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Tzu Chi Medical Journal

Case Report

Granular Cell Tumor of the Thyroid

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Article info

Article history:
Received: June 11, 2008
Revised: July 4, 2008
Accepted: July 14, 2008

Keywords:
Granular cell tumor
Schwann cell
Thyroid

Abstract

Granular cell tumors (GCT) can occur in a wide variety of organs, but are rare in the thyroid. To the best of our knowledge, only four cases of thyroid GCT have been reported in the literature. We report a GCT of the thyroid in a girl aged 12 years who presented with a painless neck mass. Thyroid function tests and the serum calcium level were within normal limits. A thyroid ultrasound demonstrated a round hypoechoic mass in the thyroid isthmus. Histologically, the tumor cells demonstrated abundant granular eosinophilic cytoplasm. The tumor cells were positive for S-100 protein and vimentin, and were negative for thyroglobulin, calcitonin, thyroid transcription factor-1, chromogranin A, synaptophysin, and cytokeratin. The patient had no recurrence and remained well at the 10-month postoperative follow-up visit. We reviewed the literature for reports of thyroid GCTs and compared them with reports of extrathyroid GCTs. (*Tzu Chi Med J* 2009;21(1):73–76)

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1. Introduction

Granular cell tumor (GCT) is a rare tumor, and comprises large cells with a highly granular cytoplasm. The histogenesis favors a Schwann cell origin. The first description of GCT was presented in 1926 by Abrikossoff, who called it a "granular cell myoblastoma". GCTs have been reported in many organs, particularly the upper aerodigestive tract. Around half of the lesions are found in the head and neck (1).

GCT of the thyroid is very rare; to the best of our knowledge, only four cases of thyroid granular cell tumor have been reported to date (2–5). Here, we report a case of GCT of the thyroid, and present a review of the literature.

2. Case report

A healthy Asian girl aged 12 years complained of a painless neck mass, which had been present for about 1 year. On physical examination, a nontender hard neck mass, about 1.4×0.5 cm, at the anterior lower neck was noted without cervical lymphadenopathy.

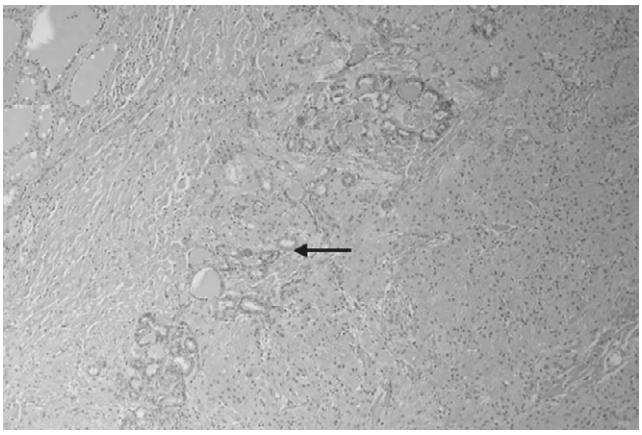

Fig. 1 — The granular cell tumor (right) shows an ill-defined capsule (left upper). At the tumor border, some thyroid follicles are infiltrated by tumor cells (arrow) (hematoxylin & eosin, 100×).

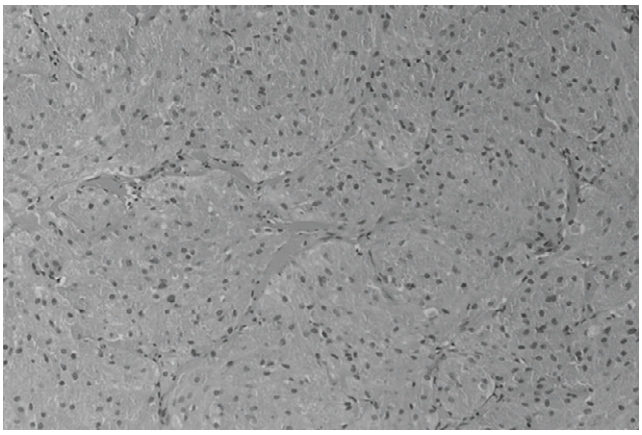

Fig. 2 — Microscopically, the tumor cells are large, with abundant eosinophilic granular cytoplasm. They are arranged in nests divided by delicate fibrous connective tissue (hematoxylin & eosin, 200×).

Thyroid function tests, including TSH, T3, and free T4, and the serum calcium level were all within normal limits. Thyroid sonography revealed a round, hypoechoic nodular lesion, 1.55×0.79 cm, in the isthmus of the thyroid. Fine-needle aspiration cytology of this nodular lesion showed only some benign follicular cells and fibrotic tissue. However, because of clinical suspicion of a thyroid neoplasm, the patient received an isthmusectomy.

Grossly, the specimen consisted of a 2.0×1.7×1.2 cm piece of red, brown and grayish soft thyroid tissue, with a 1.4×1.0×0.7 cm well-circumscribed pale gray nodular mass on the isthmus. On section, the nodular mass showed a gray-white solid cut surface.

The microscopic sections showed thyroid tissue with a partially encapsulated tumor composed of uniform large cells with abundant eosinophilic granular cytoplasm (Fig. 1). Tumor cells were arranged in nests divided by slender fibrous connective tissue septa or large sheets with no particular cellular arrangement. Nuclei were round to oval, occasionally eccentric, with small nucleoli (Fig. 2). No mitotic activity, nuclear atypia, or necrosis was seen. In some places, the tumor cells had infiltrated adjacent thyroid follicles.

The tumor cells were positive for S-100 protein (Fig. 3) and vimentin, and negative for thyroglobulin, thyroid transcription factor-1 (TTF-1), chromogranin A, synaptophysin, calcitonin, and cytokeratin on immunohistochemical (IHC) stain. The pathologic diagnosis was GCT of the thyroid. The fine needle aspiration cytology smears were reviewed. Some small scattered clusters of tumor cells containing abundant granular cytoplasm were overlooked in the initial cytological diagnosis. The patient had an uneventful postoperative course, and remained well at the 10-month postoperative follow-up visit.

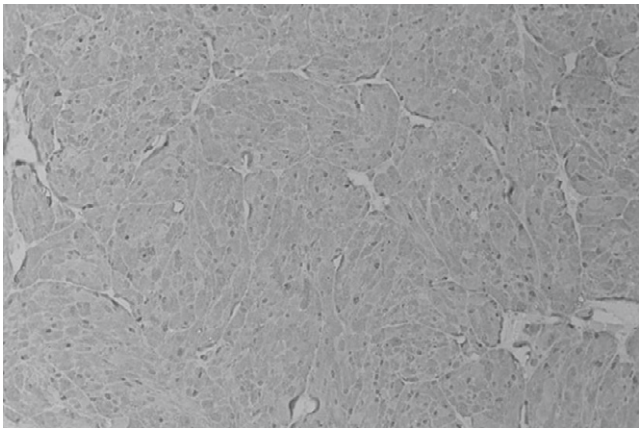

Fig. 3 — Tumor cells are positive for S-100 protein on immunohistochemical staining (200×).

3. Discussion

GCTs encompass a group of cytologically similar but clinically diverse entities characterized by proliferation of large cells with abundant granular eosinophilic cytoplasm. The histogenesis of these tumors remains controversial. Early observations suggested that the tumors were derived from skeletal muscle cells, whereas recent studies support a Schwann cell origin [6] based on histochemical reactivity for S-100 protein, and ultrastructural characteristics [7]. Under electron microscopy, the cytoplasmic granules appear to be lysozymes which arise by infolding of the cell membrane in a process similar to myelin formation around axons. These infoldings are subsequently phagocytosed by lysosomes [8].

The differential diagnosis of granular cell tumor of the thyroid includes paraganglioma, Hürthle cell

Table 1 — Five reported cases of primary granular cell tumor of the thyroid gland

Author, Year (Ref.)	Age (yr)/ Sex	Clinical history	Examination	Gross findings	Tumor extent
Mahoney et al, 1995 (2)	11.5/F	Familial tall stature, high-dose estrogen therapy, PE revealed neck nodule	1. Normal T4, TSH, thyroglobulin antibody 2. 1.7-cm hypoechoic mass at right lobe 3. ^{123}I scan: no focal areas of abnormal uptake	Light tan well-demarcated 1.5×1.2 cm, right thyroid mass	Nonencapsulated/ extension to perithyroid soft tissue
Paproski & Owen, 2001 (3)	23/F	Healthy, presented with painless neck mass	1. Normal TSH 2. Ultrasound showed a 2-cm complex mass at isthmus 3. Fine-needle aspiration: thyroid epithelial cells with possible oncocytic change	Cream-colored 1.5-cm mass at isthmus	Partially encapsulated/ confined to thyroid
Milias et al, 2004 (4)	43/F	Weakness, anxiety & palpitations	1. Mild hypothyroidism 2. Ultrasound showed thyroid enlargement with 2 nodules each in right & left lobes 3. ^{99}TcO4 scan: right nodule hyperfunction & left hypofunction	Left lobe nodule: cream-colored 2.5-cm granular cell tumor Right lobe: 1.5-cm goiter	Focal extension into thyroid capsule
Baloch et al, 2005 (5)	47/F	Sickle cell trait presented with ventral hernia; PE revealed palpable neck mass	1. Normal thyroid function tests 2. Ultrasound showed 3-cm mass at left lobe 3. Hypofunction of mass on radionuclide scan	White circumscribed 2.5-cm mass at left lobe	Confined to thyroid
Present case, 2009	12/F	Painless neck mass for about 1 year	1. Normal thyroid function tests 2. Ultrasound showed 1.55-cm hypoechoic mass 3. Fine-needle aspiration: benign follicular cells & fibrotic tissue	1.4-cm gray pale mass at isthmus	Partially encapsulated, confined to thyroid

PE=physical examination; F=female; TSH=thyroid-stimulating hormone.

tumor and oncocytic variant neoplasm. Tumor cells of a paraganglioma stain positively for chromogranin A and synaptophysin on immunohistochemistry. Hürthle cell tumors and oncocytic variant neoplasms are positive for thyroglobulin and TTF-1. Our case expressed S-100 protein, but was negative for chromogranin A, synaptophysin, thyroglobulin and TTF-1. The other four reported cases of thyroid GCTs were negative for thyroglobulin; one was negative for TTF-1. Thus, morphologic and immunohistochemical features corroborate the diagnosis of GCT of the thyroid in our patient.

The tongue is the most common site for GCTs although they have been also reported in many locations, including the skin, vulva, breast, larynx, bronchus, esophagus, stomach, appendix, rectum, anus, bile ducts, pancreas, urinary bladder, uterus, brain, pituitary gland, and soft tissue. GCT is the most common primary tumor of the posterior lobe of the pituitary gland; however, it rarely occurs in the thyroid.

To the best of our knowledge, only five cases, including our case, of thyroid granular cell tumor have been reported (2–5). Clinically, four of the five patients presented with a palpable neck mass but were otherwise asymptomatic; thyroid function tests were within normal limits. The third patient presented with anxiety, weakness and palpitations, and had mild hypothyroidism (Table 1 (2–5)). In Ordóñez's series (7), the extrathyroid GCTs were usually asymptomatic, but this tumor may cause obstructive symptoms, such as dysphagia, jaundice, or hoarseness, depending on its location. Patients presenting with hemoptysis and massive gastrointestinal bleeding have been reported.

Extrathyroid GCTs usually occur during the third to fifth decades of life, but rarely in patients under 12 years. The 42 patients with extrathyroid GCTs in Vance and Hudson's series ranged in age from 9 to 104 years old, with a median age of 37 years (9). In the series of Lack et al, the 110 patients with extrathyroid GCTs ranged in age from 16 to 58 years (mean,

32 years) [10]. The ages of the five patients with thyroid GCTs ranged from 11.5 to 47 years (mean, 27.3 years). Interestingly, thyroid GCT patients tend to be younger than patients with extrathyroid GCT; two of the five patients were only 11.5 and 12 years old. Whether or not thyroid GCTs have a higher prevalence in children cannot be definitively concluded because only five cases have been reported. Among patients with extrathyroid GCTs, females outnumbered males by a ratio of two-to-one [7]. Although all five patients with thyroid GCTs were female, the numbers were not high enough to draw any definitive conclusion regarding a higher female to male ratio in comparison with patients diagnosed with extrathyroid GCTs.

The thyroid GCTs were between 14 mm and 25 mm (mean, 18.8 mm) in diameter and were not grossly different from benign extrathyroid GCTs. In the series of Lack et al [10], the average diameter of the benign extrathyroid GCTs was 12 mm (range, 2–35 mm). Malignant GCTs tend to be larger than benign GCTs, ranging from 20 mm to 170 mm, with an average of 70 mm [7]. Grossly, thyroid GCTs are pale gray, white, tan or cream-colored (similar to extrathyroid GCTs). They are not confined to any particular location within the thyroid, and may occur in the right lobe, left lobe, or isthmus (Table 1 [2–5]).

GCTs usually have a benign clinical course. Complete excision is curative, but incompletely excised tumors may have local recurrence [10]. Malignant GCTs are rare and represent only 1–2% of all GCTs. Because of their rarity, criteria for malignancy have been difficult to establish, and remain controversial. In Fanburg-Smith et al's study, six histologic criteria were assessed: necrosis, spindling, vesicular nuclei with large nucleoli, increased mitotic activity, high nuclear to cytoplasmic ratio, and pleomorphism [11]. GCTs that met three or more of these criteria were classified as malignant; those that met one or two criteria were classified as atypical; those that met none, or had only focal pleomorphism, were classified as benign. All reported thyroid GCTs were benign tumors without metastasis at presentation despite perithyroid soft tissue involvement in one case, and focal thyroid capsule extension in another. Increasing mitotic activity, cellular atypia, and necrosis were not reported in any of the thyroid GCTs.

In conclusion, GCT of the thyroid is rare. The size, gross features, and clinical symptoms of thyroid GCTs are not obviously different from those of extrathyroid GCTs. However, all five patients with thyroid GCTs reported to date were female. Their average age at diagnosis was younger than that of patients with extrathyroid GCTs. No malignant thyroid GCTs have been described in the published literature. Complete excision was curative in all five reported cases.

Acknowledgments

We greatly appreciate the financial and technical support of Dalin Tzu Chi General Hospital and our coworkers.

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