Anaplastic Thyroid Carcinoma

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Anaplastic (undifferentiated) thyroid carcinoma is a highly aggressive malignancy that usually presents with a rapidly growing neck mass in older patients, with hoarseness, dysphasia, and vocal cord paralysis. This tumor accounts for 1–2 % of thyroid malignancies [1]. The annual incidence of anaplastic thyroid carcinoma is 1–2 in 1,000,000 people, and the overall incidence is higher in Europe and areas of endemic goiter than in the United States [2]. These tumors are composed of undifferentiated cells with immunohistochemical and ultrastructural features supporting epithelial differentiation [3]. One third of anaplastic carcinomas are associated with a better-differentiated thyroid carcinoma and may represent dedifferentiation [4]. Anaplastic carcinomas must be differentiated from poorly differentiated carcinoma metastatic to the thyroid, lymphoma, and sarcoma. The paucicellular variant of anaplastic thyroid carcinoma must be differentiated from Riedel (fibrous) thyroiditis. In small biopsy samples, the differential diagnoses may be difficult. Anaplastic thyroid carcinomas usually are positive for keratin, but most show only focal staining for thyroglobulin. Thyroid transcription factor 1 (TTF1) may be present focally, but strong diffuse staining of TTF1 throughout the tumor is not seen. These tumors are positive for vimentin and show a high Ki67 proliferative index and p53 overexpression. Decreased p27 expression, cyclin D1 overexpression, and inactivation of *PTEN* and p16 are reported [5]. *TP53* and *CTNNB1* (β-catenin) mutations and complex chromosomal alterations with allelic losses of 1q, 1p, 5, 8, 9p, 11, 17p, 19p occur [3, 6–8]. Anaplastic carcinomas are highly destructive locally with invasion of adjacent structures and metastases to lung, bone, and brain [3]. Distant metastases are present at diagnosis in almost half of patients. These tumors often are not amenable to surgical resection and may be diagnosed on biopsy and treated with radiation and chemotherapy [3]. A recent study suggested that select patients with anaplastic thyroid cancer with extrathyroid extension and no distant metastases on CT or positron emission tomography who do not have tumor extending lateral to the carotid arteries may be candidates for complete surgical resection [9]. From a multicenter registry, 677 anaplastic thyroid carcinomas from 38 institutions were subtyped; the incidental type had the best outcome, followed by anaplastic transformation at the neck, common type, and anaplastic transformation at a distant site [1]. Although the survival rate at 1 year in this study was only 18 %, 84 patients (15 %) survived longer than 1 year. Features associated with decreased survival include age ≥70 years, acute symptoms, leukocytosis, size greater than 5 cm, T4b stage, and distant metastases [1]. Anaplastic thyroid carcinomas are very aggressive, with a median survival of 2.5–6 months and a 5-year survival of 0–14 % [3, 10, 11].

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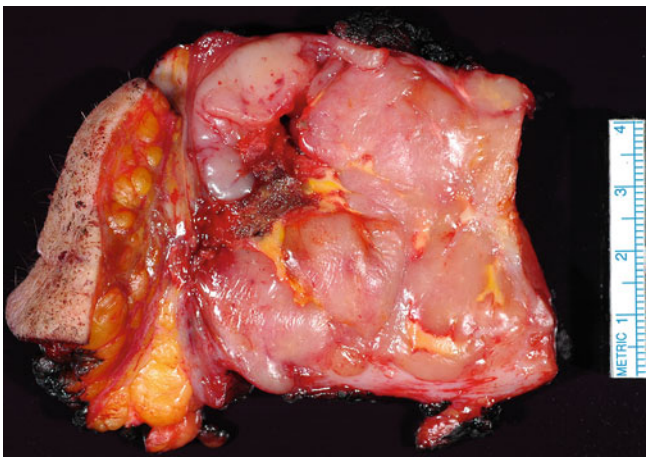

Fig. 10.1 Anaplastic thyroid carcinoma. This anaplastic thyroid carcinoma has areas of hemorrhage and necrosis. These tumors are large, often white to gray, and firm or hard, and infiltrate adjacent soft tissue and structures

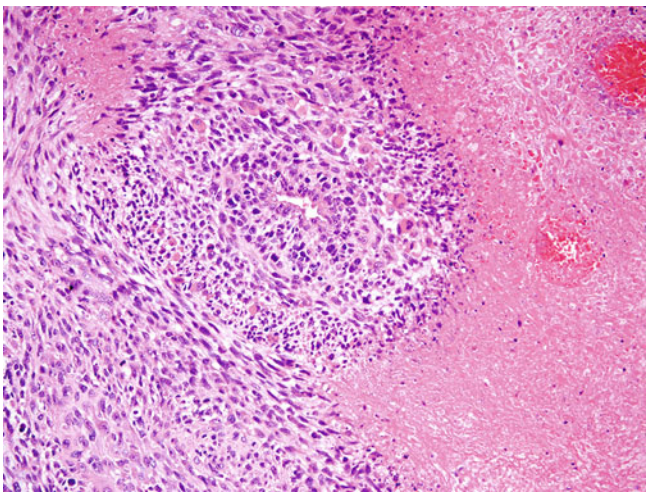

Fig. 10.3 Anaplastic thyroid carcinoma. An area of necrosis is present in this anaplastic thyroid carcinoma. Necrosis is not uncommon in anaplastic thyroid carcinoma. These are undifferentiated carcinomas that are highly malignant and composed of undifferentiated cells, usually with immunohistochemical features of epithelial differentiation

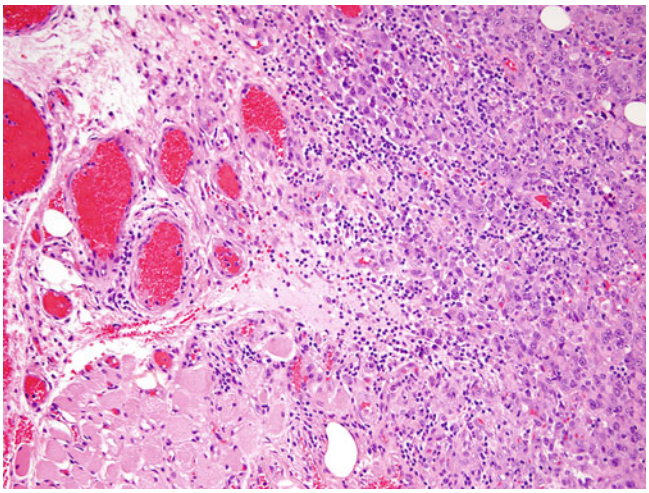

Fig. 10.2 Anaplastic thyroid carcinoma. Anaplastic thyroid carcinomas often invade adjacent structures, such as skeletal muscle, as demonstrated in this photograph. Invasion of adjacent structures in the neck, including skeletal muscle, laryngeal nerve, trachea, esophagus, and larynx, is common

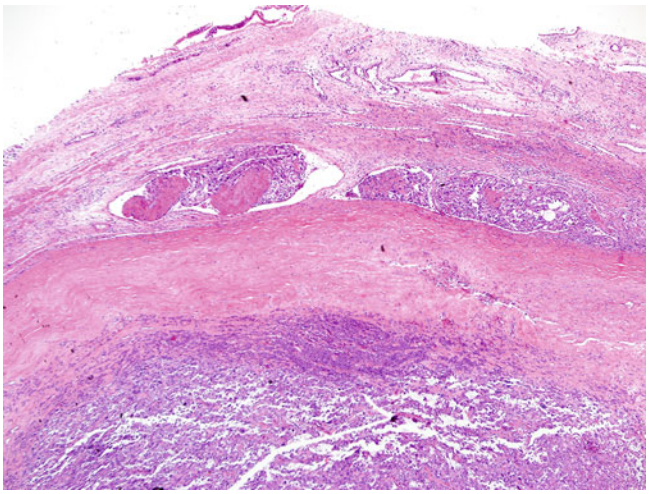

Fig. 10.4 Anaplastic thyroid carcinoma. Vascular invasion, as demonstrated in this photograph, and other aggressive histologic features, such as necrosis, prominent mitotic activity, and extrathyroid extension, are common in anaplastic thyroid carcinoma

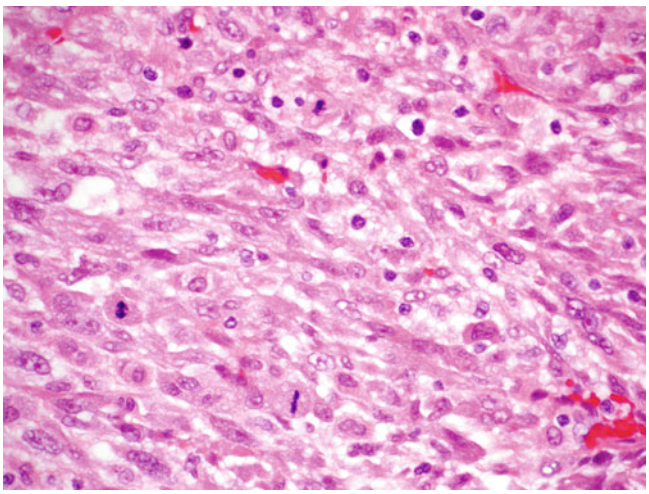

Fig. 10.5 Anaplastic thyroid carcinoma. This anaplastic thyroid carcinoma is composed of undifferentiated epithelioid and spindle cells with prominent mitotic activity. Anaplastic thyroid carcinomas often are composed of a variety of cell types, including epithelial, spindle, and pleomorphic multinucleated cells

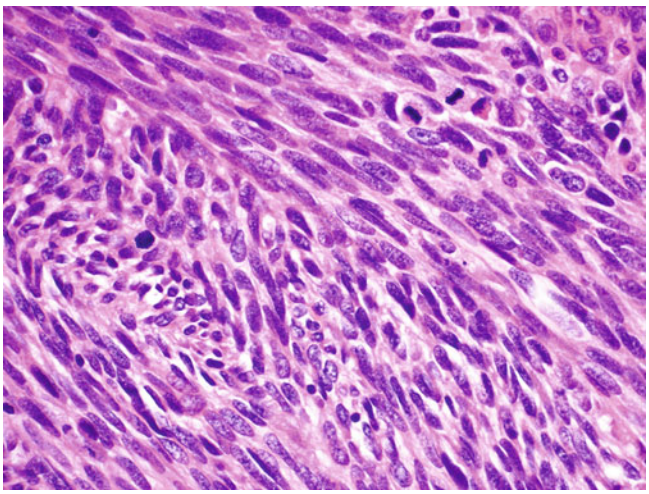

Fig. 10.7 Anaplastic thyroid carcinoma. Markedly atypical spindle cells are seen in this anaplastic thyroid carcinoma. Prominent mitotic activity is present. Anaplastic thyroid carcinomas with prominent spindle cells must be differentiated from high-grade sarcomas. Anaplastic thyroid carcinomas usually show at least focal staining for keratin and may show focal staining for thyroid transcription factor 1 (TTF1), which is helpful in identifying these tumors

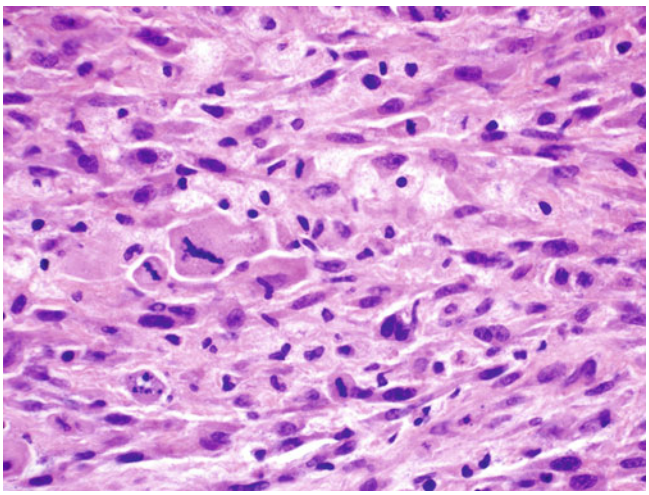

Fig. 10.6 Anaplastic thyroid carcinoma. This anaplastic thyroid carcinoma is composed of undifferentiated spindle cells and multinucleated epithelioid cells. Prominent mitotic activity is seen. Anaplastic carcinomas often are composed of a variety of cell types. In some cases, a differentiated thyroid carcinoma may be present in association with the anaplastic carcinoma, which is helpful in recognizing the undifferentiated component as anaplastic thyroid carcinoma rather than a metastasis to the thyroid

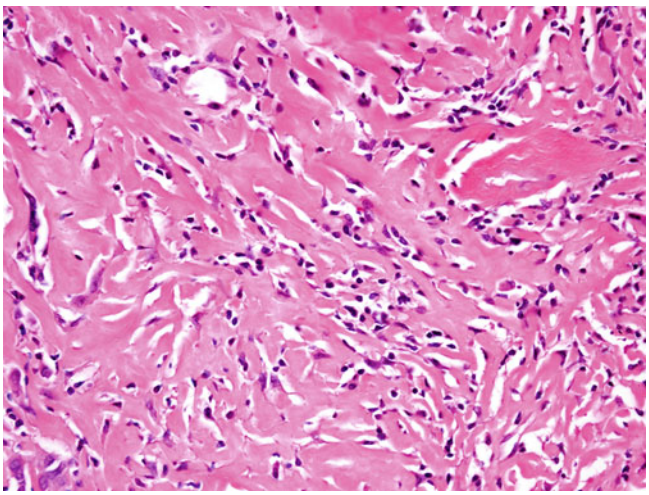

Fig. 10.8 Anaplastic thyroid carcinoma. This sclerotic cell-poor anaplastic thyroid carcinoma might be mistaken for Riedel (fibrous) thyroiditis

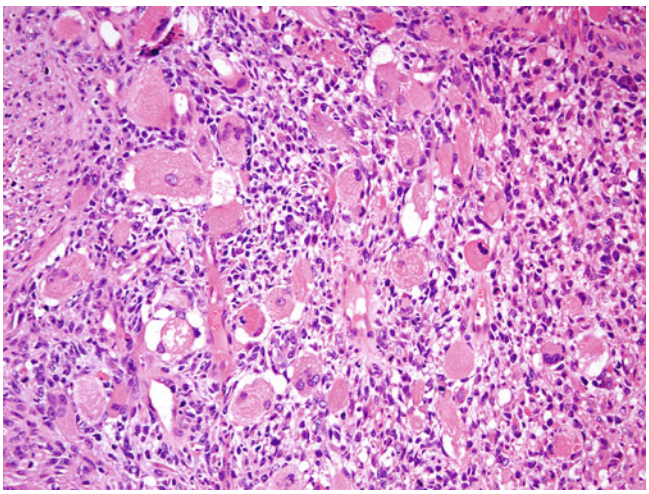

Fig. 10.9 Anaplastic thyroid carcinoma. This anaplastic thyroid carcinoma shows rhabdoid features. Rhabdoid features, as well as rhabdomyosarcomatous differentiation, may be seen in anaplastic thyroid carcinoma

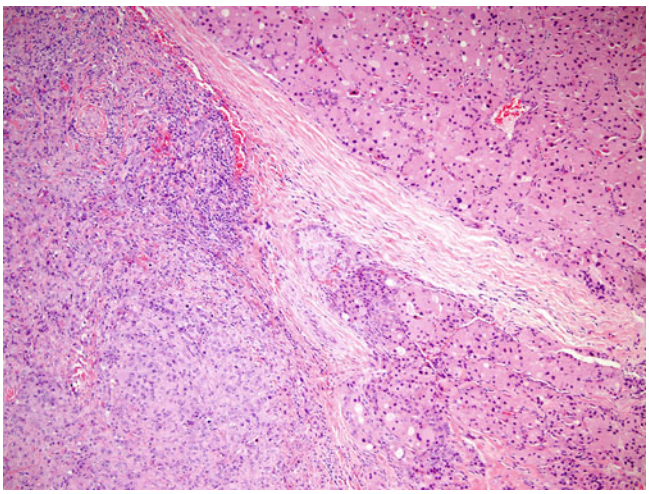

Fig. 10.11 Anaplastic thyroid carcinoma. The anaplastic thyroid carcinoma on the *left* appears to have dedifferentiated from the Hurthle cell carcinoma seen on the *right*

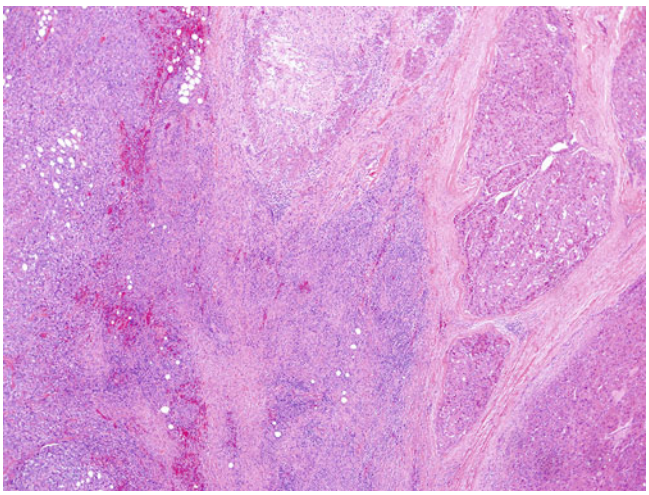

Fig. 10.10 Anaplastic thyroid carcinoma arising with Hurthle cell carcinoma. Anaplastic thyroid carcinoma is seen on the *left* arising in association with Hurthle cell carcinoma on the *right*. It is not unusual for a better-differentiated thyroid carcinoma to be identified in association with an anaplastic thyroid carcinoma, which suggests dedifferentiation. This finding also is helpful in identifying the undifferentiated tumor as anaplastic thyroid carcinoma rather than a metastasis to the thyroid

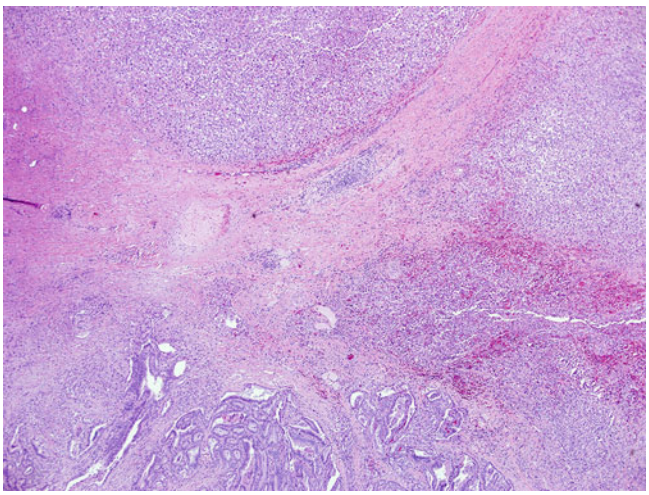

Fig. 10.12 Anaplastic thyroid carcinoma. Papillary thyroid carcinoma (PTC) is identified in the *lower portion* of the photomicrograph and is surrounded by anaplastic thyroid carcinoma. Approximately one third of anaplastic thyroid carcinomas are identified with a differentiated thyroid carcinoma [4]

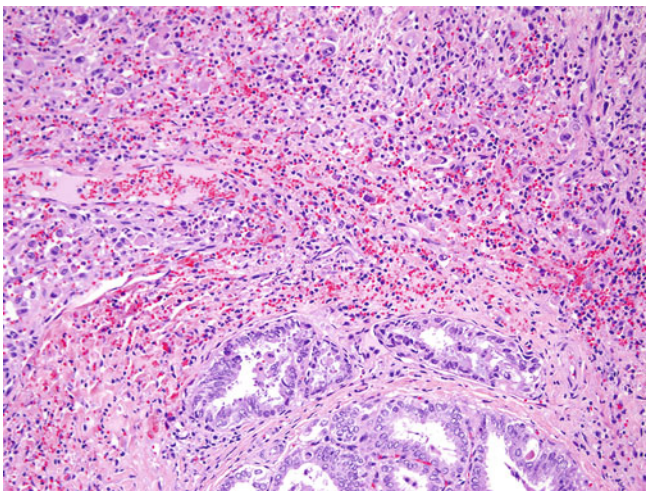

Fig. 10.13 Anaplastic thyroid carcinoma. This anaplastic carcinoma is highly vascular and may be mistaken for angiosarcoma, which may occur in the thyroid. In the *center* is a PTC. The presence of the differentiated tumor (PTC) associated with the undifferentiated carcinoma also would support a diagnosis of anaplastic thyroid carcinoma. Recent studies show that PTC with mutant *BRAF* or *RAS* may progress to poorly differentiated and anaplastic carcinoma, but additional mutations likely would be needed [12]. Similarly, *RAS* mutation in follicular carcinoma may predispose tumors to dedifferentiation with the addition of other mutations, such as *TP53* and β-catenin [12]

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