Update on Malignant Sweat Gland Tumors

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KEYWORDS

• Sweat gland tumors • Malignant • Aggressive digital papillary adenocarcinoma
• Microcystic adnexal carcinoma • Spiradenocarcinoma • Squamoid eccrine ductal carcinoma

Key Points

- Sweat gland tumors show a wide morphologic spectrum but malignant change is rare.
- Malignant sweat gland tumors are classified according to their behavior into low- and high-grade tumors. Low-grade malignant tumors are characterized by risk for locally destructive growth and local recurrence and but only rare distant metastasis, whereas high-grade tumors have significant metastatic potential and disease-related mortality.
- Precise classification and accurate diagnosis is necessary to predict behavior of these tumors.
- Immunohistochemistry and, at least as yet, molecular genetics play only a minor role in the diagnosis of sweat gland tumors.
- Cutaneous metastases from visceral primary adenocarcinomas are important considerations in the differential diagnosis of sweat gland carcinomas, and reliable separation may be impossible on morphologic and immunohistochemical grounds.

ABSTRACT

Malignant sweat gland tumors are rare cutaneous neoplasms, traditionally separated according to their behavior into low- and high-grade malignant. There is significant morphologic overlap, and outright malignant tumors may show relatively bland histologic features. They may, therefore, be mistaken easily for benign neoplasms. Recognition of these tumors and accurate diagnosis is important for early treatment to prevent aggressive behavior and adverse outcome. This article provides an overview of 4 important entities with emphasis on diagnostic pitfalls, differential diagnosis and recent developments. Microcystic adnexal carcinoma, squamoid eccrine ductal carcinoma, aggressive digital papillary adenocarcinoma, and spiradenocarcinoma are discussed in detail.

OVERVIEW

The range of skin adnexal neoplasms is broad and includes differentiation toward the hair follicle, the sebaceous gland, and the sweat gland and duct. The tumors span the spectrum from the entirely benign to high-grade malignant neoplasms with aggressive behavior and mortality. The recognition of tumors with potential for aggressive behavior is important. It poses a significant challenge for a large number of reasons. Particular problems are the rarity of skin adnexal carcinomas and the only poorly defined and often entity-specific criteria for malignancy. Furthermore, even tumors with the potential for outright aggressive disease course may show bland and innocuous histologic appearances, readily mistaken for benign neoplasms. Another important diagnostic pitfall is the separation of primary skin adnexal carcinoma

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from cutaneous metastases of visceral primary adenocarcinomas and reliable distinction may be impossible on morphology and immunohistochemistry. According to their behavior, skin adnexal carcinomas have been traditionally separated into low- and high-grade malignant neoplasms. Low-grade malignant tumors rarely metastasize, but may cause significant morbidity owing to their locally destructive growth and risk for local recurrence. High-grade malignant tumors show significant potential for distant metastasis and disease-related mortality. This separation is, however, artificial; in reality, the boundaries are somewhat blurred. This article gives an overview and update of the recent developments of a selected group of malignant sweat gland tumors. The discussion includes examples of 2 low-grade malignant tumors, namely, microcystic adnexal carcinoma and squamoid eccrine ductal carcinoma, and 2 high-grade tumors, namely, aggressive digital papillary adenocarcinoma and spiradenocarcinoma.

MICROCYSTIC ADNEXAL CARCINOMA

Microcystic adnexal carcinoma was first described by Goldstein in 1982.[1–9] It belongs to the group of low-grade malignant sweat duct tumors and is characterized by both sweat duct and follicular differentiation. It shows morphologic overlap with syringoid eccrine carcinoma, and the tumors are often regarded together.

CLINICAL PRESENTATION

Microcystic adnexal carcinoma typically presents as slowly growing plaques, and paresthesia may be an accompanying symptom. The tumors are ill-defined and extend beyond the clinically visible. They have a predilection for the central face, especially the perioral area and the nasolabial folds. There is no strong gender predilection.

MICROSCOPIC FEATURES

The tumors are based within dermis and they are characterized by a diffusely infiltrative growth with invasion of subcutis and deeper structures (**Fig. 1**A). They grow in cords and strands in a desmoplastic stroma (see **Fig. 1**B). Superficially, keratocysts and dystrophic calcifications are often seen (see **Fig. 1**C). Duct differentiation is an additional feature and is present in varying amounts. Although some tumors show prominent duct differentiation as seen in syringoid eccrine carcinoma (see **Fig. 1**D), others show almost exclusively follicular differentiation (see **Fig. 1**E). Cytologic atypia is mild and clear cell change may be prominent (see **Fig. 1**F). Mitoses are typically inconspicuous. Perineural invasion is almost invariably present. Immunohistochemistry plays no major role in the diagnosis of microscystic adnexal carcinoma. The tumors express cytokeratins and are positive for CK7 and negative for CK20. EMA and CEA staining is helpful to highlight duct differentiation and S100 and EMA are useful in identifying perineural infiltration.

BEHAVIOR AND TREATMENT

Microcystic adnexal carcinoma is characterized by locally destructive growth and high local recurrence rates, especially if complete excision cannot be achieved. Distant metastases are, however, exceptionally rare. The treatment of choice is wide local excision with tumor-free margins. Mohs micrographic surgery is an excellent alternative. Early diagnosis and adequate surgery are necessary for local disease control.

DIFFERENTIAL DIAGNOSIS

Owing to the bland histologic features, the diagnosis of microcystic adnexal carcinoma is extremely challenging, especially on superficial and partial biopsies. The differential diagnosis is summarized in **Table 1**. Microcystic adnexal carcinoma closely resembles benign skin adnexal tumors, including desmoplastic trichoepithelioma, trichoadenoma, and syringoma. Recognition of the infiltrative tumor growth is the most important differentiating feature. If the initial diagnostic biopsy does not include deeper dermis and subcutis, it is important to ask for a deeper and adequate tissue sample.

Morpheaform basal cell carcinoma and desmoplastic squamous cell carcinoma also enter the differential diagnosis. They share the infiltrative growth in a desmoplastic stroma but display more pronounced cytologic atypia and they lack the ductal differentiation. Owing to the similar behavior and treatment reliable separation on diagnostic biopsies is less important. Tumors showing predominantly duct differentiation (syringoid eccrine carcinoma) may mimic metastatic adenocarcinoma, especially of invasive ductal breast carcinoma. They are morphologically and immunohistochemically inseparable, and the diagnosis requires careful clinical correlation and screening.

SQUAMOID ECCRINE DUCTAL CARCINOMA

Squamoid eccrine ductal carcinoma is a poorly documented and likely underreported low-grade malignant sweat duct tumor first described in