Metastatic Aggressive Digital Papillary Adenocarcinoma

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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.


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.
Metastatic ADPACA

Comment

In 1987, Kao et al. 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 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 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. demonstrated a new immunohistologic marker for sweat gland malignancies. Using the immunoperoxidase technique, the polyclonal antibody to ferritin normally reacts...
with the cells of the outer layer of the eccrine duct. They described ferritin antibody marker expressed in an ADPAca. Penneys and Zlatkiss\(^3\) 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.\(^5\) 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**