

Franco Rongioletti

Cutaneous metastases of thyroid gland

Clinical Features

The occurrence of skin metastases from thyroid gland tumors is a rare event, although thyroid carcinoma is the most common endocrine malignancy. Papillary and follicular carcinomas are the most common type of tumors metastasizing to the skin; less frequently, anaplastic and medullary carcinomas are the culprit. Skin metastases arise with equal frequency in both sexes with a mean age of 65 years. Metastases present with single or multiple flesh-colored to reddish or violaceous papules and nodules that may ulcerate. The head, neck, and scalp are the most common sites of involvement. Other sites include post-thyroidectomy scar and sacral skin.

Pathology

Skin metastases recapitulate the primary tumors. Papillary carcinomas consist of complex, branching papillary structures with fibrovascular cores and psammoma bodies. The tumor shows tubules lining colloid-like material which is positive with PAS stain (Figs. 75.1–75.3). Crowded, cuboidal cells with large, oval pale nuclei with a grooved irregular contour and containing eosinophilic inclusions line the papillae. A strong association of BRAF mutation with lymph node metastasis, extrathyroidal extension, and disease recurrence has been confirmed in papillary thyroid cancer. Follicular carcinoma is characterized by multiple solid islands of epithelial cells arranged in follicles and containing colloid. A follicular-related variant called insular carcinoma presents with solid cords and nests made by small, round, and regular cells with occasional microfollicles and is associated with a more aggressive course (Fig. 75.4). Immunostaining usually reveals reactivity to thyroid transcription factor and thyroglobulins (Fig. 75.5). Differently from papillary and follicular carcinomas, thyroglobulin is usually negative in the anaplastic variant, but PAX8 is usually positive. The last histopathologic type in frequency is metastatic medullary thyroid carcinoma that arises from C cells of the thyroid and often appears in the setting of multiple endocrine neoplasia syndrome. Neoplastic cells are positive for calcitonin.

F. Rongioletti, M.D. (✉)
Section of Dermatology, Department of Health Sciences and Division of Pathology, University of Genova, Genova, Italy
e-mail: franco.rongioletti@unige.it;
franco.rongioletti@me.com

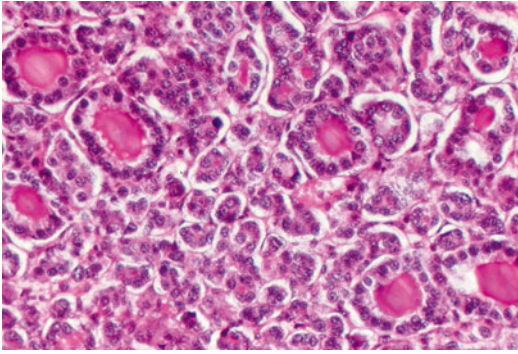


Fig. 75.1 Skin metastasis from a primary papillary thyroid carcinoma (courtesy of B.Cribier, Strasbourg, France)

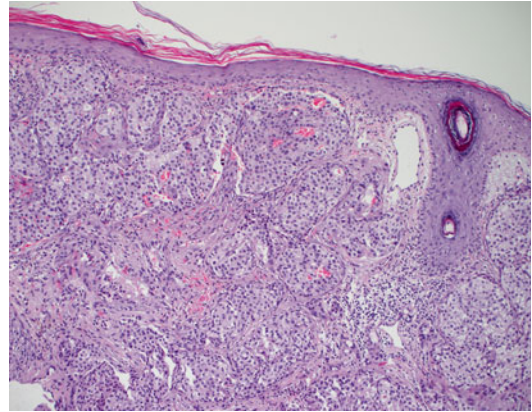


Fig. 75.4 Skin metastasis from a primary insular carcinoma, a follicular-related variant of thyroid carcinoma. Note solid cords of round or oval monotonous cells surrounded by fibrovascular septa (courtesy of W.Kempf, Zurich, Switzerland)

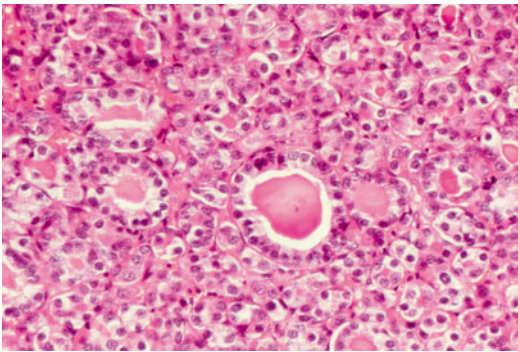


Fig. 75.2 The skin tumor is composed of tubules containing colloid-like material and lined by cells with nuclear grooves. (courtesy of B.Cribier, Strasbourg, France)

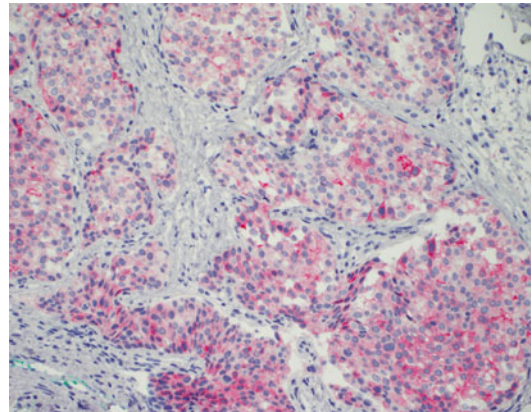


Fig. 75.5 Immunostaining reveals reactivity to thyroglobulins

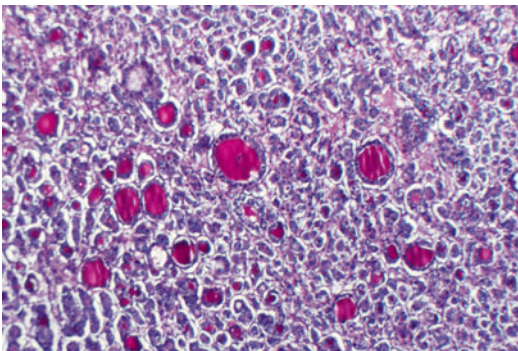


Fig. 75.3 The tumor is positive with PAS stain (courtesy of B.Cribier, Strasbourg, France)

Differential Diagnosis

Twenty-nine to 45 % of skin lesions are not suspected of being metastases due to an unusual

clinical presentation. Common clinical diagnoses which are weighed are nonmelanoma skin cancer, cutaneous lymphoma, and cutaneous sarcomas.

Prognosis

Skin metastases from thyroid malignancies are manifestations of advanced disease, independently from the histological types. Age over 45 years and follicular pathology were significant predictors of a poorest outcome. In the setting of follicular carcinoma, patients with extracutane-

ous involvement at the time of cutaneous metastasis may have a worse prognosis than those with isolated cutaneous metastases. The average length of survival after cutaneous metastasis is 19 months.

Treatment

Surgical approaches are generally the most effective as a palliative measure for single cutaneous metastasis. However, excision of select metastases does little to increase survival. Targeted therapy such as with sorafenib has shown promise in the treatment of patients with advanced or metastatic thyroid carcinoma when external beam radiation and radioiodine (¹³¹I) therapy are not suitable or give poor outcomes.

References

1. Alwaheeb S, Ghazarian D, Boerner SL, Asa SL. Cutaneous manifestations of thyroid cancer: a report of four cases and review of the literature. *J Clin Pathol.* 2004;57:435–8.
2. Quinn TR, Duncan LM, Zembowicz A, et al. Cutaneous metastases from follicular thyroid carcinoma. A report of four cases and a review of the literature. *Am J Dermatopathol.* 2005; 27:306–12.
3. Alcaraz I, Cerroni L, Rütten A, Kutzner H, Requena L. Cutaneous metastases from internal malignancies: a clinicopathologic and immunohistochemical review. *Am J Dermatopathol.* 2012;34:347–93.
4. De Giorgi V, Alfaioli B, Massi D, et al. Solitary cutaneous metastasis as the first sign of relapse of thyroid carcinoma: a clinical, dermoscopic-pathologic case study. *Dermatol Surg.* 2009;35:523–6.
5. Chen L, Shen Y, Luo Q, Yu Y, Lu H, Zhu R. Response to sorafenib at a low dose in patients with radioiodine-refractory pulmonary metastases from papillary thyroid carcinoma. *Thyroid.* 2011;21:119–24.

Additional Tumors and Patterns of Cutaneous Metastases

Laryngeal carcinoma is common in males (96 % of cases) around the age of 40 years. Skin metastases appear as solitary or multiple nodules on the head and neck region or occasionally as erythematous infiltrating plaques on the supraclavicular and infraclavicular regions. The tumor is made of malignant squamous cells arranged in solid/nesting patterns and is reactive for cytokeratins (AE1/AE3) and p53.

Sarcoma metastases to the skin are relatively rare, because most involve the deep organs such as the lung, liver, or deep soft tissues. Leiomyosarcoma is the most common source, and the scalp is the most frequent site. The skin is the initial site of metastasis in only 1–3 %, while the majority of patient with skin metastases from sarcomas harbor metastases elsewhere.

Cancer of unknown primary site (synonym: occult primary malignancy) is defined as the presence of a skin metastasis when a primary site or tissue of origin has not been possible to identify despite an intensive diagnostic approach. Its incidence is between 2 % and 6 %, and men are more often diagnosed. Only 10–20 % can primarily be discovered while 50–75 % are found only by autopsy. In 15–25 %, the primary site remains unknown even on postmortem examination. The primary sites in order of frequency include: the lung (5–35 %), pancreas (15–20 %), liver and biliary tract (10–15 %), colon (3–8 %), and kidney (3–5 %).

Bibliography

- Hussein MR. Alterations of p53 and Bcl-2 protein expression in the laryngeal intraepithelial neoplasia. *Cancer Biol Ther.* 2005;4:213–7.
- Neben K, Hubner G, Folprecht G, Jäger D, Krämer A. Metastases in the absence of a primary tumor: advances in the diagnosis and treatment of CUP syndrome. *Dtsch Arztebl Int.* 2008;105:733–40.
- Wang W, Bones Valentin RA, Prieto VG. Sarcoma metastases to the skin. A clinicopathologic study of 65 patients. *Cancer.* 2012;118:2900–4.