Coexistence of Radioactive Iodine-Resistant Benign Struma Ovarii with Cervical Primary Papillary Cancer of the Thyroid: An Unusual Cause of Thyroglobulin-Positive Radioactive Iodine-Negative Whole-Body Scans

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Dear Editor:

Struma ovarii is an ovarian neoplasm containing mature thyroid cells (1). Struma ovarii has been associated with all the pathologies affecting the cervical thyroid (2). Association of benign struma ovarii with primary follicular cell-derived cancer of thyroid origin is rare.

We present an unusual case of papillary cancer of the thyroid with highly elevated thyroglobulin (Tg) levels originating from a struma ovarii. In this case, Tg levels decreased substantially after excision of an ovarian teratoma harboring follicular thyroid cells.

A 57-year-old woman underwent thyroidectomy in 1992 for a 2.5-cm classic well-differentiated papillary thyroid cancer (Fig. 1A). After near-total thyroidectomy and excision of lymph node metastases in the neck, she received 100 mCi of iodohippurate sodium ¹³¹I radioactive iodine (RAI). The patient had additional surgery for excision of metastatic cervical lymph nodes in 1994. Subsequently, she received 2 additional RAI doses of 100 and 200 mCi in 1996 at an outside institution because of persistently elevated Tg levels. A whole-body RAI scan was negative despite an elevated Tg level of 500 ng/mL in 1997. At our institution, she had another neck excision of metastatic nodes in 2001. RAI whole-body scans after withdrawal of thyroxine therapy in 1997, 1998, and 2001 were negative for abnormal uptake, despite markedly elevated Tg levels.

Following surgery in 2001 at Mayo Clinic, the patient's serum Tg level remained elevated (91 ng/mL) with a suppressed thyrotropin level. Ultrasonographic images of the neck did not show recurrent disease. In May 2003, with a serum thyrotropin at 0.35 mIU/L, the patient had a serum Tg concentration that continued to be elevated at 83 ng/mL. Computed tomography of the neck and chest and ultrasonography of the thyroid were negative. In September 2003, she underwent neck uterosalpingo-oophorectomy for a pelvic mass found incidentally on an abdominal and pelvic computed tomographic scan when she presented to

the emergency department with a urinary tract infection. The right ovary contained an 8.5 cm × 6.5 cm × 6.0 cm mature cystic teratoma consisting largely of benign thyroid tissue (Fig. 1B). The left ovary showed a 14.5 cm × 7.5 cm × 7.0 cm mature cystic teratoma containing a 0.2 cm carcinoid tumor. In December 2003, the Tg level was reduced to 0.9 ng/mL without additional intervention (Fig. 1C) and remained low at 1.8 ng/mL at a follow-up in November 2005. In 2007, the patient developed nephrotic syndrome due to primary amyloidosis that was diagnosed through renal biopsy. Renal failure became progressive and, despite therapy in an outside institution, the patient died of renal failure in August 2008.

The majority of patients with elevated serum Tg levels and negative RAI whole-body scans after thyroidectomy and RAI therapy for follicular cell-derived thyroid cancer have sources of persistent thyroid cancer, most commonly found in cervical neck nodes. Although it has been speculated that there may be other, benign sources of Tg production in ectopic RAI-resistant thyroid tissues (3), we are not aware of previous reports of such cases. Our patient is a rare example illustrating such a possibility.

Numerous reports show an association of follicular cell-derived thyroid cancer with benign struma ovarii and describe cases of papillary, tall cell, and follicular cell thyroid cancers originating in struma ovarii (4). Primary thyroid cancer may rarely metastasize to ovaries. The present case is distinctive because of several clinical manifestations. Although thyroid tissue in the ovary did not have histologic characteristics of malignancy, the tissue was not ablated after several high therapeutic doses of RAI. In addition, no radioactive whole-body scan showed uptake in the ovaries. If repeated RAI whole-body scanning had shown uptake in the ovary by thyroid cells, the source of the elevated Tg level would have most certainly been detected earlier.

Despite the large mass of normal thyroid tissue and production of Tg by the ovarian struma, no uptake of RAI occurred. This finding is supported by the observation that

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FIG. 1. (A) Classic well-differentiated papillary thyroid cancer primary to the thyroid (hematoxylin-eosin, original magnification $\times 400$). The nuclear features of this classic papillary cancer contrast with those of the follicular cells present in this patient's right ovary. (B) Right ovary. Histologic evidence of follicular cells (hematoxylin-eosin, original magnification $\times 400$). The nuclei lack features of classic papillary thyroid carcinoma and stand in stark contrast to the nuclear characteristics of the patient's primary and metastatic papillary thyroid cancers. (C) Serum TSH and Tg levels during 8 years of follow-up. A dramatic reduction of Tg can be seen after excision of the ovarian teratoma with a struma ovarii. Tg values are in ng/mL; TSH values are in mIU/L. ¹³¹I, iodohippurate sodium ¹³¹I; RAI, radioactive iodine; Rx, therapy; Tg, thyroglobulin; TSH, thyrotropin; WBS, whole-body scan.

despite multiple doses of RAI therapy, the thyroid struma cells were not ablated. It is not clear why, in this case with histologically completely benign-appearing thyroid cells, the struma retained Tg synthesis capacity and lost RAI concentrating capacity. Although we did not examine sodium iodine symporter expression in the cells of the struma ovarii, it is likely that thyroid cells in the ovary failed to express the protein or did not successfully target it to the cell membrane.

Other reports have suggested that thyroid cells within a struma ovarii typically accumulate RAI and produce Tg, and are usually successfully ablated with RAI therapy (5). Of interest, in our patient the Tg level remained high under suppressive thyroxine therapy, indicating considerable autonomy of the struma cells for Tg production.

The presence of benign struma ovarii as a Tg source should be considered in the differential diagnosis of clinical dilemma of Tg-positive, RAI-negative follicular cell-derived thyroid cancer.

Author Disclosure Statement

No competing financial interests exist.

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