Introduction

Adenosquamous carcinoma (ASC) occurs primarily in the elderly population and has a slight male predominance.1-3 Fair-skinned individuals in areas of sun exposure and immunosuppressed patients are at greater risk.2-4 The lesion presents as a singular, erythematous, indurated, keratotic plaque often arising within actinic keratoses primarily on the head and neck.1,2,5 Lesions have, however, been described on the hand, foot, and thigh.3 The tumors are aggressive and can cause local ulceration, extensive destruction to the surrounding tissues, and in some instances metastasis that leads to death. In a case series by Banks and Cooper, five patients passed away from uncontrolled local recurrence, and two are alive with widespread disease and clinical evidence of lymph node involvement.2 In one patient the lesion caused fatal hemorrhage, and in another death by direct extension into the CNS. Wiedner and Foucar describe a similar case in which a recurrent lesion eroded the orbit.3

Case Report

An 85-year-old Caucasian male presented to our clinic with a reported two-week history of a smooth, dome-shaped, pink-to-erythematous, 0.6 cm x 0.6 cm nodule on the right superior mandible (Figure 1). Upon examination, the patient admitted to rapid growth of the lesion and a tendency to bleed.

Our clinical differential diagnosis included desmoplastic trichoepithelioma, basal cell carcinoma, cutaneous metastasis and keratoacanthoma. A biopsy was taken, and histopathological examination revealed an epidermis that was replaced by atypical keratinocytes with nests extending into the underlying dermis. Solar elastosis was also present. The squamous cells demonstrated acantholysis as well as multiple foci of ductal differentiation (Figures 2 and 3). A mucicarmine stain confirmed mucin within the ducts (Figure 4).

Discussion

Cutaneous adenosquamous carcinoma is a rare malignant neoplasm with mixed glandular and squamous differentiation and a propensity for local invasion, recurrence, and distant metastasis. ASC was first described in 1985 by Weidner and Foucar, who agreed with the view that ASC is best classified as a high-grade variant of cutaneous squamous cell carcinoma.3 Histologically, adenosquamous carcinomas often appear on a background of intense solar elastosis.4 There are features typical of classic squamous cell carcinoma, such as irregular anastomosing islands of squamous cells originating from the epidermis, keratin pearls, and intercellular bridges. The atypical squamous sheets are connected to the epidermis with intervening areas that are non-dysplastic.2 These squamous cells often exhibit a sclerosing pattern and can involve the subcutaneous tissue as well as skeletal muscle.1,4 There is true glandular differentiation with cystic spaces lined by low, columnar-to-cuboidal...
epithelial cells secreting mucin with ductular differentiation, sometimes highlighted by an eosinophilic cuticle.1-4 High-grade atypia with frequent mitotic figures is characteristic.2 There are currently only a few cases of ASC described in the literature, though some authors refer to previously described cutaneous mucoepidermoid carcinomas (cMEC) as the same entity.6 There is controversy over whether they should be regarded as singular or distinct entities. Both lesions exhibit squamous as well as adenomatous differentiation.1-5,9

Although exceedingly rare in the skin, MECs are commonly found in other organs, such as salivary glands, lungs, and the female genital tract, and are of sweat gland origin.8 MECs are low-grade, indolent neoplasms with extremely low metastatic potential.2,8 ASCs, on the other hand, are not only aggressive but exhibit high rates of both recurrence and metastasis.1-3 The reigning opinion is that ASC, due to its highly aggressive nature, should be considered separate from MEC for prognostic purposes.1-3,5,7,8 Even though ASC and MEC exhibit several mutual features, mucogenic cells, and peritumoral eosinophilic cuticle,1-4 High-grade atypia with frequent mitotic figures is characteristic.2 There are currently only a few cases of ASC described in the literature, though some authors refer to previously described cutaneous mucoepidermoid carcinomas (cMEC) as the same entity.6 There is controversy over whether they should be regarded as singular or distinct entities. Both lesions exhibit squamous as well as adenomatous differentiation.1-5,9

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ASC can resemble several other entities and must be discriminated due to differences in biological behavior and treatment approaches. Basal cell and squamous cell carcinomas are the most common leading diagnoses submitted to pathologists.7 It is important to differentiate ASC from metastasis, microcystic adnexal tumor, MEC as an extension of a primary salivary gland tumor, and primary MEC (Table 1).2,8

Histologically, ASC and MEC exhibit several mutually exclusive features. Unlike MEC, ASC is intraepidermal, well differentiated, and displays high-grade nuclear features. MEC is a dermal-based, solid or cystic tumor and has papillary features, mucogenic cells, and peritumoral fibrosis.3 Stains and immunohistochemistry can further assist in finding the right diagnosis. ASC mucin is sensitive to sialidase and resistant to hyaluronidase, indicating epithelial mucin.3 The cells lining the glandular spaces stain with CEA or mucicarmine and keratin 7, suggesting glandular differentiation.1,3,10 In addition, diffuse staining for both p63 and cytokeratin 5/6 supports a primary cutaneous origin over metastatic adenocarcinoma. MEC also stains positive for p63 and cytokeratin 5/6, but it is focal and patchy, not diffuse.11

### Table 1. Differential Diagnosis of ASC with Histopathological and Immunohistochemistry Features

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Histopathology and Immunohistochemistry Features</th>
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<tbody>
<tr>
<td>Primary cutaneous SCC</td>
<td>Hyperkeratosis, full-thickness atypia of epidermis, invasion of dermis by atypical keratinocytes</td>
</tr>
<tr>
<td>Metastatic carcinoma</td>
<td>ER PR surfactant thyroglobulin CA 199</td>
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<tr>
<td>Acantholytic SCC</td>
<td>Pseudoglandular formation, PAS-negative</td>
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<tr>
<td>MEC</td>
<td>Patchy and focal p63 and cytokeratin 5/6 staining</td>
</tr>
<tr>
<td>Cutaneous adenosquamous carcinoma</td>
<td>Diffuse p63 and cytokeratin 5/6 staining, CEA+, keratin 7+</td>
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### Treatment

Most cases report a surgical approach with Mohs microscopic surgery, in some instances followed by radiation and chemotherapy as regional recurrence is common.2,12 There are also reports on the use of cetuximab as an adjunctive therapy for the treatment of ASC. The efficacy of this recombinant human and mouse chimeric antibody against the epidermal growth factor receptor as treatment for locally advanced cutaneous ASC is still under exploration.12

### Conclusion

In summary, adenosquamous carcinoma is best considered a locally aggressive, high-risk subtype of cutaneous squamous cell carcinoma. Due to the invasive and sclerosing pattern of these lesions, surgical resection can be difficult, but it is the treatment of choice.1 It is important to take a thorough history and perform full body scans in order to rule out an alternative primary tumor origin.13 Clinicians may also consider testing for the estrogen receptor, progesterone receptor, surfactant, thyroglobulin, and CA199 antigens in order to further rule out metastatic disease.1

### References


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