Malignant Granular Cell Tumor of the Thyroid: A Case Report

Takehito Igarashi1*, Ritsuko Okamura1, Tomo Jikuzono1, Akira Shimizu2, Shinichi Tsuchiya3, Kazuo Shimizu1

1Department of Surgery, Division of Endocrine Surgery; 2Department of Analytic Human Pathology; 3Division of Diagnostic Pathology, Nippon Medical School, Japan

Abstract

Granular cell tumor is usually a benign tumor derived from nerve cells, occurring most often in the head and neck. Granular cell tumor originating from the thyroid gland is extremely rare and to date, none has been reported to exhibit malignant characteristics. We report a case of thyroid granular cell tumor with tracheal invasion. The patient was a 53-year-old man presenting a nodule in the left lobe of thyroid gland identified accidentally during a health check. The nodule was hard and elastic, and had a size of 3.5 cm in diameter. Fine needle aspiration was performed and cytology revealed clusters of cells with acidophilic cytoplasm. Considering the differential diagnosis from Hurthle cell neoplasm, diagnostic lobectomy was performed. During operation, tracheal invasion was identified, suggesting invasive follicular carcinoma. We therefore performed a total thyroidectomy with removal of the involved tracheal wall. The tumor was diagnosed postoperatively as thyroid granular cell tumor with tracheal invasion. Neither local recurrence nor distant metastasis was identified one year after the surgery. In this paper, we report and discuss this case with particular focus on the diagnostic difficulty for malignant granular cell tumor of thyroid.

Keywords: Thyroid, granular cell tumor, malignancy

Introduction

Granular cell tumor is a soft tissue tumor, which was first reported as myoblastoma by Abrikosoff and Uber Myome in 1926 (1). This entity is now thought to have a Schwann cell origin. Granular cell tumor can arise from different areas, with the head and neck region accounting for about 50% of the tumors (2). However, granular cell tumors arising from thyroid tissue are extremely rare (3-6). Granular cell tumors are usually benign, but can also be malignant (7). If metastasis is identified, a diagnosis of malignancy is easy to be made, but the diagnostic criteria for malignancy remain unclear when there are no metastases. We report an extremely rare case of granular cell tumor originating from the thyroid and showing tracheal invasion.

Patient

The patient was a 53-year-old man. A nodule was incidentally identified in the left lobe of thyroid gland during a health check, and the patient was referred to our department for further inspection. Physical examination revealed a hard, elastic nodule in the left lobe of thyroid gland. Fine needle aspiration (FNA) of the thyroid tumor was performed and the cytology revealed clusters of cells with acidophilic cytoplasm (Fig. 1). The cytological diagnosis was indeterminate, suggestive of Hurthle cell neoplasm. Preoperative computed tomography did not identify any lymph node metastases (Fig. 2). Diagnostic left lobectomy was recommended as clinical management.

![Figure 1: Fine needle aspiration smear showing small and large clusters of cells with abundant acidophilic cytoplasm (Papanicolaou stain).](image1)

![Figure 2: Computed tomography of the neck showing a low-density area of 3.5 cm in diameter in the left lobe of thyroid gland. A): plain image, B): enhanced image.](image2)

We formed a dermal flap using a collar-shaped incision and reached the thyroid gland via a midline approach. The tumor was identified having strong adhesion with the tracheal wall. At this stage, we removed the left upper pole and tried to retract the lower pole. Because a diagnosis of tracheal invasion due to follicular carcinoma was considered, total thyroidectomy was performed along with ablation of the involved tracheal wall and creation of a trachea-skin fistula. There were no postoperative complications like recurrent laryngeal nerve palsy and parathyroid dysfunction. The area of the trachea-skin stoma was stabilized, and the patient was discharged on postoperative day 11. One year after the surgery, no evidence of recurrence was identified and the skin stoma was closed by plastic surgeons.

Pathological findings

*Correspondence author: Takehito Igarashi, Department of Surgery, Division of Endocrine Surgery, Nippon Medical School, 1-1-5 Sendagi, Bunkyo-ku, Tokyo 113-8603, Japan.
Tel: +81-3-3822-2131; Fax: +81-3-5685-0985;
E-mail address: takehito@nms.ac.jp

Accepted in May 8, 2013
The surgical specimen showed a solid tumor measuring 28 x 24 mm and invading into the tracheal wall over two cartilage rings (Fig. 3). The encapsulated tumor showed invasive growth into the tumor capsule and thyroid parenchyma where chronic lymphocytic thyroiditis was noted (Fig. 4A). High magnification of the tumor nests showed polygonal large tumor cells in solid growth without forming colloid substance or follicular structures (Fig. 4B). The tumor cells had a small nucleus and acidophilic and granular cytoplasm, characteristic for granular cell tumor. Negative immunostaining for thyroglobulin and positive immunostaining for S-100 protein further supported the diagnosis of granular cell tumor. In this tumor, the Ki-67 positive cells accounted of about 10% at the typical sites. Importantly, the tumor cells invaded into the submucosal layer and tracheal cartilage, but did not block the tracheal lumen (Fig. 3B). Based on these findings, a final diagnosis of malignant granular cell tumor of thyroid was made.

**Figure 3:** A: The solid tumor is 28 x 24 mm in diameter in the left lobe of the thyroid and its cut surface is yellowish white in color. B: Note irregular polypoid elevation of the tracheal mucosa caused by invasion of the thyroid tumor.

**Figure 4:** Pathology and immunohistochemistry of the tumor. A: A low magnification of the tumor (upper field) and thyroid (lower field) showing capsular invasion and expansive growth. Note: the thyroid parenchyma has numerous lymphocytes (hematoxylin and eosin stain). B: A high magnification of the tumor showing solid medullary growth of the tumor cells without forming colloid follicles. The tumor cells had an eosinophilic granular cytoplasm and a picnotic small nucleus (hematoxylin and eosin stain). C: Immunohistochemical staining for thyroglobulin: The tumor cells (lower right) were negatively stained for thyroglobulin, while the thyroid follicles and colloid substance (upper left) were positively stained. (hematoxylin counterstain) D: Immunohistochemical staining for S-100 A: The tumor cells in the lower right were strongly positive for S-100 protein, while the thyroid parenchyma (upper left) was negatively stained (hematoxylin counterstain).

**Discussion**

Granular cell tumor is relatively rare, but may occur in different areas. A small number of tumors originating from thyroid gland have been reported. Preoperative diagnosis of granular cell tumor with a thyroid origin is challenging (8). In our case, FNA cytology showed clusters of cells with acidophilic changes, and the differential diagnosis included Huthle cell tumor, papillary carcinoma with Huthle cell changes, and medullary thyroid carcinoma. Because primary thyroid granular cell tumor is very rare, we considered the tumor to be Huthle cell tumor before surgery and oxyphilic cell variant follicular carcinoma when tracheal invasion was identified during operation. Granular cell tumor was initially considered to be myogenic origin, but recently to be Schwann cell origin based on the immunohistochemical findings of S-100 protein and neuron-specific enolase positivity (9). About 50% of the granular cell tumors have been found in the head and neck region, and there is a predilection for the 30- to 50-year-old age population (2). Women appear twice as likely to be affected as men. Granular cell tumors are usually benign, but malignant form has been reported (7). The presence of metastasis offers an easy indicator of malignancy, but no clear diagnostic criteria have been proposed when metastasis is absent. In 1998, Fanburg-Smith et al. proposed six histological criteria for a three-tier system to classify tumors as benign, atypical, or malignant (10). However, the inter-observer variation is significant and the reproducibility is poor for these criteria (11). Nasser et al. have recently proposed a new algorithmic approach to the diagnosis of granular cell tumors based on the frequency of necrosis and mitosis (11). They classified their cases as benign and uncertain malignant potential using those two parameters. In the present case, mitosis was rare, Ki-67 labeling index was <10% and only mild necrosis was found in the tumor nests.

In summary, we encountered an extremely rare case of primary malignant granular cell tumor of the thyroid. We met with some difficulty in preoperative diagnosis with FNA cytology, proper surgical treatments, and prediction of the biological behavior of the tumor. There are currently no reliable markers available for predicting recurrence of granular cell tumor and careful follow-up is necessary.

**Conflict of Interest**

None declared.

**References**