Unusual Thyroid Tumors

12

A variety of unusual tumors involve the thyroid, including sclerosing mucoepidermoid carcinoma with eosinophils, which has an unusual appearance with infiltrating glandular cells and squamoid cells. Squamous cell carcinoma may involve the thyroid by direct extension from a tumor in the neck or as a metastasis, but primary squamous cell carcinomas of the thyroid also occur. Malignant lymphoma may be primary to the thyroid, or the thyroid may be affected in systemic disease. When limited to the thyroid, Langerhans cell histiocytosis tends to be quite indolent and to remain localized. A variety of mesenchymal tumors affect the thyroid, including solitary fibrous tumor, angiosarcoma, synovial sarcoma, leiomyosarcoma, low-grade fibromyxoid sarcoma, and rhabdomyosarcoma, but angiosarcomas are among the most common and most aggressive sarcomas affecting the thyroid. Other unusual tumors in the thyroid are carcinoma showing thymus-like differentiation, teratoma, and paraganglioma.

Sclerosing Mucoepidermoid Carcinoma with Eosinophils

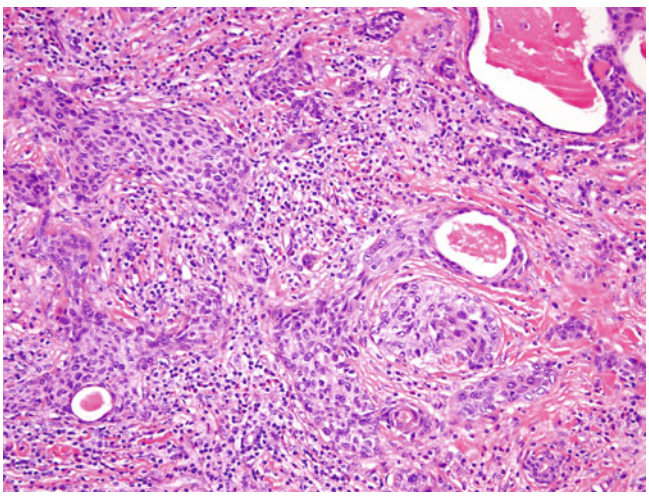

Fig. 12.1 Sclerosing mucoepidermoid carcinoma with eosinophils. Sclerosing mucoepidermoid carcinoma with eosinophils is a rare thyroid malignancy that occurs predominantly in adult women [1–3]. The tumor usually is slow growing and appears cold or hypofunctioning on radionucleotide scans. Grossly, the tumors are well circumscribed, but many extend to involve the soft tissues. The tumors are firm with a white to yellow cut surface. The tumor, as the name implies, has a sclerotic stroma and is associated with eosinophils. The infiltrating cells appear both squamoid and glandular. The tumor cells may become discohesive and appear pseudoangiomatous

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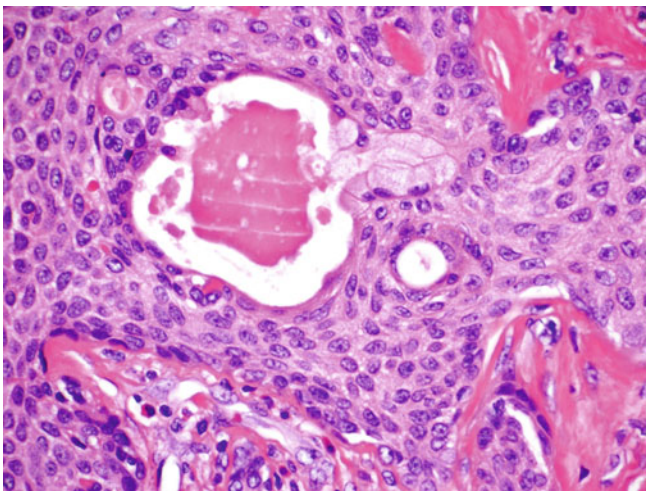

Fig. 12.2 Sclerosing mucoepidermoid carcinoma with eosinophils. Sclerosing mucoepidermoid carcinoma with eosinophils may be difficult to diagnose because the squamoid areas may be mistaken for squamous metaplasia; therefore, recognizing invasive growth is important. Perineural invasion is not uncommon. The tumor cells are positive for keratin and negative for thyroglobulin and calcitonin. Thyroid transcription factor 1 (TTF1) immunoreactivity is seen in approximately 50 % of cases [4]. Sclerosing mucoepidermoid carcinoma with eosinophils is treated surgically; approximately 50 % of patients do well, whereas others show regional or distant metastases [4]

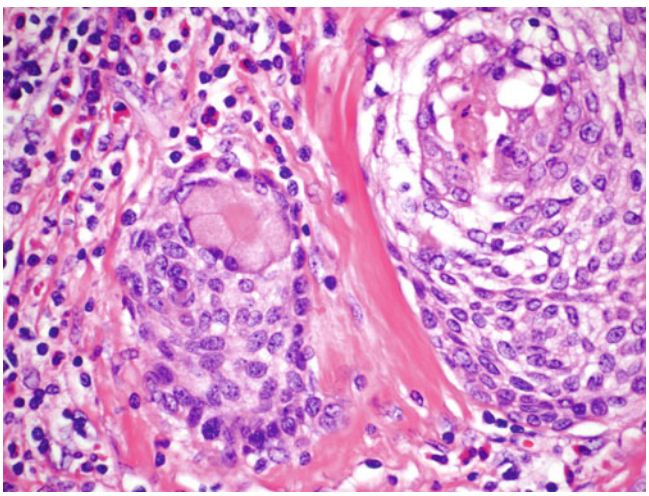

Fig. 12.3 Sclerosing mucoepidermoid carcinoma with eosinophils. Mucous cells are present but not always prominent in sclerosing mucoepidermoid carcinoma with eosinophils. The background of eosinophils and surrounding squamous areas are clues in looking for mucous cells

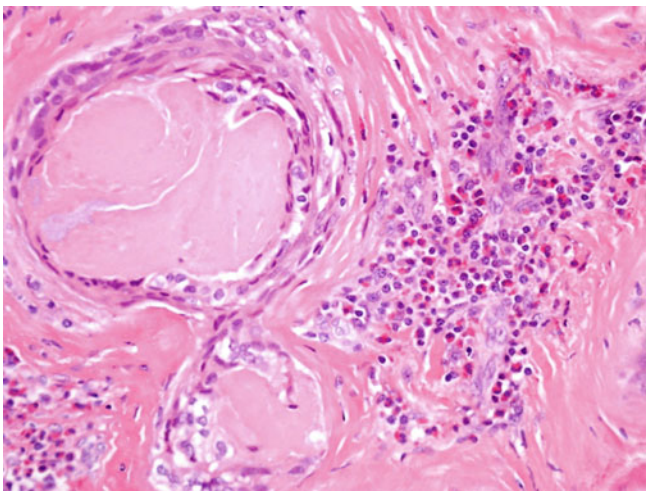

Fig. 12.4 Sclerosing mucoepidermoid carcinoma with eosinophils. The eosinophils usually are fairly prominent in sclerosing mucoepidermoid carcinoma with eosinophils. Eosinophils, sclerosis, and squamous metaplasia in a thyroid neoplasm are features that suggest sclerosing mucoepidermoid carcinoma. On further evaluation of this tumor, mucous cells are identified

Squamous Cell Carcinoma

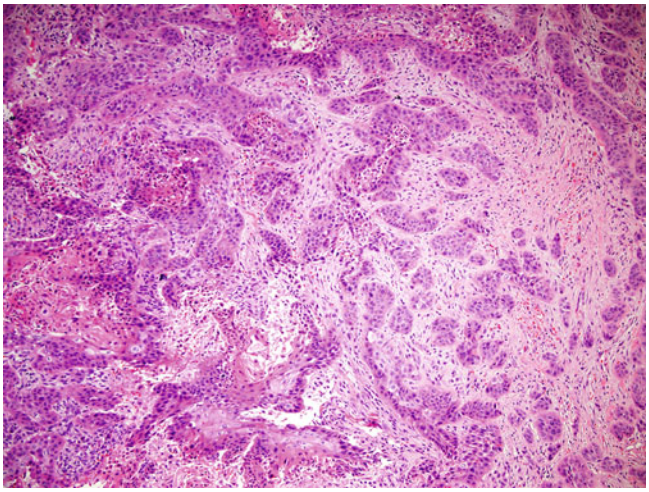

Fig. 12.5 Squamous cell carcinoma. Squamous cell carcinoma primary to the thyroid is an uncommon, rapidly growing tumor that usually occurs in adult patients and has a female predominance [5–8]. Primary squamous cell carcinoma of the thyroid has been reported in an adolescent with Hashimoto thyroiditis [9]. Presenting features include signs and symptoms of airway or esophageal obstruction or compression and neck swelling [5]. Grossly, these tumors are firm, are 2–8 cm, and may show areas of necrosis [10]. In a series of 16 patients, 12 had locoregional disease at presentation and 4 had distant metastases [6]. The median survival was 16 months, but there were three long-term survivors [6]. These tumors are aggressive and generally have a poor prognosis; however, long-term survival is possible in localized disease treated aggressively with surgery and radiotherapy [6]

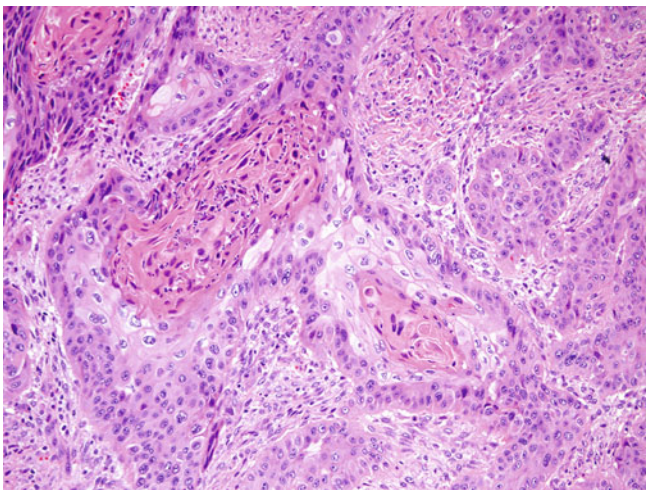

Fig. 12.6 Squamous cell carcinoma. This primary squamous cell carcinoma of the thyroid has squamous cells with keratinization. Other tumors, such as the tall cell variant of papillary thyroid carcinoma, may be identified in association with squamous cell carcinoma of the thyroid [10]. Areas of squamous differentiation also may be seen in undifferentiated carcinomas. Others have raised the possibility that some cases diagnosed solely as squamous cell carcinoma with a prognosis similar to undifferentiated carcinoma might represent extensive squamous differentiation in an undifferentiated carcinoma rather than true squamous cell carcinoma of the thyroid [11]

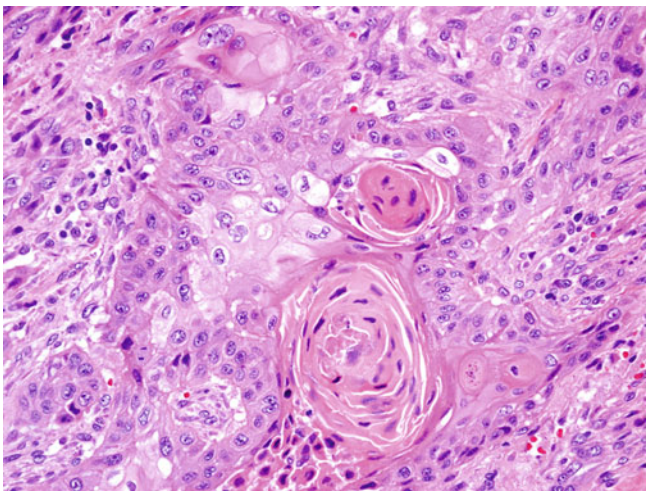

Fig. 12.7 Squamous cell carcinoma. Squamous cell carcinoma is composed of cells showing pure squamous differentiation. Other thyroid tumors may show focal squamous differentiation and should not be mistaken for the pure squamous differentiation throughout the tumor in primary squamous cell carcinoma of the thyroid. The tumor cells in thyroid squamous cell carcinoma are variably positive for keratins, including CK19, CK18, and CK7, and negative for CK1, CK4, CK10/13, and CK20 [5, 8]. Thyroglobulin usually is negative. The tumors show decreased staining for p21, and p53 expression occurs particularly in poorly differentiated cases [5, 10]. Ki67 labeling index is 30 % [10]. Differentiating primary squamous cell carcinoma of the thyroid from secondary involvement of the thyroid may be difficult histologically, and imaging studies often are helpful. TTF1 is reported to be focally positive in 37.5 % of primary squamous cell carcinomas of the thyroid, a feature, along with focal thyroglobulin staining, that may be helpful in differentiating it from squamous cell carcinoma involving the thyroid secondarily [8]

Lymphoma

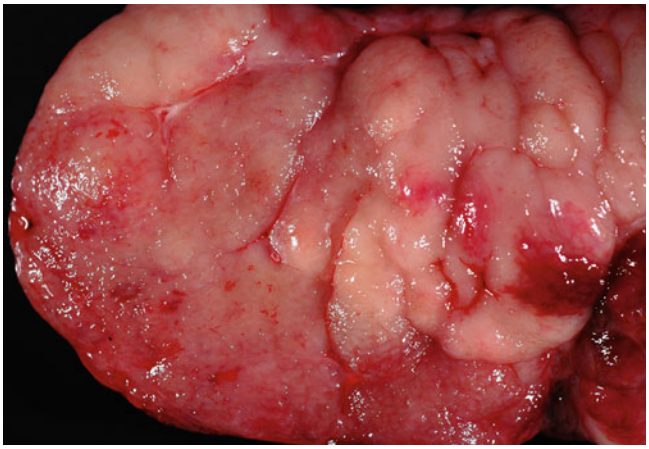

Fig. 12.8 Lymphoma. This gross photograph shows a follicular lymphoma involving the thyroid. Lymphomas constitute approximately 5 % of thyroid tumors and usually are identified in older individuals. Thyroid lymphomas often are identified in patients with a history of Hashimoto thyroiditis. Mucosa-associated lymphoid tissue (MALT) lymphomas are among the most common. The microscopic features are quite variable, ranging from small cells with sparse cytoplasm of extranodal marginal zone B-cell lymphomas to much larger cells and diffuse large B-cell lymphomas. Follicular lymphomas of the thyroid are rare. Plasmacytomas and MALT lymphomas with prominent plasma cell differentiation also occur in the thyroid

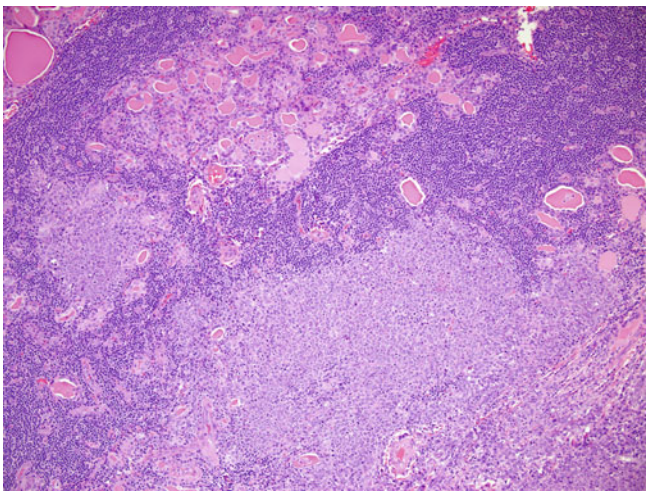

Fig. 12.9 Lymphoma. This low-power photomicrograph shows a diffuse large B-cell lymphoma of thyroid. In a retrospective review of 108 primary thyroid lymphomas, the average age was 64 years and patients presented with a thyroid mass [12]. Of the 108 primary thyroid lymphomas, 30 were marginal zone B-cell lymphomas of MALT or marginal zone B-cell lymphomas, 36 were diffuse large B-cell lymphomas with marginal zone lymphomas, 41 were diffuse large B-cell lymphomas, and 1 was follicular lymphoma. Lymphocytic thyroiditis was identified in 94 % of cases, and 69 % had perithyroidal soft tissue extension [12]

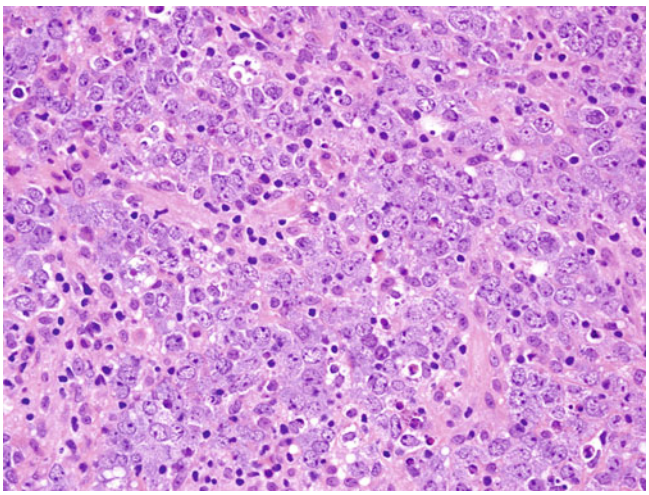

Fig. 12.10 Lymphoma. This high-power photomicrograph shows a diffuse large B-cell lymphoma of thyroid. These large cells have vesicular nuclei, nucleoli, and mitotic activity

Langerhans Cell Histiocytosis

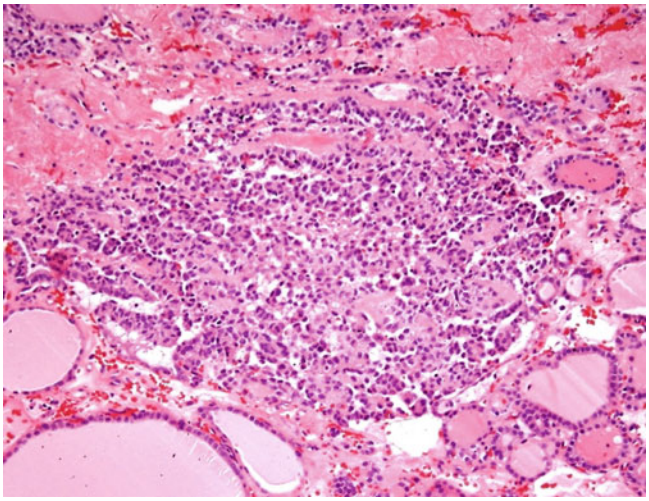

Fig. 12.11 Langerhans cell histiocytosis. Langerhans cell histiocytosis is a rare tumor of the thyroid that occurs most often in children and young adults, although it may affect a wide age spectrum. The thyroid may be involved in systemic disease; however, Langerhans cell histiocytosis localized to the thyroid is associated with good prognosis and usually does not develop into systemic disease [13]. Histologically, the thyroid may be involved focally or diffusely by Langerhans cells with intermixed eosinophils [13]

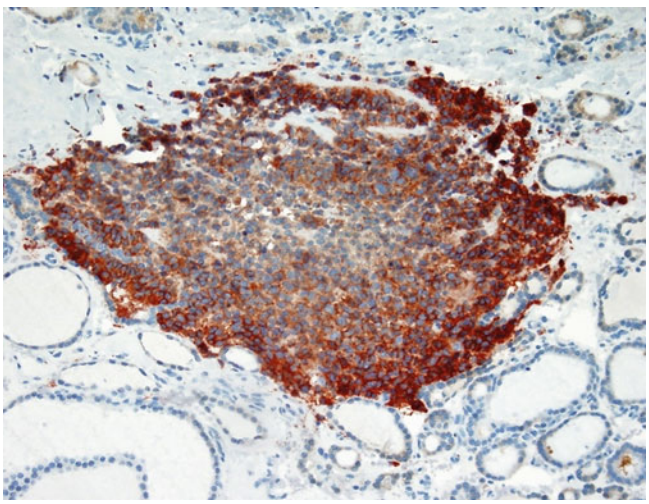

Fig. 12.12 Langerhans cell histiocytosis. CD1a immunostain highlights the Langerhans cells in this case of Langerhans cell histiocytosis of the thyroid. The Langerhans cells have grooved or folded vesicular nuclei and are positive for S100 and CD1a. Ultrastructurally, Langerhans cells have characteristic Birbeck or Langerhans granules. The surrounding thyroid may show a variety of changes, from chronic lymphocytic thyroiditis to papillary thyroid carcinoma

Solitary Fibrous Tumor

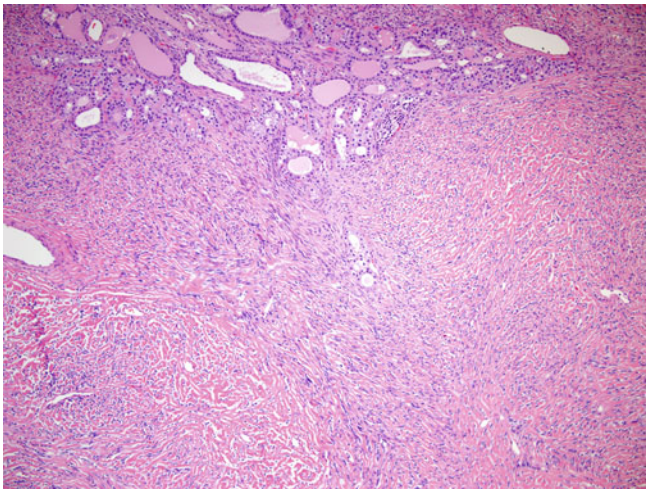

Fig. 12.13 Solitary fibrous tumor. Solitary fibrous tumors are rare tumors in the thyroid and usually are associated with indolent behavior in this location. They form a solitary circumscribed mass, 2–8 cm, in the thyroid of middle-aged adults [14, 15]

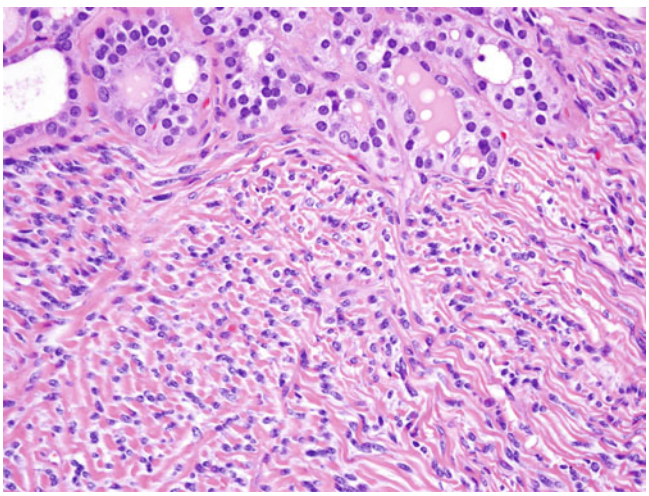

Fig. 12.14 Solitary fibrous tumor. Solitary fibrous tumors are rare. They are composed of spindle cells and have a storiform, hemangiopericytoma, or desmoid-like architecture and hypo- and hypercellular areas. The lesional cells are positive for CD34. Follicles may appear trapped at the periphery of the tumor, and the tumor cells have an infiltrative pattern among the follicles

Angiosarcoma

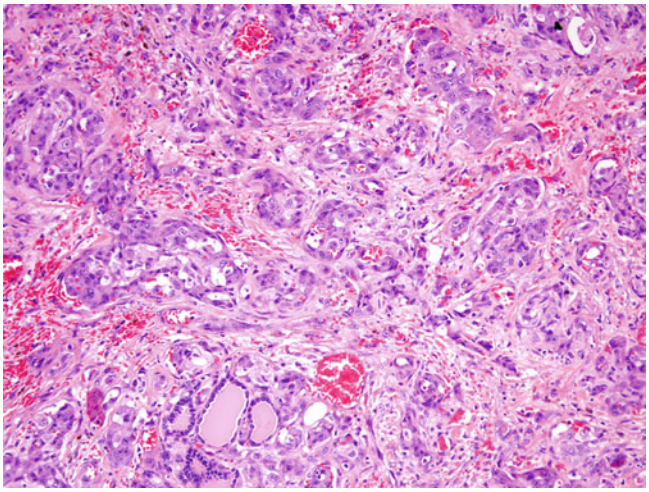

Fig. 12.15 Angiosarcoma. Angiosarcoma is the most common malignant mesenchymal tumor involving the thyroid gland [16, 17]. The tumors are large and often occur in a background of nodular goiter. They are more common in the Alpine regions of central Europe than elsewhere

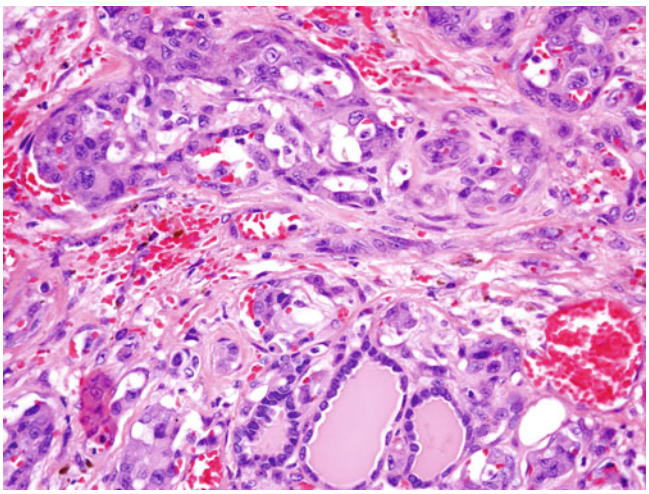

Fig. 12.16 Angiosarcoma. Angiosarcomas of the thyroid are solid and cystic and may be hemorrhagic and show necrosis. They are composed of anastomosing channels of atypical endothelial cells, often epithelioid when these tumors affect the thyroid. The tumors stain for vascular markers CD31, CD34, factor VIII, and FLI-1. Angiosarcomas with epithelioid features also often show keratin expression [16, 17]. Angiosarcomas are highly aggressive tumors, and survival often is less than 6 months

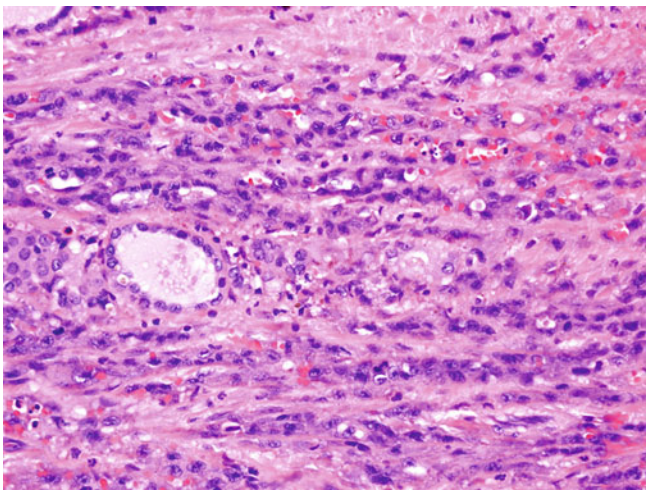

Fig. 12.17 Angiosarcoma. Angiosarcomas of the thyroid must be differentiated from metastasis to the thyroid and carcinomas and angiomatoid features, although they are all aggressive tumors with a poor prognosis [18]

Synovial Sarcoma

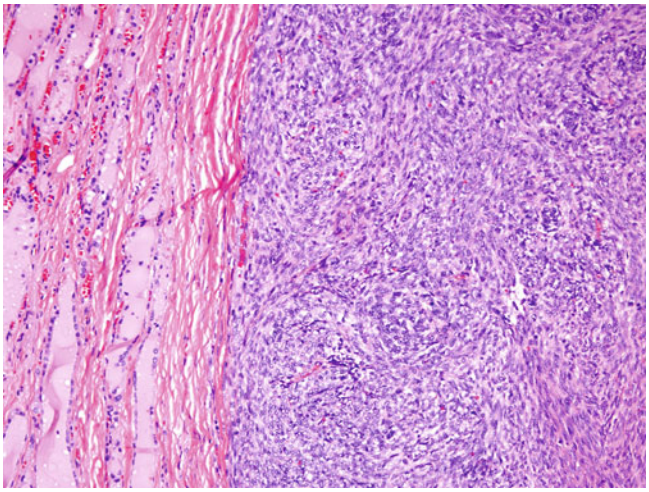

Fig. 12.18 Synovial sarcoma. Synovial sarcoma of the thyroid is present on the *right*, with normal thyroid parenchyma on the *left*. Like other uncommon mesenchymal tumors, synovial sarcoma rarely may involve the thyroid [19, 20]

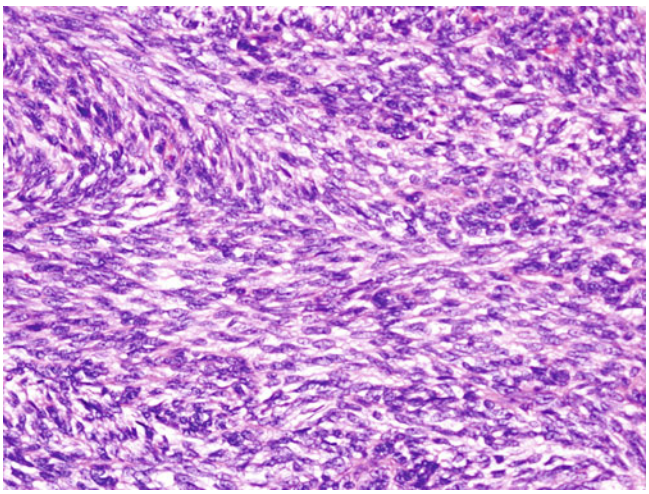

Fig. 12.19 Synovial sarcoma. This synovial sarcoma of the thyroid has a monophasic pattern. These tumors may be biphasic, with both epithelial and spindle components, or monophasic, with a pure spindle pattern. The spindle cells have stippled chromatin, indistinct cell margins, and scant cytoplasm and grow in sheets or fascicles. These tumors often have thick ropy collagen bundles, hemangiopericytoma-like vessels, and calcifications. They show keratin positivity and have a characteristic translocation t(X;18/p11;q11), resulting in an SYT/SSX fusion transcript that has been used to confirm the diagnosis of synovial sarcoma of the thyroid [19]

Low-Grade Fibromyxoid Sarcoma

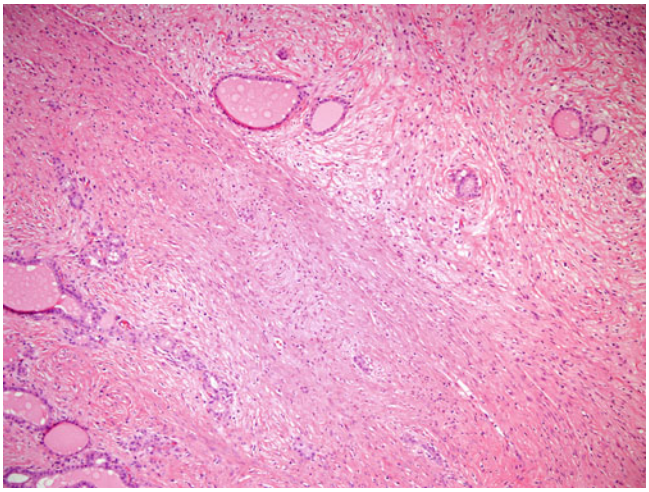

Fig. 12.20 Low-grade fibromyxoid sarcoma. Low-grade fibromyxoid sarcoma rarely affects the thyroid and is quite uncommon, and the literature is limited to case reports [21, 22]. These tumors appear deceptively benign and often are indolent, but they can metastasize. This tumor shows bland fibroblasts in a linear arrangement and alternating areas or less cellular myxoid and more cellular areas

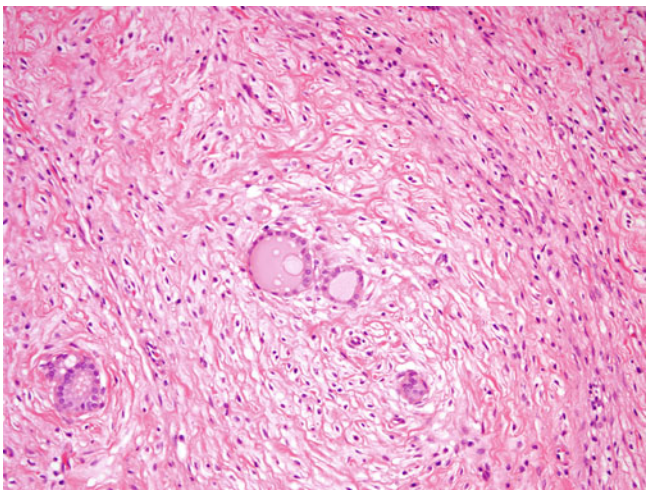

Fig. 12.21 Low-grade fibromyxoid sarcoma. The cells in this low-grade fibromyxoid sarcoma have weakly eosinophilic cytoplasm and ovoid nuclei with indistinct nucleoli and lack significant nuclear atypia. Mitotic figures are absent or sparse. These tumors have a characteristic balanced translocation, resulting in a *FUS*/*CREB3L2* fusion gene [23]

Rhabdomyosarcoma

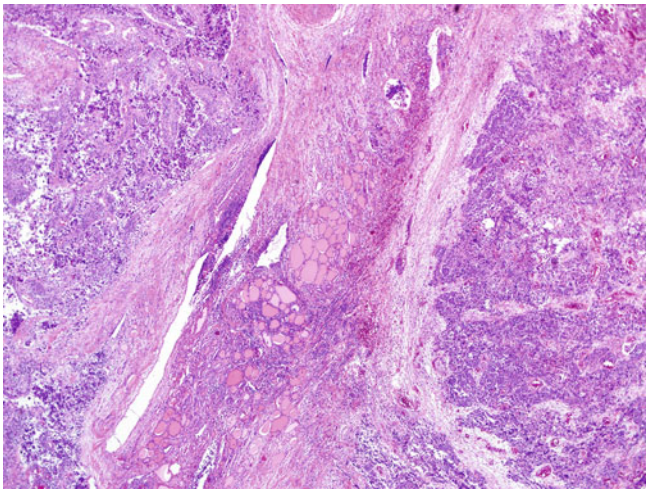

Fig. 12.22 Rhabdomyosarcoma. Rhabdomyosarcoma is a rare sarcoma, particularly with regard to the thyroid. Shown is a primitive embryonal rhabdomyosarcoma with an area of residual thyroid follicles in the center of the field

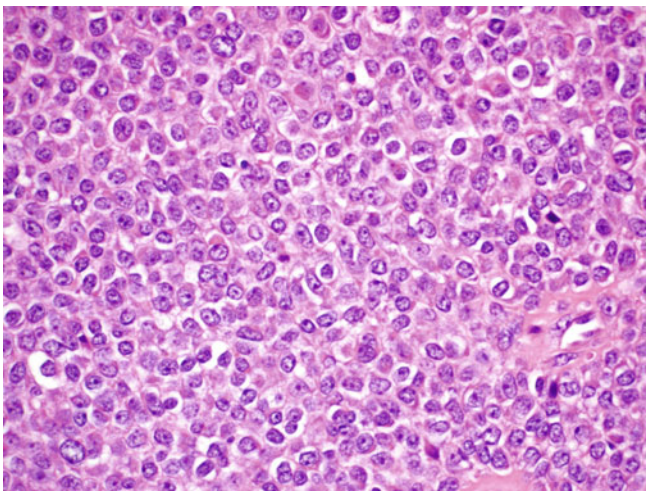

Fig. 12.23 Rhabdomyosarcoma. Poorly differentiated primitive, predominantly embryonal rhabdomyosarcoma in the thyroid gland. Rhabdomyosarcomatous differentiation also may be seen in anaplastic carcinoma in the thyroid [24]

Carcinoma Showing Thymus-Like Differentiation

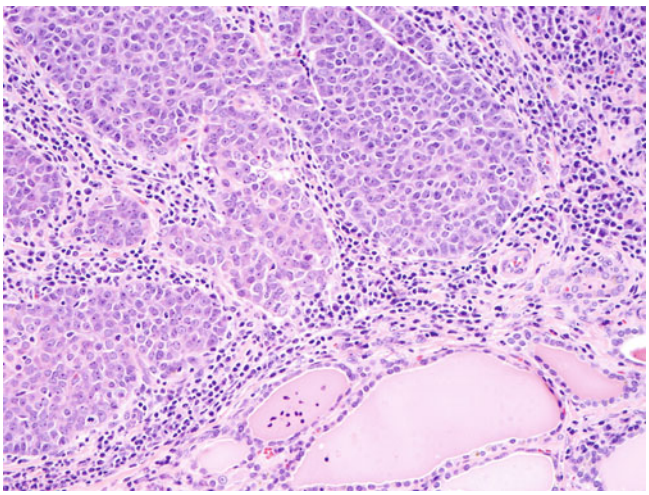

Fig. 12.24 Carcinoma showing thymus-like differentiation (CASTLE). CASTLE is a rare malignant neoplasm postulated to arise from intrathyroidal thymic rests or thymic rests within the thyroid or remnants of the branchial pouch. It may show thymic differentiation, including solid cell nests [25–28]. This tumor also is known as intrathyroidal epithelial thymoma/carcinoma showing thymus-like differentiation, intrathyroidal epithelial thymoma, thymic carcinoma of thyroid, and lymphoepithelioma-like carcinoma of thyroid. CASTLE resembles thymic lymphoepithelioma-like carcinoma and squamous cell carcinoma and is positive for CD5, which is negative in thyroid carcinomas, including those with squamous differentiation [26]. Lymph node metastases are found at surgery in 40 % of cases; other metastatic sites are bones, liver, and lungs. The overall survival rate is 71 % [27]

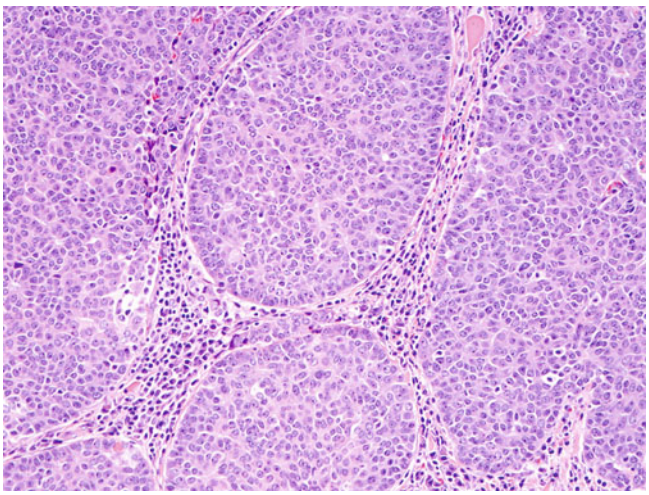

Fig. 12.25 Carcinoma showing thymus-like differentiation. The cells of this CASTLE tumor are epithelial and have distinct nucleoli. Three histologic subtypes may occur: keratinizing squamous cell carcinoma, nonkeratinizing basaloid cell carcinoma (lymphoepithelioma-like), and neuroendocrine carcinoma. These subtypes correspond to those of the mediastinal thymic carcinomas [27]

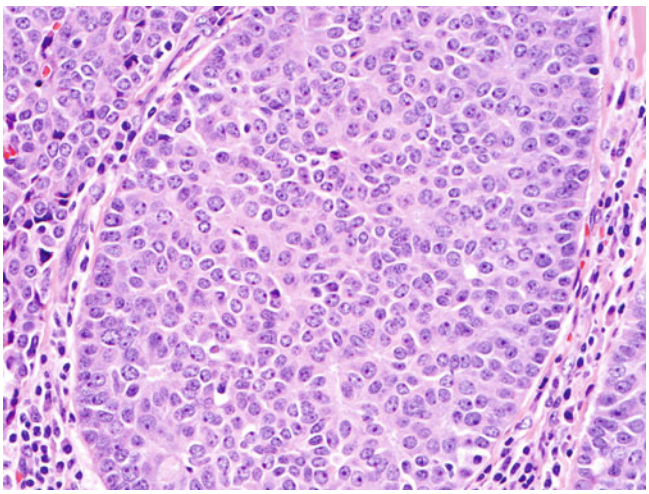

Fig. 12.26 Carcinoma showing thymus-like differentiation. This CASTLE tumor is growing in solid sheets. Immunopositivity for CD5, p63, and KIT (and negative staining for TTF1, thyroglobulin, and calcitonin) is helpful in differentiating CASTLE from undifferentiated or poorly differentiated carcinoma, medullary thyroid carcinoma, and squamous cell carcinoma of the thyroid [27]. CD5, high molecular weight kininogen (HMWK), carcinoembryonic antigen (CEA), and p63 may be used to help distinguish CASTLE from other thyroid neoplasms, as CASTLE and most thymic carcinomas are positive for these markers and other thyroid tumors usually are negative [28]. Solid cell nests, thymomas, and normal thymus stain for p63, HMWK, and CEA, which supports the hypothesis that CASTLE may be of thymic origin and may arise from branchial pouch remnants, such as solid cell nests in the thyroid [28]

Teratoma

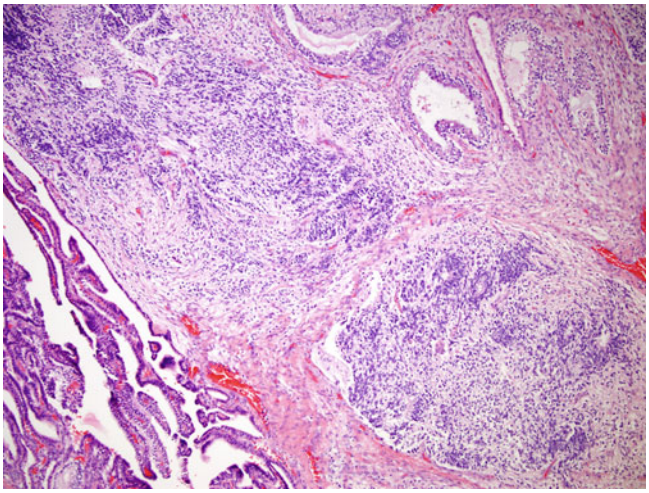

Fig. 12.27 Teratoma. This is an immature teratoma from the thyroid of an infant. Thyroid teratomas are rare tumors with trilineage (ectoderm, mesoderm, and endoderm) differentiation and show varying degrees of maturity [29]. In a study of 30 thyroid teratomas, males and females were affected equally, patient age ranged from newborns to 56 years (mean age, 12.4 years), and all presented as a thyroid mass measuring 2–13 cm (mean, 6 cm) [29]. The tumors in this study were divided into benign (7), immature (14), and malignant (9) by an increasing proportion of primitive mesenchymal or neural-type tissue and found outcome depending on age, tumor size, and proportion of immature tissue [29]. The authors suggested the tumors be excised surgically, with adjuvant therapy reserved for malignant cases [29]

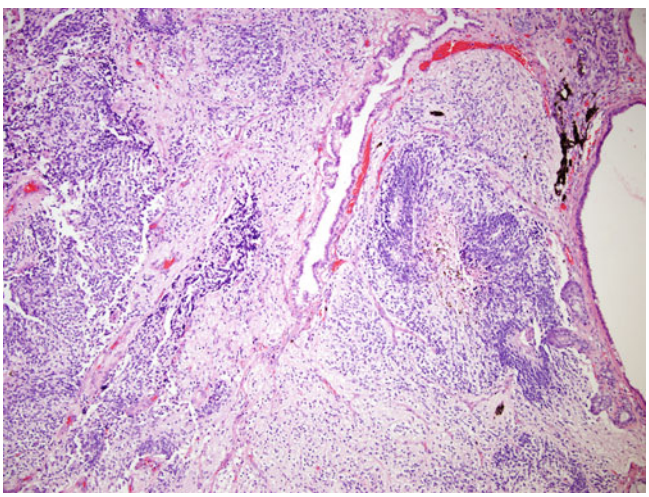

Fig. 12.28 Teratoma. This immature teratoma is from the thyroid of an infant. In a study of 11 cervical teratomas containing thyroid tissue, 8 were thought to be of thyroid origin because of an intimate admixture of thyroid and other tissues with or without a surrounding fibrous pseudocapsule [30]. All these tumors were congenital, measured 3.5–13.5 cm (median, 6.9 cm), were excised surgically, and had a follow-up of 1–45 years (median, 17 years) with no recurrence in any patient [30]. The authors concluded that "histologic immaturity in congenital thyroid teratomas is not the harbinger of adverse behavior as seen in adolescents and adults" [30]

Paraganglioma

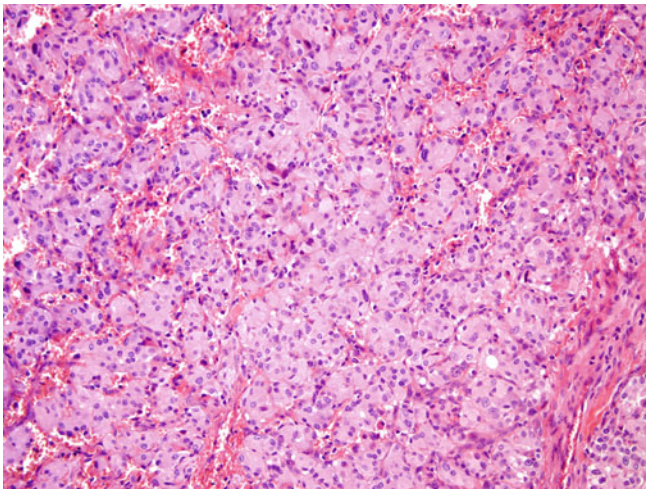

Fig. 12.29 Paraganglioma. Paraganglioma of the thyroid is an extremely rare entity. These tumors have a female predominance, occur in young adults, and present as a neck mass. They are slow-growing neuroendocrine tumors that, in the thyroid, are thought to represent a subset of laryngeal paraganglioma [31]. Patients may have associated carotid body tumors or glomus vagale [32]. Multiple paragangliomas often are associated with syndromes with corresponding succinate dehydrogenase mutations. Less than 10 % of paragangliomas are malignant. Locally aggressive thyroid paragangliomas have been reported [33, 34], but metastases have not been reported. Paragangliomas are treated by surgical excision

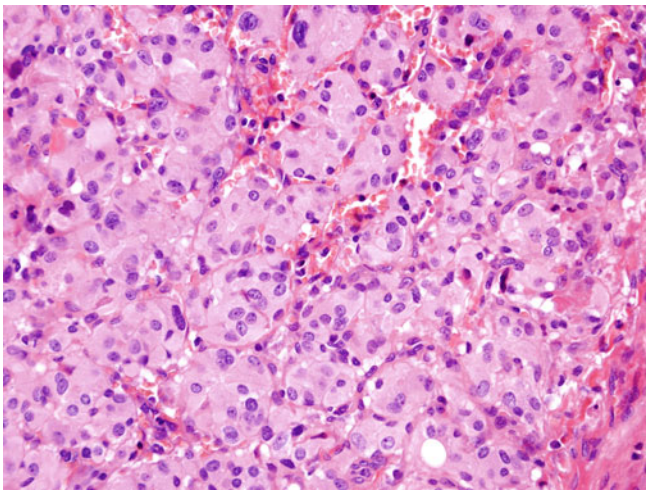

Fig. 12.30 Paraganglioma. Paraganglioma of the thyroid histologically resembles paraganglioma of other sites. Paragangliomas characteristically have a "zellballen" or nested growth pattern but may have alveolar or lobular growth patterns and are highly vascular. Paragangliomas are composed of chief cells that are polygonal and have eosinophilic cytoplasm and round nuclei. Sustentacular cells are delicate spindle cells best seen with S100 immunostain. The main problem in diagnosing thyroid paraganglioma is considering it in the differential diagnosis of tumors such as medullary thyroid carcinoma, hyalinizing trabecular tumor, and thyroid adenomas with unusual growth patterns. Paragangliomas are positive for synaptophysin and chromogranin, with sustentacular cells staining for S100. Thyroid paragangliomas are negative for keratin, thyroglobulin, TTF1, calcitonin and CEA [35]

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