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Primary vs. Metastatic Mucinous Adenocarcinoma of the Skin: a Case Report and Discussion of Immunohistochemical Techniques

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Abstract. *Background:* Primary mucinous adenocarcinoma of the skin is a rare malignant sweat gland tumor, which is difficult to distinguish from metastatic adenocarcinoma. *Purpose:* Describe a case of mucinous adenocarcinoma of the scalp and discuss the usefulness of immunohistochemical techniques in the diagnosis of primary vs. metastatic mucinous adenocarcinoma. *Case Report:* A 58 year old female presented with a cyst on her scalp, which was initially diagnosed as a metastatic mucinous adenocarcinoma. After radiological evaluation the malignancy was determined to be a primary mucinous adenocarcinoma of the scalp. Treatment included wide excision and radiation therapy with no recurrence or metastasis on follow up. *Conclusion:* This case report describes challenges in the diagnosis of primary vs. metastatic mucinous adenocarcinoma of the skin.

1. Introduction

Primary mucinous adenocarcinoma of the skin is a rare subtype of malignant sweat gland tumor first described by Lennox et al. in 1952 [1]. This tumor has a benign appearing clinical presentation and runs an indolent course. The differential diagnoses include: epidermal inclusion cyst, lipoma, hemangioma, cystic basal cell carcinoma, melanoma, squamous cell carcinoma, and most importantly metastatic mucinous adenocarcinoma. Mucinous adenocarcinomas that most commonly exhibit cutaneous metastasis are breast, gastrointestinal (GI) tract, lung, ovary and prostate malignancies [2]. Since primary mucinous adenocarcinoma of the skin has a more favorable clinical outcome than metastatic lesions, it is not only important to identify mucinous adenocarcinoma as a possible malignancy, but also to determine if this is a primary neoplasm or a cutaneous metastasis from a primary tumor.

2. Experiment, Results, Discussion, and Significance

Case Report: A 58 year old Caucasian female was seen in the dermatology clinic with a complaint of a “bump” on her head. The lesion presented as a 2 to 3 cm nodular cyst in the left parietal region of the scalp. The patient denied any pain, headaches, fever, chills, night sweats, numbness, weakness, paresthesias or blurred vision. Past medical history included squamous cell carcinoma, gastroesophageal reflux, depression, osteoporosis, hyperlipidemia and osteoarthritis. Past surgical history included tonsillectomy. The patient’s medications included esomeprazole (Nexium®) 40 mg once daily, paroxetine (Paxil®) 12.5 mg once daily, alendronate (Fosamax®) 70 mg once weekly and ezetimibe/simvastatin (Vytorin®) 10/20 mg once daily. She was allergic to sulfa agents, amoxicillin, celecoxib (Celebrex®) and rofecoxib (Vioxx®). Patient’s family history was significant for a maternal aunt having colon cancer. Physical examination and review of systems were negative. The lesion was clinically diagnosed as a sebaceous cyst and the patient was told to monitor the lesion for any changes. The patient came back for further evaluation 15 months later. At that time she was still asymptomatic and no noticeable changes to the lesion occurred. At a follow-up appointment 18 months after the initial diagnosis, the patient reported increased swelling and redness, as well as tenderness to palpation. Skull radiographs were performed, which were grossly negative. At the next evaluation 20 months after the initial diagnosis, a biopsy of the lesion was performed and the pathology report identified the tumor as a mucinous adenocarcinoma. Differential diagnosis was that of metastatic mucinous adenocarcinoma. As the majority of cases of mucinous adenocarcinoma of the skin are noted to be cutaneous metastasis from another site, such as breast, GI tract and lung, among other sites, investigations were initiated in search of a primary tumor. A computerized tomography (CT) scan of the chest, abdomen and pelvis was performed, which showed no evidence of occult mass pathology. Upper and lower GI series, positron emission tomography scan, mammogram and pelvic sonogram were all negative for a primary tumor. A wide excision of the lesion with sentinel lymph node biopsy was performed, which demonstrated clear excision margins and extensive sentinel lymph node, as well as perinodal involvement. Neoplasm closely approached the deep margin of excision, but did not appear to cross it. The specimen also tested estrogen and progesterone receptor positive. The patient received

regional radiation therapy and was started on tamoxifen. Follow up CT scans of the chest, abdomen and pelvis six months, one year and two years later showed no evidence of local or distant malignancy.

Discussion: Clinical presentation of primary mucinous adenocarcinoma of the skin varies. The most common manifestation is an asymptomatic, well circumscribed, cystic nodule with benign appearance [2]. When evaluating a patient for a possible primary mucinous adenocarcinoma of the skin, a differential diagnosis of metastatic mucinous adenocarcinoma from a distant site cannot be excluded. Because the presence of metastatic lesions carries a less favorable prognosis and requires aggressive treatment, a correct diagnosis is crucial in preventing delay in implementation of appropriate evidence-based treatment protocols. Most common primary sites of metastasis include the breast, GI tract, lung and ovary. Of these, mucinous adenocarcinoma of the breast most commonly resembles the tumor histologically [2].

Immunohistochemical Techniques: Studies have demonstrated that primary mucinous adenocarcinomas of the skin can demonstrate remarkably diverse morphology and can be morphologically indistinguishable from metastatic cutaneous neoplasms, especially mucinous adenocarcinomas of the breast [2]. Various immunohistochemical panels have been used by several authors in an attempt to accurately distinguish between primary and metastatic mucinous adenocarcinoma of the skin. Immunohistochemical markers used in previous studies included cytokeratin (CK) 20, myoepithelial cells, transcription factor p63, CK 5/6, CK 7 and human milk fat globulin (HMFG) [3]. To date, only positive staining for CK 20 has been a consistent indicator of metastasis from the GI tract. In contrast, the absence of CK 20 expression cannot reliably confirm diagnosis of primary mucinous adenocarcinoma of the skin [3]. In addition, immunostaining for transcription factor p63, a newly discovered homolog of the p53 gene, is often positive in primary neoplasms and negative in metastatic lesions [4]. However, it may also be negative in primary mucinous adenocarcinoma, and therefore cannot be reliably used to discriminate between the two [3, 4]. Expression of other immunohistochemical markers, including CK 5/6, CK7 and HMFG so far has not been very promising in differentiating primary mucinous adenocarcinoma of the skin from metastatic lesions, as these markers are often positive in both primary and metastatic lesions [3]. Despite some promising recent research, distinguishing primary mucinous adenocarcinoma of the skin from a cutaneous metastasis remains a challenging task, complicated by the rarity of this tumor and unavailability of complete immunohistochemical data. At the same time, immunohistochemical profiles using multiple markers can be helpful in establishing a correct diagnosis and should be used in conjunction with other clinical information, including patient history, location of the lesion, and a careful workup to rule out cutaneous metastasis from another site.

3. Conclusions

Primary mucinous adenocarcinoma of the skin is a rare malignant tumor of sweat gland origin. Because it occurs so infrequently, many health care providers may be unaware of this malignancy and its classical clinical presentation. Delays in diagnosis of this neoplasm can lead to local tissue destruction, regional lymph node invasion, and even distant metastasis. This case deserves attention not only for the rarity of the tumor, but also for the challenges in diagnosing primary vs. metastatic mucinous adenocarcinoma, since both types of neoplasms share similar morphological presentation and several immunohistochemical markers. This case report also illustrates that the differential diagnosis of metastatic mucinous adenocarcinoma can be ruled out only after careful investigation with the use of appropriate immunohistochemical panels, and extensive search for other possible primary sites utilizing relevant imaging techniques.

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