

# Squamoid Eccrine Ductal Carcinoma

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## PRACTICE POINTS

- Squamoid eccrine ductal carcinoma (SEDC) is an extremely rare cutaneous tumor of unknown etiology.
- A high index of suspicion with SEDC in the differential diagnosis should be maintained in elderly men with slow-growing, solitary, nodular lesions of the scalp, nose, arms, legs, or trunk.
- Development of a second or even a third primary malignancy in patients with SEDC is increasingly being reported in CLL patients.

Squamoid eccrine ductal carcinoma (SEDC) is an extremely rare cutaneous tumor of unknown etiology. We report the case of a 77-year-old man with a history of treated chronic lymphocytic leukemia along with numerous basal cell and squamous cell carcinomas who presented for evaluation of a 5-cm, stellate, sclerotic plaque on the left chest of approximately 2 years' duration and a suspicious 3-mm pink papule on the right nasal sidewall of 2 months' duration. Initial histology of both lesions revealed carcinoma with squamous and ductal differentiation that extended from the undersurface of the epidermis, favoring a diagnosis of SEDC. It was later determined that the patient had distant metastasis of SEDC. This report of an immunocompromised patient with SEDC is a rare case of distant metastasis of SEDC. A review of the literature on the diagnosis, treatment, and surveillance of SEDC also is provided.

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Eccrine carcinomas are uncommon cutaneous neoplasms demonstrating nonuniform histologic features, behavior, and nomenclature. Given the rarity of these tumors, no known criteria by which to diagnose the tumor or guidelines for treatment have been proposed. We report a rare case of an immunocompromised patient with a primary squamoid eccrine ductal carcinoma

(SEDC) who was subsequently treated with radical resection and axillary dissection. It was later determined that the patient had distant metastasis of SEDC. A review of the literature on the diagnosis, treatment, and surveillance of SEDC also is provided.

## Case Report

A 77-year-old man whose medical history was remarkable for chronic lymphocytic leukemia (CLL) and numerous previous basal cell carcinomas and squamous cell carcinomas (SCCs) presented with a 5-cm, stellate, sclerotic plaque on the left chest of approximately 2 years' duration (Figure 1) and a 3-mm pink papule on the right nasal sidewall of 2 months' duration. Initial histology of both lesions revealed carcinoma with squamous and ductal differentiation extending from the undersurface of the epidermis, favoring a diagnosis of SEDC (Figure 2). At the time of initial presentation, the patient also had a 6-mm pink papule on the right chest of several months duration that was consistent with a well-differentiated sebaceous carcinoma on histology.

Further analysis of the lesion on the left chest revealed positive staining for cytokeratin (CK) 5/14 and p63, suggestive of a cutaneous malignancy. Staining for S100 protein highlighted rare cells in the basal layer of tumor aggregates. The immunohistochemical profile showed negative staining for CK7, CK5D3, epithelial membrane antigen (EMA), estrogen receptor, progesterone receptor, and human epidermal growth factor 2.

Diagnosis of SEDC of the chest and nasal lesions was based on the morphologic architecture, which included ductal formation noted within the tumor. The chest lesion also had prominent squamoid differentiation. Another histologic feature consistent with SEDC was poorly demarcated, infiltrative neoplastic cells extending into the dermis and subcutis. Although there was some positive focal staining for carcinoembryonic antigen (CEA), variegation within the tumor and the prominent squamoid

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component might have contributed to this unexpected staining pattern.

The patient was admitted to the hospital for excision of the lesion on the chest wall. Initial workup revealed macrocytic anemia, which required transfusion, and an incidental finding of non–small-cell lung cancer. The chest lesion was unrelated to the non–small-cell lung cancer based on the staining profile. Material from the lung stained positive for thyroid transcription factor 1 (TTF-1) and exhibited rare staining for p63; however, the chest lesion did not stain positive for TTF-1 and had strong staining affinity for p63, indicative of a cutaneous malignancy.

The lesion on the chest wall was definitively excised. Pathologic analysis revealed a dermal-based infiltrative tumor of irregular nests and cords of squamoid cells with focal ductal formation in a fibromyxoid background stroma, suggestive of an adnexal carcinoma with a considerable degree of squamous differentiation and favoring a diagnosis of SEDC. Focal perineural invasion was noted, but no lymphovascular spread was identified; however, metastasis was identified in 1 of 26 axillary lymph nodes. The patient underwent 9 sessions of radiation therapy for the lung cancer and also was given cetuximab.

Three months later, the nasal tumor was subsequently excised in an outpatient procedure, and the final biopsy report indicated a diagnosis of basal cell carcinoma. One-and-a-half years later, in follow-up with surgery after removal of the chest lesion, a 2×3-cm mass was excised from the left neck that demonstrated lymph nodes consistent with metastatic SEDC. Careful evaluation of this patient, including family history and genetic screening, was considered. Our patient continues to follow-up with the dermatology department every 3 months. He has been doing well and has had multiple additional primary SCCs in the subsequent 5 years of follow-up.

## Comment

Eccrine carcinoma is the most common subtype of adnexal carcinoma, representing 0.01% of all cutaneous tumors.<sup>1</sup> Squamoid eccrine ductal carcinoma is rare, with as few as 13 cases reported in the literature; 3 of these patients were treated with Mohs micrographic surgery (MMS).<sup>1,2</sup> Recently, two series of 7 and 30 cases, respectively, were longitudinally followed and described.<sup>3,4</sup> We report an additional rare case of SEDC in an immunocompromised patient with distant metastases that was treated with radical resection and axillary dissection.

Eccrine carcinoma is observed clinically as a slow-growing, nodular plaque on the scalp, arms, legs, or trunk in middle-aged and elderly individuals.<sup>1</sup> Squamoid eccrine ductal carcinoma also has been reported in a young woman.<sup>5</sup> Another immunocompromised patient was identified in the literature with a great toe lesion that showed follicular differentiation along with the usual SEDC features of squamoid and ductal differentiation.<sup>6</sup> The etiology of SEDC is controversial but is thought to be an

SCC arising from eccrine glands, a subtype of eccrine carcinoma with extensive squamoid differentiation, or a biphenotypic carcinoma.<sup>1,7</sup>

Histologically, SEDC is poorly circumscribed with an infiltrative growth pattern and deep extension into the dermis and subcutaneous tissue. The lesion is characterized by prominent squamous epithelial proliferation superficially with cellular atypia, keratinous cyst formation, squamous eddies, and eccrine ductal differentiation.<sup>1</sup>

The differential diagnosis of SEDC includes SCC; metastatic carcinoma with squamoid features; and eccrine tumors, including eccrine poroma, microcystic adnexal carcinoma, and porocarcinoma with squamous differentiation.<sup>1</sup>

Immunohistochemistry has a role in the diagnosis of SEDC. Findings include positive staining for S100 protein, EMA, CKs, and CEA. Glandular tissue stains positive for EMA and CEA, supporting an adnexal origin.<sup>1</sup> Positivity for p63 and CK5/6 supports the conclusion that this is a primary cutaneous malignancy, not a metastatic disease.<sup>1</sup>

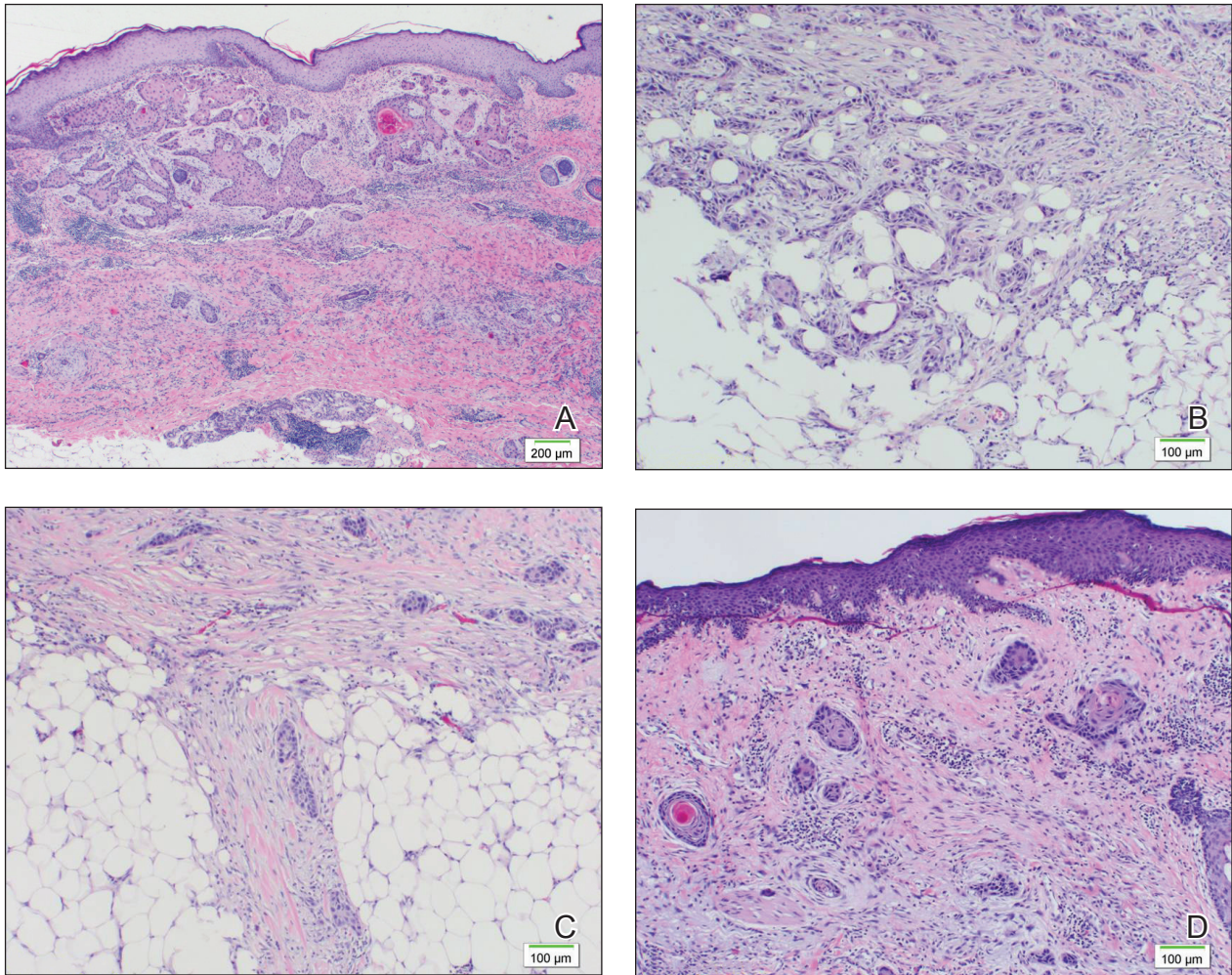
Squamoid eccrine ductal carcinoma has an indeterminate malignant potential. There is a disparity of clinical behavior between SCC and eccrine cancers; however, because squamous differentiation sometimes dominates the histological picture, eccrine carcinomas can be misdiagnosed as SCC.<sup>1,8</sup> Eccrine adnexal tumors are characterized by multiple local recurrences (70%–80% of cases); perineural invasion; and metastasis (50% of cases) to regional lymph nodes and viscera, including the lungs, liver, bones, and brain.<sup>1</sup> Squamous cell carcinoma, however, has a markedly lower recurrence rate (3.1%–18.7% of cases) and rate of metastasis (5.2%–37.8%).<sup>1</sup>

Squamoid eccrine ductal carcinoma is classified as one of the less aggressive eccrine tumors, although the low number of cases makes it a controversial conclusion.<sup>1</sup> To our knowledge, no cases of SEDC metastasis have been reported with SEDC. Recurrence of SEDC has been



**FIGURE 1.** Squamoid eccrine ductal carcinoma presenting as a 5-cm, stellate, sclerotic plaque on the left chest.





**FIGURE 2.** Squamoid eccrine ductal carcinoma. Histology revealed infiltrative nests and cords of squamoid cells with epidermal involvement and some ductal formation within the dermis and subcutis, extending to fat lobules (A and B)(H&E, original magnification  $\times 40$  and  $\times 100$ , respectively). Tumor nests extended to fibrous septae in adipose tissue (C)(H&E stain, original magnification  $\times 100$ ), and subtle tumor nests within a fibromyxoid background in the superficial dermis were noted (D)(H&E, original magnification  $\times 100$ ).

reported locally, and perineural or perivascular invasion (or both) has been demonstrated in 3 cases.<sup>1</sup>

Since SEDC has invasive and metastatic potential, as demonstrated in our case, along with elevated local recurrence rates, physicians must be able to properly diagnose this rare entity and recommend an appropriate surgical modality. Due to the low incidence of SEDC, there are no known randomized studies comparing treatment modalities.<sup>1</sup> Other works in the literature have suggested treating SEDC with the same approach as lesions with similar histologic features and behavior, such as eccrine carcinoma and SCC.<sup>1,5-7</sup>

Surgical extirpation with complete margin examination is recommended, as SEDC tends to be underestimated in size, is aggressive in its infiltration, and is predisposed to perineural and perivascular invasion. The literature has shown that MMS has demonstrated lower recurrence rates (3.1%–5%) than other treatments at 5-year follow-up

for SCC and (0%–5%) for eccrine carcinoma (average follow-up, 31 months).<sup>1,5</sup> Further studies are needed to understand the clinical progression of SEDC, and more experience is necessary with close follow-up of this subset of patients. Follow-up is determined at the present time from anecdotal experience and patient history.

Along with the rarity of SEDC in our patient, the simultaneous occurrence of 3 primary malignancies also is unusual. Patients with CLL have progressive defects of cell- and humoral-mediated immunity, causing immunosuppression. In a retrospective study, Tsimberidou et al<sup>9</sup> reviewed the records of 2028 untreated CLL patients and determined that 27% had another primary malignancy, including skin (30%) and lung cancers (6%), which were two of the malignancies seen in our patient. The investigators concluded that patients with CLL have more than twice the risk of developing a second primary malignancy and an increased frequency of

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certain cancer types.<sup>9</sup> Furthermore, treatment regimens for CLL have been considered to increase cell- and humoral-mediated immune defects at specific cancer sites,<sup>10</sup> although the exact mechanism of this action is unknown. Development of a second primary malignancy (or even a third) in patients with SEDC is increasingly being reported in CLL patients.<sup>9,10</sup>

A high index of suspicion with SEDC in the differential diagnosis should be maintained in elderly men with slow-growing, solitary, nodular lesions of the scalp, nose, arms, legs, or trunk.

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