Cytological features of malignant eccrine acrospiroma presenting as a soft tissue mass axilla: A rare sweat gland tumor with histologic correlation

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Abstract

Malignant eccrine acrospiroma is an infrequent, highly malignant primary skin tumor derived from eccrine sweat glands. Though fine-needle aspiration cytology (FNAC) is a well-established diagnostic tool, but if a skin adnexal tumor or primary skin lesion is suspected clinically, the usual approach is biopsy due to easy accessibility. Being itself rare, cytologic features of this lesion is hardly encountered in case reports. As a result, very little is known about the appearance of adnexal tumors like malignant eccrine acrospiroma on fine-needle aspiration samples. A 50-year-old man presented with swelling in the left axilla, clinically suspected to be a soft tissue sarcoma. Fine-needle aspiration was advised, and a cytological diagnosis of malignant eccrine acrospiroma was rendered which was later confirmed on histological examination. Rapid, accurate diagnosis of these tumors is imperative as they have very poor prognosis and an aggressive course with recurrence and/or metastasis. FNAC plays a decisive and easy diagnostic modality in these unusual, rare cases of highly malignant primary skin tumor, and awareness of the lesions is indispensable in their management.

Key words: Aspiration cytology, clear-cell hidradenocarcinoma, fine-needle, malignant eccrine acrospiroma, sweat gland tumor

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Introduction

Malignant eccrine acrospiroma is a rare, aggressive tumor of eccrine sweat gland origin. Since its first description in 1954 by Keasbey and Hadley,[1] several names have been used in the literature to designate this entity, including clear-cell hidradenocarcinoma, malignant clear-cell hidradenoma, malignant clear-cell acrospiroma, clear-cell eccrine carcinoma, nodular hidradenocarcinoma, malignant nodular clear-cell hidradenoma, and mucoepidermoid hidradenocarcinoma. It is a rare tumor with a predilection for the face and extremities,[2] but may appear in any area. It seems to be slightly more frequent in women than in men, with the mean age of 50 years, but cases have been also reported in children[3] and neonates.[4]

We hereby describe a case that was diagnosed as malignant eccrine acrospiroma presenting as a soft tissue mass of axilla on fine-needle aspiration cytology (FNAC), and was later confirmed on histological examination. An attempt is made to document the cytological features of malignant eccrine acrospiroma in the present case with discussion of differential diagnosis.

Case Report

A 50-year-old man presented with a swelling in the left axilla of 2 months duration. Initially, it was a small swelling that had increased progressively and reached a size of 7 cm × 5 cm. The patient was febrile on and off for last 2 months. He had no significant past or medical history. There was no regional...
lymphadenopathy; general physical and systemic examination was within normal limits. Local examination of left axilla revealed a large, firm, nontender pedunculated swelling of size 7 cm × 5 cm. Skin overlying the swelling was inflamed and ulcerated. With a clinico-radiological diagnosis of soft tissue sarcoma, the patient was referred for FNAC.

Cytological findings
Highly cellular smears showed cohesive cell clusters of malignant cells composed of two cell population; polyhedral cells with dense basophilic cytoplasm along with glycogen containing pale/clear cells with a clear cytoplasm. The nuclei were cytologically pleomorphic, hyperchromatic, round to oval with coarse chromatin and prominent nucleoli. The nuclei were eccentrically located within a moderate amount of basophilic cytoplasm, with a relatively well-defined cell borders imparting a plasmacytoid appearance. There were many bi- and multinucleated cells [Figures 1a and b]. Few cells were showing squamous differentiation. At places acinar pattern and tubule formation along with numerous mitotic figures were seen. Cytological diagnosis of malignant eccrine acrospiroma was offered. Subsequently, surgical excision with adequate margins was done and sent for histopathological examination.

Histological findings
Gross examination revealed an ulcerated skin covered well-circumscribed solid mass measuring 5 cm × 4 cm × 3 cm [Figure 1c]. Cut section was grey-brown with areas of hemorrhage and necrosis. Microscopic examination showed a skin covered tissue revealing sharply demarcated lobules of tumor cells located in the dermis and extending into the subcutaneous tissue. There was no connection between the epidermis and the tumor. Most of the lobules were solid and some contained cystic spaces filled with homogenous, eosinophilic material and lined with a thick coat of tumor cells. Interstitial hyaline collagen changes were present around lobules. The cell population was made up of two cells types; predominantly clear cell type and fusiform cell type with eosinophilic cytoplasm [Figure 1d]. The tumor cells were highly pleomorphic with irregular nuclear membrane, coarsely clumped nuclear chromatin, prominent nucleoli, and clear cytoplasm. Numerous mitotic figures and atypical mitotic figures were appreciated [Figure 2]. Tumor cells were seen invading into the surrounding stroma. Angioinvasion was visible along with focal areas of necrosis. No basaloid, sebaceous, or trichilemmal differentiation were noted. Periodic acid-schiff (PAS) positive diastase-resistant material was demonstrated in clear cytoplasm. Hence, a diagnosis of malignant eccrine acrospiroma was made.

Discussion
Malignant eccrine acrospiroma is an infrequent, highly malignant primary skin tumor derived from eccrine sweat glands. They have very poor prognosis, and an aggressive course with recurrence and/or metastasis. The neoplasm does not have any distinctive clinical features and usually presents as a slow growing solitary dermal or subcutaneous nodule and can be present for several years without apparent change. They can appear as de novo disease or as a malignant transformation of nodular hidradenoma. In a review by Hernández-Pérez and Cestoni-Parducci, 6.7% of cases of malignant variant arose in preexisting benign nodular hidradenoma. Diagnosis is very difficult, and often the preoperative diagnosis is incorrect, as in our patient who was diagnosed clinico-radiologically as soft tissue sarcoma. In a review of 35 cases of eccrine adenocarcinoma, Mehregan et al. showed that none were diagnosed correctly preoperatively, and specifically, the two cases of nodular hidradenocarcinoma

![Figure 1a](image1a.png): Fine-needle aspiration smears showing cohesive cell clusters of malignant cells composed of two cell population; polyhedral cells with dense basophilic cytoplasm along with cells with clear cytoplasm. (MGG stain, ×200)

![Figure 1b](image1b.png): High power view revealing highly pleomorphic atypical basaloid cells, bi- and multinucleated tumor cells with atypical mitotic figure (arrow). (MGG stain, ×400)
were misdiagnosed. The diagnosis is primarily based on histopathological, immunohistochemical, or ultrastructural features. These tumors, therefore, can be considered clinico-pathological dilemmas with an unpredictable biological behavior. Rarely diagnosed clinically, they are often encountered as histological surprise.\(^7\)

Grossly, they appear as nodular dermal masses with or without skin changes with a firm, fibrous appearance simulating a connective tissue tumor.\(^5,8\) The histology of malignant eccrine acrospiroma resembles that of its benign counterpart. The histologic features characteristically entail a prominent nodular (lobular) pattern. Usually, there is no connection between the epidermis and the tumor, but the surface epithelium may be ulcerated. The tumor may display increased mitotic activity with focal areas of necrosis.\(^9,10\) The reliable criteria of malignancy include infiltrative growth, presence of nuclear atypia, number of mitotic figures, predominantly solid islands, as well as perineural and angiolymphatic invasion.\(^11\) Some authors have proposed a subclassification of malignant eccrine acrospiroma into high grade, low grade, and atypical hidradenoma with focal atypia.\(^6\)

The neoplastic cells are usually positive for PAS but negative for PAS with diastase digestion, indicating glycogen content rather than mucin. Immunophenotypically, they show reactivity for cytokeratin (AE1/AE3, CAM5.2, CK5/6, etc.), Carcinoembryonic antigen and epithelial membrane antigen decorate the luminal border of ductal structures. They are characteristically negative for the androgen receptor and myoepithelial markers (smooth muscle actin, calponin, etc.).\(^12,13\)

If a skin adnexal tumor or primary skin lesion is suspected clinically, the usual approach is biopsy due to easy accessibility. However, on rare occasions, these tumors do undergo fine-needle aspiration. As a result, there is a paucity of case reports describing the cytomorphological features of adnexal tumors like malignant eccrine acrospiroma. As it is an uncommon tumor and rarely undergo aspiration, only infrequent case reports describing the cytologic features are available in the literature.\(^14,15\) The rarity of this neoplasm and failure to identify its morphologic features may lead to misdiagnosis. They are usually reported only after histopathological examination. In our case, the cytodagnosis of malignant eccrine acrospiroma of the axilla was rendered on account of the presence of cohesive cell clusters, two cell patterns composed of polyhedral cells with dense cytoplasm and a basaloid appearance and glycogen containing pale/clear cells, with a clear cytoplasm, tubular formation, nuclear anaplasia and increased number of mitotic figures. Later, it was confirmed by histopathology to be a malignant eccrine acrospiroma.

The histopathological differential diagnosis generally includes other tumors with clear cell change such as sebaceous carcinoma, trichilemmal carcinoma, clear cell changes in
squamous cell carcinoma, balloon cell melanoma, basal cell carcinoma, porocarcinoma, and metastatic renal clear cell carcinoma.\[11\]

Sebaceous cell carcinoma and trichilemmal carcinoma, which may have the most overlapping features with malignant eccrine acrospiroma, both lack cuticles and show at least focally microvesicular cytoplasm and indented nuclei in sebaceous cell carcinoma and trichilemmal-type keratinization in trichilemmal carcinoma. Furthermore, the majority of sebaceous cell carcinoma show immunoreactivity for androgen receptor markers, which are not expressed in malignant eccrine acrospiroma.\[11\]

Basal cell carcinoma, clear cell changes in squamous cell carcinoma, and porocarcinoma generally have an intraepidermal component, and they also lack cuticular differentiation.\[11\] Balloon cell melanoma does not demonstrate squamous or cuticular differentiation and the tumor cells are always cytokeratin negative and usually S100 and HMB45 positive.\[11\] While metastatic renal cell carcinoma to the skin may be nodular and composed of clear and eosinophilic epithelial cells, the presence of rich sinusoidal vascular network and often the existing history of primary renal neoplasm should help in establishing the correct diagnosis.\[11\]

Prognosis for malignant eccrine acrospiroma is generally very poor. The tumor has up to 50% local recurrence rate and a 60% metastatic rate within the first 2 years.\[16\] Metastasis favors the regional lymph nodes followed by the lung and the bone.\[11\] Disease-free 5-year survival has been reported at less than 30%.\[16\] Treatment is surgical excision with adequate margins to minimize the risk of recurrence followed by histological confirmation of adequacy of excision.\[9,17\]

Malignant eccrine acrospiroma is an infrequent malignant tumor that is often misdiagnosed preoperatively, and that must be treated with aggressive multimodality therapy for increased survival. Rapid, accurate diagnosis of these tumors is imperative as they have very poor prognosis and an aggressive course with recurrence and/or metastasis. FNAC plays a decisive and easy diagnostic modality in these unusual rare cases of highly malignant primary skin tumor, and awareness of the lesions is indispensable in their management.

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