Syringocystadenocarcinoma papilliferum with orbital invasion: a case report with literature review

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Abstract: We present a case of Syringocystadenocarcinoma papilliferum that originated in the eyelid and extended into the orbit. These tumors are very rare and have the potential to metastasize. A literature review of all the previous cases has been compiled from the Medline, EMBASE, and PubMed databases. We found that the majority of cases present on the head and neck and up to 17% of cases showed metastatic progression. This is the first case to show orbital involvement and highlights the need to remain vigilant with such lesions, as they have a tendency to become aggressive.

Keywords: eyelid, orbit, Syringocystadenocarcinoma papilliferum

Introduction
Syringocystadenocarcinoma papilliferum (SCACP) is a rare malignant sudoriferous gland tumor that is related to its more common, benign counterpart, syringocystadenoma papilliferum (SCAP). Since the original description of SCAP in 1917, only 43 cases of SCACP have been described in the literature. To date, only one has appeared in the eyelid. SCACP is thought to develop from SCAP, nevus sebaceous, and linear nevus verrucous lesions. However, due to the rarity of this tumor, little is known regarding its etiology and origin.

In this study, we report the first case of SCACP with orbital involvement. Interestingly, it recurred following exenteration. An informed written consent was obtained from the patient for the publication of medical data and images.

Case report
A 63-year-old man presented with a lesion on the right upper eyelid that had been present for 7 years. The lesion was nodular, measuring 5.0 cm × 7.0 cm, ulcerated, indurated, and erythematous. It involved the lower eyelid (Figure 1). The patient had no light perception with the right eye, his intraocular pressure could not be measured, and it was found to be 18 mmHg on the left.

The left orbital examination did not reveal any abnormalities. A full examination of his local lymph nodes and lacrimal duct did not reveal any abnormalities. He explained that he did not have any previous therapy for this lesion. He was otherwise systemically well with no relevant family history. He did not have any history of trauma and informed us that he was a farmer by occupation.

A computed tomography (CT) scan of the orbit revealed right anterior orbital invasion with no bony or lacrimal gland involvement (Figure 2). A subsequent incisional biopsy revealed squamous cell invaginations extending from the epidermis into the dermis. The invaginations and papillary projections were lined with a bilayer epithelium: the luminal layer was composed of columnar cells with decapitation secretion and the outer layer was composed of small cuboidal cells. These cells had significant nuclear pleomorphism, prominent nucleoli, and increased mitotic activity (Figure 3). Immunohistochemical staining demonstrated positivity for epithelial membrane antigen (EMA),
**Figure 1.** Lesion on presentation.

**Figure 2.** CT imaging of the lesion at presentation.

**Figure 3.** Hematoxylin and eosin staining (H&E): (a) the transition between squamous and glandular epithelium (100×). (b) Large areas of superficial epithelium were sphacelated. Glandular invaginations showed a characteristic funnel shape. Papillary structures can be identified inside a dermal cyst (100×). (c) The papillary structures are lined with a stratified atypical epithelium. Micropapillae and secretion by decapitation can be seen (100×). (d) At high power magnification, atypical nuclei are evident. Large atypical nuclear shapes are seen and increased mitotic activity is observed (*).
### Table 1. Previous case reports on SCACP.

| Reference                      | Age  | Sex | Location         | Size (mm)       | Duration | Diagnosis         | Association          | Follow-up            | Treatment          |
|-------------------------------|------|-----|------------------|-----------------|----------|--------------------|----------------------|---------------------|--------------------|
| Dissanayake and Salm         | 74   | F   | Scalp            | 65              | 30 years | SCACP in situ     | SCAP                 | NED [6.75 years]    | Surgery            |
| Seco Navedo and colleagues    | 50   | F   | Scalp            | 65              | N/A      | SCACP invasive    | Nevus sebaceous      | NED [7 years]       | Surgery            |
| Numata and colleagues        | 52   | F   | Chest            | 130 × 80        | 20 years | SCACP invasive    | N/A                  | NED [7 years]       | Surgery            |
| Bondi and Urso               | 47   | M   | Scalp            | 25              | N/A      | SCACP invasive    | N/A                  | N/A                 | Surgery            |
| Ishida-Yamamoto and colleagues | 61   | M   | Perianal         | 60              | 10 years | SCACP in situ     | N/A                  | NED [11 months]     | Surgery            |
| Arai and colleagues          | 64   | M   | Scalp            | 35              | 2 years  | SCACP in situ     | SCAP                 | N/A                 | Surgery            |
| Chi and colleagues           | 60   | M   | Auricle          | 40 × 10         | Since childhood | SCACP invasive  | SCAP                 | NED [72 months]     | Surgery            |
| Woestenborghs and colleagues | 81   | F   | Scalp            | 15              | N/A      | SCACP in situ     | SCAP                 | N/A                 | Surgery            |
| Park and colleagues         | 65   | M   | Suprapubic region | 35             | 2 years  | SCACP in situ     | N/A                  | NED [24 months]     | Surgery            |
| Langner and Ott             | 83   | M   | Perianal         | 15              | N/A      | SCACP in situ     | SCAP                 | N/A                 | Surgery            |
| Sroa and colleagues         | 77   | M   | Calf             | 25              | 9 years  | SCACP invasive    | N/A                  | NED [15 months]     | Surgery            |
| Kazakov and colleagues      | 56   | F   | Neck             | 20              | 10 years | SCACP in situ     | SCAP                 | NED [9 months]      | Surgery            |
| Kazakov and colleagues      | 58   | M   | Forehead         | 25              | 25 years | SCACP invasive    | SCAP                 | NED [4 years]       | Surgery            |
| 46   | F   | Scalp            | 35              | N/A              | SCACP invasive | SCAP              | NED [6 years]        | Surgery            |
| 67   | M   | Scalp            | 25              | N/A              | SCACP in situ     | SCAP                 | NED [2 years]        | Surgery            |
| 60   | F   | Scalp            | 30              | >30 years        | SCACP invasive    | SCAP                 | N/A                 | Surgery            |
| 81   | M   | Scalp            | 20              | N/A              | SCACP invasive    | SCAP                 | NED [21 months]      | Surgery            |

(Continued)
| Reference                  | Age  | Sex  | Location      | Size (mm) | Duration         | Diagnosis          | Association | Follow-up              | Treatment                           |
|---------------------------|------|------|---------------|-----------|------------------|--------------------|-------------|------------------------|-------------------------------------|
| Leeborg and colleagues17 | 86   | F    | Neck          | 45        | 4 months         | SCACP invasive     | Invasive     | Local recurrence [18 months] | Surgery + Rt                        |
| Abrari and Mukherjee18    | 62   | M    | Axilla        | 35        | 6 months         | SCACP invasive     | N/A          | N/A                    | Surgery                            |
| Aydin and colleagues19    | 67   | M    | Scalp         | 40        | Since childhood  | SCACP invasive     | SCAP         | NED [2 years]          | Surgery                            |
| Hoekzema and colleagues20 | 83   | F    | Arm           | 30        | 7 years          | SCACP invasive     | SCAP nevus verrucosus | N/A                  | Surgery                            |
| Hoguet and colleagues21   | 86   | M    | Eyelid        | 4         | N/A              | SCACP invasive     | N/A          | NED [3 months]         | Surgery                            |
| Plant and colleagues22    | 83   | M    | Penis         | 12        | N/A              | SCACP in situ      | N/A          | N/A                    | Surgery                            |
| Bakhshi and colleagues23   | 45   | F    | Scalp         | 60 × 30   | 12 months        | N/A                | SCAP         | NED [12 months]        | Surgery in situ                    |
| Zhang and colleagues24    | 75   | F    | Arm           | 15        | 12 months        | SCACP invasive     | SCAP         | NED [6 months]         | Surgery                            |
| Peterson and colleagues25  | 65   | M    | Scalp         | 30 × 30   | 12 months        | SCACP invasive     | SCAP         | NED                    | Surgery                            |
| Arslan and colleagues26    | 66   | M    | Scalp         | N/A       | 20 years         | SCACP invasive     | SCAP         | 3; Local lymph node, lymph node metastasis | Surgery + Rt [NED—15 months]         |
|                           | 66   | F    | Scalp         | 30        | >12 months       | SCACP invasive     | N/A          | NED [2 years]          | Surgery                            |
| Castillo and colleagues27  | 32   | F    | Scalp         | 22        | N/A              | SCACP in situ      | N/A          | Local recurrence [8 years] | Surgery                            |
| Paradiso and colleagues28  | 88   | M    | Shoulder      | 15 × 15   | N/A              | SCACP invasive     | N/A          | Died from other cause  | N/A                                |
| Shan and colleagues29      | 93   | M    | Popliteal fossa | 20        | >10 years        | N/A                | SCAP         | NED                    | Surgery                            |
| Mohanty and colleagues30   | 80   | F    | Scalp         | 50        | 8 years          | SCACP in situ      | N/A          | NED [5 years]          | Surgery                            |
| Satter and colleagues31    | 42   | M    | Scalp         | 45 × 40   | >1 month         | SCACP invasive     | SCAP and Nevus sebaceous | Lymph node metastasis | Surgery                            |
| Parekh and colleagues32    | 74   | M    | Scalp         | 20        | Since childhood  | SCACP invasive     | SCAP, nevus sebaceous of Jadassohn, trichoblastoma | Lymph node metastasis | Surgery                            |
| Reference                  | Age | Sex | Location   | Size (mm) | Duration | Diagnosis                           | Association                                                                 | Follow-up                        | Treatment            |
|---------------------------|-----|-----|------------|-----------|----------|-------------------------------------|----------------------------------------------------------------------------|-----------------------------------|----------------------|
| Chen and colleagues<sup>30</sup> | 60  | F   | Scalp      | 28 × 20   | 12 months| SCACP in situ                       | Nevus sebaceous                                                            | N/A                               | Surgery              |
| Singh and colleagues<sup>31</sup> | 60  | F   | Back       | 15 × 10   | >10 years| SCACP in situ with macular amyloidosis | Left axillary lymph node and bilateral lung metastases, DOD 2 months after diagnosis | N/A                               | Surgery              |
| Zhang and colleagues<sup>32</sup> | 26  | M   | Chest      | 50        | 22 years | SCACP in situ                       | Invasive adenocarcinoma subcutis                                           | N/A                               | Surgery + Ct         |
|                           | 47  | M   | Abdomen    | 15        | 23 years | SCACP in situ                       | N/A                                                                         | NED (9 years)                     | Surgery              |
|                           | 67  | M   | Left Axilla| 20        | 6 years  | SCACP in situ                       | Invasive adenocarcinoma subcutis                                           | N/A                               | Surgery + left axilla lymphadenectomy |
|                           | 64  | M   | Scalp      | 20        | 1 years  | SCACP in situ                       | Invasive adenocarcinoma in dermis + mucinous metaplasia                    | Metastases to multiple distant lymph nodes and lung metastases, DOD 34 months after diagnosis | Surgery + Rt         |
|                           | 63  | M   | Chest      | 10        | 10 years | SCACP in situ                       | Invasive adenocarcinoma in dermis                                          | NED (36 months)                   | Surgery              |
|                           | 74  | M   | Chest      | 20        | 6 years  | SCACP in situ                       | Invasive adenocarcinoma subcutis                                           | NED (30 months)                   | Surgery              |
|                           | 63  | F   | Axilla     | 50        | 3 months | SCACP in situ                       | Invasive adenocarcinoma + invasive squamous cell carcinoma                | Widespread subcutaneous metastases, DOD 20 months after diagnosis           | Surgery + right axilla lymphadenectomy |
|                           | 40  | M   | Chest      | 50        | 5 years  | SCACP in situ                       | Invasive adenocarcinoma subcutis                                           | NED (14 months)                   | Surgery + bilateral lymphadenectomy + Ct |
|                           | 29  | F   | Forehead   | 15        | 2 years  | SCACP in situ                       | Invasive squamous cell carcinoma                                           | NED (10 months)                   | Surgery              |
|                           | 64  | M   | Axilla     | 22        | 10 years | SCACP in situ                       | Invasive adenocarcinoma subcutis                                           | NED (3 months)                    | Surgery + right axilla lymphadenectomy + Ct |
| Present case              | 63  | M   | Eyelid     | 50 × 70   | >6 years | SCACP invasive                      | SCAP                                                                        | Local recurrence                   | Surgery              |

Ct, chemotherapy; Rt, radiation therapy; N/A, not available; NED, no evidence of disease; DOD, died of disease.

Table 1. (Continued)
Cytokeratin 8/18, and a Cytokeratin cocktail of high and low density (Figure 3). It was negative for GCDFP-15 (protein 15 of the fibrocystic disease of the breast), which excluded a lesion of breast origin and carcinoembryonic antigen (CEA). The diagnosis of SCACP was therefore confirmed. A positron emission tomography (PET) scan did not reveal any metastatic spread.

The patient was treated with exenteration of the right orbit to remove the tumor. After 11 months of follow-up, we noted local recurrence of the original tumor (confirmed with biopsy) in the anophthalmic orbit. There was no associated lymph node enlargement on examination, though the patient refused any further imaging. Radical exenteration with adjuvant radiotherapy has been planned for the patient.

**Discussion**

SCACP is an extremely rare adnexal neoplasm of the sweat glands and has only been documented 43 times in the literature. It is believed to arise from a malignant transformation of SCAP lesions.\(^4\) Clinically, it may present as an asymptomatic long-standing lesion, which may be flat or nodular, cystic, or ulcerated. We performed a literature review of the Medline, EMBASE, and Cochrane databases to characterize the cases previously listed in the literature (Table 1).

The tumor appears to affect middle-aged or elderly individuals\(^1\) and does not seem to have a gender bias. The most frequent location is the head and neck (53%), with only one case in the eyelid. Other locations where these lesions occur frequently are the back, chest, suprapubic, and perianal regions.

Treatment is based on a complete tumor resection with oncological margins, which is essential for a better prognosis. Mohs surgery has also been successfully used for this purpose.\(^11\) Sentinel lymph node biopsy may be feasible in some cases when there is suspicion of lymph spread, although lymphatic spread has been shown to be rare with this tumor (6 of the 42 documented cases; Table 1). Radiotherapy and chemotherapy have also been used rarely, but the experience with these treatments is scarce due to the rarity of the lesion.\(^25\)

SCACP characteristically presents with squamous cell invaginations extending from the epidermis into the dermis. The invaginations and papillary projections are lined by two-layer epithelium: the luminal layer composed of columnar cells with decapitation secretions and the outer layer composed of small cuboidal cells. The immunohistochemical features of SCACP are still under study, but the most frequently reported markers are CEA,\(^15,20,28\) followed by EMA,\(^9,28\) GDFP-15,\(^20,28,32\) and cytokeratin.\(^11,28,32\)

Of the cases that reported head and neck involvement, 16 (72.72%) were in remission following therapy, 2 (9.09%) had local recurrence, 3 (13.63%) had regional lymphatic invasion, and 1 (4.54%) had distant metastases. Of the reports describing involvement of the thorax, abdomen, and pelvis, 17 (85%) went into remission following therapy, none had local recurrence, 1 (5%) had regional lymphatic invasion and 2 (10%) had distant metastases.

This is the first reported case of SCACP with extension into the anterior orbit. While SCACP is an exceedingly rare tumor, we found that of the reported cases, 16% showed signs of metastasis. It is therefore an important diagnosis to consider when reviewing skin lesions around the orbit. It also encourages us to monitor patients with SCAP more closely as our literature review suggests that SCACP may be more aggressive than previously considered.

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