Poorly Differentiated Thyroid Carcinoma

9

Poorly differentiated thyroid carcinomas are diagnostically controversial, as there is a lack of consensus regarding diagnostic criteria [1–3]. Poorly differentiated thyroid carcinomas usually occur in older patients (>50 years) and are more common in Italy and Latin America (4–7 % of thyroid carcinomas) and less common in the United States [4]. These tumors are morphologically and prognostically intermediate between well-differentiated and anaplastic thyroid carcinoma [2, 5]. An operational pathologic definition offered in 2007 included insular and trabecular variants, but not solid lesions or more differentiated tumors that may have a poor prognosis, such as tall cell, columnar, diffuse sclerosing, and oncocytic lesions [2]. At a consensus conference in Turin in 2006, 12 thyroid pathologists evaluated 83 tumors without knowledge of clinical parameters and devised a diagnostic algorithm for the diagnosis of poorly differentiated thyroid carcinoma to include "(1) presence of a solid/trabecular/insular pattern of growth, (2) absence of the conventional nuclear features of papillary carcinoma, and (3) presence of at least one of the following features: convoluted nuclei; mitotic activity $\geq 3 \times 10$ HPF [high-power fields]; and tumor necrosis" [5]. A subsequent study of 56 cases from the Mayo Clinic and 96 from the University of Turin in northern Italy validated the Turin criteria [6]. The prevalence of poorly differentiated carcinoma in the United States was 1.8 and 6.7 % in the northern Italy cases. Tumor characteristics were similar, except extensive vascular invasion and prevalent insular growth was less common in the US cases than the Italian cases [6]. The Turin criteria work well for cases from mountain areas such as northern Italy, where most thyroid carcinomas with high-grade features also have a solid/trabecular/insular growth pattern [3]. However, this algorithm may not work as well for cases from other geographic areas that may have tumors with more heterogeneous architectural and cytologic features, and some pathologists base their diagnosis on only high-grade features, mitotic index, and necrosis, irrespective of the growth pattern [3]. Tumor necrosis and high mitotic activity, rather than growth pattern or histologic subtype, may be prognostic in thyroid tumors [1]. Poorly differentiated tumors have lower relapse-free and cause-specific survival rates than well-differentiated tumors, and poor differentiation and age affect survival [7]. Extrathyroidal infiltration also affects disease-free survival [7]. Aggressive surgery for tumors with gross extrathyroidal extension has resulted in satisfactory locoregional control [8]. Although the benefit of iodine-131 is unclear, it has been recommended for all patients postoperatively because of its lack of morbidity and potential for benefit [2]. External-beam radiotherapy has been suggested for T3 tumors without distant metastasis, all T4 tumors, and all tumors with regional node metastases [2]. The 5-year overall survival rate for poorly differentiated thyroid carcinoma is 47 % [8].

L.A. Erickson, *Atlas of Endocrine Pathology*, Atlas of Anatomic Pathology,
DOI 10.1007/978-1-4939-0443-3_9, © Springer Science+Business Media New York 2014

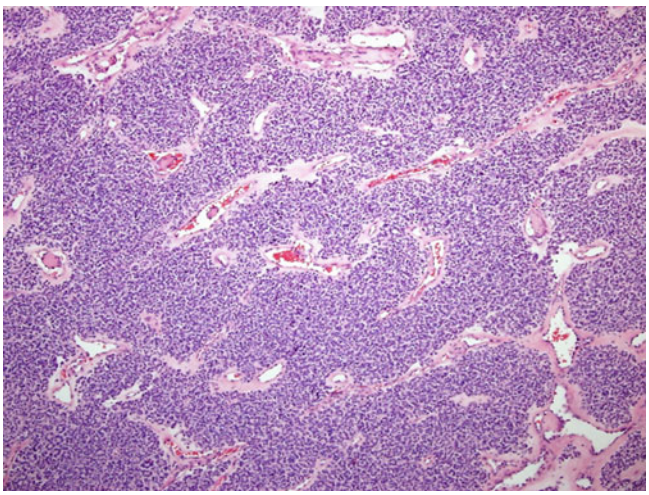

Fig. 9.1 Poorly differentiated thyroid carcinoma. This poorly differentiated thyroid carcinoma has a characteristic insular growth pattern. Growth patterns vary, but the most common are insular, trabecular, and solid [5]. A peritheliomatous pattern admixed with fibrosis and/or necrosis also may occur [9]

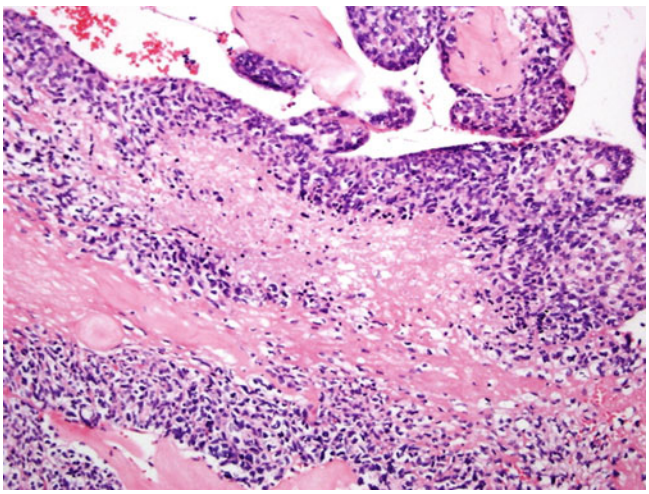

Fig. 9.2 Poorly differentiated thyroid carcinoma. Areas of necrosis are seen in this poorly differentiated thyroid carcinoma. The differential diagnosis of poorly differentiated thyroid carcinoma includes medullary thyroid carcinoma, follicular carcinoma, the solid variant of papillary thyroid carcinoma (PTC), and carcinoma metastatic to the thyroid. Follicular carcinomas lack necrosis and show a lower grade of cytomorphology and less prominent mitotic activity compared with poorly differentiated carcinomas. The solid variant of PTC has nuclear PTC cytomorphology. Medullary thyroid carcinoma has neuroendocrine nuclei with stippled chromatin and is positive for chromogranin, synaptophysin, and calcitonin. Poorly differentiated carcinomas stain with thyroid transcription factor 1 (TTF1) and thyroglobulin, although thyroglobulin may be focal [10]. Carcinoma metastatic to the thyroid usually is negative for TTF1, except for lung adenocarcinomas

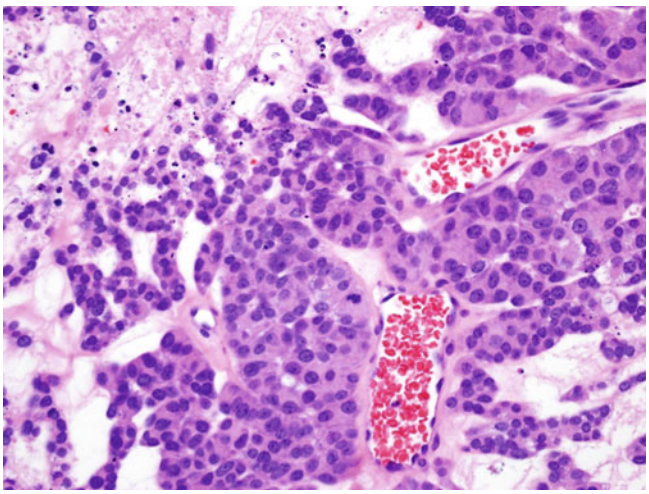

Fig. 9.3 Poorly differentiated thyroid carcinoma. This poorly differentiated thyroid carcinoma has focal necrosis, hyperchromatic tumor cells, and mitotic activity. These tumors show a high Ki67 proliferative index; p53 staining, when present, may be focal [10]. *TP53* mutations are identified in 20–30 % and aberrant p53 overexpression in 40–50 % of cases [11]. *BRAF*, *RET*/PTC, and *NTRK1* abnormalities occur in a small percentage of patients [11]. *H-*, *K-*, and *N-RAS* mutations are identified in about 50 % of cases [12]. In a series of 65 poorly differentiated thyroid carcinomas, *RAS* mutations in codon 61 were the most common genetic abnormality (23 %), whereas no *KRAS*, *RET*/PTC, or *PAX8*/peroxisome proliferator-activated receptor-γ alterations and only a single *BRAF* mutation were found (in a tumor with residual tall cell PTC) [13]. *RAS* mutation was a negative prognostic parameter in these tumors [13]

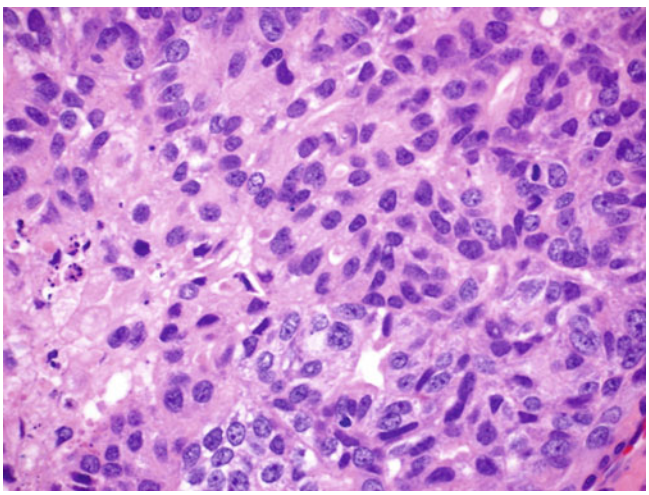

Fig. 9.4 Poorly differentiated thyroid carcinoma. This poorly differentiated thyroid carcinoma has uniform tumor cells with hyperchromatic nuclei containing small nucleoli. Vesicular nuclei are focally present. Although the nuclei are atypical, extensive anaplastic nuclear features, as seen in anaplastic thyroid carcinoma, are not identified

References

1. Tallini G. Poorly differentiated thyroid carcinoma. Are we there yet? Endocr Pathol. 2011;22(4):190–4.
2. Sanders Jr EM, et al. An evidence-based review of poorly differentiated thyroid cancer. World J Surg. 2007;31(5):934–45.
3. Volante M, Papotti M. Poorly differentiated thyroid carcinoma: 5 years after the 2004 WHO classification of endocrine tumours. Endocr Pathol. 2010;21(1):1–6.
4. DeLellis RA, Lloyd RV, Heitz PU. WHO classification of tumours—pathology and genetics. In: DeLellis RA, Lloyd RV, Heitz PU, editors. Tumours of endocrine organs. Lyon: IARC Press; 2004.
5. Volante M, et al. Poorly differentiated thyroid carcinoma: the Turin proposal for the use of uniform diagnostic criteria and an algorithmic diagnostic approach. Am J Surg Pathol. 2007;31(8):1256–64.
6. Asioli S, et al. Poorly differentiated carcinoma of the thyroid: validation of the Turin proposal and analysis of IMP3 expression. Mod Pathol. 2010;23(9):1269–78.
7. Tanaka K, et al. Analysis of clinical outcome of patients with poorly differentiated thyroid carcinoma. ISRN Endocrinol. 2011; 2011:308029.
8. Ibrahimpasic T, et al. Poorly differentiated thyroid carcinoma presenting with gross extrathyroidal extension: 1986–2009 Memorial Sloan-Kettering Cancer Center experience. Thyroid. 2013;23(8):997–1002.
9. Papotti M, et al. Poorly differentiated thyroid carcinomas with primordial cell component. A group of aggressive lesions sharing insular, trabecular, and solid patterns. Am J Surg Pathol. 1993;17(3):291–301.
10. Volante M, et al. Poorly differentiated carcinomas of the thyroid with trabecular, insular, and solid patterns: a clinicopathologic study of 183 patients. Cancer. 2004;100(5):950–7.
11. Nikiforov YE. Genetic alterations involved in the transition from well-differentiated to poorly differentiated and anaplastic thyroid carcinomas. Endocr Pathol. 2004;15(4):319–27.
12. Albores-Saavedra J, Carrick K. Where to set the threshold between well differentiated and poorly differentiated follicular carcinomas of the thyroid. Endocr Pathol. 2004;15(4):297–305.
13. Volante M, et al. RAS mutations are the predominant molecular alteration in poorly differentiated thyroid carcinomas and bear prognostic impact. J Clin Endocrinol Metab. 2009; 94(12):4735–41.