Metastatic Aggressive Digital Papillary Adenocarcinoma

CPT Coleman E. Altman, MC, USA; LTC Randy L. Hamill, MC, USA; Dirk M. Elston, MD

A 52-year-old white man presented with 2 complex cystic masses in his left inguinal region. On histopathologic examination, an asymptomatic nodule between the third and fourth metatarsal heads was diagnosed as an aggressive digital papillary adenocarcinoma (ADPAca), and the complex cysts from the groin represented metastatic disease from the primary acral tumor. The primary tumor was focally positive for immunoreactivity to ferritin antibody, an immunohistologic marker for sweat gland malignancies. Ferritin antibody may prove useful in the diagnosis of aggressive digital papillary adenoma (ADPA) and ADPAca.

Cutis. 2003;72:145-147.

Aggressive digital papillary adenocarcinoma (ADPAca) typically presents as solitary painless nodules in an acral location. We describe the case of a 52-year-old white man with an ADPAca who presented with groin metastases.

Case Report

A 52-year-old white man presented with a mass in his left groin that had been present for 2 months. Findings from the physical examination revealed a firm, mobile, and nontender mass of the left inguinal region. Results from an ultrasound revealed 2 discrete, complex cysts with thick walls and fluid-filled centers. Surgical exploration was performed to remove the cysts. Each cyst measured 4 cm, had papillary projections emanating from the cyst lining, and was filled with a greenish brown fluid. Histologically, the proliferations were interpreted as distant metastasis from an unknown primary tumor.

On subsequent physical examination, a 3-cm, round, mobile mass at the plantar aspect of the patient's left foot was noted. He reported that this mass had been present for 2 years. The tumor was located in the soft tissue between the third and fourth metatarsal bones. A magnetic resonance imaging (MRI) scan of the left foot demonstrated a 2.4×2.4×2.6-cm mass with thin septations. The signal intensity was isointense to fat on Triplane T1 and hyperintense to fat on T2 fast spin-echo images. The bone was not involved, and there were no erosive changes suggested by MRI. This was confirmed by a bone scan. The patient underwent a local wide excision of the mass. On serial sectioning of the foot mass, a cystic cavity was revealed.

Microscopic examination of the left foot mass showed a poorly circumscribed neoplasm involving the dermis and subcutis. Tubuloalveolar and ductal structures were observed, with areas of papillary projections protruding from the cyst wall. Scattered mitoses and cellular atypia were observed (Figure 1). Subsequently, the left inguinal region was surgically reexplored, and 9 lymph nodes were removed for histologic examination. A focus of tumor cells involving the capsular area of a single lymph node was discovered. Within this specimen, there was a well-formed cystic lumen with papillary projections, identical to those described for the foot mass (Figure 2). The original specimens from the left groin exhibited identical histologic features. The primary tumor was positive for cytokeratin 7, CAM 5.2, and a polyclonal keratin mix. Ferritin antibody, S-100 protein (Figure 3), and epithelial membrane antigen were focally positive. The following markers were negative: cytokeratin 20, carcinoembryonic antigen (CEA), prostate-specific antigen, chromogranins, synaptophysin, and α-fetoproteins.

Annual follow-up examination included physical examination and computed tomographic scans of the chest, abdomen, and pelvis. No local recurrence or metastatic disease had been noted 60 months after excision.

Accepted for publication December 31, 2002.

Dr. Altman is from the Department of Dermatology, Brooke Army Medical Center, San Antonio, Texas. Dr. Hamill is from the Department of Pathology, Eisenhower Army Medical Center, Fort Gordon, Georgia. Dr. Elston is from the Departments of Dermatology and Laboratory Medicine, Geisinger Medical Center, Danville, Pennsylvania.

The opinions expressed herein are the private views of the authors and are not to be construed as official or reflecting the views of the Department of the Army or the Department of Defense.

The authors report no conflict of interest.

Reprints: CPT Coleman E. Altman, DO, Department of Dermatology, Brooke Army Medical Center, Building 3600, San Antonio, TX 78234 (e-mail: coleman.altman@amedd.army.mil).

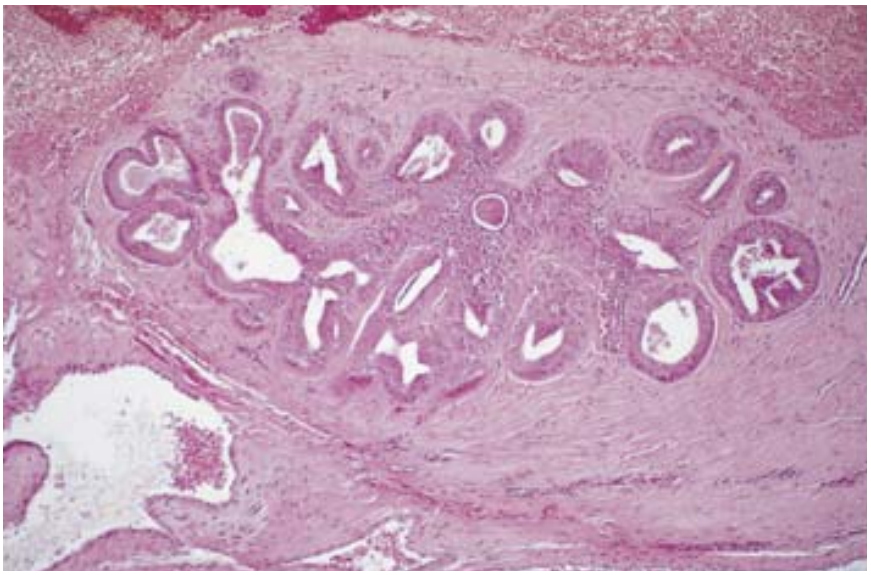

Figure 1. Scattered mitoses and cellular atypia (H&E, original magnification ×100).

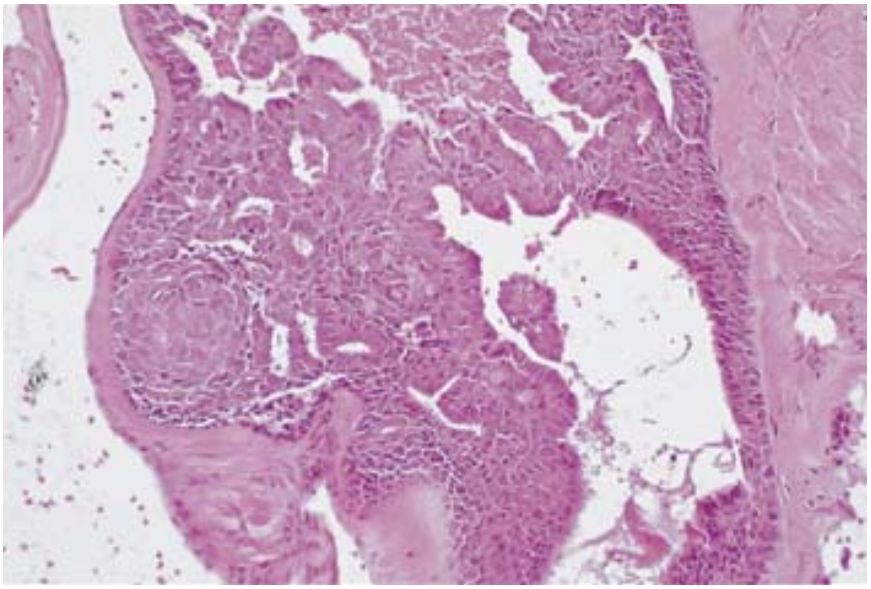

Figure 2. A well-formed cystic lumen with papillary projections, identical to those described for the foot mass (H&E, original magnification ×200).

Comment

In 1987, Kao et al[1] published findings (culled from the files of the Armed Forces Institute of Pathology) on 57 cases, 40 of which were identified as ADPA and 17 as ADPAca. Most of these tumors occurred in white men (94%) ranging in age from 40 to 60 years (76.4%). The nodules were acral in location, having been diagnosed in either the digit of the hand (53%) or foot (47%). Local recurrence was noted in 47% of cases, of which 62.5% recurred 2 or more times. Metastases developed in 7 of the 17 (41.2%) patients with ADPAca, as late as 19 years after initial treatment. Five of those tumors metastasized to lung (71.4%). Three patients died of metastases, 5 to 20 years after surgical treatment of the primary tumor.

Criteria for ADPAca included poor glandular differentiation, necrosis, cellular atypia and pleomorphism, invasion of soft tissue and bone, and invasion of blood vessels. Nine cases of recurrence and 3 cases of metastasis in tumors, originally diagnosed as adenoma by the Armed Forces Institute of Pathology, prompted Duke and coworkers[2] to review an additional 67 cases of ADPA and ADPAca from 1980 to 1995. They concluded that a distinction between ADPA and ADPAca could not reliably be made on a histologic basis. Singla and Shearin[3] noted that the recurrence rate was 5% in patients who underwent subsequent reexcision or amputation within 6 months of initial excision versus 50% in patients without follow-up procedures.

In 1990, Ceballos et al[4] demonstrated a new immunohistologic marker for sweat gland malignancies. Using the immunoperoxidase technique, the polyclonal antibody to ferritin normally reacts

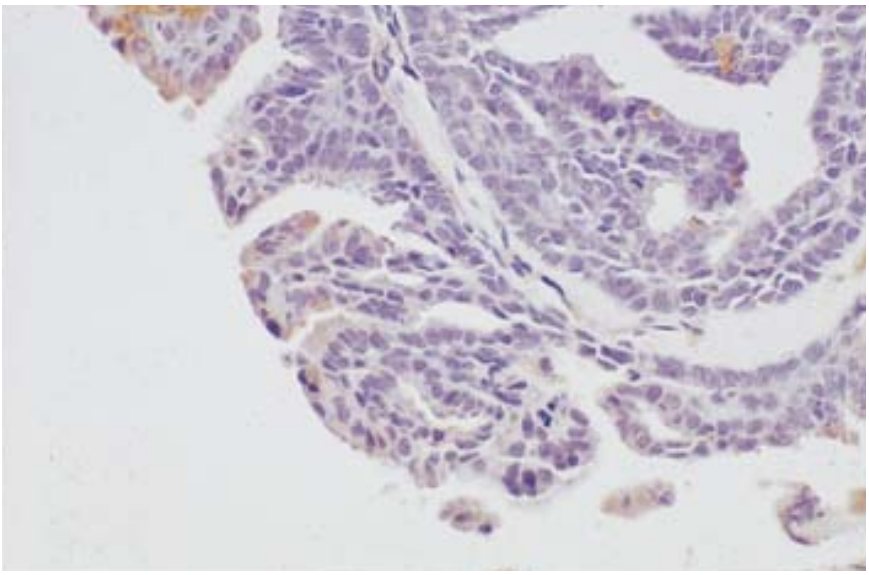

Figure 3. S-100 was focally positive (original magnification ×400).

with the cells of the outer layer of the eccrine duct. They described ferritin antibody marker expressed in an ADPAca. Penneys and Zlatkiss[5] discovered 2 distinct binding patterns of ferritin antibody. The first pattern, the binding of ferritin antibody to the outermost layer of cells in the epithelial cords of syringoma, produced a characteristic ring when seen on cross-section. This pattern did not occur in other neoplasms related to the eccrine duct, such as dermal duct tumor and eccrine poroma. The second pattern, observed in acrospiroma and adnexal carcinomas, was more diffuse. They noted that a diffuse ferritin antibody expression had been described in malignant neoplasms in tissues other than the skin. They proposed that diffuse expression reflects biologic activity and may be useful in assessing the presence of malignancy.

The differential diagnosis of ADPAca includes metastatic breast cancer. Well-differentiated papillary carcinoma of the breast is a low-grade malignancy from which distant metastases rarely develop.[6] Positive immunoperoxidase staining for CEA is characteristic of ADPA and ADPAca.[7-12] However, this finding should not rule out metastatic adenocarcinoma from the lung, breast, or gastrointestinal tract. Ferritin antibody markers may prove to be useful for future confirmation of biologically aggressive ADPA and ADPAca.

REFERENCES

1. Kao GF, Helwig EB, Graham JH. Aggressive digital papillary adenoma and adenocarcinoma. a clinicopathological study of 57 patients, with histochemical, immunopathological, and ultrastructural observations. *J Cutan Pathol.* 1987;14:129-146.
2. Duke WH, Sherrod TT, Lupton GP. Aggressive digital papillary adenocarcinoma. *Am J Surg Pathol.* 2000;24:775-784.
3. Singla AK, Shearin JC. Aggressive surgical treatment of digital papillary adenocarcinoma. *Plast Reconstr Surg.* 1997;99:2058-2060.
4. Ceballos PI, Penneys NS, Acosta R. Aggressive digital papillary adenocarcinoma. *J Am Acad Dermatol.* 1990;23:331-334.
5. Penneys NS, Zlatkiss I. Immunohistochemical demonstration of ferritin in sweat gland and sweat gland neoplasms. *J Cutan Pathol.* 1990;17:32-36.
6. Haagesen CD. The papillary type of mammary carcinoma. In: Haagesen CD. *Diseases of the Breast.* Philadelphia, Pa: WB Saunders Co; 1971:528.
7. Maiorana A, Nigrisoli E, Papotti M. Immunohistochemical markers of sweat gland tumors. *J Cutan Pathol.* 1986;13:187-196.
8. Penneys NS. Immunohistochemistry of adnexal neoplasms. *J Cutan Pathol.* 1984;11:357.
9. Penneys NS, Nadji M, McKinney EC. Carcinoembryonic antigen present in human eccrine sweat. *J Am Acad Dermatol.* 1981;4:401-403.
10. Penneys NS, Nadji M, Morales A. Carcinoembryonic antigen in benign sweat gland tumors. *Arch Dermatol.* 1982;118:225-227.
11. Penneys NS, Nadji M, Ziegels-Weissman J, et al. Carcinoembryonic antigen in sweat-gland carcinomas. *Cancer.* 1982;50:1608-1611.
12. Terui T, Obata M, Tagami H. Immunohistochemical studies on epithelial cells in mixed tumors of the skin. *J Cutan Pathol.* 1986;13:197-206.