The adjusted annual incidence of SA is estimated at around 16.5/100,000 in men and 19/100,000 in women (1) compared to 16/100,000 for women and 5.6/100,000 for men in 2008 for PTC (2). The true numbers of asymptomatic patients with SA cannot be reliably determined, since many of them escape diagnosis, however, a few studies reported that 30–50% of patients were found to be asymptomatic at the time of diagnosis (3). We present 4 patients whom PTC with lymph node (LN) metastasis and SA coexisted.

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Ahmet Bahadir Ergin, MD,
Ergin AB, Thyroid cancer and Sarcoidosis
E-mail: bahadirergin@gmail.com

Patients:

Patient 1

A 48 year-old female with SA involving the lungs, lacrimal glands and skin was referred for evaluation of calcified thyroid nodules and cervical adenopathy found incidentally on computed tomography (CT). Fine needle aspiration (FNA) of a right level III LN and a right thyroid nodule was performed and that showed PTC and non-diagnostic cytology respectively. She underwent thyroidectomy and right selective LN neck dissection; histology showed multifocal bilateral PTC, predominantly of tall cell variant, the largest focus measuring 1.3 cm with focal extrathyroidal extension in right lobe. Multiple metastatic LNs and LNs with non-necrotizing granulomatous inflammation (NNGI) were found in central and lateral neck compartments (Figure 1). One mediastinal LN showed only NNGI.

Patient 2

A 54 year-old female with a history of PTC, presented with fever, non-productive cough, weakness and fatigue and was found to have a palpable left cervical LN. Periodic neck ultrasound (US) studies demonstrated a left supra-clavicular lymph node which was measured 7 mm and had grown to 12 mm over time. One of the LNs was initially reported as metastatic PTC at another institution. Later, the patient had 2 additional FNAs at yet another institution for lateral LNs, one was reported as atypical cells concerning for malignancy and the other reported NNGI. CT of the chest showed bulky lymphadenopathy throughout the chest, including hilar, subcarinal, mediastinal, and para-tracheal LNs. Because of the suspicious features on US including microcalcifications (Figure 2), we performed a sonographically-guided FNA with Thyroglobulin (Tg) wash-out of that LN and those were consistent with only NNGI.

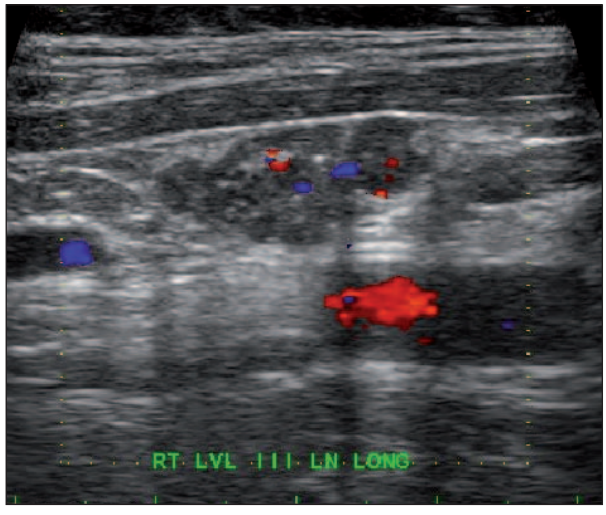

Fig. 1. Grayscale ultrasound with color Doppler showing Level III LN, with irregular border, internal punctate calcifications, disorganized blood flow and absent hilum. Pathology showed NNGI (Patient 1)

Patient 3

A 35 year-old male with no known SA noticed a lump on the right side of his neck. On examination, he was found to have a right thyroid nodule and a right lateral neck adenopathy. Sonographically-guided FNAs of a suspicious right cervical LN and of the thyroid nodule were both positive for PTC. He underwent total thyroidectomy and right lateral neck LN dissection. Pathology showed 4-LNs with extensive NNGI, concurrently with PTC in 3 central LNs. Fluorodeoxyglucose-positron emission tomography (FDG-PET)/CT scan showed diffuse, extensive lymphadenopathies including but not limited to right neck, mediastinal, bilateral hilum with maximal standardized uptake value of 10.6. Serum angiotensin converting enzyme was elevated at 106 U/L (normal being less than 46 U/L) in our lab. On the 6-month follow-up neck US, he was found to have an abnormal right central neck LN (Figure 3).

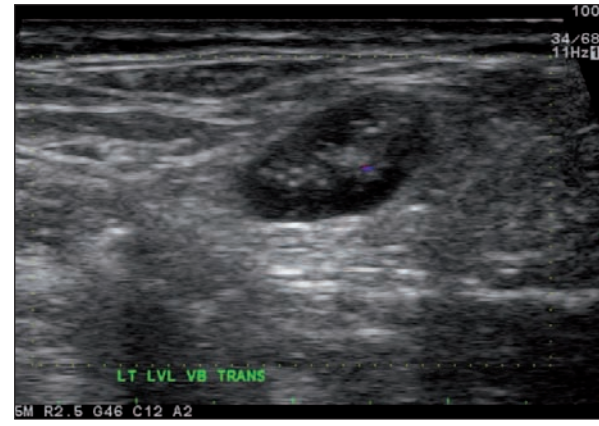

Fig. 2. Grayscale ultrasound of level Vb lymph node which appears hypoechoic with microcalcifications in the center (Patient 2)

This was biopsied, and was proven to be PTC. Therefore, he was taken to the operating room for re-operative central neck lymph node dissection. At histology, one LN was positive for PTC and 4 other LNs showed NNGI without PTC.

Patient 4

A 49 year-old male patient presented initially with increasing fatigue, dyspnea, and cough; neck and chest imaging revealed a diffusely enlarged thyroid gland extending substernally (Figure 4). US of the thyroid showed a 2.1 x 1.4 x 2.2 cm nodule in the lower pole of the left thyroid lobe. FNA of the thyroid lesion was suggestive of a follicular neoplasm.

Total thyroidectomy and bilateral neck exploration were performed. Final pathology showed 3 microscopic foci of PTC and chronic lymphocytic thyroiditis with patchy NNGI and fibrosis involving thyroid and 3 perithyroidal lymph nodes. The patient was also found to have intrathoracic lymph node prominence and multiple pulmonary nodules.

All the described PTC patients went through extensive work up including Gomori methenamine silver and acid-fast bacilli stains being performed on lymph nodes to rule out fungal organisms and acid-fast bacilli, respectively and the final diagnosis was SA in all these patients.

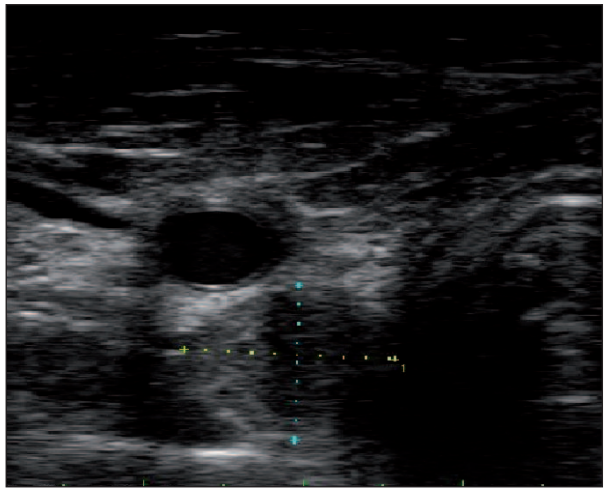

Fig. 3. Grayscale ultrasound of right thyroid bed showing a suspicious lymph node with round configuration, abutting the carotid artery (Patient 3).

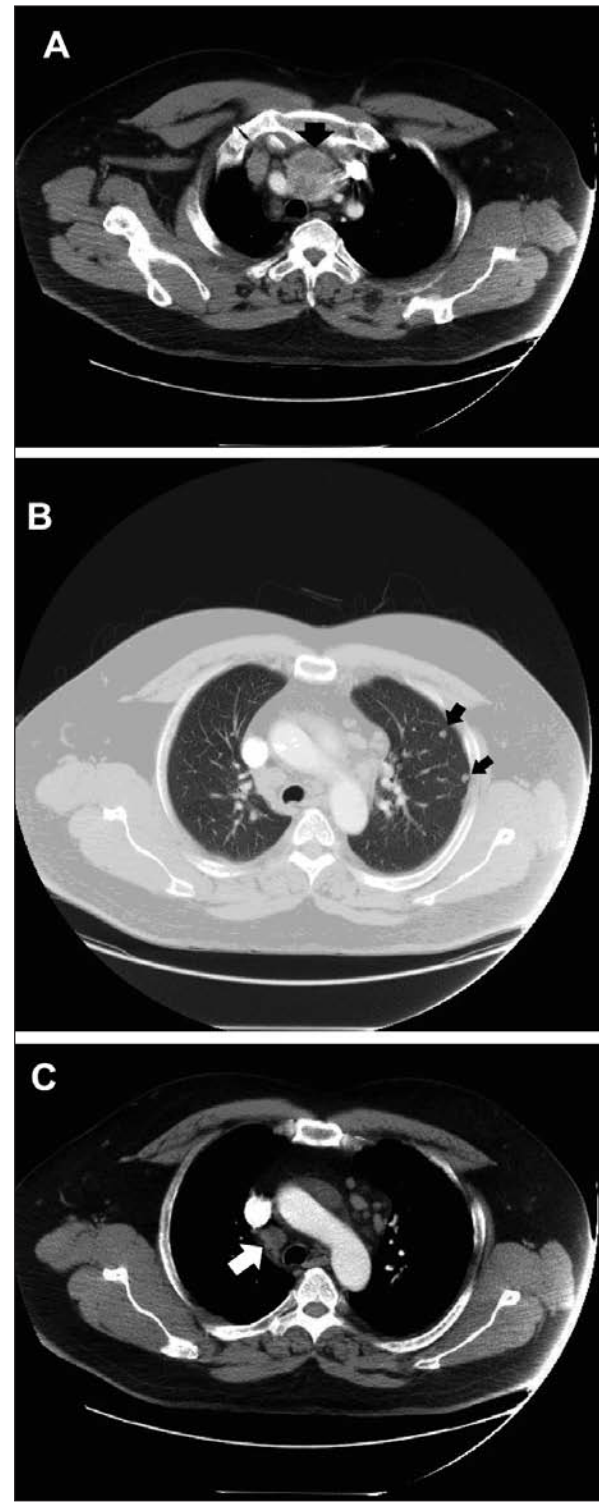

Fig. 4. A) Contrast-enhanced CT of the chest demonstrates retrosternal extension of goiter (Arrow); B) lung window showing two non-calcified parenchymal nodules (Arrows); C) multiple enlarged lymph nodes including a precarinal node (Arrow) (Patient 4).

Discussion

SA is a well recognized multi-system granulomatous disorder. It was used by Caesar Boeck, a Norwegian dermatologist in 1899 to describe skin nodules characterized by compact, sharply defined foci of "epithelioid" cells with large pale nuclei and along with a few giant cells (4). SA most commonly involves the lungs, eyes, skin and LN (5). Thyroid involvement with SA has been reported in 4% of post-mortem cases (6).

Anectodal reports of clinically important involvement is not more than 1% of cases which can present as hypothyroidism, hyperthyroidism with Graves' disease and/or goiter or nodule (7-16). In Patient 4, there was involvement of the thyroid with SA and the other 3 patients had only LN involvement with SA. PTC, as the most common thyroid malignancy, accounts for 80% of the all thyroid cancers. Management of co-existing PTC and SA can prove difficult because both can affect the same organs and the incidences of both diseases are very similar.

The co-existence of PTC and SA has been described in the past in individual case reports (16-24). The total number of reported cases is not more than a dozen. In recent years, 4 patients were seen at the Cleveland Clinic Thyroid Center which stimulated our curiosity to a possible relationship between SA and PTC and led to a few management caveats. Although we cannot prove causality, these cases bring a management challenge on the practicing endocrinologist in the decision making process.

The first challenge is that both diseases can present in the neck and they may have unexpected recurrences. Patient 1 who had a history of SA, presented with an incidentally-found.

Thyroid nodule and a cervical adenopathy on CT of the neck. A history of SA may distract the physician and lead to insufficient work up.

We suggest performing FNA of both the nodule and LN because cancer in a lymph node may be missed since the clinician may be biased by the common LN involvement in SA. The clinician should be extra careful when selecting suspicious LN for biopsy to justify a selective neck dissection by proving metastasis in the lymph nodes in patients with SA. If FNA is negative but there is suspicious LN, the patient should still be sent for selective neck dissection.

Furthermore, at times SA can be found incidentally as in patient 2 who was erroneously diagnosed with PTC on FNA cytology, perhaps because of the bias from the patient's medical history. After the patient presented to our clinic for a second opinion, FNA of the same LN with Tg wash-out was negative for PTC. Serum Tg was undetectable (negative Tg antibodies) which raised our suspicion for another possible etiology. Repeat FNA was consistent with granulomatous reaction and sarcoidosis was the final diagnosis in that patient.

Patient 3 also did not have a history of SA, but was later incidentally found to have widespread LN involvement with SA on FDG-PET scan. The clinician should be more vigilant and aware of the fact that coexistence of both diseases can be seen. Not surprisingly, this patient presented with biopsy proven LN metastasis at 6-month follow up and taken to the operating room for a second surgery. Clinically attributing cervical LN to SA may lead to undertreatment.

The pathology in patient 4 found NNGI along with PTC in both thyroid gland and 3 lymph nodes. As a caveat, one should be aware of the difference between a sarcoid reaction and SA. Sarcoid reaction is defined as a non-caseating granuloma found in the primary tumor, its vicinity, or within the lymph nodes draining the neoplasm when evidence of systemic SA does not exist (25). In the fourth patient, this may be an alternative explanation to co-existing SA hypothesis. In the second patient, however, CT showed bulky lymphadenopathy throughout the chest which was suggestive of systemic sarcoidosis.

Finally, lung involvement in both diseases may be intriguing to clinicians when SA and PTC co-exist in the same patient. In a case report, a patient presented with a jugulo-digastric mass which was found to be PTC at work up (18). Chest radiograph showed bilateral, diffuse, reticular-nodular infiltrates. The Initial differential diagnosis included lung metastasis, however, later bronchoscopy with trans-bronchial biopsy found SA. Given all the data presented here, clinicians should be prepared for possible incidental SA diagnosis during their work up for PTC and the converse can be true.

A detailed history including past history of PTC and SA and a detailed physical exam can make a difference in the diagnosis and management of patients who may have both SA and PTC.

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