CASE

Benign Thyroid Teratomas Manifest Painful Cystic and Solid Composite Nodules

Three Case Reports and a Review of the Literature

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Benign thyroid teratomas are rare in adolescents and adults. We report on three cases of benign thyroid teratomas that presented as painful tumors in the neck after puberty. The tumor adjacent to the thyroid in each case showed rapid enlargement with predominant cystic lesions within several months. Ultrasonography and computed tomography revealed few findings suggesting the origin of the tumor. Cytological examination and culture of the aspirate failed to show cells originating from the thyroid or infectious findings, but revealed a small population of columnar epithelial cells or squamous epithelial cells. Chemical analysis of the aspirate showed levels of pancreatic enzymes higher than those in serum. The accumulation of cystic fluid in each case was refractory to drainage treatment or percutaneous ethanol injection therapy. The patients subsequently underwent resection of the tumor, and microscopic examination revealed various types of tissue including pancreas, adipose, cartilage, muscle, and skin, and the cystic wall was lined by gastric, intestinal, respiratory, and stratified squamous epithelium. Surgical resection was curative, and subsequent histologic examination revealed mature benign teratomas of the thyroid. The main characteristic of our cases presented the painful tumors due to the enlarged cystic formation lined by a variety of different types of epithelium, which agreed with previous cases of benign thyroid teratomas in adolescents and adults.

Key Words: Benign thyroid teratoma; painful nodule; cyst; digestive enzyme; ectopic thymus.

Introduction

Teratomas are defined as neoplasms of germ-cell derivation composed of tissues derived from three germ-cell layers. They have been described in a variety of sites and organs, including the ovaries, testes, the retroperitoneal region, anterior mediastinum, and presacral and coccygeal regions. The head and neck regions account for 3–6% of all teratomas (1,2), with exceptionally rare cases found in association with the thyroid gland (3,4). Although the criteria for distinguishing cervical teratomas from thyroid teratomas remains controversial, the standard definition of thyroid teratoma is a tumor that occupies a portion within or adjacent to the thyroid gland with mature or immature tissues from three germ-cell layers (5). Since the first case was reported by Hess in 1854 (6), approx 300 cervical teratomas, including thyroid teratomas, have been reported (3,4). Although most of cervical teratomas display histologically benign features in fetuses and children (2), they are detected in stillbirths or present dramatically in infancy as respiratory or esophageal obstruction (3). In adolescents and adults, they almost invariably present as a mass in the neck, and some behave in a malignant fashion with local recurrence or metastasis even after surgery (4,7,8). Because benign teratomas in adolescents and adults are rarer than those in fetuses and children, their clinical features are poorly known. We report on three cases of benign thyroid teratomas after puberty, which presented with neck pain and developed cystic and solid composite nodules refractory to drainage treatment or percutaneous ethanol injection therapy during follow-up.

Case Report

Case 1

A 15-yr-old boy complained of mild tenderness on the left side of the neck. Laboratory investigations and thyroid function tests revealed no abnormalities. Computed tomography (CT) of the neck revealed a cystic and solid composite nodule, 1.7 cm in maximum diameter, adjacent to the left thyroid lobe (Fig. 1A). The left-sided neck pain gradually increased, and hoarseness appeared 2 mo after initial
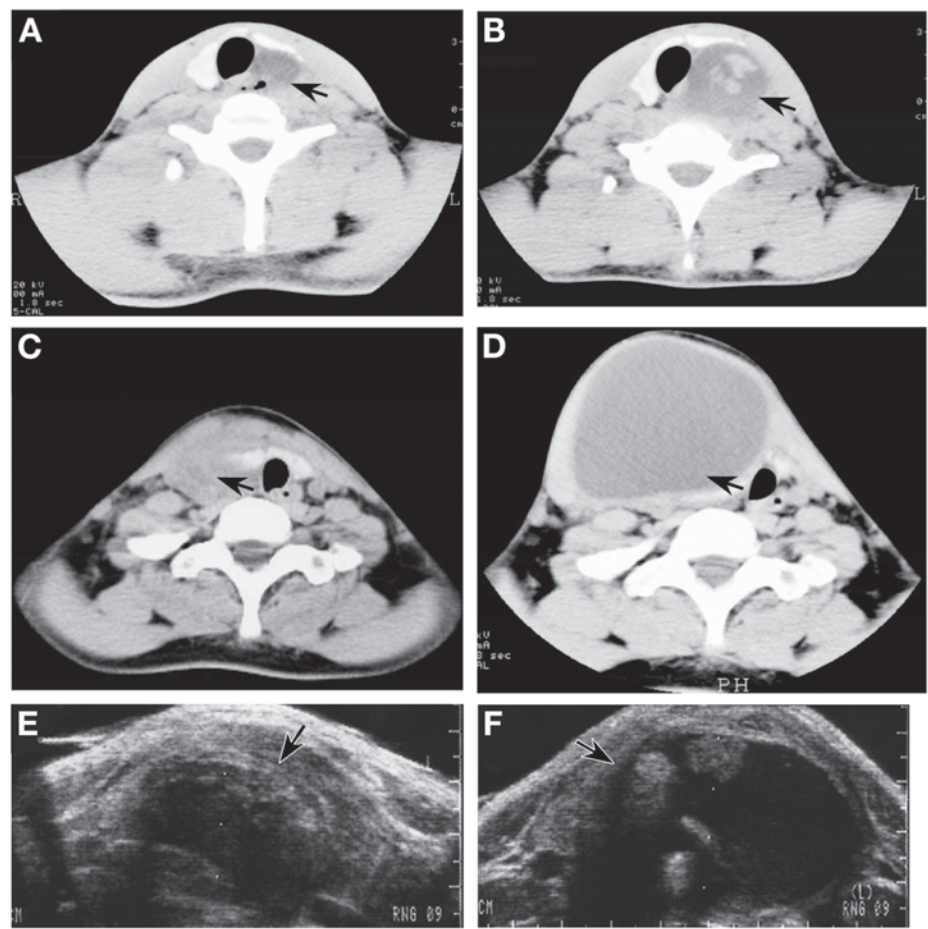
Fig. 1. CT scans of the neck in case 1 (**A** and **B**) and case 2 (**C** and **D**) and ultrasonography in case 3 (**E** and **F**). **A**, **C**, and **E** are initial examinations, and **B**, **D**, and **F** are examinations just before surgery. A cystic mass adjacent to the left lobe of the thyroid (**A**) and an enlarged cystic mass accompanied by a solid component inside (**B**). A heterogeneous mass showing isodensity to low density adjacent to the right lobe of the thyroid (**C**) and the enlarged cystic mass (**D**). The trachea and the normal thyroid gland, showing higher density on CT, are displaced by these enlarged cystic masses (**B** and **D**). Ultrasonography revealed hypoechoic lesions surrounded by a heterogeneous wall adjacent to the left thyroid lobe (**E**) and the enlarged cystic mass (**F**). Arrows indicate the location of teratomas.

consultation. Laryngoscopic examination confirmed paralysis of the left vocal cord. Laboratory investigations revealed slightly elevated levels of C-reactive protein, but thyroid function tests revealed no abnormalities in the absence of antithyroid antibodies (Table 1). Barium swallow examination revealed no findings indicating piriform sinus fistula. Because CT revealed that the cystic component had enlarged to 5.0 cm in diameter, the cystic lesion was punctured with a fine needle, and 30 mL of viscous dark brown fluid was aspirated. Culture of the aspirate failed to show infectious findings. Aspirated fluid contained foam cells, multinucleated giant cells, lymphocytes, neutrophils, and some clusters of small intestinal epithelia. The aspirate showed a low thyroglobulin concentration (<2.0 ng/mL), but elevated amylase (55550 IU/L/37°C) and lipase (64500 IU/L/37°C), while thyroglobulin, amylase, and lipase concentrations in serum were 26.9 ng/mL, 150 IU/L/37°C and 26 IU/L/37°C, respectively. Two weeks after additional drainage treatment, CT revealed re-accumulation of cystic fluid, a solid component, and displacement of the trachea to the

Table 1
Thyroid Function Tests and Laboratory Findings in Each Case

	Case 1	Case 2	Case 3
FT4 (ng/dL)	1.14	1.37	1.55
TSH (mIU/L)	0.99	1.10	1.18
Tg (ng/mL)	26.9	14.2	14.3
WBC (/μL)	4100	5900	9000
CRP (mg/dL)	1.0	2+	1+

FT4, free thyroxine (normal: 0.70–1.60 ng/dL); TSH, thyrotropin (normal: 0.30–5.00 mIU/L); Tg, thyroglobulin (normal: <35 ng/mL); WBC, white blood cell; CRP, C-reactive protein (normal: <0.5 mg/dL or –).

right side (Fig. 1B). The patient finally underwent resection of the tumor, which adhered to the posterior side of the left thyroid lobe with inflammatory fibrous connective tissue. Twelve paraffin blocks were made for microscopic examination. Histologically, the tumor was cystic and the
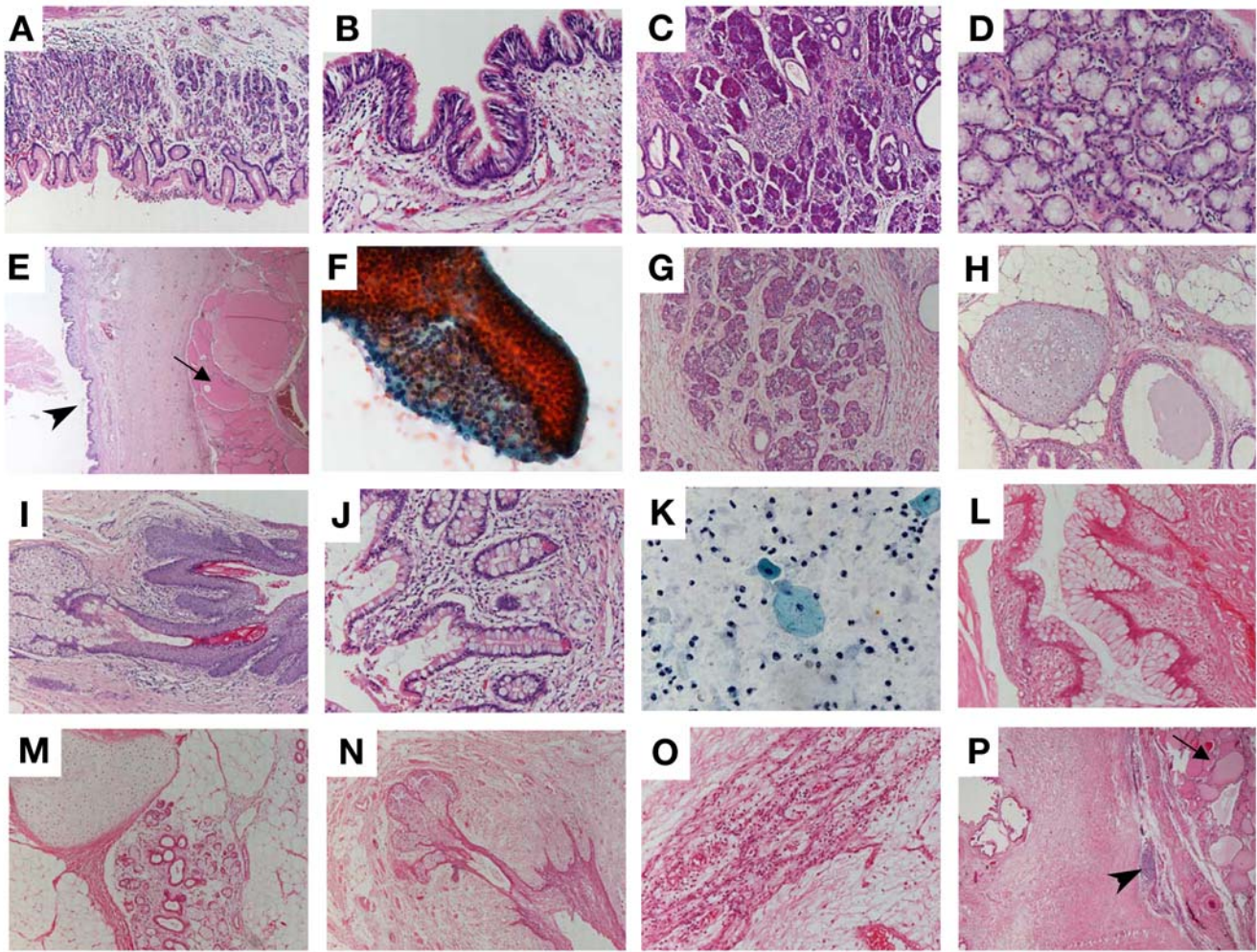
Fig. 2. Histological and cytological findings showing thyroid teratomas in case 1 (**A–E**), case 2 (**F–J**), and case 3 (**K–P**). **A**, gastric mucosa; **B**, pseudostratified ciliated columnar epithelium resembling a respiratory component; **C**, pancreatic tissue with islets; **D**, salivary gland; **E**, respiratory mucosa (arrowhead) and thyroid gland (arrow); **F**, a cluster of small intestinal epithelia; **G**, pancreatic tissue with islets; **H**, an islet of cartilage surrounded by mature adipose tissue; **I**, stratified squamous epithelium accompanied by sebaceous glands; **J**, small intestinal epithelium; **K**, squamous cells; **L**, large intestinal epithelia; **M**, an islet of cartilage surrounded by mature adipose tissue with apocrine sudoriferous gland; **N**, stratified squamous epithelium accompanied by sebaceous glands; **O**, thymus; **P**, thymus (arrowhead) and thyroid gland (arrow). Hematoxylin and eosin stain, magnification ×4 (**E**, **H**, **I**, **M**, **N**, **P**), ×10 (**A**, **G**), ×20 (**B**, **C**, **D**, **J**, **L**, **O**), and ×40 (**F**, **K**).

wall was composed of granulation tissue, necrotic tissue, and acute inflammatory cell infiltrate. The inner surface of the wall was partially covered with respiratory mucosa (Figs. 2B,E). The remaining portion contained the pancreas including Langerhans islands, stomach, skeletal muscle, smooth muscle, and salivary gland (Figs. 2A,C,D). There was no evidence of immature components or malignant cells. The neck pain and hoarseness resolved, and no paralysis of the left vocal cord or evidence of recurrence has been observed for 6 yr after excision.

Case 2

A 23-yr-old woman complained of a painful swelling of the right side of the neck. Laboratory investigations and thyroid function tests revealed no abnormalities in the absence of antithyroid antibodies. Ultrasonography revealed a 2.3-cm-diameter hypoechoic lesion surrounded by a heterogeneous wall adjacent to the right thyroid lobe. Three months later, a severely painful swelling of the right side of the neck developed. Laboratory investigations revealed elevated levels of C-reactive protein, with normal thyroid function (Table 1). CT revealed enlargement of a cystic and solid composite nodule, 5.0 cm in diameter (Fig. 1C). The cystic lesion was punctured with a fine needle, resulting in 23 mL of viscous dark brown fluid. Aspirated fluid contained foam cells, multinucleated giant cells, lymphocytes, neutrophils, and some clusters of small intestinal epithelia (Fig. 2F), but culture of the aspirate failed to show infectious findings. Barium swallow examination revealed no findings suggesting piriform sinus fistula. Percutaneous ethanol injection therapy was performed twice in 4 mo but failed to prevent re-accumulation of cystic fluid in the tumor. CT

showed the tumor had enlarged to 11.0 cm in diameter, mostly owing to the cystic component with displacement of the trachea to the left (Fig. 1D). The cystic component showed a high thyroglobulin concentration (7400 ng/mL) compared with a serum thyroglobulin concentration of 20.3 ng/mL. The patient finally underwent resection of the tumor, which was attached to the anterior side of the right thyroid lobe. Nine paraffin blocks was microscopically examined. The cystic tumor was separated from the thyroid with granulation tissue and fibrous capsule of the tumor. Inner portion of the cyst was inflamed, necrotic, or covered with the skin, small intestine, and respiratory mucosa (Figs. 2I, J). Solid area contained the pancreas containing Langerhans islands, cartilage, smooth muscle, adipose tissue, and parathyroid (Figs. 2G, H). The immature components or malignant cells were not observed. Microscopic focus of ectopic thymus was present close to the tumor. The neck pain resolved, and no inflammatory signs or evidence of recurrence have been observed for 10 yr after excision.

Case 3

A 13-yr-old girl complained of tenderness on the left side of the neck. Laboratory investigations revealed slightly elevated levels of C-reactive protein, but results of thyroid function tests were normal in the absence of antithyroid antibodies (Table 1). Ultrasonography revealed 2.7-cm-diameter hypoechoic lesions surrounded by a heterogeneous wall adjacent to the left thyroid lobe (Fig. 1E). Barium swallow examination revealed no findings indicating piriform sinus fistula. Three months later, a severely painful swelling of the left neck developed, and ultrasonography revealed enlargement of the cystic lesion to a diameter of 4.3 cm (Fig. 1F). The cystic lesion was punctured with a fine needle, resulting in 40 mL of viscous brown fluid. The aspirate showed a high thyroglobulin concentration (>160 ng/mL) compared with a serum concentration of 14.3 ng/mL. Culture of the aspirate failed to show infectious findings. Cytologic examination of tissue obtained by fine-needle aspiration revealed a small population of squamous cells with an abundance of inflammatory cells, comprising neutrophils and foam cells (Fig. 2K). The patient underwent resection of the tumor, which was attached to the left lobe of the thyroid. The microscopic preparations obtained from 16 paraffin blocks revealed that the wall of the cystic tumor was composed of respiratory mucosa, stomach, small and large intestine, skin, pancreas-containing Langerhans islands, adipose tissue, smooth muscle, and cartilage (Figs. 2L–N). Some portion of the wall was markedly inflamed and revealed necrotic tissue and granulation tissue. Immature components or malignant cells were not noted. Microscopic-sized ectopic thymus laid between the thyroid and the tumor (Figs. 2O, P). The neck pain resolved, and no inflammatory signs or evidence of recurrence have been observed for 1.5 yr after excision.

Discussion

The cervical and thyroid regions are rarely identified as categories of teratomas, and most of them are noted at birth or in stillborn fetuses. Approximately 10% of thyroid teratomas are found after puberty, and less than half of cases are proven benign according to the literature (4,7,8). Benign thyroid teratomas in adolescents and adults rarely present with respiratory or esophageal obstruction (3,9–15). However, benign teratomas often present as cystic and solid composite nodules, whose development can be influenced by several triggers and can be accelerated in adolescents and adults. Indeed, our three cases presented with neck pain before the tumor enlarged over several months. In all three cases, ultrasonography or CT confirmed that tumor enlargement was due to the markedly increasing cystic components; however, imaging studies failed to show characteristics, such as a fat component and calcification, to differentiate the teratomas from other tumors. Fine-needle aspiration of cystic components yielded viscous brown to dark brown fluid, and cytological examination showed that most cellular components were neutrophils and foam cells, suggesting inflammatory findings, whereas a small population of columnar epithelial cells and squamous cells were consistent with teratomas. One possible reason for the neck pain is the increase in cystic fluid. Irritation due to increased secretion from pancreatic tissue in mature teratomas is thought to play a role in cystic formation and inflammatory reactions (16,17). Pathological examination reveals pancreatic tissue in 40–60% of mediastinal teratomas (18). Approximately 7% of thyroid teratomas contain pancreatic tissue, according to one report (4), although all three of our teratomas contained pancreatic tissue. The cystic lesion in each case was lined by intestinal epithelium with or without gastric mucosal cells. Digestive enzymes were probably secreted from each epithelial cell, resulting in cystic accumulation and inflammation.

Only 11 benign thyroid teratomas, including 3 poorly documented cases, in patients older than 12 yr have been reported in the English-language literature (4,9–15) (Table 2) and in addition to several other cases reported in other languages. Of the eight tumors listed in Table 1, six were in females and two were in males and ranged from 5 to 8 cm in larger diameter. Microscopic examination has revealed that cartilage is the most common tissue, followed by pancreas, gastric glands, and intestinal gland (Table 2). About 80% of tumors show cystic changes and all tumors are lined by a variety of different types of epithelium (Table 2). Another pathological feature is the relative rarity of neuronal tissue (Table 2), which is in contrast to the neuronal elements often found in benign thyroid teratomas in fetuses and children and in malignant thyroid teratomas (3,4,7,19). Interestingly, ectopic thymus was present within the fibrous capsule of the teratoma or between the thyroid and the tumor in the present cases. The traditional view of teratoma pathogene-

Table 2
Benign Teratomas of the Thyroid in Adolescents and Adults

Cases	Age (yr)	Sex	Tumor size (cm)	Cystic changes	Histological features												References
					Pancreas	Stomach	Intestine	Respiratory mucosa	Skin	Cartilage	Bone	Salivary	Brain	Muscle	Adipose	
1	24	M	NR	NR	+	+	+	+	+	+	–	–	+	+	+	9
2	18	M	7	+	–	–	–	+	+	+	+	–	+	–	–	10
3	20	F	6	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	11
4	14	F	6	+	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	11
5	72	F	6	–	–	–	–	–	–	+	+	–	–	+	+	12
6	26	F	5	+	+	+	+	+	+	+	–	–	–	+	+	13
7	21	F	7	+	+	+	+	+	+	+	–	–	–	–	–	14
8	15	F	8	+	+	–	–	+	+	+	–	–	–	+	+	15
9–11	13–56	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	4
P1	15	M	5	+	+	+	–	+	–	–	–	+	–	+	–	
P2	23	F	11	+	+	+	+	+	+	+	–	–	–	+	+	
P3	13	F	4	+	+	+	+	+	+	+	–	–	–	+	+	

NR: not reported; +: present; –: absent. P: present case.

sis is that tripotential embryonic cells that escaped the influence of the primary organizer are misplaced, commonly into midline structures, during early embryonic development. Thyroid teratomas most likely arise from the embryonic thyroid analog *(20)*, which includes three germ layers. It is not defined yet whether the ectopic thymus is an organ simply attached to the teratoma. We postulate that another possible pathogenesis concerning thyroid teratomas may be related to the thymus where teratoma usually occurs *(21)*.

Benign thyroid teratomas in our three cases were accompanied by normal thyroid function and slight inflammatory findings at the onset of neck pain (Table 1), followed by unusual enlargement of cystic and solid composite nodules. Surgical resection was curative, and subsequent histologic examination established the diagnosis of benign teratomas, which attached to the thyroid without malignancy in each case. Benign teratomas occasionally rupture into adjacent organs, which can produce life-threatening complications. Amylase activity is thought to be the most likely cause of the rupture *(22,23)*. The first case presented with paralysis of the left vocal cord, and in all cases enlargement of the cystic lesions could not be controlled, even with drainage and percutaneous ethanol injection therapy. Therefore, surgery for benign thyroid teratomas should be performed without delay.

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