

Fine-Needle Aspiration Cytology of Metastatic Eccrine Porocarcinoma

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Eccrine porocarcinoma (EP), although rare, is widely recognized as the most common malignant sweat gland tumor. EP typically grows slowly and usually is cured by surgical excision with clear margins. An elevated mortality rate, however, is observed when regional lymph nodes are involved. We herein describe cytohistologic findings in a case of metastatic EP. An 86-year-old man with a history of EP of the left lateral ankle and squamous cell carcinoma in situ (Bowen's disease) of the penis presented with enlarged left inguinal lymph nodes. A superficial fine-needle aspiration (FNA) was performed and demonstrated a hypercellular sample with discohesive clusters and/or individual tumor cells. The tumor cells were round or oval with most of the cells showing dense, refractile cytoplasm. Intracytoplasmic vacuoles were readily appreciated in some of the cells. Nuclear enlargement, high N/C ratio, nuclear hyperchromasia, bi- and multinucleation, and prominent nucleoli were seen. A diagnosis of metastatic eccrine porocarcinoma was rendered. Enlarged retroperitoneal lymph nodes were detected and CT-guided left retroperitoneal core biopsy was performed 1 week later. The biopsy revealed features consistent with metastatic eccrine porocarcinoma. Diagn. Cytopathol. 2009;37:755–758. © 2009 Wiley-Liss, Inc.

Key Words: fine-needle aspiration; cytology of porocarcinoma; metastatic porocarcinoma

Eccrine porocarcinoma (EP) is a rare malignant adnexal tumor of the skin derived from the eccrine sweat gland. Pinkus and Mehregan first described the entity in 1963¹ and Mishima and Morioka introduced the term of EP later in 1969.² The tumor reported by the latter authors was described as an intraepidermal proliferation of tumor cells and intraepidermal ducts among the tumor cells, the latter

resembled eccrine sweat ducts in the epidermis and clefts. The authors further identified the intraepidermal portion of the eccrine sweat duct (the acrosyringium) as the point of origin of the tumor and the term of porocarcinoma (poro = duct) was thus coined. EP may result from malignant transformation of a benign eccrine poroma or occur de novo.^{3–5} The largest series of cases studied to date demonstrated that EP most commonly involves lower extremities, trunk, and head.⁶ There is a predilection for elderly patients in the fifth to eighth decades of life.^{7–10} Inconsistent observations have been reported with regard to gender preference.^{11–14} The natural course of EP varies. EP characteristically grows slowly and is usually cured by wide surgical excision with clear margins.¹⁵ However, this neoplasm may behave in a more aggressive fashion and ~20% of patients experience local recurrence and/or regional lymph node metastasis.^{1,4,11} When regional lymph nodes are involved, an elevated mortality rate of >65% is observed.¹¹ We herein report the cytohistologic findings in a case of EP that metastasized to regional lymph nodes.

Case Reports

An 86-year-old man with a history of EP of the left lateral ankle and squamous cell carcinoma in situ (Bowen's disease) of the penis, presented with a 0.5-cm palpable left inguinal lymph node. A superficial fine-needle aspiration (FNA) of a left inguinal lymph node was performed using a 25-gauge needle. A total of five passes were performed. For each pass, two direct smears were prepared and the needle was then rinsed in the CytoLyt solution from which a cell block was prepared and a 4- μ m section was stained with hematoxylin and eosin. Half of the smears were air-dried and stained with Diff-Quick. The remaining smears were rapidly fixed by the Sprayfix™ and later stained with Papanicolaou technique. The smears were hypercellular and consisted of discohesive sheets and clusters of round and oval neoplastic cells, as well as

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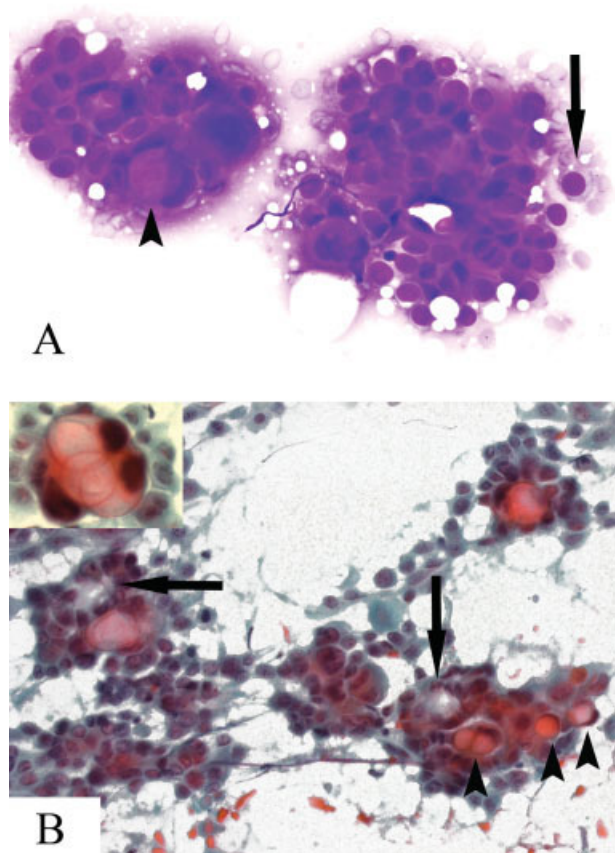


Fig. 1. Diff-Quik stain (A) and Pap stain (B) show clusters of neoplastic cells with high N/C ratio, nuclear pleomorphism, hyperchromasia, and occasionally prominent nucleoli. A: Cells with squamoid features (arrow), and intracytoplasmic vacuoles (arrowhead) in Diff-Quik ($\times 400$). B: Intracytoplasmic vacuoles (arrowhead) and acinar configuration (arrow) in Papanicolaou stain ($\times 400$). The insert also shows intracytoplasmic vacuoles (Papanicolaou stain, $\times 600$). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

single scattered cells. Some cells showed squamoid features that were manifested by ill- to well-defined intercellular boarder, moderate to dense refractile cytoplasm which appeared deep blue on Diff-Quick stain and cyanophilic on Papanicolaou stain. Other cells attempted to form acini and exhibited intracytoplasmic vacuoles. High N/C ratio, nuclear enlargement, pleomorphism in size and shape of nuclei, nuclear hyperchromasia, and occasionally prominent nucleoli were appreciated (Fig. 1). Bi- and multinucleation were rarely seen. The cell block contained some tumor cells with intracytoplasmic vacuoles which were highlighted with polyclonal carcinoembryonic antigen (CEA) antibody. Based upon these findings, a diagnosis of metastatic eccrine porocarcinoma was rendered.

Enlarged retroperitoneal lymph nodes were detected and CT-guided left retroperitoneal core biopsy was per-

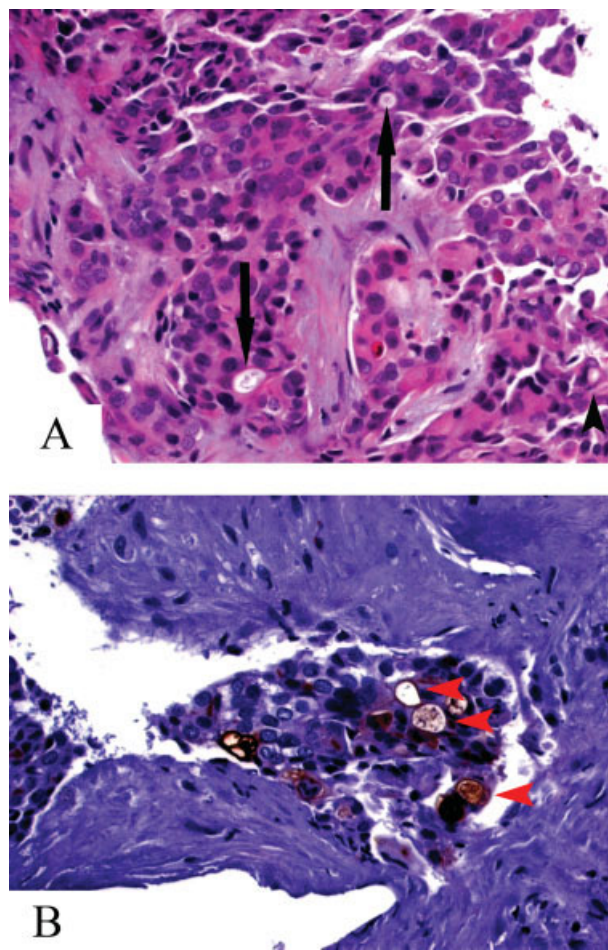


Fig. 2. (A) H&E stain shows neoplastic cells arranged in sheets and infiltrative cords. Duct differentiation is manifested by epithelial cell-lined ducts (arrow) and intracytoplasmic vacuoles (arrowhead) (core biopsy, H&E, $\times 400$). (B) Immunostain shows that intracytoplasmic vacuoles (arrowhead) are highlighted by polyclonal CEA antibody (core biopsy, CEA immunostain, $\times 400$). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

formed 1 week later. The biopsy revealed neoplastic cells arranged in sheets and infiltrative cords. The cells possessed abundant eosinophilic cytoplasm, pleomorphic and vesicular nuclei and occasional nucleoli. Various extent of duct differentiation was appreciated, which was manifested by epithelial cell-lined ducts or intracytoplasmic vacuoles. The tumor cells were positive for cytokeratin 5/6 and cytokeratin 7 and the epithelial cell-lined ducts and intracytoplasmic vacuoles were highlighted by polyclonal CEA antibody (Fig. 2). The morphology and the immunoprofile were consistent with metastatic eccrine porocarcinoma.

Discussion

To date, less than 300 cases of EP have been reported in the English literature.¹⁶ Despite its rarity, the clinical and

Table I. Comparison of EP and Selected Differential Diagnostic Entities

<i>Diagnosis</i>	<i>Cytoarchitecture</i>	<i>Cell borders</i>	<i>Cytoplasm</i>	<i>Nucleus</i>	<i>Intracytoplasmic vacuole</i>
EP	Round/oval cells dispersed singly or in discohesive clusters/sheets	Ill to well-defined	Variable amount. Vacuolated to dense and refractile	Pleomorphic, hyperchromatic. Coarse chromatin. Occasional prominent nucleoli	Present
Nonkeratinizing SCC	Round/oval cells dispersed singly or in discohesive two-dimensional geographic sheets	Well-defined	Variable amount. Dense and refractile	Hyperchromatic. Coarse chromatin. Prominent nucleoli	Absent
BCC	Tight clusters of tumor cells with peripheral palisading	Ill-defined	Scant	Small or inconspicuous nucleoli	Absent
Met. AdC	Single cells. Tight clusters of round-oval cells that attempt to form acini	Ill-defined	Variable amount. Formy or vacuolated	Pleomorphic, hyper/hypo-chromatic. Coarse chromatin, prominent nucleoli	Present
MM	Single or loosely associated epithelioid or spindle cells	Well-defined	Melanin may be seen	Eccentric. Intranuclear inclusions	Absent

EP, eccrine porocarcinoma; SCC, squamous cell carcinoma; BCC, basal cell carcinoma; Met. AdC, metastatic adenocarcinoma; MM, malignant melanoma.

histopathological features of EP have been well described.^{6,16} Data are limited, however, on the cytologic features of metastatic EP. Our case is the third reported describing the FNA cytology of metastatic EP.^{17,18}

Similar to what previously described,^{17,18} FNA cytology of metastatic EP in the current case revealed discohesive clusters of tumor cells and single scattered cells. A majority of the cells had dense, refractile cytoplasm. Intracytoplasmic vacuoles were readily appreciable in some cells. Nuclear enlargement, high N/C ratio, nuclear pleomorphism, and hyperchromasia, and occasional prominent nucleoli were observed. Bi- and multinucleated tumor cells were also identified. Neither tumor necrosis, which was reported by the previous investigators nor individual apoptotic cells were identified in the current case.^{17,18}

The clinical presentation of EP may resemble both malignant and benign conditions such as squamous cell carcinoma in situ (Bowen's disease), invasive squamous cell carcinoma, basal cell carcinoma, amelanotic melanoma, metastatic carcinoma, seborrheic keratosis, verruca vulgaris, and pyogenic granuloma.^{10,15} EP commonly presents as a verrucous plaque or nodule, up to 5 cm in diameter, with frequent ulceration. Definitive diagnosis relies on pathologic examination. EP may have some histologic overlap with eccrine poroma with a proliferation of basaloid to squamoid epithelium, broad based connection to the epidermis, and ductule lumina. Key to differentiating EP from eccrine poroma is identifying cytologic atypia, which may be high-grade. In addition, EP may demonstrate an infiltrative growth pattern, tumor necrosis and/or angiolymphatic invasion.

The cytologic features of metastatic EP are characteristic but by no means specific. Table I summarizes cytologic features of EP along the differential diagnoses. With

regard to the current case in which the patient's past medical history was significant for EP and Bowen's disease, the cytologic differential diagnosis rested primarily between metastatic EP and metastatic nonkeratinizing squamous cell carcinoma. The aspirate did show tumor cells with features of squamous differentiation manifested by ill- to well-defined intercellular border, moderate to dense refractile cytoplasm. In addition, some tumor cells attempted to form and exhibited intracytoplasmic vacuoles. Combination of these findings strongly favored a diagnosis of EP over squamous cell carcinoma.

Besides metastatic squamous cell carcinoma, other malignant lesions should also be considered in the differential diagnoses of EP. The lesions include but are not limited to metastasis of basal cell carcinoma, melanoma and adenocarcinoma. Generally, metastatic basal cell carcinomas are rare. FNA biopsy revealed single and tight clusters of small, round tumor cells with hyperchromatic oval to spindle-shaped nuclei, minimal cytoplasm, high N/C ratio, and inconspicuous or small nucleoli. Some of tumor cells in the clusters showed peripheral palisading.¹⁹⁻²¹

Metastatic melanoma is notorious for mimicking other tumors due to its various morphologic appearances. Classically, FNA biopsy reveals hypercellular smear with predominantly single, epithelioid-looking cells. Multinucleation, large and eccentric nuclei, intranuclear inclusion, prominent nucleoli, and intracytoplasmic melanin pigments have been described in various degrees.²² It is noteworthy that rare variants of metastatic melanoma reveals other cell types, raising a diagnostic challenge. In this regard, metastatic melanomas with predominant population of spindle cell, lipid-rich balloon cell, signet-ring cell, and rhabdoid cell have been reported.²³⁻²⁶ Correlation of FNA cytologic findings with patient's known his-

tory of melanoma and previous histologic findings (if available) plays a vital role in the diagnosis of metastatic melanoma. The diagnosis can be confirmed by positive immunostaining for S-100, MelanA, and/or HMB-45.

In the current setting, the presence of intracytoplasmic vacuoles, confirmed with positive immunostaining for polyclonal CEA antibody, was a critical finding allowing for accurate diagnosis of metastatic EP. However, we need to emphasize that the presence of intracytoplasmic vacuoles is not specific for EP. Other tumors particularly metastatic adenocarcinoma, e.g., lobular carcinoma of the breast, may exhibit the similar cytologic features. It is common that lobular carcinoma shows population of small, uniform, single tumor cells with eccentric nuclei and intracytoplasmic vacuoles containing targetoid inclusions.²⁷ Although single cells may be seen in EP, it appears that EP tends to form clusters. Tumor cells of EP also exhibit more cytologic pleomorphism compared to that of lobular carcinoma, the latter is well known for bland, uniform appearance. As always, correlation of the cytological features with the clinical presentation is crucial for making a correct diagnosis in a challenge situation.

In summary, careful consideration of previous history is very important. Our experience suggests that there are unique cytopathologic features of metastatic EP and in the right setting such a cytologic diagnosis can be rendered.

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