Primary Mucinous Adenocarcinoma of Skin: Myoepithelial Cells are a Clue to its Diagnosis

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Abstract
Primary mucinous adenocarcinoma is a rare adnexal neoplasm of eccrine gland. Fewer than 200 cases are reported in literature. Clinically, it can be mistaken as a benign lesion. The primary challenge in these lesions is to differentiate these rare primary lesions from more frequent mucinous secondary deposits. Morphologically, they are similar to metastatic deposits of mucinous carcinoma from other viscera such as breast, lung, or gastrointestinal tract. Use of ancillary techniques and a thorough metastatic work up are mandatory to differentiate these lesions from metastases. We report a case of primary mucinous carcinoma of nasojugal region in a 51-year-old female. It was diagnosed on fine-needle aspiration cytology, and later, the lesion was excised and diagnosis confirmed on histopathological examination and immunohistochemistry.

Key Words: Adenocarcinoma, mucinous, myoepithelial cell

Introduction
Primary mucinous adenocarcinoma of the skin is an uncommon neoplasm of eccrine glands. There have been sporadic reports of this entity, after its first description by Lennox et al. in 1952.[1] It has a good prognosis with a high recurrence rate and occasional regional node metastasis. Visceral mucinous carcinomas can metastasize to skin and histologically mimic this lesion. Therefore, it is important to recognize this entity, as treatment and prognosis are different. We report a case of primary mucinous carcinoma of the skin in a 51-year-old female in the nasojugal area, describing the pathological differential diagnosis and a brief review of literature.

Case Report
A 51-year-old female patient presented with a swelling in the nasojugal region of 2-year-duration. The swelling was slowly growing. There was no history of pain or discharge from the swelling. There was no history of trauma. She was a known diabetic for the past 9 years; not a known hypertensive.

On examination, there was a skin colored, non tender swelling measuring 2 cm × 1.5 cm. No sinus or punctum was seen [Figure 1]. The swelling was firm and the overlying skin was not pinch-able. It was mobile, edges were well-defined. Maxillary and mandibular contours appeared normal. No restriction of opening of mouth was observed.

A fine-needle aspiration cytology was done from the swelling which revealed cellular smears. Cells were round to polygonal with moderate eosinophilic cytoplasm. These were arranged in cords and in small clusters. There was mild anisonucleosis. Nuclear chromatin was fine. Few clumps of cells had abundant cytoplasm with eccentrically placed nuclei resembling myoepithelial cells [Figure 2a]. There was an abundant mucoid background. A cytological diagnosis of mucinous neoplasm probably of adnexal origin was suggested in view of cells morphologically resembling myoepithelial cells. An excision biopsy of the lesion was done. Specimen measured 2 cm × 1.5 cm. Cut section was mucoid. Sections revealed tissue lined by keratinized stratified squamous epithelium with a

What was known?
Primary mucinous adenocarcinoma is an uncommon neoplasm of the eccrine gland. It is important to differentiate it from metastatic deposits from other viscera like gastrointestinal tract, lung and breast.

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lesion in the dermis, compartmentalized into lobules by fibrous septae [Figure 2b]. Cells were seen in clumps, islands, and tubules floating in pools of mucin [Figure 2c]. Mucin was periodic acid–Schiff (PAS) positive. Cytoplasm was eosinophilic. There was mild nuclear pleomorphism; mitosis was sparse. These cells were strongly CK7 positive [Figure 2d], CK 20, and TTF negative. The patient was investigated with chest X-ray and ultrasonography abdomen. Before wide excision, the patient had an extensive oncological evaluation which included a positron emission tomography/computed tomography scan. An upper and lower gastrointestinal endoscopy was performed. There was no detectable primary. The lesion was diagnosed as primary mucinous adenocarcinoma of the skin. A wide local excision with at least one centimeter margin was done subsequently, which is the recommended treatment modality in primary mucinous carcinoma of the skin. The patient was put on a biannual follow-up programme and is under regular follow-up with no evidence of recurrence.

Discussion

Primary mucinous carcinoma of skin is a rare adnexal neoplasm. It is an adenocarcinoma the eccrine gland. This tumor was first described by Lennox et al. in 1952.[1] It was later designated by Mendoza and Helwig in 1971.[2] Breiting et al.[3] studied close to 200 cases described in the literature and standardized the incidence as 0.07/million person-years. Mucinous carcinoma most commonly arises in head-and-neck region. The recorded site of occurrence of the tumor is eyelids 41%, scalp 17%, face 14%, axilla 9%, vulva 4%, chest and abdominal wall 7%, neck 2%, canthus 2%, extremity 2%, groin 1%, and ear 1%.[4] Primary mucinous carcinoma is more common in men than in women in a ratio of 2:1. It affects people in the age group of 50–70 years. The tumor was variously designated as adenoid cystic carcinoma, colloid carcinoma, mucinous carcinoma, mucoeipidermoid carcinoma, mucin-secreting carcinoma, and gelatinous carcinoma. With the exception of studies of Mendoza and Helwig most are individual case reports highlighting the rarity of the tumor.

Mucinous carcinoma has varied clinical presentation. Lesions vary from painless papules to nodules. They may be present for several, even up to 20 years.[5] The size varies from 5 mm to 8 cm. They are usually single. The surface may be smooth, ulcerated, or crusted. Clinical differential diagnosis includes sebaceous cyst, hemangioma, lipoma, melanoma, chalazion, neurofibroma, pilomatrixoma, and metastatic deposits. These lesions are slow growing but have a recurrence rate of 29.4% and has a low metastatic rate of 9.6%.[4] Most metastatic deposits are to regional lymph nodes although distant metastasis is described. Aggressive tumors may involve the underlying bone in 7% of cases. Death is reported in 2% of cases. The hypothesis proposed for its slow growth by Mendoza and Helwig is that the copious mucin secretion interferes with cellular nutrition and replication, and these tumors are typically avascular, a factor that helps in low metastasis.

The main histological differential diagnosis for this tumor is a metastatic deposit of mucinous carcinomas arising from other viscera like breast, gastrointestinal tract, respiratory tract, salivary and lacrimal glands and urinary bladder, and prostate and paranasal sinuses. Primary mucinous carcinomas of gastrointestinal tract produce nonsulfated, neutral, and sulfated mucins. The mucin in primary mucinous carcinoma of the skin is PAS positive, mucicarmine positive, and colloidal iron positive; it is hyaluronidase resistant and sialidase labile indicating it is a sialomucin. This helps in differentiating it from metastatic deposits which is usually sulfomucin. Qureshi et al.[6] indicated the presence of myoepithelial...
component in primary mucinous carcinoma as an important feature to differentiate it from metastatic deposits.

Immunohistochemically, these tumors are AE1/AE3, epithelial membrane and carcinoembryonic antigen positive. There is a strong positivity for estrogen receptors and variable positivity for progesterone receptors and S100 protein. The tumor has a low proliferating index by ki-67. These cells express CK7, CK5/6, and p63. They are CK 20 negative. Occasionally, these tumors show focal neuroendocrine differentiation and stain positive to chromogranin and synaptophysin.[7]

Treatment of these tumors is wide local excision with a surgical margin of 1 cm. It is resistant to chemo and radiotherapy. Bad prognostic features include younger age of presentation, Asian background, tumor on the trunk, and swelling more than 1.5 cm. These features are associated with recurrence and metastasis.[8]

Frequent follow-up to look for local recurrence, enlarged lymph nodes will help detect recurrence early so that extensive surgeries can be avoided.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

What is new?
Ancillary techniques like immunohistochemistry play an important role in differentiating primary mucinous carcinoma from secondary deposits. Surgical excision with margins of 1 cm is the treatment of choice. Lesion is resistant to chemotherapy and radiotherapy.

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