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Primary mucinous adenocarcinoma of the scalp: A case report and literature review

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ABSTRACT

INTRODUCTION: Primary mucinous adenocarcinoma or mucinous eccrine carcinoma of the skin is a rare malignant neoplasm showing predilection to the head and neck. Distinguishing between these primary neoplasms and the more frequent metastatic mucinous deposits on the skin from primaries in the breast and gastrointestinal tract constitutes a diagnostic dilemma.
PRESENTATION OF CASE: We report a case of a 61-year-old lady who presented with a slow-growing, painless scalp nodule. Upon excision, it was diagnosed as "primary mucinous adenocarcinoma". An extensive work-up in search for another primary tumour failed to show a primary malignancy elsewhere and the diagnosis of a primary eccrine mucinous adenocarcinoma of the skin was rendered.
DISCUSSION: A review of the literature on this entity is presented, discussing diagnostic challenges and therapeutic options that of interest to surgeons, pathologists and dermatologists.
CONCLUSION: These tumours are indolent and low-grade, with a tendency for local, sometimes multiple, recurrences. Proper patient counselling and follow-up are important in treatment. Sound collaboration between clinicians and pathologists, for good therapeutic results, is of utmost importance.

1. Introduction

Mucinous sweat gland carcinoma is a rare malignant tumour of the skin. We report herein the case of a 61-year-old lady who presented with a scalp mass. After excision, histopathological examination of the mass revealed mucinous adenocarcinoma. Extensive metastatic work-up, including a total body computed tomographic and positron emission scan (PET/CT scan), showed the neoplasm to be a primary mucinous adenocarcinoma of the skin. Distinguishing this primary neoplasm from metastatic mucinous adenocarcinoma originating from other primary sites in particular from the breast presents a diagnostic dilemma. A review of the literature of this rare, yet challenging, entity follows.

2. Report of a case

A 61-year-old lady, of Caucasian origin, presented to our care with a slow growing, painless, spherical, scalp nodule overlying the right temporal region, measuring 1.5 × 1 cm. The mass was subcutaneous, being tethered to the skin, yet mobile with respect to the underlying skull. It was firm, non-compressible, non-pulsatile and showed no central punctum. The nodule was present for the last 5 years with no history of pain, secretions or overlying redness. Upon examination, no regional lymphadenopathy or abnormal findings in the head or neck region could be noticed. The patient had been medically followed up in the past with regular screening for breast cancer and gastrointestinal disease, namely colorectal cancer.

An excisional biopsy of the nodule was done under local anaesthesia with no adverse events and the skin defect was primarily closed. Histopathological examination of the mass showed hair-bearing skin with underlying lakes of mucin separated by delicate fibrous septae. Floating in between the mucinous lakes were nests, clusters, and cords of predominantly uniform round to cuboidal epithelial cells that exhibit mild to moderate nuclear variability. Focal areas show duct formation. Occasional tumour nests show prominent proliferation of cells with cribriforming. The tumour showed no connection to the overlying skin or adnexal structures (See Fig. 1). The neoplastic cells were strongly positive for cytokeratin 7 (CK7) and oestrogen and progesterone receptors. The cells were negative for cytokeratin 20 (CK20) and Her-2-neu (See Fig. 2).

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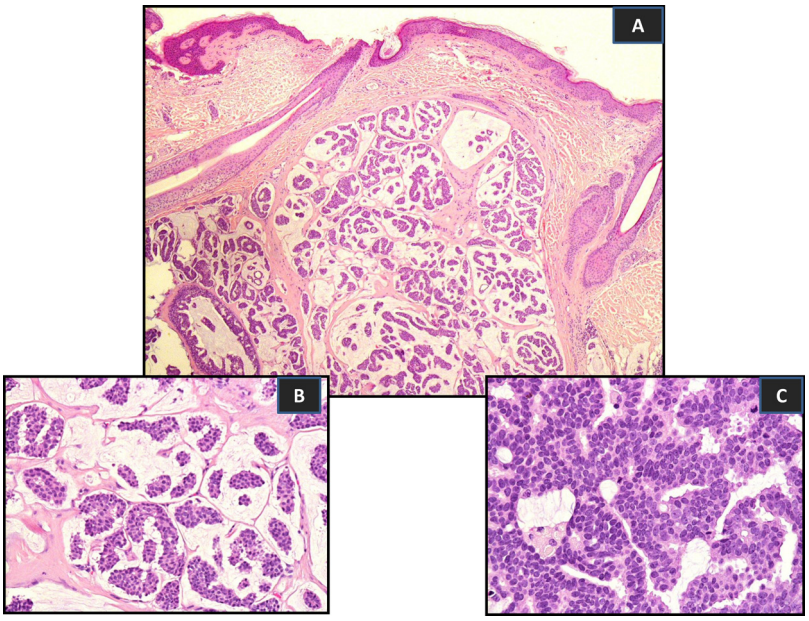

Fig. 1. A. Low power view of the skin nodule exhibiting skin with underlying lakes of mucin compartmentalised by delicate fibrous septae and floating nests and ducts of tumour cells B&C. Higher power showing variability in cellularity and proliferation of neoplastic cells ranging from less cellular nests/ducts to more cellular areas with cribriforming.

The morphologic and immunohistochemical features were consistent with mucinous adenocarcinoma. As the histopathological distinction between primary eccrine mucinous adenocarcinoma and metastatic mucinous tumour is almost impossible, it was recommended to do a complete workup to exclude the presence of a primary involving an extracutaneous site, especially the breast.

At this stage, the patient was referred to a cancer centre. She had an extensive oncological evaluation, including a detailed clinical assessment and a PET/CT scan, in search of a possible primary mucinous adenocarcinoma originating mainly in the breast and gastrointestinal tract, resulting in a negative metastatic work-up. Therefore, the diagnosis of a primary eccrine mucinous adenocarcinoma of the scalp was confirmed. She underwent Moh's micrographic surgery until negative margins were obtained. Having no evidence-based data regarding treatment, follow-up and recurrence rates of this tumour, the patient was put on a biannual follow-up programme for possible early detection of local recurrence or metastasis in relation to this unusual tumour.

3. Discussion

Primary eccrine mucinous adenocarcinoma of the skin is a rarely described pathological entity. This neoplasm was first described by Lennox et al. [1,2] in 1951, it affects more men than women in an approximately 2:1 ratio, mostly seen in 5–7th decade with an average age at occurrence of 61 years (range 8–84 years) [3,4]. There is an increased predilection to white rather than African American, East Asian or Indian individuals [5,21]. The majority of these tumours are located in the head and neck; however, less frequently, they may arise from other areas of the body [6]. More than 50% of reported cases are located in the peri-orbital region and the hair-bearing scalp [1,7].

Typically, these tumours present as slow growing, painless, soft, sometimes indurated, reddish or grey-blue, non-ulcerating nodules that have been present for several years [1,3], with longer courses for up to 20 years prior to presentation being reported [8]. The presentation of these neoplasms in the form of ulcers or cysts has also been described [3]. The tumours usually range in size between 1 and 8 cm [4], the mean diameter prior to excision being reported to be around 1.8 cm [21]. However, larger variants have been described in literature [4]. The nodules are well circumscribed, unencapsulated, and often fixed to the dermis making them unable to be "shelled out". The cut surface is mostly gelatinous.

These tumours are considered low-grade malignant neoplasms with an indolent course, having a tendency for local recurrence (19.6%) and metastasis (6.1%) after surgical treatment over a mean follow-up period of 37.4 months [21], with most metastases being to the regional lymph nodes [9,10]. Distant metastases have been reported in 2–7 percent of affected patients [6]. However, these tumours more frequently invade tissues by direct extension, due to the presence of satellite islands of tumour cells present around the main nodule, and via regional lymph node invasion [11,12]. Death due to mucinous adenocarcinoma of the skin is exceptional with only less than 5 cases reported thus far, most associated with multiple tumour recurrences and widespread metastatic disease [13].

The clinical presentation of mucinous carcinoma is nonspecific and the differential diagnosis includes epidermoid cyst, pyogenic granuloma, melanoma, sebaceous cyst, sebaceous carcinoma, cystic basal cell carcinoma, neuroma, lacrimal sac tumour, haemangioma, pilomatricoma, lipoma and metastatic adenocarcinoma [5,14].

Histogenesis of this tumour has not been clearly elucidated. There is strong evidence that these neoplasms arise from eccrine ducts, however, some studies support that at least a subset of these tumours to be originating from apocrine ducts [15].

The primary challenge in diagnosis lies in differentiating these rare primary skin neoplasms of sweat gland origin from the more frequent mucinous secondary deposits to the skin from primaries elsewhere. Mucin-producing primary tumours are known to originate in the breast, gastrointestinal tract, lung, kidney, ovaries, pancreas and prostate [3,16]. Metastatic lesions from the breast and colon are most likely to mimic mucinous carcinoma of the skin, knowing the fact that 19% of men with colon cancer and 6% of women with breast cancer have metastatic skin disease [14,17]. Differentiating secondary deposits, particularly from these two sites from primary mucinous skin carcinoma based on morphologic evaluation alone is almost impossible. Therefore, the

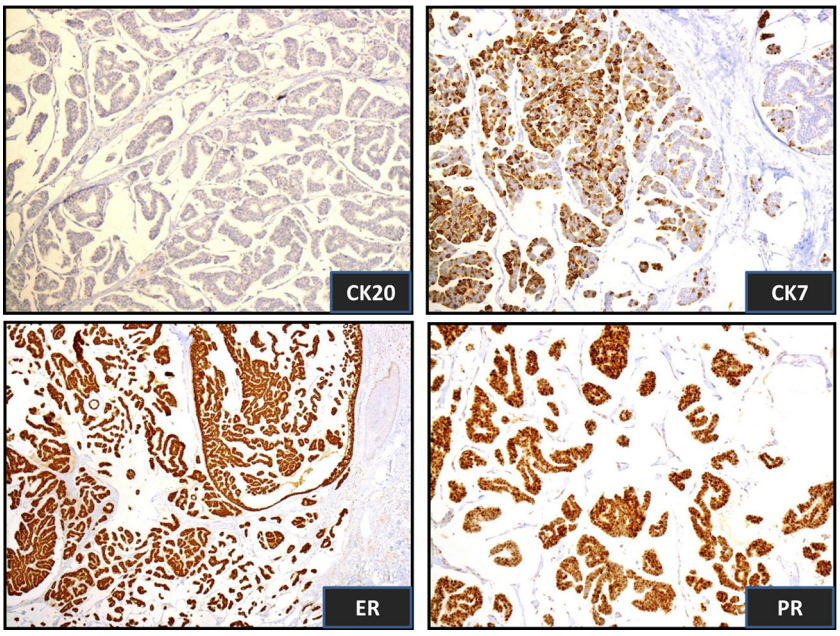

Fig. 2. Immunohistochemistry shows tumour cells to be strongly positive for CK7, oestrogen receptors (ER), and progesterone receptors (PR) and negative for CK 20.

differentiation is mainly based on firstly, ruling out the presence of another primary malignant site through a full oncological evaluation and, secondly, on certain histological and pathological characteristics of the mucinous lesion.

Histologically, these tumours are generally well circumscribed, unencapsulated, asymmetric, dermal nodules that may extend to involve subcutis and even deeper tissue planes. Most tumours show no connection to the overlying epidermis or skin adnexae. Characteristically, there are pools of basophilic mucin compartmentalised by delicate thin fibrous septae creating a honey comb pattern. Within these mucinous lakes are small islands, clusters, and/or tubules of floating epithelial cells (Fig. 1A). The neoplastic cells are round to cuboidal with abundant eosinophilic to clear cytoplasm, small central nuclei, minimal nuclear pleomorphism, and only rare mitotic figures (Fig. 1B&C). These tumour cells are often grouped in nests and duct-like structures reminiscent of eccrine and apocrine sweat glands. Some glandular structures show prominent proliferation and may form a cribriforming pattern. Smaller tumour satellites may occur around the primary nodule. Epidermotism by these neoplastic cells is an unusual feature [3,14]. The presence of copious amounts of mucin has been hypothised to serve as a physical barrier to spread, compressing the tumour stroma and restricting growth, as well as inhibiting DNA synthesis, decreasing the rate of angiogenesis [3,16], and consequently metastatic disease [9].

Histologic distinction between primary and secondary tumours may be impossible, albeit the latter may show certain features supporting metastasis such as less abundance of mucin, larger tumour clusters and sheets with predominance of malignant epithelial cells over mucin, and lack of honey combing due to the absence of fibrous septae in-between the mucinous lakes [18].

Histochemical and immunohistochemical staining can assist in differentiating tumour types. The tumour cells express cytokeratin AE1/AE3, epithelial membrane antigen (EMA), and carcinoembryonic antigen (CEA) in keeping with its derivation from secretory lobule. There is strong nuclear staining for oestrogen receptors and variable but mostly positive staining for progesterone receptors (Fig. 2). The cells are also often positive for alpha-lactalbumin, salivary amylase, beta-2-microglobulin, cytokeratin CAM 5.2, and gross cystic disease fluid protein -15 (GCDFP-15). There is variable expression of S-100 protein. The tumour shows a low proliferation index by Ki-67. In addition, the cells are negative for CK20, a helpful feature in distinguishing it from metastasis from primary gastrointestinal tumours that are often CK20 positive (Fig. 2). Primary tumours may occasionally show focal neuroendocrine differentiation as evidenced by positive reaction by Grimilius, and positive staining by chromogranin, synaptophysin, and neuron specific enolase (NSE) [3,15,18]. Alcian blue staining of primary skin lesions is positive at a pH of 2.4 but is negative at a pH of 0.4, differentiating them from other sweat gland tumours [14]. The mucin in primary skin lesions is a sialomucin which is resistant to digestion with diastase and hyaluronidase but sensitive to sialidase [3,16], unlike mucinous lesions from gastrointestinal primaries that contain sulphomucin [14,19]. Moreover, cytokeratin 20 (CK20) is commonly expressed in gastrointestinal neoplasms but absent in skin primaries. Additionally, the expression of cytokeratin 5, 6 and 7 (CK5/6/7) (Fig. 2) and p63 in primary eccrine carcinoma of the skin (indicating the presence of myoepithelial cells) can help exclude metastatic mucinous breast carcinoma [20]. In summary, although helpful, histopathological features cannot exclude metastatic disease with 100% certainty; therefore, the importance of a full metastatic work-up cannot be overemphasised.

As for treatment, surgical excision of primary eccrine mucinous adenocarcinoma of the skin is the therapeutic mainstay in most cases. Because of the recurring nature of the tumour, adequate excision with wide margins (at least 1 cm) is advocated. Moh's micrographic surgery can be a particularly advantageous treatment modality in this setting. These tumours are generally resistant to radiotherapy and chemotherapy and these tools are not usually employed [3,14]. Finally, patients are to be counselled about the importance of frequent follow-up to rule out local tumour recurrence or the development of regional lymphadenopathy. Knowing that younger patient age at presentation, Asian background, location of the tumour on the trunk, tumours larger than 1.5 cm and longer follow-up periods are factors that could be associated with poor outcomes, namely, recurrence and metastasis [21].

4. Conclusion

Before a diagnosis of a primary mucinous adenocarcinoma is established, a primary mucinous carcinoma of breast, gastrointestinal tract, or other organs must be excluded as the majority of cutaneous mucinous carcinoma cases, in fact, represent metastasis. Primary mucinous carcinoma of the skin, in contrast to other sweat gland carcinomas, is an indolent low-grade malignant tumour with tendency for local, sometimes multiple, recurrences. Distant metastasis is rare and is often limited to regional lymph nodes. Primary eccrine mucinous adenocarcinoma of the skin poses challenges in relation to its diagnosis and differentiation from metastatic adenocarcinoma to the skin and with regard to its treatment. Its rarity precludes comparative evaluation of therapeutic options. However, sound collaboration between clinicians and pathologists, for a good therapeutic result, is of utmost importance. Proper patient counselling and follow-up are important in treating this low-grade, indolent and frequently recurring tumour.

Conflicts of interest

Nothing to declare.

Sources of funding

Nothing to declare.

Patient's consent

Informed consent has been obtained from the patient and a copy of this document is available when requested. The figures related to the article are pathological slides and contain no information that may affect patient's privacy in any way.

Authors contribution

Osama S. Al Beteddini: The corresponding author. General surgeon. He has written the case report and collected relevant data for the literature review.

Salwa Sheikh: Author, pathologist. She has provided all information related to the histopathological properties of the tumour. She has further provided the pathological slides. She has reviewed the article and rewritten the section on pathology of the article.

Faisal Shareefi: Author, plastic and reconstructive surgeon. He is the attending physician of the patient. He has reviewed the article.

Rana Shahab: Author, dermatologist. She has referred the patient to surgical care. She has reviewed the article.

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