Primary Mucinous Carcinoma of the Skin: A Review
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Citation

Abstract
Background: Primary mucinous carcinoma of the skin (MCS) is a rare subtype of sweat gland tumor. We report a case of primary MCS.

Method: A literature search from 1966 to 2004 was conducted. Keywords were: mucinous carcinoma, mucinous adenocarcinoma, adenocystic carcinoma and mucoepidermoid carcinoma.

Results: 100 cases of primary MCS were reported. Of these, 58.8% were male and 41.2% female. Ages ranged from 8 to 87 years (mean, 62.6). The eyelid was most commonly affected (41%). MCS also affected the scalp (17%), face (14%), axilla (9%), chest/abdominal wall (7%), vulva (4%), neck (2%), extremity (2%), canthus (2%), groin (1%) and ear (1%). Local recurrence occurred in 29.4% and metastases in 9.6%. The overall mortality rate was 2%.

Conclusion: Differentiation from metastatic mucinous carcinoma is difficult and a search for a primary tumor is warranted. Local recurrence is common. Treatment includes wide excision and lymph node dissection for clinically positive nodes.

INTRODUCTION
Primary mucinous carcinoma of the skin (MCS) is an uncommon subtype of sweat gland tumor. While some debate exists as to the apocrine or eccrine origins of this tumor, most authors favor eccrine differentiation based on evidence obtained from immunohistochemical studies and electron microscopic ultrastructural analysis. Lennox et al. first described primary mucinous carcinoma of the skin in 1952. The tumor has been identified variously as adenocystic carcinoma, colloid carcinoma, mucinous adenocarcinoma, mucoepidermoid carcinoma, mucin-secreting carcinoma and gelatinous carcinoma. With the exception of case series presented by Mendoza and Helwig (1971) and Wright (1979), most reports have been individual case reports or incomplete reviews. We present a case of primary mucinous carcinoma of the skin, review the 100 cases reported in the English literature, and provide guidelines regarding diagnosis, treatment and follow-up.

CASE REPORT
A 78 year old white male presented to general surgery clinic at the Northport VA Medical Center for evaluation of a painless, superficial nodular mass in his left axilla that had slowly grown over the course of approximately three years to measure 1.0 x 1.0 cm. The mass was not discolored but was hyperkeratotic and ulcerated at its apex. There was neither surrounding lymphadenopathy nor telangiectasia. The lesion was excised with 1 cm margins under local anesthesia. Gross pathology revealed a subcutaneous nodule of tan, gelatinous tissue measuring 1.5 x 1.0 x 1.0 cm. Microscopic examination revealed islands of eosinophilic cells surrounded by lakes of mucin consistent with the diagnosis of mucinous carcinoma (Figure 1).
Figure 1

Figure 1: Characteristic findings of cellular islands separated from lakes of mucin by fibrous septae under low power, (1A) and high power, (1B)

Keywords used included mucinous carcinoma, mucinous adenocarcinoma, adenocystic carcinoma, and mucopidermoid carcinoma. The bibliographies of these papers were searched for these keywords to obtain additional cases, particularly those prior to 1966. Only cases of primary mucinous carcinoma of the skin were included in this review. All cases were compiled and the age, sex and race of individuals determined. The size and location of the lesion was noted, as well as any evidence of metastasis or recurrence.

Since its first description, 100 cases of primary mucinous carcinoma of the skin have been reported in the English literature (Table 1). Mucinous carcinoma of the skin affects men (58.8%) more than women (41.2%). It tends to occur in more elderly individuals (average age 62.6 years, range 8-87 years), although the disease has been reported in a patient as young as 8 years old. Out of 100 patients in the current review, race was indicated in 64 (64%). Of these, 39 (60.9%) were White, 15 (23.4%) were Black, and 10 (15.6%) were Asian. Mucinous carcinoma most commonly arises in the head or neck, with the eyelid being the most common site (41%). Mucinous carcinoma also affected the scalp (17%), face (14%), axilla (9%), vulva (4%), chest/abdominal wall (7%), neck (2%), extremity (2%), canthus (2%), groin (1%) and ear (1%). Because of the scarce number of cases reported, data on incidence and prevalence are unknown.

**DISCUSSION**

A Medline and Cancerlit search was performed for the years encompassing 1966-2003 and 1983-2004, respectively.
Mucinous carcinoma of the skin has a varied clinical presentation. Lesions have been described as painless, papular or nodular, with sizes ranging from 5 mm to 120 mm. They are frequently single, isolated lesions with color reported as red, pink, gray, blue or purple. Telangiectasia
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may or may not be present. The surface may be smooth, ulcerated or crusted. The differential diagnosis of primary mucinous carcinoma of the skin includes sebaceous cyst, hemangioma, adenocystic basal cell carcinoma, lipoma, melanoma, epidermal inclusion cyst, chalazion, neuroma, Kaposi’s sarcoma, pilomatrixoma, squamous cell carcinoma and metastatic adenocarcinoma. [59,62,72,73,77,78,144,147,149,150,164,165,168,171,199,200,309,311,314,325,326,327,328,329,330,331,332,333,334,335,336,337,338,339,40,41,42,43,44] Of these, the most important to consider is mucinous carcinoma of the skin metastatic from another site.

Mucinous carcinoma arises most commonly from the breast, and gastrointestinal or respiratory tract, but may also originate from salivary and lacrimal glands, the urinary tract, prostate, or paranasal sinuses. Colon carcinoma metastatic to the skin most commonly involves the anterior abdominal wall, not the head and neck where most primary tumors are found. Additionally, primary mucinous carcinomas of the skin produce a nonsulfated mucin while mucinous carcinomas of gastrointestinal origin produce nonsulfated, neutral and sulfated mucins.[1,2,3,5,6,8,11,12,13,14,15,16,17,18,20,21,22,23,25,26,27,30,31,33,35,36,37,38,39,40,41,42,43,44] Similar to colon carcinoma, mucinous breast carcinoma metastatic to the skin is most commonly found on the anterior chest wall.[10,30,144] It is uncommon for mucinous carcinoma to metastasize to the skin of the extremities, head and neck, groin and axilla.[11,10,30,144] The rarity of primary mucinous carcinoma of the skin relative to primary sites in the lung, breast or GI tract, necessitates a thorough work-up to search for a source of metastasis. All patients should undergo a complete history and physical examination, with special attention to breast examination, CBC, SMA-7, liver transaminases, colonoscopy or barium enema, mammography, and CT scan of the chest, abdomen and pelvis.

Primary mucinous carcinoma of the skin typically has an indolent course. Local recurrence occurs frequently (29.4%) following excision, but the rate of metastasis is low (9.6%). Most metastases are to regional lymph nodes, although widespread metastases have been reported.[12,59,146] Aggressive bony invasion has also been reported (7%), but is uncommon.[2,3,22,72,35,48,49] Two deaths have been reported (2%).[12,59,146] Microscopic examination reveals nests of tumor cells separated from pools of mucin by fibrous septae. Cells tend to have a round to cuboidal nucleus, a prominent nucleolus and abundant eosinophilic cytoplasm.[1,2,3,5,6,8,11,12,13,14,15,16,17,18,20,21,22,23,25,26,27,29,30,31,33,35,36,37,38,39,40,41,42,43,44] There are few mitotic figures. As opposed to classic eccrine sweat gland tumors, which are locally invasive and metastasize in 50% of patients, invasive mucinous carcinoma of the skin exhibits slow local growth and relatively low rates of metastasis (28.6%). Mendoza and Helwig (1971) assert that copious mucin secretion produced by mucinous carcinomas of the skin interferes with cellular nutrition and replication.[1,2] Mucin production is consistent with retained cellular function and an indication that the tumor is well-differentiated. Additionally, mucinous carcinomas are typically avascular, a factor that helps explain its low rate of metastasis. Under light microscopy, two cell populations are identified: peripherally located dark cells and centrally located pale cells.[1,2,3,5,6,8,10,12,16,27] Electron microscopy reveals that the dark cells contain large amounts of cell product, presumably mucin, relative to the centrally located pale cells.[11,15,17,20,27,29] Ultrastructurally, the dark cells of mucinous carcinoma resemble the dark cells of the eccrine secretory coil, lending support to the theory of the tumor’s eccrine origin.[11,15,27]

Histochemically the mucin produced by the tumor is periodic acid-Schiff (PAS) and colloidal iron positive, but is resistant to hyaluronidase and diastase. Alcian blue is positive at pH 2.5 but negative at pH 0.4 or in the presence of sialidase. This histochemical profile is consistent with the presence of a non-sulfated mucoprotein, most likely sialomucin.[2,3,5,6,8,10,12,16,27,30,31,33,35,36,37,38,39,40,41,42,43,44] Additionally, mucinous carcinoma of the skin is positive for cytokeratins, vimentin, epithelial membrane antigen (EMA), β-actin, S-100 protein, CEA, succinyl dehydrogenase, β-glucoronidase, as well as estrogen and progesterone receptors.[2,3,5,6,8,10,12,16,27,30,31,33,35,36,37,38,39,40,41,42,43,44] P53 and c-erbB-2 have stained negatively.[1,2]

Treatment for primary mucinous carcinoma of the skin is wide local excision. Surgical margins were reported in 11 of 100 (11%) cases with the average margin noted to be 12.5 mm in least dimension. Given that local recurrence is a significant, it seems reasonable to recommend excision with at least 1 cm margins. Moh’s micrographic surgery has been suggested as an alternative to wide local excision.[9,14,15,20,32,44,47,48] Success with Moh’s procedure, however, assumes a lesion is contiguous, with low rates of lymphatic and hematogenous metastasis. As this may not apply to all mucinous carcinomas of the skin, wide excision is preferable. Moh’s procedure may be helpful for smaller, superficial lesions, and those involving the eyelid, where wide resection is difficult due to anatomic or cosmetic
restraints. While metastasis to regional lymph nodes is rare, lymph node resection is indicated if nodes are clinically involved. Mucinous carcinoma of the axilla is most frequently associated with regional lymph node involvement (33.3%). Given the potentially locally invasive nature of the tumor, we opted to perform prophylactic axillary lymph node dissection in our case and suggest similar management for any mucinous carcinoma of the axilla. Prophylactic lymph node dissection should similarly be considered for recurrent, locally aggressive, or poorly differentiated tumors. Mucinous carcinoma is resistant to both chemotherapy and radiation as primary therapy. As local recurrence is a frequent complication, clinical follow-up at yearly intervals is indicated.

CONCLUSION

Primary mucinous carcinoma of the skin is an uncommon variant of sweat gland tumor with an indolent course and infrequent metastasis relative to true sweat gland tumors. Clinical differentiation from mucinous carcinoma metastatic from another site is difficult, and an aggressive search for a primary tumor site is warranted. Treatment includes wide local excision and lymph node dissection in the setting of clinically positive nodes. Prophylactic lymph node dissection should be considered in tumors of the axilla, as these have a higher rate of metastasis. Because of frequent local recurrences, close follow-up is warranted.

References

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