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Concurrent Intrathyroidal Thyroid Cancer and Thyroid Cancer in Struma Ovarii: A Case Report and Literature Review

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Context: The presence of differentiated thyroid cancer in mature cystic teratomas in the ovaries is rare, and usually incidentally found on surgical pathology specimens. We present a case of simultaneous intrathyroidal thyroid cancer and thyroid cancer within a struma ovarii, presenting specific diagnostic challenges.

Case Description: A 55-year-old woman had an intrathyroidal, encapsulated 1.2-cm papillary thyroid carcinoma, follicular variant, which was resected. Laboratory studies showed an elevated thyroglobulin level of 35 ng/mL while on suppressive levothyroxine therapy. During preparation for radioactive iodine ablation, thyroglobulin increased dramatically to 3490 ng/mL. A pretreatment whole-body scan showed residual tracer uptake in the thyroid bed and increased radiotracer uptake in the pelvis that raised concern for a pelvic metastasis, given the marked thyroglobulin elevation. After ablation, the posttreatment scan showed intense focal uptake in the pelvis. Single-photon emission computed tomography–computed tomography confirmed that the tracer uptake corresponded to a right adnexal mass. The patient underwent a laparoscopic bilateral salpingo-oophorecotomy with pelvic washings. The final pathology of the right ovary showed papillary thyroid carcinoma arising in a mature cystic teratoma. In addition, there was abundant normal thyroid tissue with colloid surrounding the carcinoma, indicating a source for the dramatic rise in thyroglobulin levels and suggesting that the ovarian papillary thyroid cancer arose within the teratoma and was not metastatic disease. Thyroglobulin measurements have been undetectable for 5 years since surgery and radioiodine treatment.

Conclusions: Concurrent intrathyroidal thyroid cancer and differentiated thyroid cancer in struma ovarii are very rare, but can often be distinguished on clinical grounds.

Freeform/Key Words: thyroid cancer, struma ovarii, papillary thyroid cancer

Struma ovarii is a rare clinical condition comprising thyroid tissue originating in mature cystic teratomas in the ovaries. It is recognized when more than 50% of the teratoma is occupied by thyroid tissue. Abdominal pain, bloating, and abnormal menses occasionally lead to the finding of struma ovarii. The presence of thyroid cancer in struma ovarii is even rarer and occurs in approximately 0.5% to 5% of cases [1, 2]. The presence of differentiated thyroid cancer in struma ovarii is usually reported on the pathological examination of the surgical specimen, and the presence of thyroid cancer both intrathyroidal and within a struma has not often been reported. We present an unusual case of a patient with a 1.2-cm papillary thyroid

Abbreviation: SPECT-CT, single-photon emission computed tomography–computed tomography.

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cancer of the neck, follicular variant, which subsequently and unexpectedly showed rising thyroglobulin levels after completion thyroidectomy. There was concern for possible metastatic disease, and whole-body scanning was performed. Pelvic uptake was found, and the patient was eventually diagnosed with an additional papillary thyroid cancer originating in struma ovarii.

1. Case Presentation

A 55-year-old woman was found to have an incidental 2.5-cm nodule in the left lower thyroid lobe on physical examination. Ultrasound-guided fine-needle aspiration showed "follicular neoplasm" on cytology. A left hemithyroidectomy was performed and pathology was consistent with a 1.2-cm papillary thyroid carcinoma, follicular variant. The tumor was encapsulated and intrathyroidal, and no additional lymph nodes were sampled. The patient had no family history of thyroid cancer and no personal history of radiation to the head and neck. The patient underwent a completion thyroidectomy 2 years later, which showed no additional foci of thyroid cancer. Laboratory studies performed while taking levothyroxine replacement therapy showed a thyrotropin concentration of 0.82 mIU/L and a thyroglobulin concentration of 35 ng/mL in the absence of antithyroglobulin antibodies. The patient agreed to undergo radioactive iodine ablation.

During preparation for the pretreatment I-123 whole-body scan with thyroid hormone withdrawal, the patient's thyrotropin concentration increased to 102 mIU/L, but the thyroglobulin concentration increased dramatically to 3490 ng/mL. A whole-body scan was performed and showed residual tracer uptake in the thyroid bed, estimated at 6%, and no evidence of metastatic disease in the neck or mediastinum [Fig. 1(a)]. There was also increased radiotracer uptake in the pelvis that likely represented radiotracer within the bladder, but also raised concern for a pelvic metastasis given the marked elevation in thyroglobulin. Single-photon emission computed tomography–computed tomography (SPECT-CT) to confirm the localization was unavailable at the time of the I-123 pretreatment scan. The patient subsequently received 150-mCi I-131. The posttreatment scan showed intense activity in the thyroid bed, compatible with recent remnant ablation, as well as intense focal uptake in the pelvis [Fig. 1(b)]. SPECT-CT scanning was now available and confirmed tracer uptake that corresponded to a right adnexal mass [Fig. 1(c)]. A pelvic ultrasound showed that

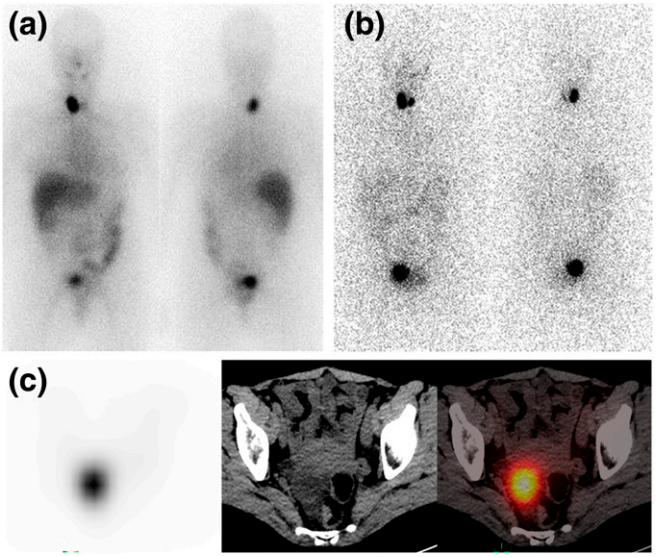

Figure 1. (a) Diagnostic I-123 whole-body scan (pretreatment) scan showing uptake in the thyroid and right adnexal region. (b) Posttreatment I-131 whole-body scan showing uptake in the thyroid and right adnexal region. (c) SPECT-CT scan showing uptake in the right adnexa.

the right adnexal mass was located in the ovary, indicating a possible struma ovarii tumor. The patient underwent a laparoscopic bilateral salpingo-oopherectomy with washings. Final pathology of the right ovary showed papillary thyroid carcinoma (~1.5 cm in greatest dimension) arising in a mature cystic teratoma (Fig. 2). In addition, there was abundant normal thyroid tissue with colloid adjacent to the carcinoma, suggesting the papillary thyroid cancer within the struma arose within the teratoma and was not metastatic disease. Staining was positive for TTF-1 and thyroglobulin, and background tissue showed Hürthle-cell changes with atypia, consistent with a recent history of radioactive iodine ablation. The pelvic washings were negative.

Postoperatively, the patient recovered well. Mutation analysis was performed. The BRAFV600E mutation was negative on both the original 1.2-cm thyroid cancer as well as the thyroid carcinoma in the struma ovarii. The thyrotropin concentration became suppressed and the thyroglobulin concentration has been undetectable for 5 years since radioiodine treatment.

2. Discussion

The diagnosis of papillary thyroid cancer originating in struma ovarii is quite rare and has not often been reported in a patient with a history of intrathyroidal papillary cancer. Multiple case reports show the incidental finding of papillary thyroid cancer in struma ovarii after surgery for either gynecological or abdominal symptoms and subsequent discovery of cervical thyroid cancer [3–6]. One case report described the finding of a benign struma ovarii on I-131 scanning during evaluation and treatment of Graves disease [7]. In our case, the patient had previously been diagnosed with a follicular variant of papillary thyroid cancer, and the elevated and rising thyroglobulin concentration, as well as pelvic uptake on I-123 scanning, raised concern for metastatic disease, possibly involving the ovaries. Whereas this can usually be differentiated from struma ovarii based on clinical grounds [4], there is currently no established definitive marker available for clinical use. Characteristics that can help differentiate between metastatic disease and synchronous tumors are dissemination pattern, site of ovarian involvement (bilateral vs unilateral), and the presence of teratomatous features [8]. Zhu *et al.* [9] have suggested the possibility of measuring CK19 or TTF-1 expression levels, and others have suggested tumor profiling by oncogene expression [8]. Additionally, magnetic resonance imaging findings of "multiloculated ovarian cystic mass with solid component and variable signal intensity between locules" may point toward struma ovarii [4].

A striking finding in this case was the dramatic rise in thyroglobulin concentration in preparation for radioiodine treatment. Thyroid hormone withdrawal increased the

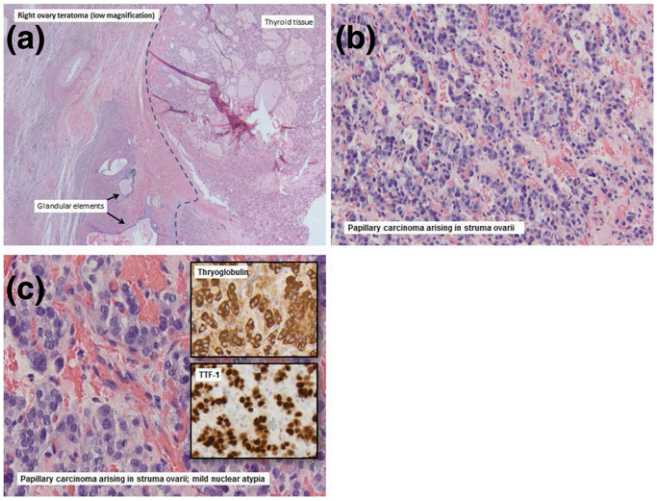

Figure 2. (a–c) Hematoxylin and eosin staining of right ovary surgical pathology specimen confirming the presence papillary thyroid carcinoma arising in struma ovarii.

thyrotropin concentration up to 102 mIU/L and the thyroglobulin to 3490 ng/mL, which suggested a large source of thyroid-like tissue, such as a metastasis, even when the original tumor was considered "low risk" according to the American Thyroid Association's guidelines [10]. Efforts are ongoing to better classify thyroid cancers in the neck, including the proposed reclassification of encapsulated follicular variant of papillary thyroid cancer, primarily based on the indolent clinical behavior [11]. Given that our patient had this variant of papillary thyroid cancer, metastatic disease was thought to be highly unlikely [12]. In cases of marked thyroglobulin rise with pelvic uptake on the pretreatment scan, struma ovarii should be investigated. In addition, despite the abundant "normal" thyroid tissue in the struma ovarii, the thyrotropin concentration rose appropriately after thyroid hormone withdrawal, demonstrating that the tissue was nonfunctional, or at least unable to produce thyroxine in large enough amounts to normalize thyrotropin. The reason for this observation is unknown, but suggests that, although a teratoma can differentiate into thyroid tissue that appears histologically normal and produces thyroglobulin, it is still not fully functional.

Long-term outcome data of thyroid cancer originating in struma ovarii have recently become available [13]. A retrospective analysis followed 68 patients over 28 years and showed survival rates of up to 85% over 20 years. Although there are no evidence-based guidelines for differentiated thyroid cancer in struma ovarii, most authors recommend oophorectomy followed by thyroidectomy and radioactive iodine ablation so that thyroglobulin levels can be monitored as a tumor marker. A case series review, supported by data from the Surveillance, Epidemiology, and End Results Program database, suggests that a more aggressive approach may be restricted to patients showing extraovarian or distant metastases [13, 14].

3. Conclusion

Although papillary thyroid cancer originating in struma ovarii can be incidentally found [3, 5, 6, 8], this case highlights the importance of considering struma ovarii as a cause of rising thyroglobulin measurements after resection of a generally low-risk papillary thyroid cancer. Any pelvic uptake on radioactive iodine imaging in the treatment of a patient with established papillary thyroid cancer of the neck may also indicate presence of a struma ovarii. The finding of papillary thyroid cancer originating in struma ovarii can often be clinically distinguished from papillary thyroid cancer of the neck, but immunohistochemical and molecular characterization techniques may be helpful in the management of these rare cases.

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