Primary Thyroid Teratomas in Children

A Report of 11 Cases With a Proposal of Criteria for Their Diagnosis

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Abstract: Cervical teratomas are uncommon neoplasms, although the commonest neck tumors in newborns and infants. Presence of associated thyroid tissue often causes speculation as to the site of origin, ie, arising from within thyroid, adjacent soft tissue with secondary involvement of thyroid, or as innate part of a cervical teratoma. Twenty-eight cases of cervical teratomas were identified over 75 years, including 11 cases containing associated thyroid tissue. Clinical history, treatment, and follow-up were reviewed and the neoplasms analyzed regarding location, size, degree of maturity, and relative arrangement of thyroid and other tissues. All thyroid teratomas were congenital, measured 3.5 to 13.5 cm in diameter (median size, 6.9 cm), and were resected. Follow-up ranged from 1 to 45 years (median, 17 years) without recurrent disease in any patient. Neuroglial tissue predominated in 10 of 11 tumors. Intimate admixture of thyroid and other tissues with or without surrounding fibrous pseudocapsule was present in 8 cases, suggesting thyroid as origin. Histologic immaturity in congenital thyroid teratomas is not the harbinger of adverse behavior as seen in adolescents and adults. Intimate intermingling of thyroid tissue with teratoma and presence of a pseudocapsule seem to be the most significant criteria for establishing thyroid as origin.

Key Words: teratoma, thyroid, newborn, immaturity, pseudocapsule

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Teratomas are classically defined as neoplasms of germ cell derivation comprised of different tissue components from all three germ cell layers, ie, ectoderm, endoderm, and mesoderm.[12] The most common sites of occurrence in childhood are the sacrococcygeal region, gonads, mediastinum, and pineal region.[2] Teratomas have occasionally been described in the head and neck region, with exceptionally rare cases found in association with the thyroid gland.[11] Most head and neck teratomas arise in neonates and infants and are usually clinically benign[6]; however, they have also been described in the adult population where they often behave in a malignant fashion and carry an ominous prognosis.[2]

Teratomas, regardless of location, display various degrees of differentiation, encompassing a spectrum from primitive somatic elements to very complex organized axial and metameric structures that, in their most extreme form of presentation, have been designated as fetus-in-fetu.[11] The degree of immaturity of the teratomatous tissue components, ie, presence of immature neuroglial tissues in the adult and adolescent population, has been correlated with poor prognosis, which is in strong contrast to the excellent prognosis of head and neck teratomas in infants (with the exception of brain and spinal cord). In this age group, adverse outcome is more dependent on age at diagnosis and anatomic site of origin.[6]

Presence of thyroid tissue within a cervical teratoma has consistently led to significant confusion and controversy among clinicians and pathologists as to the possible site of origin of neck teratomas, resulting in various interpretations and debate over possible criteria distinguishing cervical teratomas from teratomas of the thyroid. Some authors accept the thyroid gland as the site of origin if the tumor occupies portions of the thyroid, shows continuity with the gland, or has supposedly replaced the gland, ie, no thyroid gland is identified intraoperatively or on imaging studies. Others think that the presence of thyroid tissue within cervical teratomas does not necessarily prove thyroid origin since the tissue might represent well-differentiated elements of the teratoma, native thyroid encased by the tumor, or residual thyroid tissue in which the teratoma arose.[1,4,8,15]

Review of the world literature on cervical teratomas with special emphasis on thyroid origin somehow does not resolve the controversy. While around 300 cervical teratomas have been reported, many of them are included in reviews of teratomas in general and lack detailed anatomic or histologic description.

METHODS

Twenty-eight cases of cervical teratomas were identified at Children's Hospital Boston over a 75-year period. Eleven of these neoplasms are the subject of this review and were located in the anterior neck, at the anatomic site of the normal thyroid, and all contained thyroid tissue. The remaining cervical teratomas were located in anatomic regions remote from the thyroid region, eg, oral cavity, oropharynx, posterior pharynx, nose, parotid gland as well as larynx, and therefore, were excluded from our study. Clinical information of the 11 cases was obtained

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from review of pertinent medical records or from referring clinicians and pathologists. Approval to conduct the study was granted from the Committee on Clinical Investigation from Children's Hospital Boston on May 12, 2004 (protocol no. M04-05-123) and May 25, 2004 (protocol no. S04-05-49). Past medical history, location and size of the neoplasms, as well as individual treatment modalities were reviewed. Up-to-date follow-up information was available in most cases.

Imaging studies of the neck were available for review in 5 patients (3 males, 2 females). Fetal ultrasonography and magnetic resonance imaging (MRI) were obtained in 3 patients using single shot fast spin-echo T2 weighted images. In 1 of these patients, a preoperative multiplanar MRI examination with contrast-enhanced images was also obtained on the first day of life prior to surgical resection of the mass. One additional patient underwent a preoperative ultrasound examination with Doppler ultrasonography on the first day of life. The last patient was imaged with preoperative computed tomography (CT) and MRI with contrast-enhanced images at the first and second days of life, respectively.

Routine stained sections of each teratoma were examined (average 17 sections per case), and all tumors were analyzed regarding their different tissue composition, degree of maturity (immature vs. mature), arrangement of thyroid and other tissues in relation to each other, and the presence of a fibrous pseudocapsule.

RESULTS

Clinical Features

All cervical teratomas were congenital (Fig. 1A,B), meaning that the lesions were present at the time of birth or were detected before birth in the setting of prenatal imaging techniques such as ultrasound and/or MRI. Other tumors were immediately detected after birth, especially in cases antedating these sensitive imaging procedures. Precise anatomic location as well as size of the lesions was determined (Table 1). The neoplasms ranged in size from nonpalpable (3.5 cm) to the largest that measured 13.5 cm (median, 6.9 cm).

All tumors were surgically resected, and the patient follow-up ranged form 1 to 45 years (median, 17 years); none of the patients experienced a recurrence over this period of time (Table 1). Most neoplasms were resected in the newborn period, especially when they were associated with significant medical problems, which included distortion of the neck anatomy with resulting breathing difficulties and secondary overinflation of the lungs due to congenital high airway obstruction syndrome. Some patients presented with pulmonary atelectasis rather than overinflation secondary to the lack of aeration due to subtotal airway narrowing. Other patients had feeding and swallowing problems because of oral tumor protrusion of which case no. 3 is an example; the clinical notes of this patient refer to grotesque distortion of the facial features. Sometimes, swallowing difficulties in the fetus resulted in polyhydramnios of the mother with the subsequent need for repeated amniotic fluid drainage to maintain the pregnancy. The prenatal history of some patients indicated poor weight gain in utero, displacement and/or compression of cervical vascular structures, and mild facial asymmetry on active motion of lips as well as postnatal dyspnea and stridor. Smaller lesions sometimes demonstrated palpable fullness in the submandibular region. In cases in which no respiratory or functional problems had been encountered, tumors were electively removed at a later point in time, ie, within the first few months of life.

Imaging Characteristics

In more recent years, when preoperative ultrasonography, CT, and MRI became readily available, characteristic

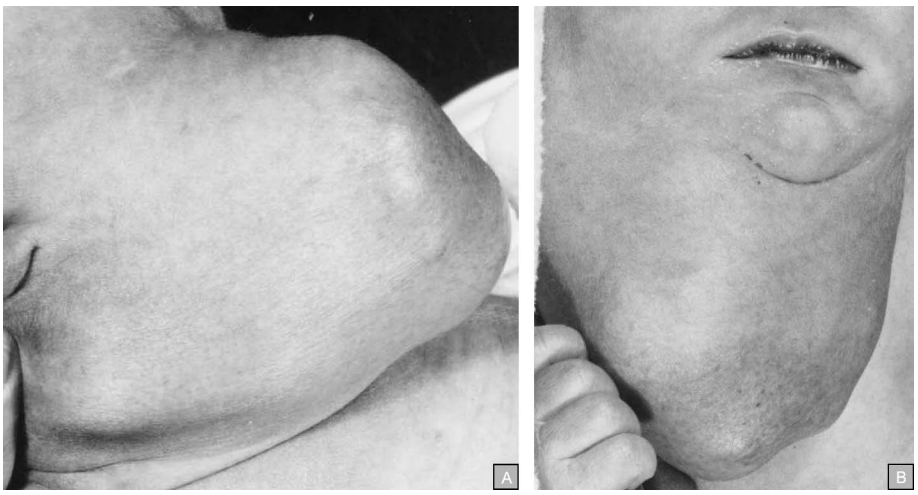

FIGURE 1. The patient (case no. 9) was the product of a full-term, spontaneous breech delivery with external version. A large neck mass was noted after birth, which was predominantly midline with extension to the right side of the neck and caused gross distortion of the anterior neck with limitation in flexion of the neck. The mother had polyhydramnios during her pregnancy. On the third hospital day, the patient underwent complete resection of the neck tumor. A 6-month follow-up showed an excellent cosmetic result without evidence of residual tumor. A, Right lateral view of neonatal presentation of a cervical teratoma (9.0 × 6.5 × 5.5 cm) causes marked fullness of neck. B, Frontal view shows the same marked grotesque distortion of the neck.

TABLE 1. Comparison of Thyroid Teratomas by Gender Distribution, Site of Origin, Size, Follow-up, Admixture With Thyroid Tissue, and Histologic Criteria

Patient No./Gender	Location	Size (cm)	Follow-up (yr.mo)	Admixture With Thyroid Tissue	Histologic Grade	Capsule Identified
1/Male	R NECK/*THYROID*	3.5	NED-1.3	Yes	Immature	No
2/Female	R NECK/*THYROID*	4.5	NED-1.9	No	Immature	Yes
3/Female	NECK	13.5	NED-1.2	No*	Immature	No
4/Male	R NECK/*THYROID*	8	NED-4.2	Yes	Immature	Yes
5/Male	L NECK/*THYROID*	7	NED-8	Yes	Immature	Yes
6/Male	NECK/*THYROID*	7	NED-19	Yes	Immature	Yes
7/Male	R NECK/*THYROID*	4.3	NED-29	No	Mature	No
8/Male	NECK/*THYROID*	5.5	NED-33	Yes	Immature	Yes
9/Male	R NECK/*THYROID*	9	NED-37	Yes	Immature	Yes
10/Female	NECK/*THYROID*	7	NED-30	Yes	Immature	No
11/Female	R NECK/*THYROID*	6	NED-24	No†	Immature	No

R, right; L, left; NED, no evidence of disease.
Note: All patients were newborn.
*Abundant necrosis.
†Thyroid not found.

imaging findings were discovered in some tumors (Fig. 2). Five patients had sharply circumscribed, infrahyoidal masses, four had neoplasms arising in the right cervical region, and one in the left neck. Figures 3A–C and 4A show 2 patients with a right and a left cervical tumor, respectively. In each case, the tumor was surrounded by a smooth glistening capsule (Figs. 3D, 4B,C). In each case, the tumor was heterogeneous and contained solid and cystic areas (Figs. 3C,E, 4C). Some tumors had scattered calcifications on CT examination (Fig. 4A).

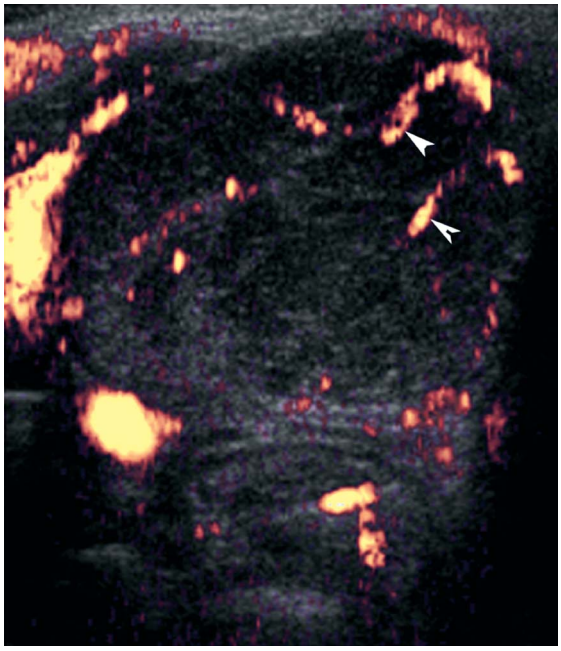

FIGURE 2. A female newborn (case no. 2) was noted to have a 4.5-cm tumor, located in the right neck region. This power Doppler image examination illustrated prominent vascularity within the tumor (arrow heads) as well as feeding vessel.

The characteristic appearance on imaging studies permitted the correct preoperative diagnosis of teratoma in all 5 patients. In all radiographically examined patients, the thyroid gland on the side of the tumor was either compressed or almost entirely replaced. In 1 patient, the tumor clearly had a ring of thyroid tissue stretched around the periphery of the tumor, suggesting thyroid gland as the site of origin of the tumor (Fig. 3A–C).

Pathology

Seven of 11 tumors showed a smooth glistening capsule on gross examination, with some of them having a rather multinodular appearance. Congested subcapsular vessels and focal subcapsular hemorrhage were observed in some cases. On cross section, the neoplasms revealed a variable degree of predominantly solid, predominantly cystic, or a mixed solid-cystic pattern. Conclusions regarding the specific tissue composition of a given tumor could not be drawn based on the gross appearance, as most tumors showed thyroid and other tissues intimately intermixed with each other (Table 1).

Immature neuroglial tissue predominated in 10 of the 11 tumors (Fig. 3H,L,M), and an intimate admixture of thyroid and other tissues with or without surrounding fibrous pseudocapsule was present in 8 cases, strongly suggesting thyroid as origin (Table 1; Figs. 3F–I, 4D–F). Of the remaining 3 cases, 1 contained only mature tissues, 1 large necrotic areas, and 1 showed no thyroid on imaging studies or intraoperatively (Table 1).

Based on review of clinical history, adequate follow-up when possible, and correlation with gross and microscopic features, the presence of immature elements in congenital thyroid teratomas in infancy did not result in adverse behavior as seen in adolescents and adults. A distinct intimate intermingling of thyroid and other tissue components and/or the presence of a fibrous pseudocapsule in an anterior cervical teratoma seemed to be the most significant criterion in establishing the diagnosis of thyroid teratoma.

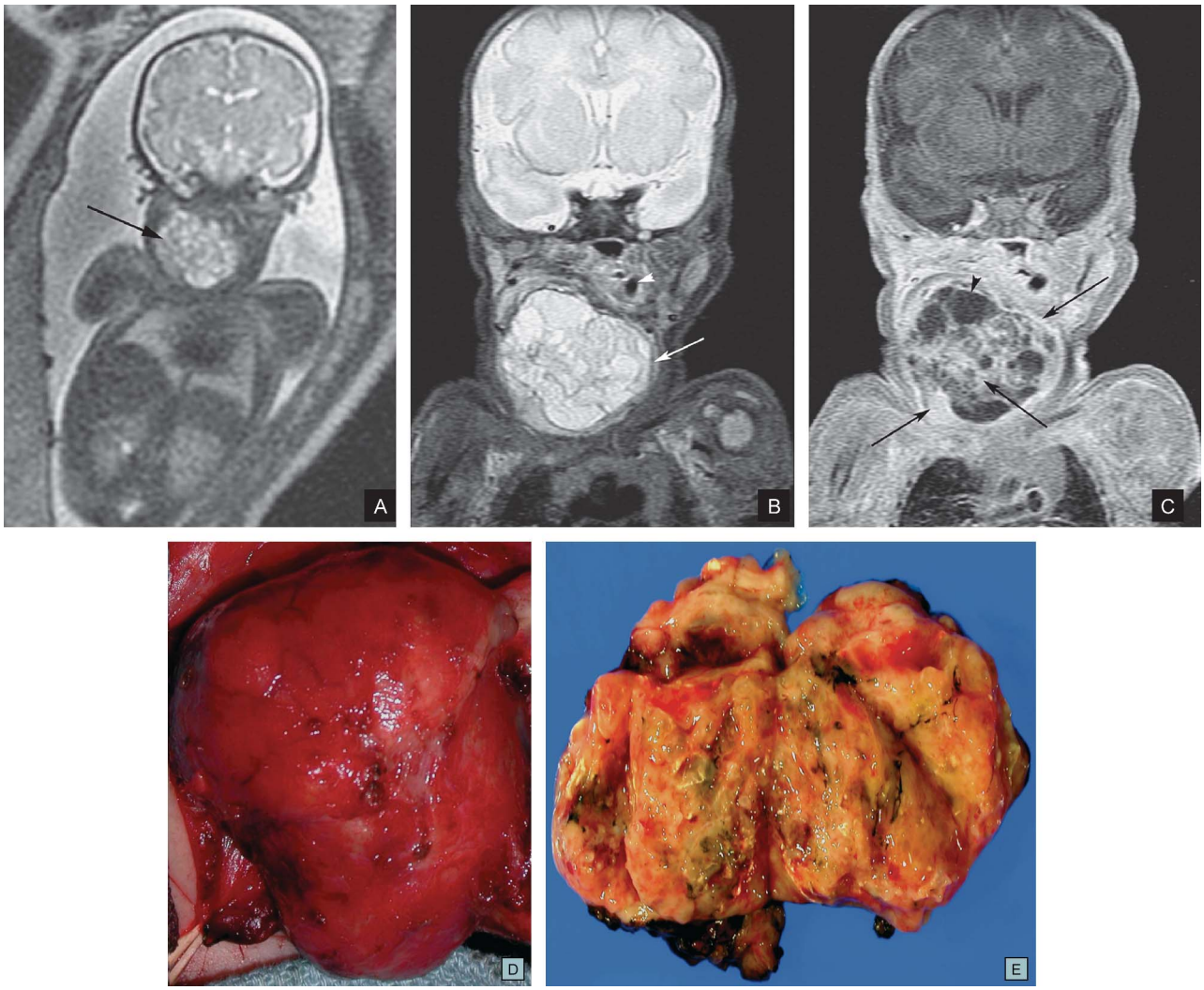

FIGURE 3. A, Coronal single shot fast spin echo T2-weighted MR image of a male fetus (case no. 1) during the third trimester reveals a heterogeneous cystic and solid mass (black arrow) within the neck on the right. B, Coronal fast spin echo inversion recovery MR image obtained of the baby boy at 1 day of age demonstrates the mass (white arrow) that has enlarged during the interim. There is distortion and compression of the airway (white arrowhead). C, Gadolinium-enhanced, fat-suppressed T1-weighted MR image shows the cystic components (black arrowhead) and enhancing solid components (black arrows). The peripheral and inferior component on the right (right inferior arrow) cannot be clearly separated from thyroid tissue. D, Intraoperative clinical picture demonstrates well-demarcated tumor surrounded by a glistening capsule. E, Bisected tumor reveals glistening solid and cystic cut surface. F, Low power photomicrographs of lesion revealing a distinct fibrous pseudocapsule (original magnification ×4). G, Medium power view of lesion showing intimate intermingling of thyroid and other tissue components (original magnification ×10). H, Immature neuroglial tissue (rosette) was present (original magnification ×20). I, High power view demonstrating intimate intermingling of thyroid follicles and neuroglial tissue (original magnification ×40). J and K, Medium power (original magnification ×10) and low power views (original magnification ×4), respectively, of teratoma showing intermixed ectodermal (black arrows), mesodermal (yellow arrows), and endodermal elements (red arrows). L, Low power view of immature neuroglial tissue (green arrows) and adjacent mesodermal and endodermal elements (original magnification ×4). M, High power view of immature neuroglial elements (original magnification ×40).

DISCUSSION

The current study is the second largest evaluating exceedingly rare primary thyroid teratomas of infancy with an average follow-up of 17 years. Thompson et al[13] reported the only larger study that included a few more neonates and infants (18 vs. 11) with about the same number of years regarding long-term follow-up (16.9 vs. 17.1 years). However, this study is the first report attempting to systematically evaluate histopathologic criteria for establishing the definitive diagnosis by postulating morphologic characteristics and distinct features of these lesions not previously cited in the medical literature.

Many previous reports of head and neck teratomas in general and of thyroid teratomas in particularly only cite individual cases and, even more significantly, there are only

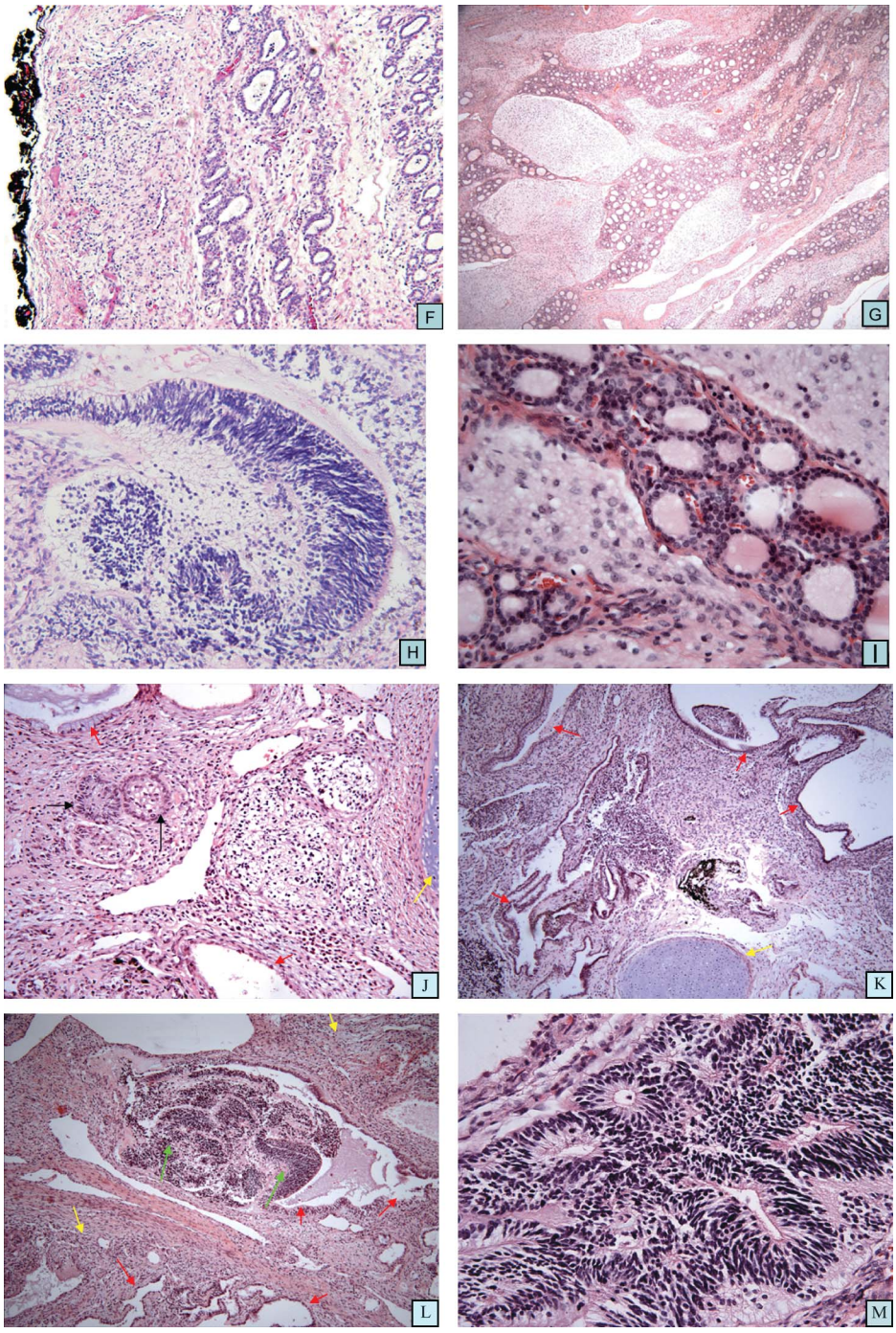

FIGURE 3. (*continued*)

a few articles reporting three or more original cases, most recently listed in a work by Thompson et al.[13] Considering the rarity of these lesions as well as the still unresolved debate as to the possible origin, we reviewed the files at Children's Hospital Boston for head and neck teratomas and directed our focus of interest to those neoplasms within the anterior cervical area that had associated thyroid tissue. All of the patients were diagnosed with an anterior neck mass in the newborn period and subsequently treated with surgical resection, which is widely accepted as optimal treatment of primary head and neck teratomas without malignant components.[6]

No difference in outcome was noted among patients with immature or mature teratomas since none of the neoplasms recurred with adequate follow-up, although only 1 of our cases was interpreted as mature teratoma. There seems to be no obvious difference in outcome based on the degree of immaturity of thyroid teratomas in infancy, an observation that is in concordance with the literature interpreting histologic

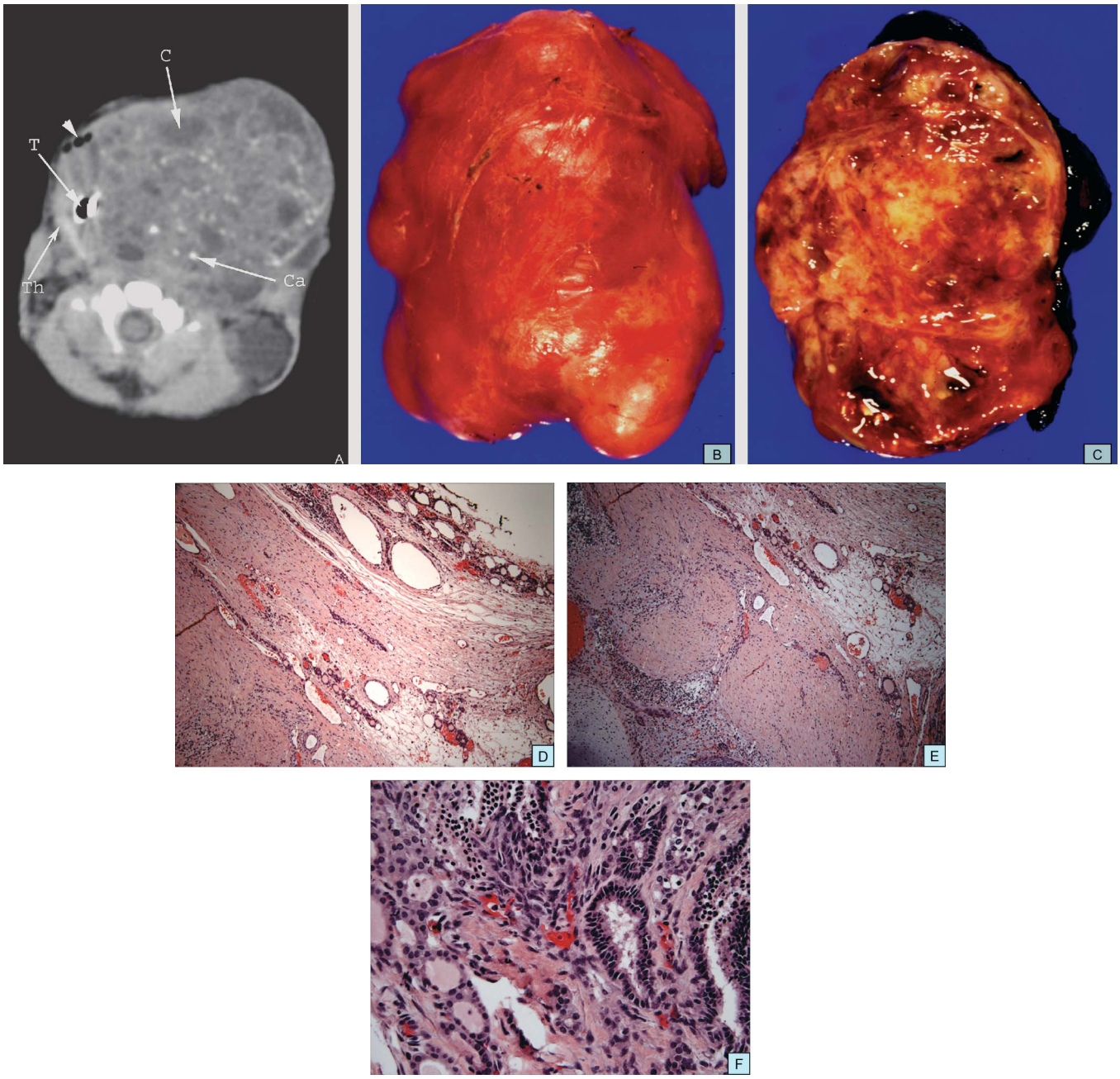

FIGURE 4. A, CT image of a heterogenous, solid and cystic (arrow C) mass with scattered calcifications (arrow Ca), located within the left side of the neck in a 1-day-old baby boy (case no. 5), compressing and displacing the trachea to the right (arrow T) with visible thyroid tissue on the right side of the mass (arrow Th). B, Encapsulated lobulated resection specimen in frontal and dorsal views with focal subcapsular hemorrhage. C, Cystic and solid lobulated and focal hemorrhagic cut surface of the mass. D, Medium power photomicrograph of teratoma surrounded by distinct fibrous pseudocapsule (original magnification ×10). E & F, Low power and high power views, respectively, demonstrate thyroid follicles intermingled with neuronal type tissue (original magnifications: E, ×4; F, ×40).

immaturity by itself as not being a predictor of malignant behavior.[3,14] An overtly malignant component, such as endodermal sinus tumor, however, must additionally be treated with adjuvant chemotherapy, although it is very uncommon and more often noted in other locations such as ovaries, testes, or the sacrococcygeal region.[9]

Radiologic differential diagnostic entities include lymphatic malformation (cystic hygroma), congenital hemangioma, congenital infantile fibrosarcoma, and rhabdomyoma. Certain distinct imaging features can help characterize and differentiate teratomas from those entities, such as the heterogeneous solid and cystic nature of the mass, sometimes

with additional fatty or calcific elements. On the other hand, lymphatic malformations exclusively appear cystic in nature, while the remainder of the differential diagnostic entities usually have a more homogeneously solid appearance. Additionally, prominent vascularity, as depicted in Figure 2, is often a feature of congenital hemangioma and, on occasion, of congenital infantile fibrosarcoma and teratoma.[7]

Our results suggest that the distinct tissue composition of cervical teratomas could provide essential clues regarding the most likely origin in cases of clinical doubt, ie, immature neuronal elements intimately admixed with thyroidal tissue in all but 1 case. More importantly, the presence of a fibrous pseudocapsule seemed to be the single most significant criterion in establishing the histopathologic diagnosis of primary thyroid teratomas in so far as it could be viewed as an unbroken barrier, separating the neoplasm from its surrounding environment and thereby excluding the possibility of secondary invasion into the thyroid gland.

Interestingly, previous reports attempting to provide some guidelines for interpretation of origin have not commented on the presence or absence of a fibrous pseudocapsule.[5,10,15]

There were no gross morphologic features, eg, necrosis, hemorrhage, predominantly cystic or predominantly solid tissue composition, that could accurately predict the microscopic tissue ingredients. Indeed, in 1 case, even the gross appearance of a "capsule" did not hold true after microscopic examination; there were instead large areas of necrosis that, theoretically, could have obscured an original pseudocapsule. Review of the literature also did not indicate any gross morphologic feature to draw significant conclusions regarding the possible tissue composition.

Three cases had neither a fibrous pseudocapsule nor intimate association of thyroid and teratoma. One case was exclusively composed of mature tissues with some scattered foci of atrophic thyroid follicles, most probably being part of the teratoma itself since no other case showed these atrophic follicles. The second case contained large amounts of necrosis, and no thyroid was identified on preoperative imaging studies or intraoperatively in the third case; this suggests that extensive tumor necrosis, degeneration, or the neoplastic process itself might have obscured or entirely replaced the thyroid gland.

In summary, very stringent criteria should be applied before one can confidently diagnose a primary thyroid teratoma; spatial continuity of thyroid and teratoma, commented upon in some reports,[13] should be regarded as a questionable argument in favor of this exotic diagnosis.

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