Aggressive digital papillary adenocarcinoma: A clinicopathological study of 19 cases

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Background: Aggressive digital papillary adenocarcinomas (ADPA) are malignant tumors of sweat glands having recurrence/metastatic potential.

Objective: We sought to describe the clinical/histopathological characteristics of a series of ADPA.

Methods: This is a retrospective case series of 19 ADPA.

Results: The tumors occurred in 17 men and 2 women (mean age: 47 years). They involved digits (15), big toe (3), and palm (1), and measured from 3 to 30 mm. They were mostly solid and cystic, with papillary projections and tubular structures. Atypia was mostly mild to moderate. Tumors tested positive for p63, keratin 7, keratin 77 (eccrine duct-specific), PHLDA1, and epithelial membrane antigen in most cases, and for carcinoembryonic antigen, smooth muscle actin, S100 protein, estrogen, progesterone, and androgen receptors in 50%. Mean Ki67 proliferation index was 15%. Local recurrence was observed in 4 cases. One patient had axillary lymph node metastasis. Histopathologic parameters were not predictive of evolution. Conservative surgical treatment, performed in 7 of 19 cases, did not result in more recurrences than amputation.

Limitations: The study was retrospective and the number of cases is small.

Conclusion: ADPA are histologically variable, but papillary projections are always present. Keratin 77 expression suggests an eccrine origin. P63 is helpful to exclude metastasis. Conservative surgery may be sufficient in some cases. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2017.02.028.)

Key words: aggressive digital papillary adenocarcinoma; complete excision; conservative surgery; eccrine adnexal tumor; hormonal receptors; keratin 77; sweat gland.

Aggressive digital papillary adenocarcinomas (ADPA) are rare cutaneous tumors of sweat gland origin, described by Helwig in 1979 (American Academy of Dermatology Clinical Pathology Conference, Chicago, unpublished data, December 1979). The name comes from their aggressive potential, with a high rate of recurrence and their predominantly digital location.

Only 2 large studies on ADPA have been conducted. In 1987, Kao et al[1] described 57 cases and defined criteria to distinguish papillary digital adenomas and adenocarcinomas. In 2000, Duke et al[2] worked on the same cohort with longer-term follow-up and observed that in the 30 cases included in the adenoma group, 9 cases had recurred, 3 had metastasized, and no clinical or histologic criteria could distinguish between benign and malignant behavior. In 2012, 31 cases of ADPA were described by Suchak et al,[3] confirming that histologic criteria are insufficient to determine prognosis.

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We describe here the clinicopathologic characteristics of 19 ADPA, with immunohistochemical and follow-up data. As the eccrine sweat gland origin is sometimes controverted,[4] we have studied keratin 77 (a type II epithelial keratin, originally named keratin 1b, specifically expressed by luminal cells of the eccrine sweat duct[5-8]) immunohistochemical expression.

CAPSULE SUMMARY

- Aggressive digital papillary adenocarcinoma is a rare malignant sweat gland tumor, with potential for recurrence or metastasis.
- This study of 19 cases illustrates the morphologic/immunohistochemical characteristics and behavior of this tumor.
- Conservative surgical treatment may be sufficient in some cases.

METHODS

Patient selection

This retrospective study includes cases of ADPA in France and Switzerland. Nineteen patients were included in the study, given a diagnosis in the Strasbourg University Hospital between 1999 and 2015 and referred by other pathologists for expert opinion. The institutional review board approved this study. Patients provided informed consent.

Histologic analysis

Hematoxylin and eosin–stained slides were reviewed to define the following features: site, extent of demarcation, pattern (uni/multinodular, solid/cystic), presence of tubules, strands, papillary structures, aspect of cells, atypia, malpighian, apocrine or sebaceous differentiation, hyalinized stroma, necrosis, mitotic index, inflammation, angioinvasion, and perineural invasion.

Immunohistochemical analyses

Immunohistochemical studies were performed on 4 μm-thick slides from formalin-fixed paraffin-embedded tissue blocks. At least 1 immunohistochemical marker could be tested in 17 of 19 cases. The antibodies and protocol used are indicated in Supplemental Table I (available at http://www.jaad.org). Immunohistochemical analyses were performed on a Benchmark XT with ultraView universal diaminobenzidin detection kit (Ventana, Roche, Meylan, France). For 2 antibodies, manual detection used a labeled streptavidin biotin Ultravision (Dako, Glostrup, Denmark) detection kit.

Clinical/follow-up data

Clinical/follow-up data were requested from referring physicians: sex, age at diagnosis, site/size of tumor, duration before surgery, prior trauma, clinical diagnosis evoked, nature of initial/complementary treatment, quality of excision (complete, incomplete, or marginal, that is to say with very close margins, <1 mm), extension staging, pathological diagnosis initially proposed, notion of recurrence or metastasis, and date of last follow-up.

Statistical analysis

Associations between variables were appreciated with the χ^2 test or Fisher exact test. Statistical analysis was performed using software (SPSS Statistics, Version 20.0.0, IBM Corp, Armonk, NY). Statistical significance was set at a P value below .05.

RESULTS

Clinical features

Data are summarized in Table I. The patients were 17 men and 2 women, with a mean age of 47 years (range: 19-63 years). All lesions were solitary tumors (Fig 1), located on a digit (15/19), big toe (3/19), or palm (1/19). Clinical presentation was that of a mass, with progressive growth. The clinical diagnosis was pyogenic granuloma, glomangioma, or angioma (n = 4); cyst (n = 3); mucoid cyst (n = 3); giant cell tumor (n = 2); wart (n = 1); encapsulated hematoma (n = 1); or foreign body granuloma (n = 1). ADPA was never clinically evoked. Size ranged from 3 to 30 mm (mean: 14.4 mm). In 2 cases, there was prior trauma. Lesions had been present for 1 month to 10 years before diagnosis (mean: 24.4 months). Four cases in our series recurred (21% of patients): case 1 was diagnosed as an "eccrine hidradenoma," and recurred 8 years after initial excision (whether complete or incomplete is unknown); case 5 was diagnosed as a "sweat gland tumor, presumed benign but with some mitoses" and recurred 2 years after marginal excision without secondary surgical revision; case 7 was diagnosed as "trichoblastoma" and recurred 4 months after incomplete excision; and case 11 was located on the ring finger and recurred on the palm 9 years after incomplete excision followed by digit amputation, and this recurrence was associated with an axillary lymph node metastasis. Metastatic evolution was thus observed in 1 patient (5%). Surgical observations were rarely reported: the surgeon described a bluish mass in 3 cases (Fig 1, *C*).

Initial pathological diagnosis

The initial pathological diagnosis was known in 9 cases: ADPA (n = 3) and benign sweat gland tumor