

Syringomatous Carcinoma in a Young Patient Treated With Mohs Micrographic Surgery

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GOAL

To gain a thorough understanding of syringomatous carcinoma (SC) to better manage patients with this condition

OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Describe the clinical presentation of SC.
2. Discuss the histopathology of SC lesions.
3. Explain the treatment options for patients with SC.

CME Test on page 37.

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Syringomatous carcinoma (SC) has typically been observed in middle-aged and older patients. We report a case of SC mimicking an epidermoid cyst in a 23-year-old Asian man.

Histopathologic examination results showed a dermal neoplasm consisting of nests of basaloid cells, focal areas of ductal differentiation, moderate dermal fibrosis, and moderate nuclear atypia consistent with a diagnosis of SC. No perineural involvement was noted. Results of immunohistochemical analysis revealed positivity for high- and low-molecular-weight cytokeratins, as well as for carcinoembryonic antigen (CEA). There was scattered immunoreactivity to S-100 protein. The tumor was completely excised using Mohs micrographic surgery (MMS). This case demonstrates the importance of differentiating SC from other benign or malignant entities,

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the value of a prompt diagnosis of SC, and the effective treatment of SC with MMS.

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Syringomatous carcinoma (SC), considered by some to be a variant of microcystic adnexal carcinoma (MAC),¹ is a rare malignant neoplasm of sweat gland origin. SC encompasses a range of neoplasms with different degrees of differentiation, and its nomenclature has varied over the years. SC also has been referred to as syringoid eccrine carcinoma,² basal cell tumor with eccrine differentiation,³ malignant syringoma,⁴ and sclerosing sweat duct carcinoma.⁵ Its diagnosis has been a dilemma in a number of reported cases, probably due to the combination of its rarity and thus limited clinical and histopathologic information, microscopic similarities to other benign and malignant neoplasms, and characteristic histologic features that may only be apparent in surgical excisions containing deeper tissue. We report a case of SC that masqueraded as an epidermoid cyst in an unusually young patient.

Case Report

A 23-year-old Asian man, who was otherwise healthy, presented with an asymptomatic slowly enlarging nodule of one year's duration on the right medial eyebrow. Prior treatment with intralesional steroid injections resulted in minimal improvement. The patient had no personal or family history of skin cancers. Physical examination results demonstrated a well-demarcated, mobile, nontender subcutaneous nodule measuring 7 mm in diameter. The clinical presentation favored a diagnosis of an epidermal inclusion cyst, and the patient underwent surgical excision of the lesion.

Results of the histopathologic examination revealed a neoplasm in the dermis consisting of bands and nests of pale staining basaloid cells extending between the collagen fibers (Figure 1). There were focal areas of ductal differentiation, scattered individual necrotic cells, moderate dermal fibrosis, and chronic inflammation with numerous eosinophils. Moderate nuclear atypia also was present (Figure 2). Perineural involvement was not seen.

Results of immunohistochemical analysis revealed positive staining for high- and low-molecular-weight cytokeratins, as well as carcinoembryonic antigen (CEA)(Figure 3). There was scattered positivity with S-100 protein in occasional cells lining lumina and in dendritic cells (Figure 4). The histopathologic findings supported the diagnosis of SC. Because the neoplasm extended to the surgical margins of the specimen, repeat surgical excision with continuous microscopic control under the Mohs micrographic technique was performed to prevent local recurrence and spare normal tissue. At the 18-month follow-up visit, no local recurrence was seen.

Comment

SC is a rare, malignant sweat gland neoplasm that usually occurs in the fourth and fifth decades of life.⁴⁻⁸ SC typically presents as a slow-growing, solitary, painless nodule or indurated plaque on the head or neck region.⁶⁻⁸ It has been frequently found on the upper and lower lips; however, it also has been reported to occur on the finger and breast.^{9,10} Predisposing factors for the development of SC are unclear¹¹ but may include previous radiation to the

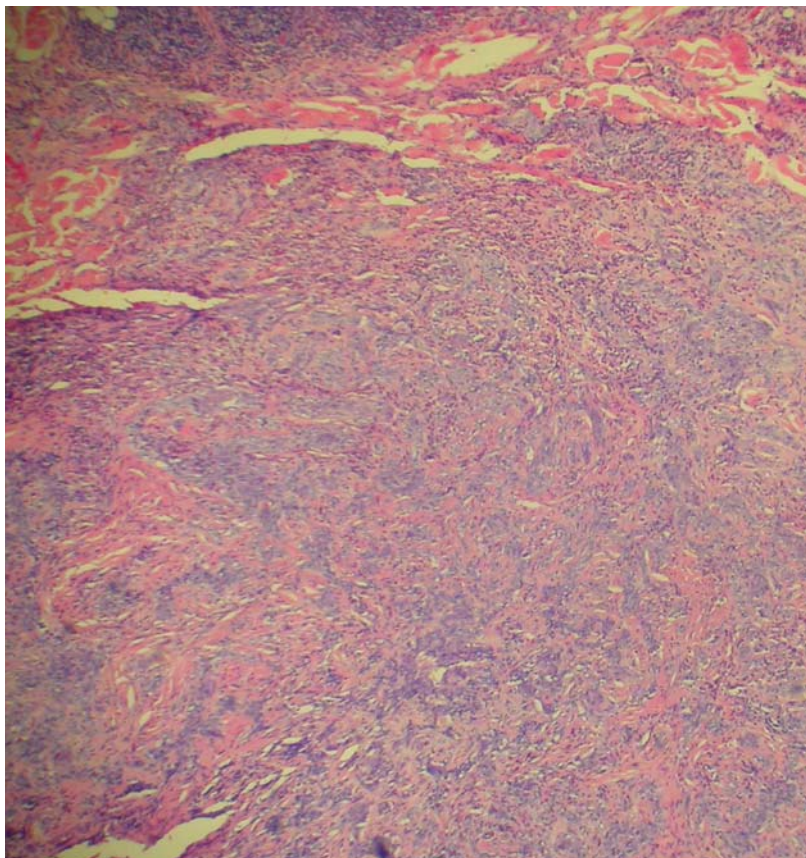


Figure 1. A neoplasm in the dermis consisting of bands and nests of pale staining basaloid cells extending between the collagen fibers (H&E, original magnification $\times 40$).

face and history of receiving an organ transplant with immunosuppressive drug therapy.¹²⁻¹⁷

Histopathologically, SC is characterized by asymmetric and deep dermal invasion of tumor cells, perineural involvement, ductal formation, keratin-filled cysts, multiple nests of basaloid or squamous cells, and desmoplasia of the surrounding dermal stroma (Table 1).^{5,6} Some authors consider SC to be closely related to MAC but generally describe SC as more basaloid with larger tubules and a more sclerotic stroma than MAC.¹⁸⁻²⁶ If histologic examination of SC is limited to the superficial dermis, SC demonstrates similarities to other neoplasms, including syringomas, trichoadenomas, trichoepitheliomas, basal cell carcinomas, or squamous cell carcinomas. In the reported cases in which SC was initially misdiagnosed as another benign or malignant neoplasm, many misdiagnoses were due to either a benign clinical appearance of the lesion or biopsy specimens that were too superficial to contain the deeper characteristic histologic features of SC.^{8,9,11,27-30}

Immunohistochemical studies can facilitate the diagnosis of SC and differentiate it from other neoplasms. SC stains positively for CEA,

S-100 protein, epithelial membrane antigen, cytokeratin, and gross cystic disease fluid protein 15,³¹ all of which aid in the confirmation of a sweat gland neoplasm (Table 2).^{8,32,33,39} Positivity for CEA in the ductal lining cells and the luminal contents of tumor ducts confirms sweat gland differentiation.^{25,33,34} This ductal immunoreactivity to CEA appears to be one of the most reliable findings to differentiate SC and MAC from other adnexal tumors, especially desmoplastic trichoepithelioma, which may be one of the more challenging histopathologic differential diagnoses.³⁵ In addition, epithelial membrane antigen positivity can be found in the areas showing glandular features.³⁵ This can assist in distinguishing SC from a desmoplastic trichoepithelioma or sclerosing type basal cell carcinoma, both of which demonstrate negativity to epithelial membrane antigen.³⁵ S-100 protein positivity in dendritic cells, as well as in some cords and ducts in SC, further verifies dendritic differentiation toward sweat gland structures and is useful as an adjunct in the confirmation of glandular differentiation.^{25,33,34,36}

Without proper and timely diagnosis and management, SC can cause severe patient morbidity. Although SC rarely metastasizes and can have an indolent course, it can be locally destructive and lead to potentially disfiguring outcomes.⁵⁻⁷ SC can invade deeply and infiltrate into the dermis, subcutaneous fat tissue, muscle, perichondrium, periosteum, and galea.⁸ Goto et al⁹ reported a case of an SC that was initially misdiagnosed as a basal cell carcinoma of the left middle finger. The deeper, characteristic features of SC were not recognized until after the affected finger required amputation due to erosion of the bone. Hoppenreijts et al¹¹ described an aggressive case of an SC arising at a site of previously irradiated squamous cell carcinoma of the lower eyelid. Extensive involvement of the SC in the orbit led to the recommendation of an orbital exenteration; however, it was not performed because of the poor clinical condition of the patient.

Treatments for SC have included wide local excision and Mohs micrographic surgery (MMS). SC treatment with wide local excision often resulted in incomplete excision of

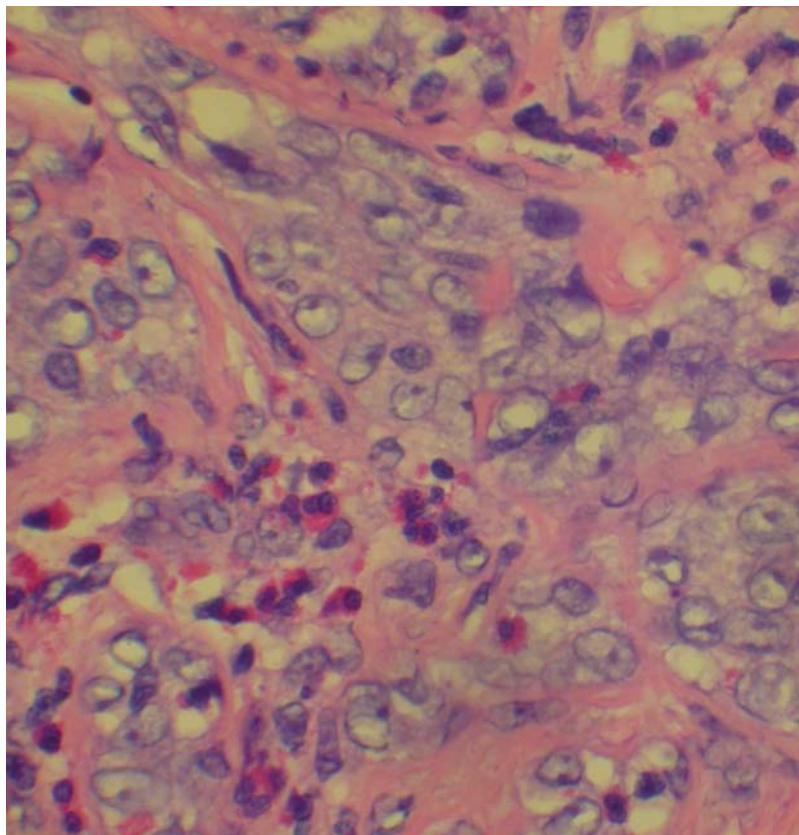


Figure 2. Focal areas of ductal differentiation, scattered individual necrotic cells, moderate dermal fibrosis, and chronic inflammation with numerous eosinophils. Moderate nuclear atypia also was present (H&E, original magnification $\times 400$).

the neoplasm despite having taken an adequate margin around the clinically assessable tumor.⁵ Cases of SC treated with wide local excision had a recurrence rate of 47%.⁵ The positive surgical margins following wide local excision may be due to the deep infiltration of SC, which frequently exceeds the clinically predicted size of the tumor.⁵ Due to the close relationship of MAC and SC, we feel that MMS treatment of SC will reduce recurrences as it has for MAC. Currently, there is strong support for the treatment of MAC with MMS as a gold standard to ensure complete clearance of the neoplasm and to reduce the local recurrence rate.^{12,13,17,21,22,37,38}

In a study of MAC by Chiller et al,³⁷ the authors demonstrated a median 4-fold increase in defect size when they compared the clinically estimated pretreatment size of the lesion with the MMS-determined posttreatment size of the lesion. The authors therefore suggest that, similar to the MMS-treated lesions, the lesions completely treated with wide local excision also would produce a defect size that is at least 4 times greater than the predicted pretreatment size of the lesion. Because wide local excision relies on predicted margins of the lesion, which the authors have shown can be greatly underestimated, Chiller et al³⁷ argue that the use of MMS, which does not rely on predicted margins, is a reasonable first-line therapeutic modality for effectively treating patients with MAC. Furthermore, MMS allows for the examination of the entire peripheral and deep margins of the lesion, which is critical when considering the deep infiltrative nature of MAC. The reported local recurrence rate of MAC treated with MMS is 0% to 5%,^{12,13,21,26,38} which is much lower than the reported local recurrence rate following treatment with wide local excision. This reduced recurrence rate found in MAC cases treated with MMS is probably due to the ability to confirm complete removal of the neoplasm with MMS.

Conclusion

To our knowledge, this case report describes the occurrence of SC, a rare sweat gland neoplasm, in the youngest reported patient and is only the second reported case of SC treated with MMS. Adequate

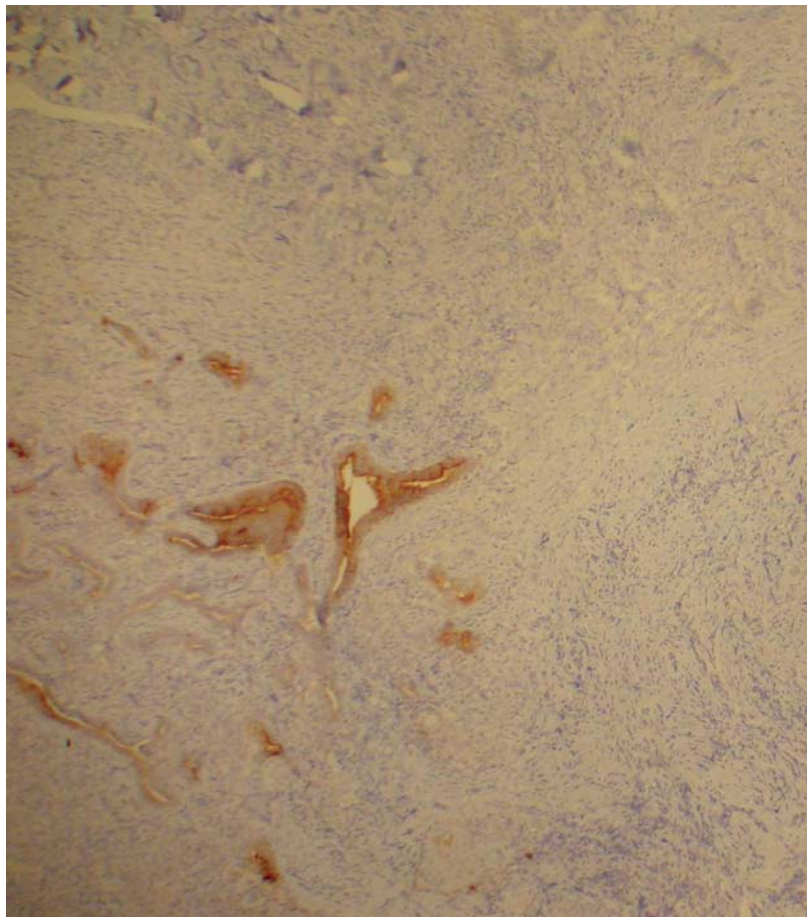


Figure 3. Positivity for carcinoembryonic antigen (original magnification $\times 40$).

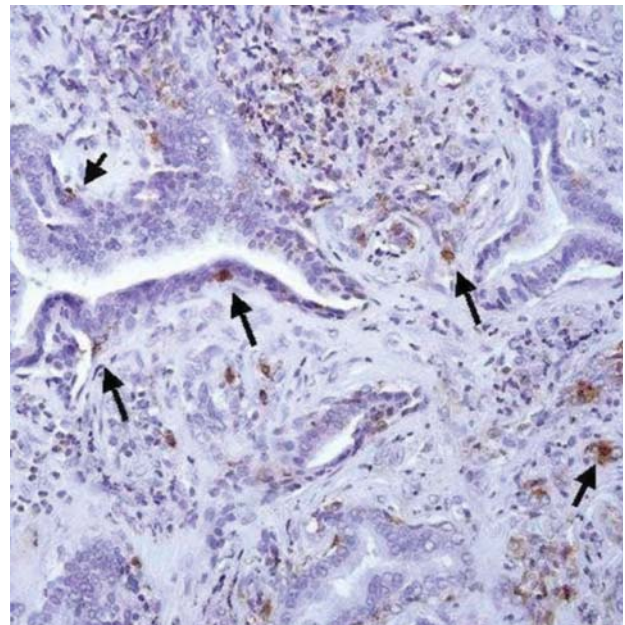


Figure 4. Scattered positivity with S-100 protein in occasional cells (arrows) lining the lumina, as well as in dendritic cells (original magnification $\times 200$).

Table 1.

Differential Diagnoses of Syringomatous Carcinoma and the Corresponding Histopathologic Features*

| Tumor | Deep Invasion | Perineural Involvement | Ductal Structures | Horn Cysts |
|--------------------------------|---------------|------------------------|-------------------|------------|
| Syringomatous carcinoma | + | + | + | + |
| Desmoplastic trichoepithelioma | – | – | – | + |
| Trichoadenoma | – | – | – | + |
| Syringoma | – | – | + | – |
| Sclerosing-type BCC | – | – | +/- | +/- |

*BCC indicates basal cell carcinoma.

Table 2.

Differential Diagnoses of Syringomatous Carcinoma and the Corresponding Immunohistochemical Features*^{8,32,33,39}

| Tumor | CEA | S-100 | EMA | CKs | GCDFP-15 |
|--------------------------------|-----|-------|-----|-----|----------|
| Syringomatous carcinoma | + | + | + | + | + |
| Desmoplastic trichoepithelioma | – | – | – | + | – |
| Trichoadenoma | – | – | – | + | – |
| Syringoma | + | – | + | + | – |
| Sclerosing-type BCC | – | – | – | + | – |

*CEA indicates carcinoembryonic antigen; EMA, epithelial membrane antigen; CKs, cytokeratins; GCDFP-15, gross cystic disease fluid protein 15; BCC, basal cell carcinoma.

sampling of tissue with an excisional biopsy allowed for appropriate evaluation with histologic and immunohistochemical studies to arrive at the diagnosis that could easily have been missed with a superficial biopsy. In our patient, histopathologic evaluation showed typical nests of basaloid cells, ductal differentiation, and ductal fibrosis seen in SC. However, perineural involvement that is particularly characteristic of SC was not present. This may portend a better prognosis for our patient whose tumor was completely excised after one stage of MMS and has not shown evidence of recurrence at the 18-month

follow-up visit. MMS allowed for evaluation of the entire surgical margin and decreased risk of local recurrence resulting from an incomplete excision. In addition, it also allowed for sparing of normal tissue in a cosmetically sensitive area where SC commonly occurs. In summary, this case highlights the importance of including SC in the differential diagnosis of an enlarging cystic lesion in a younger patient and its successful treatment with MMS.

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