# Primary Thyroid Teratomas

## *A Clinicopathologic Study of 30 Cases*

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**BACKGROUND.** Primary thyroid teratomas are rare thyroid gland neoplasms of germ cell derivation that display features of trilineage differentiation.

**METHODS.** The histologic and immunophenotypic features of 30 cases of thyroid teratomas were reviewed, patient follow-up was obtained, and the results were analyzed statistically.

**RESULTS.** The patients included 15 females and 15 males ages newborn–56 years (mean, 12.4 years). All patients presented clinically with a mass in the thyroid, ranging in size from 2.0–13 cm in greatest dimension (mean, 6.0 cm). Histologically, the tumors usually were well circumscribed, although occasionally infiltrative into the thyroid parenchyma. Derivatives of all three germ layers (ectoderm, mesoderm, and endoderm) were present in varying degrees of maturity. The tumors were divided into benign (n = 7 tumors), immature (n = 14 tumors), and malignant (n = 9 tumors) as determined by an increasing percentage of tumor volume comprised of primitive mesenchymal or neural-type tissue. All the microscopically malignant tumors occurred in the adult population. Surgical excision was performed in 28 patients, followed by adjuvant therapy in 5 patients. Follow-up was obtained in 26 patients; 8 patients had died from or with tumor (5 neonates with immature histology and 3 adults with malignant histology; mean, 0.6 years) and 18 patients were alive with no evidence of disease at a mean of 16.9 years of follow-up.

**CONCLUSIONS.** Thyroid teratomas are rare neoplasms that can be divided into three types depending on the presence and proportion of the immature component. The outcome is dependent largely on the age of the patient, the size of the tumor at the time of initial presentation, and the presence and proportion of immaturity. Surgical excision is the treatment of choice, with adjuvant therapy reserved for the malignant cases. ***Cancer* 2000;88:1149–58.** © *2000 American Cancer Society.*

**KEYWORDS: thyroid, teratoma, mature, immature, malignant, grading, prognosis, immunohistochemistry, neonate, child, adult.**

Teratomas are tumors of germ cell derivation comprised of tissues derived from all three germ cell layers: ectoderm, endoderm, and mesoderm. They are most frequent in the gonads, sacrococcygeal region, mediastinum, and pineal region, although they also occur in the cervical region, and a number of these primarily involve the thyroid gland. Although there are many single case reports of thyroid teratomas, to our knowledge there are only a few articles containing three or more original cases.[1–14] In view of the rarity of thyroid teratoma and the lack of a comprehensive clinicopathologic study on the entity, we undertook a study of what we believe to be 30 heretofore unreported cases to evaluate their clinical, morphologic, and immunohistochemical features and to correlate those parameters with long term patient outcome.

## METHODS

Twenty-four cases of primary thyroid teratomas were retrieved from the files of the Endocrine and Otorhinolaryngic-Head & Neck Tumor Registry of the Armed Forces Institute of Pathology (AFIP), Washington, DC, between 1952–1997, and 6 cases from the consultation files of one of the authors (J.R.). The AFIP cases were identified in a review of 27,934 (0.1%) benign or malignant primary thyroid gland tumors seen in consultation during the same time. Twenty-three cases were obtained from civilian sources, including university medical centers and foreign contributors, and 7 were from military hospitals.

Hematoxylin and eosin stained slides for all cases were reviewed. All cases met the standard definition of thyroid teratoma (i.e., a mass lesion present within or adjacent to the thyroid gland and histologically displaying mature or immature tissues from the three embryonic layers).[15]

Although to our knowledge there are no currently accepted grading criteria for cervical/thyroid teratomas, grading criteria for gonadal and sacrococcygeal teratomas are well established.[16–20] We separated our tumors into three categories: benign, immature, and malignant. Benign tumors contained only mature elements (Grade 0). Immaturity, identified as immature tissues that resemble those of the embryo (usually immature neuroectodermal tissues arranged in primitive neuroepithelial rosettes and tubules), was divided into three grades to separate immature from malignant tumors, by a modification of the grading of ovarian and sacrococcygeal teratomas[16–18] as follows: Grade 1: a limited degree of immaturity, with embryonal-type tissue in only 1 low-power magnification field ($\times$4 objective with a $\times$10 ocular, using an Olympus BX40 microscope; Olympus, Melville, NY); Grade 2: $>$ than 1 but $<$ 4 low-power fields of immature foci; Grade 3: $>$ 4 low-power fields of immature tissue, along with mitoses and cellular atypia. By these definitions, tumors that we graded as Grade 0 were called benign, Grade 1 or Grade 2 tumors were categorized as immature, and Grade 3 immature tumors were considered malignant. The presence of embryonal carcinoma or yolk sac tumor also would have placed a teratoma into a malignant category, but none of the cases in the current study had these components.

The information already present regarding these patients in the files was supplemented by a review of the patient demographics, symptoms at presentation, medical history, surgical pathology reports, surgical reports, and oncology data records by specific questionnaires or direct communication with the physician or patient. Follow-up data included information regarding tumor location, treatment modalities, and current patient status. This clinical investigation was conducted in accordance and compliance with all statutes, directives, and guidelines of the Code of Federal Regulations, Title 45, Part 46, and the Department of Defense Directive 3216.2 relating to human subjects in research.

Immunophenotypic analysis was performed in cases with suitable material (n = 17) (according to the standardized avidin-biotin method of Hsu et al.[21]) on 4-$\mu$m thick, formalin fixed, paraffin embedded sections. The commercially available immunohistochemical antibody panel used in this study is listed in Table 1. Predigestion was performed with 0.05% Protease VIII (Sigma Chemical Co., St. Louis, MO) in a 0.1 M phosphate buffer at a pH of 7.8 at 37 °C for 3 minutes. Antigen enhancement was performed by placing the sections in a buffered citric acid solution and heating them for 20 minutes in a calibrated microwave oven. After this, the sections were allowed to cool at room temperature in a citric acid buffer solution for 45 minutes before the procedure was continued.[22] Appropriate positive and negative (serum) controls were used.

For the statistical studies, categoric variables were analyzed using chi-square tests to compare observed and expected frequency distributions. The Fisher exact test was used as a substitute for the chi-square test when numbers involved fewer than five patients. Comparison of means between groups were made with Student $t$ tests for unpaired data or one-way analysis of variance, depending on whether there were two groups or more than two groups, respectively. Multiple comparisons were analyzed using the Tukey method. Confidence intervals of 95% were generated for all positive findings. The $\alpha$ level was set at $P < 0.05$. All analysis was conducted using Statistical Package for the Social Sciences (SPSS) 8.0 for PCs (SPSS, Inc., Chicago, IL).

## RESULTS

### Clinical

A summary of the clinical information is given in Table 2 and Figure 1. There were 15 females and 15 males. Their ages at presentation ranged from newborn to 56 years, with an average age of 12.4 years. The average was slightly skewed by the 2 older patients (ages 50 years and 56 years, respectively), whereas the median age at presentation was newborn. Two distinct groups can be created by separating the neonates and infants from the children and adults: 18 patients in the first group, ranging in age from newborn to 2 years (average, 0.32 years), and 12 patients in the second group, ranging in age from 13–56 years (aver-

**TABLE 1**
**Immunohistochemical Panel**

| Antibody/antigen | Primary antibody | Company | Dilution | Antigen unmasking |
|---|---|---|---|---|
| Cytokeratin (AE1/AE3 and CK1) | | Boehringer Mannheim Biochemicals, Indianapolis, IN, and Dako, Carpinteria, CA | 1:50<br>1:200 | Protease treatment |
| Thyroglobulin | | Dako | 1:1600 | None |
| CD99 | | Boehringer Mannheim Biochemicals | 1:20 | Enzyme pretreatment |
| Chromogranin | | | 1:3,200 | None |
| Calcitonin | Mouse monoclonal | Dako | 1:100 | None |
| Vimentin | | BioGenex Laboratories, San Ramon, CA | 1:800 | Microwave pretreatment |
| Smooth muscle actin | | Sigma ImmunoChemicals, St. Louis, MO | 1:800 | None |
| Actin | | Enzo Inc., Farmingdale, NY | 1:80 | None |
| Desmin | | Dako | 1:100 | Enzyme pretreatment |
| Myo-D1 | | NovoCastra, New Castle-upon-Tyne, U.K. | 1:10 | Microwave pretreatment |
| Myoglobin | | | 1:1600 | None |
| S-100 protein | Rabbit polyclonal | Dako | 1:800 | None |
| Glial fibrillary acidic protein | | | 1:2000 | Protease treatment |
| NSE | Mouse monoclonal | | 1:200 | None |
| NFP | | Dako | 1:200 | Enzyme pretreatment |
| Synaptophysin | | | 1:400 | None |
| AFP | Rabbit polyclonal | | 1:640 | None |
| PLAP | | Biomeda Corp., Foster City, CA | 1:320 | None |

NSE: neuron specific enolase; NFP: neural filament protein; AFP: $\alpha$-fetoprotein; PLAP: placental alkaline phosphatase.

age, 30.2 years). Whereas the average age at presentation for females was older than males (16.9 years vs. 7.8 years), there was no statistically significant difference between them ($P = 0.157$).

All the patients presented with a mass lesion in the neck, which in one case (a stillborn infant) was complicated by a nuchal umbilical cord. There was no predilection for a particular side. In addition, nine patients reported dyspnea or difficulty breathing, two patients presented with stridor, and four patients reported both stridor and difficulty breathing.

## Radiographic Studies

Twelve of the patients had thyroid scans and/or ultrasound examinations performed prior to surgery. Four of these patients were found to have a single cold nodule and three showed a diffuse decreased iodine uptake. In the other patients there is no record that these tests demonstrated thyroid abnormalities.

## Pathologic Features

### *Macroscopic*

The tumors ranged in size from 2–13 cm in greatest dimension, with an average of 6.0 cm. There was no statistically significant difference in tumor size at presentation between males and females (males, 5.7 cm and females, 6.3 cm). Tumors associated with stridor and difficulty breathing were on the average larger (8.0 cm) than those in which these symptoms were absent (5.2 cm) ($P = 0.044$).

Macroscopically, the outer tumor surface varied from smooth to bosselated or lobulated, the consistency from firm to soft and cystic, and the color from gray-tan or yellow-white to translucent. The tumor borders ranged from well circumscribed to widely infiltrative into the surrounding thyroid parenchyma (Fig. 2). The cut surface usually was multiloculated, with the cystic spaces containing white-tan creamy material, mucoid glairy material, or dark brown hemorrhagic fluid admixed with necrotic debris. Material resembling brain tissue frequently was identified, often in association with areas of black pigmentation. Islands of gritty material consistent with bone and cartilage often were noted.

### *Microscopic findings*

Characteristically, these tumors displayed a wide array of tissue types and growth patterns within a single lesion. A multitude of small cystic spaces were observed lined by a variety of different epithelia: squa-

**TABLE 2**
**Clinical Features of Thyroid Teratomas**

| | Histology | | | |
|---|---|---|---|---|
| | All | Mature | Immature | Malignant |
| All cases | 30 | 7 | 14 | 9 |
| Gender | | | | |
| Females | 15 | 2 | 6 | 7 |
| Males | 15 | 5 | 8 | 2 |
| Age at presentation | | | | |
| All (average) | 12.4 yrs | 8.5 yrs | Newborn | 34.1 yrs |
| All (range) | 1 day–56 yrs | 0.2–25 yrs | 1 day–1 yr | 20–56 yrs |
| Females (average) | 16.9 yrs | 21.0 yrs | 0.2 yrs | 29.6 yrs |
| Males (average) | 7.8 yrs | 3.5 yrs | Newborn | 50.0 yrs |
| Age groups | | | | |
| Neonates and infants | 18 | 4 | 14 | 0 |
| Children and adults | 12 | 3 | 0 | 9 |
| Type of presentation | | | | |
| Mass | 15 | 6 | 2 | 7 |
| Mass with dyspnea, difficulty breathing, and/or stridor | 15 | 1 | 12 | 2 |
| Tumor size (cm) | | | | |
| Range | 2.0–13.0 | 4.5–6.0 | 3.0–13.0 | 2.0–10.5 |
| Average | 6.0 | 5.0 | 6.3 | 6.3 |

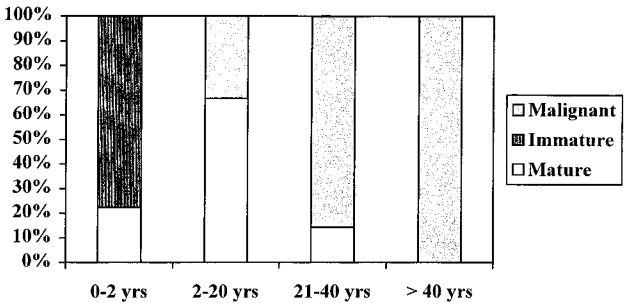


**FIGURE 1.** Age distribution at the time of presentation based on histology.

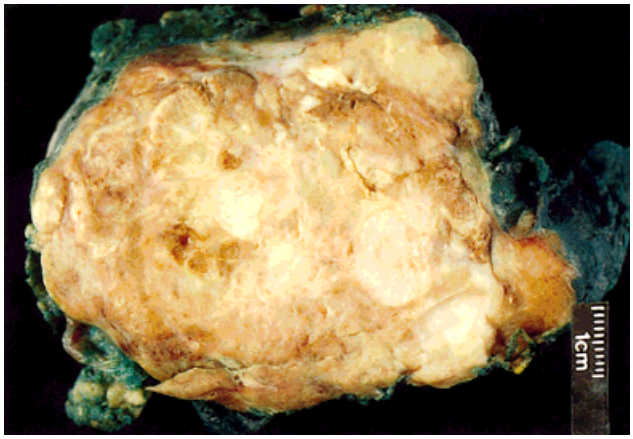


**FIGURE 2.** Macroscopic appearance of a thyroid teratoma demonstrating compressed thyroid parenchyma at the periphery with areas of cartilage interspersed with areas of degenerated tissue.

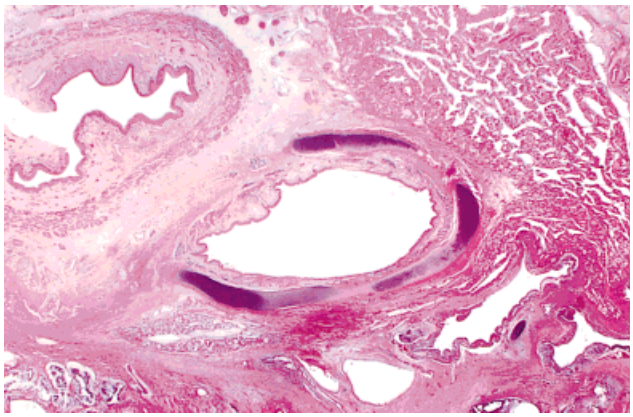

**FIGURE 3.** One area demonstrating an embryonic trachea and esophagus next to an area of choroid plexus in a mature teratoma.

mous epithelium (simple and stratified), pseudostratified ciliated columnar epithelium (respiratory) (Fig. 3), cuboidal epithelium (with and without goblet cells), glandular epithelium, and transitional epithelium. Pilosebaceous and other adnexal structures were noted in association with the squamous epithelium. Well differentiated areas of pancreatic (two cases), hepatic (two cases), and lung parenchyma (two cases) (Fig. 4) were noted. The various epithelia often blended with each other in a single cystic space. All cases contained a large component of neural tissue, which was comprised variously of mature glial elements, choroid plexus, pigmented retinal anlage, or immature neuroblastemal elements (Fig. 3, Figs. 5–7). The latter were comprised of small to medium-sized cells with dense hyperchromatic nuclei accompanied by mitoses, arranged in sheets or rosette-like structures (Fig. 8). The neural tissue was exclusively mature in 7 cases (Grade 0), predominant mature in 14 cases (Grade 1 and 2), and predominantly or exclusively immature in 4 cases (Grade 3 or malignant). Cartilage (n = 14) (Fig. 4), bone (n = 6), striated skeletal muscle (n = 18) (Fig. 9), smooth muscle (n = 18), adipose tissue, and loose myxoid to fibrous embryonic mesenchymal connective tissue was identified in the background (Fig. 6 and Fig. 9). Bone marrow elements occasionally were identified within the bone matrix.

Thyroid parenchyma was detected intermingled or contiguous to the teratoma in 24 cases (Fig. 5). It is interesting to note that the six cases in which no thyroid gland was identified were all immature or malignant.

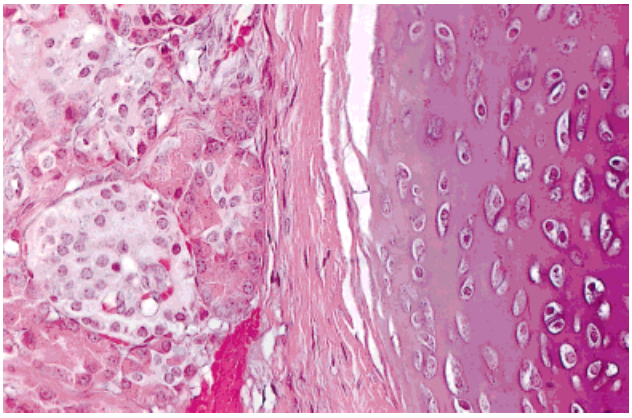

**FIGURE 4.** Cartilage was juxtaposed with pancreatic tissue, including islets and acini.

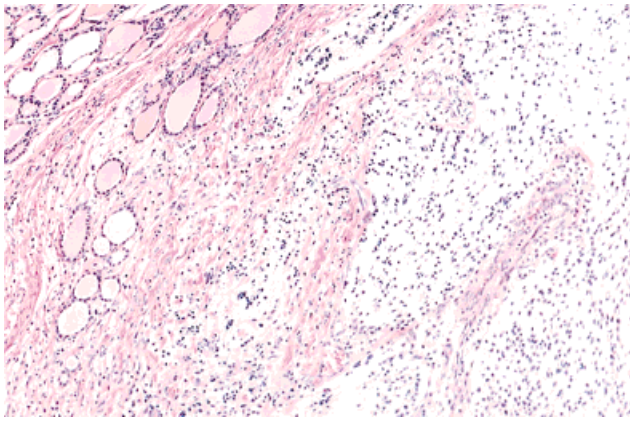

**FIGURE 5.** Thyroid parenchyma was present in the majority of most cases, here in the presence of neural tissue (brain) in a mature teratoma.

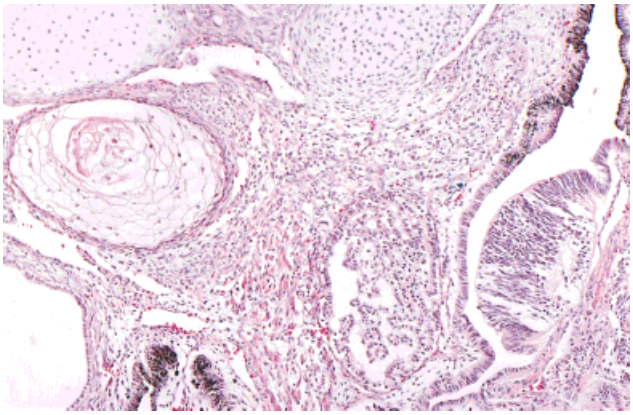

**FIGURE 6.** Retinal anlage was present along with immature elements in this immature, benign thyroid teratoma.

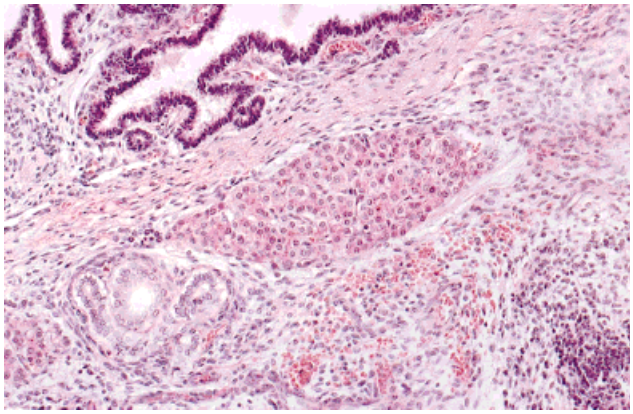

**FIGURE 7.** Salivary gland type tissue juxtaposed with columnar epithelium and immature elements.

### *Immunohistochemical results*

In all cases tested, immunoreactivity for epithelial, mesenchymal, and neural markers was found in the corresponding tissue types as predicted from their appearances in routine sections. The immature elements reacted with a variety of markers including S-100 protein, glial fibrillary acidic protein, neuron specific enolase, and neurofilament protein. Chromogranin reactivity was centered in the pancreatic islets, $\alpha$-fetoprotein immunoreactivity in the hepatic parenchyma, and desmin in the areas of skeletal muscle. Myo-D1 was reactive in immature mesenchymal areas, consistent with early skeletal muscle differentiation.

## Treatment and Follow-Up

Initially, all patients were treated by surgical excision, except for the 2 cases of infant deaths (1 of these infants was stillborn and the other lived only 1 hour) (Table 3). In addition to surgical excision, two patients with malignant teratoma initially were treated with radiation, two with chemotherapy, and one with a combination of the two. Four patients were lost to follow-up after the initial surgery. There was adequate follow-up for the remaining 26 patients. Of these, 18 patients were alive and well at last follow-up (average follow-up, 16.9 years), 5 patients had died on the day of delivery as a result of tracheal compression and lack of normal neck development (but without evidence of metastasizing tumor), and 3 patients had died as a result of the tumor aggressiveness (average follow-up, 1.7 years), manifested as recurrent local disease and/or lung metastases (metastatic tumor deposits were not reviewed histologically by the authors). All three patients were adults with histologically malignant teratomas. The fourth patient in this category was alive without evidence of disease 11.1 years after his disease, which was metastatic to the mediastinal lymph nodes and lungs (detected 3 months after pre-

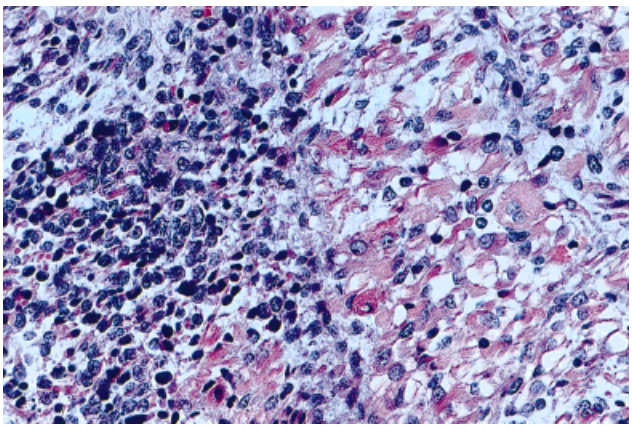

**FIGURE 8.** Undifferentiated and immature neural elements were the dominant findings in malignant thyroid teratomas.

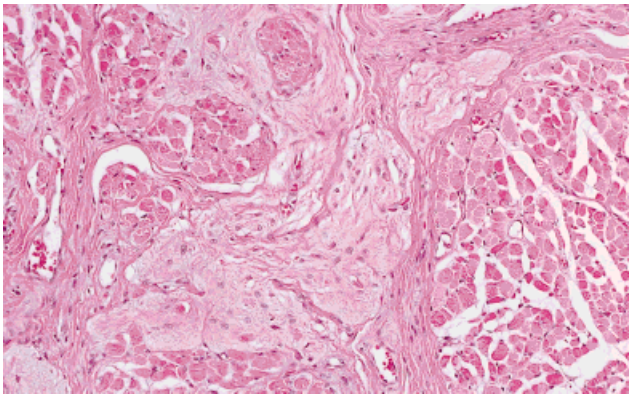

**FIGURE 9.** Mature muscle was interspersed with mature neural elements in the center of this thyroid teratoma.

sentation), was managed with a combination of radiation and chemotherapy.

## Clinicopathologic Correlations

The clinical outcome was evaluated against several clinical and pathologic parameters.

### *Age at presentation*

A striking correlation was found between age at presentation and tumor histology. Among the neonates and infants, there was a preponderance of immature (Grade 1 or 2 immaturity) over mature teratomas and an absence of malignant tumors. Conversely, among children and adults there was a preponderance of malignant teratomas (Grade 3 immaturity) over mature teratomas, with absence of immature forms (solely Grade 1 or 2 immaturity). These differences were reflected in the clinical outcomes among the various age groups. Thus, among the 17 neonates and infants, 5 (29.4%) died as a result of tracheal compression or lack of development of vital structures, but none as a result of tumor spread. Conversely, the 3 deaths among the 9 children and adults (33.3%) were due to tumor recurrence or metastases.

**TABLE 3**
**Outcome Depending on Patient Age and Tumor Histology**

| | Cases | A, NED | D, NED | D, D |
|---|---|---|---|---|
| Neonates and infants | | | | |
| Mature | 3 (27.5 yrs) | 3 (27.5 yrs) | 0 | 0 |
| Immature | 14 (10.5 yrs) | 9 (15.8 yrs) | 5[a] | 0 |
| Malignant | 0 | 0 | 0 | 0 |
| Children and adults | | | | |
| Mature | 1 (8.1 yrs) | 1 (8.1 yrs) | 0 | 0 |
| Immature | 0 | 0 | 0 | 0 |
| Malignant | 8 (8.7 yrs) | 5 (12.9 yrs) | 0 | 3 (1.7 yrs) |

A, NED: alive, no evidence of disease; D, NED: dead, no evidence of disease; D, D: dead with disease.
[a] Died on day of delivery, related to tracheal compression and lack of normal neck development, but did not have disseminated tumor.

### *Type of presentation*

Patients in whom the neck mass was associated with stridor and difficulty breathing had a statistically significant worse outcome than those presenting with a mass only ($P = 0.004$). However, it should be noted that all the patients belonging to the first category presented at birth. Also, tumors in which the cervical mass was symptomatic were much more likely to have immature microscopic elements ($P = 0.045$).

### *Tumor size*

When a dimension of 5.4 cm (the median rank) was used as a cutoff value, patients with a larger tumor size had a shorter median survival ($P = 0.046$).

### *Histology*

None of the tumors showing a mature or immature histology developed metastatic disease, whereas this was true for four of eight cases with clinical follow-up in the microscopically malignant group. However, 5 of the 17 patients with clinical follow-up in the mature/immature group died as a result of the mass impinging on vital neck structures or as the result of surgical complications.

### *Treatment*

There was no apparent statistically significant difference in overall patient outcome based on the type of initial treatment. Patients who went on to receive additional therapy (radiation therapy or chemotherapy) had a shorter survival ($P = 0.037$), but in all likelihood

this derives from the fact that only the patients with clinically malignant tumors received such treatment.

## DISCUSSION

Teratomas are germ cell tumors featuring tissues from the three primordial layers (i.e., ectoderm, mesoderm, and endoderm). A subset of these tumors is found in the neck, and a few of these are located within or in close anatomic relation to the thyroid. Review of the literature shows that, in general, tumors of the cervical region have been regarded as thyroid teratomas if one or more of these features were present: 1) the tumor occupies a portion of the thyroid gland; 2) there is direct continuity between the tumor and the thyroid gland; and 3) a cervical teratoma is accompanied by total absence of the thyroid gland.[1,2,23,24] The latter cases have been explained by hypothesizing that there might have been total replacement of the gland by the tumor or, alternatively, that the teratoma had arisen from a thyroid anlage that failed to develop into a mature thyroid gland.[2] We followed these criteria for the inclusion of cases in the current series. Specifically, we regarded a cervical teratoma as being of thyroid origin if normal thyroid tissue was found intermingled or in contiguity with the tumor mass (24 cases) or if the tumor was located in the anterior midneck and the thyroid gland was unidentifiable (6 cases). We fully acknowledge the fact that the determination of a thyroidal origin for a cervical teratoma is to some extent arbitrary. Moreover, in a given case it may be difficult to rule out the possibility that the thyroid tissue found adjacent to the teratoma may represent either normal thyroid gland secondarily invaded by a primary teratoma of soft tissues or yet another component of the teratoma.[23]

To our knowledge there are well in excess of 250 case reports in the world literature of cervical (including thyroid) teratomas. However, many of these cases are included in reviews of teratomas in the pediatric patient population or of teratomas in general, and are not sufficiently detailed. Moreover, many of the case reports have been duplicated in different journals at various times by the same authors or institutions.[5,9–11,25,26] Therefore, in the interest of presenting a meaningful review of the literature, only the first report given for these cases has been included in the current review, along with any report that contains at least three new cases (Tables 4 and 5). Perusal of the literature revealed that thyroid teratomas have been reported in all ages, with the majority of the cases occurring in patients falling into the neonates/children category.[1–14,27–29] We attempted to assign them to the categories of mature, immature, or malignant whenever possible, based on the authors' diagnoses when provided or our own interpretation of the pathologic description and illustrations when they were not, using the grading method described. On the basis of this admittedly arbitrary exercise, it appears as if the large majority of neonatal and pediatric teratomas display a mature or immature histology, whereas a significant proportion of those appearing in adult life are malignant.[30–32] It also becomes apparent that thyroid teratomas in infants can cause significant morbidity, despite their generally favorable histology, because of respiratory distress or the presence of associated malformation of vital structures in the neck. Therefore, surgery for mature thyroid teratomas should be instituted without delay because the preoperative mortality is significant.[18]

We divided the patients in the current series into 2 groups according to age at presentation (age $<$ or $>$ 2 years) and tumor histology (mature, immature, and malignant) (Table 2) (Fig. 1). The gender ratio was equal for the entire group (female:male [F:M] = 15:15), but there was a striking and unexplained difference in gender involvement when the tumors were divided according to histology (mature, F:M = 2:5; immature, F:M = 6:8; and malignant, F:M = 7:2). There was no difference in age at presentation between the genders. The clinical presentation of the cases in the current study did not differ significantly from that documented in the literature.[1–14,27–29]

When the various clinicopathologic parameters were related to outcome, a number of interesting correlations appeared. The worse outcome observed in patients presenting with stridor and difficulty breathing versus those presenting with an asymptomatic mass was mirrored in the literature[1–14,27–29] and most likely is explained by the fact that the majority of these patients presented at birth.

No differences in outcome were detected among the patients with mature and immature teratomas, confirming the observation made at other sites (such as the sacrococcygeal region)[16,17] that histologic immaturity in teratomas (particularly when restricted to neuroepithelial tissues) should not be regarded in itself as evidence of malignancy. Whatever morbidity or mortality was found in these tumors was due to their mass effect and/or postoperative complications. Conversely, the microscopically malignant teratomas occurring after the neonatal period manifested a clinically malignant behavior, thus emphasizing the importance of their morphologic identification and their distinction from the immature type.

The majority of thyroid teratomas are easily recognizable as such on clinical and pathologic grounds. At the clinical level, entities to be considered in the differential diagnosis, particularly in neonates, include

**TABLE 4**
**Review of the Literature Regarding Thyroid Teratomas (Listed in Chronologic Order)**

| Author | Year of publication | Age | Gender | Tumor size (cm) | Pathologic type | Patient outcome |
|---|---|---|---|---|---|---|
| Hess[28] | 1854 | Newborn | M | n/r | Benign | n/r |
| Pupovac[29] | 1896 | 9 wks | M | n/r | Malignant | D, perioperative |
| Carter[27] | 1903 | Newborn | F | n/r | Benign | n/r |
| McGregor and Workman[34] | 1906 | 2 wks | F | n/r | Immature | A, 5 mos |
| Lurje[30] | 1908 | 53 yrs | F | n/r | Malignant | D |
| Fritzsche[35] | 1920 | 41 yrs | F | n/r | Malignant | D, 1 mo/2 mos |
| Bell[36] | 1926 | Stillborn | M | n/r | Immature | D, 1 hr |
| Saphir[1] | 1929 | Stillborn | F | 11 | Benign | D, stillborn |
| Bale[2] | 1950 | Newborn | F | 12 | Benign | D, 1 day |
| | | 6 mos | F | 10 | Benign | D, 1 day |
| | | Fetus | n/r | n/r | Benign | D, 1 day |
| | | 2 mos | M | 15 | Benign | n/r |
| McGoon[3] | 1952 | 6 mos | F | 4 | Benign | D, 2 wks |
| | | Newborn | M | 7.5 | Benign | D, 1 hr |
| | | 8 mos | M | 6 | Benign | A |
| | | Newborn | M | 5 | Benign | D, 2 wks |
| Batsakis et al.[25] | 1964 | Newborn | M | 4 | Benign | D, 3 days |
| | | Newborn | F | 12 | Malignant | A, 1 yr |
| Retief[4] | 1966 | 7 mos | M | 6 | Benign | A |
| | | 18 yrs | M | 7 | Benign | A |
| | | 2 mos | n/r | n/r | Benign | D, perioperative |
| Kemp[32] | 1967 | 85 yrs | F | n/r | Malignant | A, 7 mos |
| Stone et al.[5] | 1967 | 20 yrs | F | 6 | Benign | A, 10 yrs |
| | | 6 yrs | F | 1 | Benign | A |
| | | 2 yrs | F | 1.5 | Benign | A |
| | | 3 yrs | F | 3.5 | Benign | A |
| | | 14 yrs | F | 6 | Benign | A |
| Berry et al.[6] | 1969 | 3 days | F | n/r | Immature | D, 1 day |
| | | 3 wks | F | n/r | Benign | A, 3 yrs |
| | | 4 mos | F | n/r | Benign | A, 5 mos |
| Chappel[7] | 1970 | Newborn | F | n/r | Benign | A |
| | | Newborn | F | n/r | Benign | A |
| | | Newborn | F | n/r | Benign | D, perioperative |
| Grosfeld[8] | 1976 | 1 yr | M | n/r | Benign | A |
| | | 14 mos | M | n/r | Benign | A |
| | | 30 mos | M | n/r | Benign | A |
| Colton et al.[31] | 1978 | 77 yrs | M | n/r | Malignant | n/r |
| Idobaev[37] | 1980 | 55 yrs | M | n/r | Benign | n/r |
| Gundry et al.[9] | 1983 | Newborn | F | n/r | Benign | A, 5 yrs |
| | | Newborn | F | 12 | Malignant | A, 1 yr |
| | | Newborn | M | 4 | Benign | D, 3 days |
| | | Newborn | F | n/r | Benign | D, < 1 hr |
| | | Newborn | M | n/r | Benign | A, 4 yrs |
| | | Newborn | M | 5 | Benign | A, 6 mos |
| Tapper and Lack[10] | 1983 | Newborn | F | 6 | Immature | A, 3 yrs |
| | | Newborn | F | 5.5 | Immature | A, 12 yrs |
| | | Newborn | F | 7 | Immature | A, 9 yrs |
| | | Newborn | M | 4.3 | Benign | A, 8 yrs |
| | | Newborn | M | 5 | Immature | A, 8 yrs |
| | | Newborn | M | 9 | Malignant | A, 16 yrs |
| Lack[11] | 1985 | Newborn | F | 6 | Immature | A, 3 yrs |
| | | Newborn | M | 5.5 | Immature | A, 12 yrs |
| | | Newborn | F | 7 | Immature | A, 9 yrs |
| | | Newborn | M | 4.3 | Benign | A, 8 yrs |
| | | Newborn | F | 5 | Immature | A, 8 yrs |
| | | Newborn | M | 9 | Malignant | A, 16 yrs |
| Wolvos et al.[38] | 1985 | 72 yrs | F | 6 | Benign | A, 3 yrs |
| Jordan and Gauderer[12] | 1988 | Newborn | F | n/r | Benign | A, 2 yrs |
| | | Newborn | F | 6.5 | Benign | A, 6 mos |
| | | Newborn | F | 5 | Benign | A, 7 yrs |
| | | Newborn | F | 8 | Benign | D, 1 hr |
| | | Fetus | F | 11 | Immature | D, stillborn |
| Schmitz et al.[39] | 1990 | 6 yrs | F | 3.7 | Immature | A |
| Zerella and Finberg[13] | 1990 | Newborn | F | n/r | Benign | A |
| | | Newborn | F | n/r | Benign | A |
| | | Newborn | F | n/r | Benign | n/r |
| Cudennec et al.[40] | 1992 | 51 yrs | M | 10 | Benign | A, 14 yrs |
| Vujanic et al.[14] | 1994 | 3 mos | M | 3 | Benign | A, 3 yrs |
| | | 18 mos | M | 4 | Benign | A, 4 yrs |
| | | Newborn | M | 12 | Benign | D, same day |
| | | Newborn | M | 8 | Benign | A, 3 mos |

M: male; n/r: not reported; D: dead; F: female; A: alive.

**TABLE 5**
**Literature Summary**

| | Histology | | | |
|---|---|---|---|---|
| | **All** | **Mature** | **Immature** | **Malignant** |
| All cases[a] | 71 | 49 | 13 | 9 |
| Gender | | | | |
| Females | 40 | 25 | 10 | 5 |
| Males | 29 | 22 | 3 | 4 |
| Age at presentation | | | | |
| Range, all | Newborn–85.0 yrs | Newborn–72.0 yrs | Newborn–6.0 yrs | Newborn–85.0 yrs |
| Average, all | 7.2 yrs | 5.1 yrs | 0.5 yrs | 28.5 yrs |
| Females (average) | 7.6 yrs | 4.7 yrs | 0.6 yrs | 35.8 yrs |
| Males (average) | 7.2 yrs | 6.0 yrs | Newborn | 19.2 |
| Age groups | | | | |
| Neonates and infants | 57 | 40 | 12 | 5 |
| Children and adults | 14 | 9 | 1 | 4 |
| Tumor size (cm) | | | | |
| Range | 1–15 | 1–15 | 3.7–11.0 | 9–12 |
| Average | 6.7 | 6.4 | 6.2 | 10.5 |
| Outcome | | | | |
| Alive (not specified further) | 45 | 30 | 10 | 5 |
| Dead (not specified further) | 20 | 14 | 3 | 3 |

[a] Parameter was not always stated in the report, and therefore the numbers do not necessarily equal the total values in the columns.[1–14,25,27–32,34–40]

cystic lymphangioma (cystic hygroma), thyroglossal ductal cyst, and branchial cleft cyst, all of which should be easily recognizable at the microscopic level. Histologically, immature and malignant teratomas largely comprised of neural tissue need to be distinguished from extraskeletal Ewing sarcoma/primitive neuroectodermal tumor, small cell carcinoma, malignant lymphoma, and other malignant small cell tumors.[24,33] The diagnosis of teratoma under these circumstances is largely dependent on the identification of other tissue elements, the immature/malignant neural tissues, and a confirmatory immunohistochemical panel.

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