Papillary Squamous Cell Carcinoma, Not Otherwise Specified (NOS) of the Penis: Clinicopathologic Features, Differential Diagnosis, and Outcome of 35 Cases

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Abstract: There is a group of low-grade papillomatous squamous cell carcinomas (SCC) of the penis, collectively designated as "verruciform," that are difficult to classify. A proposal of classification grouped these tumors in warty (condylomatous), verrucous, and papillary carcinomas. Papillary SCC, not otherwise specified is the third distinctive type of penile low-grade verruciform neoplasms. We are presenting clinicopathologic features of 35 cases from 2 institutions. All specimens were penectomies or circumcisions. Mean age was 57 years. Sites of involvement were glans alone in 18 cases (51%), glans, coronal sulcus and foreskin in 13 cases (37%), glans and sulcus in 3 cases (9%), and foreskin in 1 case (3%). Papillary carcinomas were large (mean 5.6 cm) exophytic low-grade squamous neoplasms with hyperkeratosis and papillomatosis. Papillae were variable in length and shape. The tip was straight, undulated, spiky, or blunt. There was no koilocytosis. The interface between tumor and stroma was characteristically jagged and a moderate stromal reaction was evident in most cases. The majority of the tumors (94%) showed a low-grade histology with focally present poorly differentiated areas in 6% of the cases. The mean thickness of the tumor was 9.4 mm. The most commonly invaded anatomic levels were the corpus spongiosum and/or dartos (77% cases). Corpus cavernosum was invaded in 8 cases (23%). Vascular and perineural invasion were unusual. Frequent associated lesions were squamous hyperplasia, differentiated penile intraepithelial neoplasia, and lichen sclerosus (74%, 46%, and 34%, respectively). Nodal metastases were identified in 3 of 12 patients with bilateral groin dissections. Of the 20 patients followed, 18 were either with no evidence of disease (15 cases) or died from unrelated causes (3 cases). One patient was alive with evidence of systemic metastases and 1 died from disseminated penile cancer 32 months after original penectomy. In conclusion, papillary carcinomas were exophytic albeit, often deeply invasive low-grade neoplasms, with a low rate of nodal metastasis characterized by complex papillae, irregular fibrovascular cores, and jagged tumor base. Papillary SCC should be distinguished from other penile verruciform tumors, including verrucous and variants, warty and papillary basaloid carcinomas, and carcinoma cuniculatum. Helpful morphologic features for differential diagnosis are provided.

Key Words: penile cancer, squamous cell carcinoma, papillary carcinoma, verruciform tumor, HPV, prognosis

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There is a distinct geographic distribution of penile cancer, with a low incidence in the United States, Europe, Japan, Korea, and Israel, with an age-standardized rate of 0.1 to 1.0/100.000 inhabitants, and a high incidence in tropical regions of America, Africa, and Asia, with an age-standard rate of 1.0 to 4.0/100.000 inhabitants. Highest rates are reported in Paraguay and Northern Brazil.[11,18] A vast majority of penile carcinomas, except rare cases of Paget disease or basal cell carcinomas, are squamous cell carcinomas (SCC). About one third of them are represented by grossly exophytic and microscopically low-grade papillomatous tumors, collectively designated as "verruciform" that are problematic to classify.[3,4,16] There has been some confusion in the nomenclature of these neoplasms. A proposal classified these tumors in condylomatous (warty), verrucous, papillary not otherwise specified (NOS), and giant condylomas.[3] A recently described tumor, the carcinoma cuniculatum, also belongs to the verruciform group.[1] Distinguishing morphologic features are related to the pattern of papillae, presence of koilocytosis, and the appearance of the interface between the tumor and the underlying stroma.[5,13] Papillary SCC, NOS was originally mentioned with other penile tumors in a study evaluating the presence of HPV in penile carcinomas[15] and in other series,[3,4,16] but we found no specific clinical or morphologic description and outcome features of this tumor entity. The aims of this study were to characterize these features in 35 papillary carcinomas and to discuss the differential diagnosis of penile verruciform tumors.