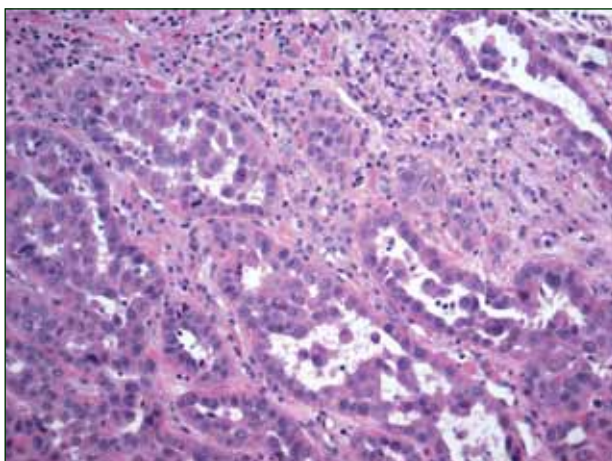


H&E, original magnification  $\times 40$ .



H&E, original magnification  $\times 100$ .

## The best diagnosis is:

- a. adenoid basal cell carcinoma
- b. angiosarcoma
- c. eccrine carcinoma
- d. metastatic adenocarcinoma of the skin
- e. pseudoglandular squamous cell carcinoma

PLEASE TURN TO PAGE 104 FOR DERMATOPATHOLOGY DIAGNOSIS DISCUSSION

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The authors report no conflict of interest.

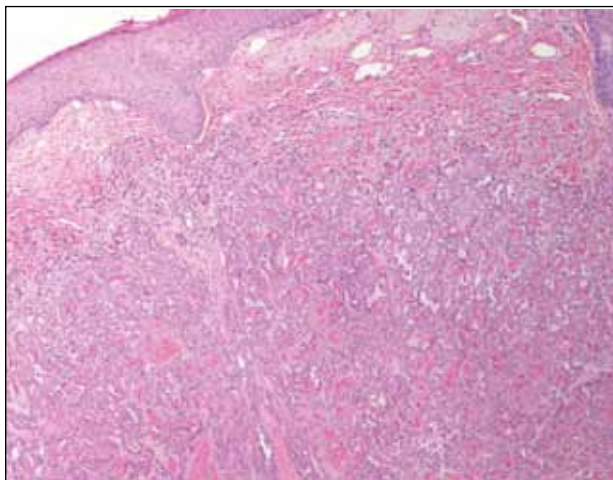
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## Pseudoglandular Squamous Cell Carcinoma

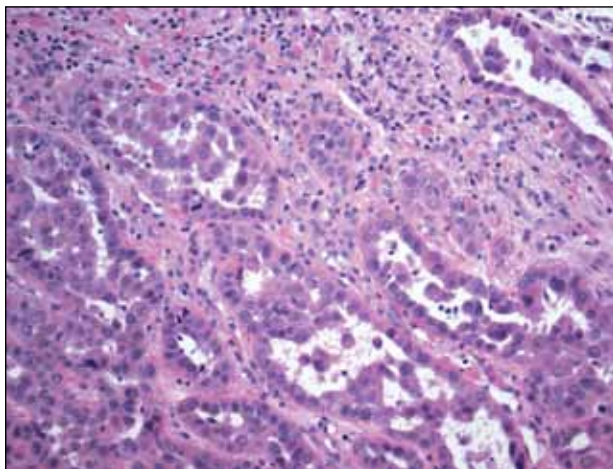
Squamous cell carcinoma (SCC) is the second most common form of skin cancer. Pseudoglandular SCC, also known as adenoid SCC or acantholytic SCC, is an uncommon variant that was first described by Lever<sup>1</sup> in 1947 as an adenoacanthoma of the sweat glands. Of the many variants of SCC, pseudoglandular SCC generally is considered to behave aggressively with intermediate (3%–10%) risk for metastasis.<sup>2</sup> The metastatic potential of pseudoglandular SCC may be conferred in part by diminished expression of intercellular adhesion molecules, including desmoglein 3, epithelial cadherin, and syndecan 1.<sup>3,4</sup> Pseudoglandular SCC presents most often on sun-damaged skin of elderly patients, especially the face and ears, as a pink or red nodule with central ulceration and a raised indurated border. It may be mistaken clinically for basal cell carcinoma (BCC) or keratoacanthoma.

On microscopic examination, the lesion is predominantly located in the dermis and may extend to the subcutis. There usually is connection to the overlying epidermis, which often shows hyperkeratosis and parakeratosis. Epidermal squamous dysplasia may be present. The dermis typically contains nests of squamous cells with a variable degree of central acantholysis. The morphology on low-power magnification consists of tubules of irregular size and shape, which are present either focally or throughout the lesion (Figure 1). The tubules are typically admixed with foci of keratinization. One or more layers of cohesive cells line the tubules. Partial keratinization may be found in the lining of tubules with more than 1 cell layer. The tumor cells are polygonal with eosinophilic cytoplasm, ovoid hyperchromatic or vesicular nuclei, and prominent nucleoli. Mitoses are common. The tubular lumina are filled with acantholytic cells, either singly or in small clusters, which may demonstrate residual bridging to tubular lining cells (Figure 2). The acantholytic cells show some variability in size and may be large, multinucleated, or keratinized. The tubules may contain material that is amorphous, basophilic, periodic acid–Schiff positive, diastase sensitive, and mucicarmine negative.<sup>5</sup> Eccrine ducts at the periphery of the tumor may show reactive dilatation and proliferation. Tumor cells show positive immunostaining for epithelial membrane antigen, 34 $\beta$ E12, CK5/6, and tumor protein p63.<sup>6-8</sup> There is negative immunostaining for carcinoembryonic antigen, amylase, S-100 protein, and factor VIII.<sup>5</sup>

The differential diagnosis includes adenoid BCC, angiosarcoma, eccrine carcinoma, and



**Figure 1.** Glandlike tubular structures admixed with foci of keratinization (H&E, original magnification  $\times 40$ ).

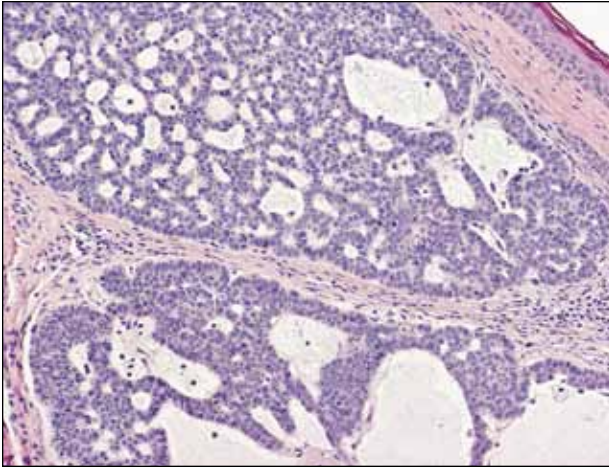


**Figure 2.** Pseudoglandular spaces containing acantholytic cells (H&E, original magnification  $\times 100$ ).

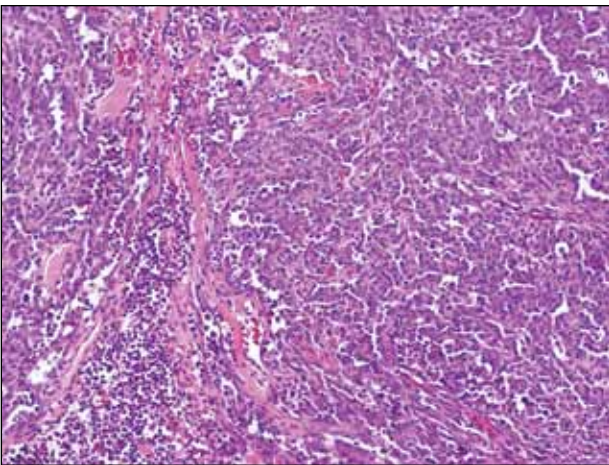
metastatic adenocarcinoma of the skin. In adenoid BCC, excess stromal mucin imparts pseudoglandular architecture (Figure 3). However, features of conventional BCC, including peripheral nuclear palisading and retraction artifact often are present as well.

Angiosarcoma shows slitlike vascular spaces lined by hyperchromatic endothelial cells (Figure 4). Further, there is positive immunostaining for vascular markers CD31 and CD34.

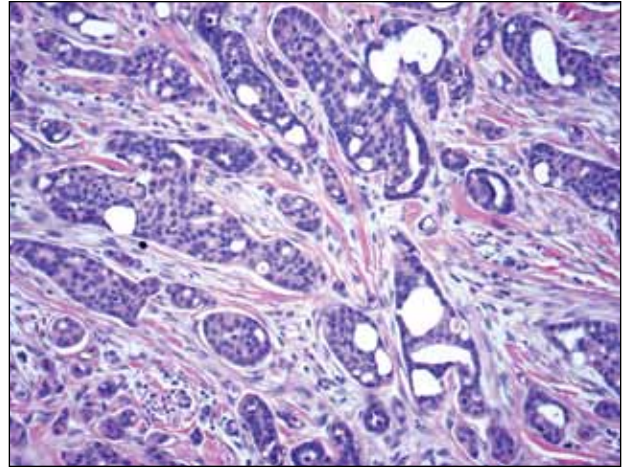
In eccrine carcinoma, there are invasive ductal structures lined by either a single or double layer of cells that may contain luminal material that is



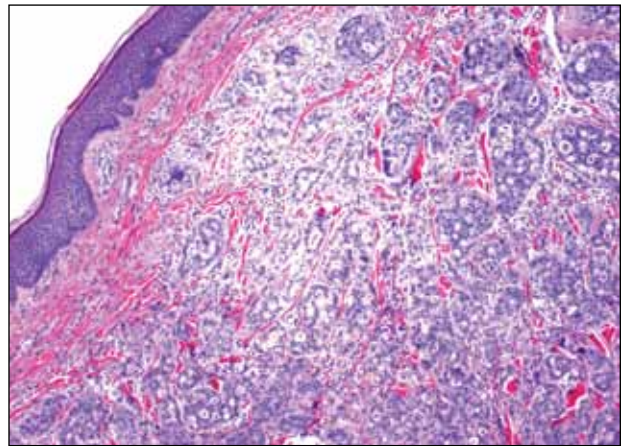
**Figure 3.** Thin strands of basaloid cells in a reticulate pattern with prominent stromal mucin in adenoid basal cell carcinoma. There also is palisading and retraction artifact of conventional basal cell carcinoma (H&E, original magnification  $\times 40$ ).



**Figure 4.** Slitlike vascular spaces lined by hyperchromatic endothelial cells in angiosarcoma (H&E, original magnification  $\times 100$ ).



**Figure 5.** Invasive ductal structures of malignant eccrine carcinoma (H&E, original magnification  $\times 100$ ).



**Figure 6.** The dermis is filled with malignant glandular epithelium that is CK7 positive, CK20 negative, and thyroid transcription factor 1 positive (immunohistochemistry not shown), consistent with metastatic adenocarcinoma of lung origin (H&E, original magnification  $\times 40$ ).

periodic acid–Schiff positive and diastase resistant (Figure 5).<sup>9</sup> The tumor cells show positive immunostaining for cytokeratins, epithelial membrane antigen, carcinoembryonic antigen, and S-100 protein.<sup>10</sup>

Pseudoglandular SCC is susceptible to misdiagnosis as adenocarcinoma by sampling error if biopsies do not capture areas with typical features of SCC, including dysplastic squamous epithelium and keratinization. Metastatic adenocarcinoma of the skin is more likely to present with multiple nodules in older individuals. Lack of epidermal connection of the tumor and minimal to no acantholytic

dyskeratosis further support cutaneous metastasis (Figure 6). Review of the patient's clinical history might be helpful if adenocarcinoma was previously diagnosed. Immunohistochemical evaluation may aid in the prediction of the primary site in patients with metastatic adenocarcinoma of unknown origin.<sup>11</sup>

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