



Histologic classification of penile intraepithelial neoplasia

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 Warty penile intraepithelial neoplasia

Penile squamous cell carcinomas (SCCs) and their corresponding precancerous lesions can be classified in 2 major groups: human papillomavirus (HPV) related and HPV unrelated. In the former (warty and basaloid SCC), there is a predominance of undifferentiated basaloid cells. In the latter (eg, usual, papillary, and verrucous SCC), the predominant cell is larger with abundant eosinophilic cytoplasm. Based on these morphologic features, a new term, “penile intraepithelial neoplasia” (PeIN), was proposed. PeIN was further subclassified into differentiated and undifferentiated, with the latter being subdivided into basaloid, warty, and warty–basaloid subtypes. Macroscopically, PeIN subtypes are indistinguishable. Microscopically, differentiated PeIN is characterized by acanthosis, parakeratosis, enlarged keratinocytes with abundant “pink” cytoplasm (abnormal maturation), and hyperchromatic cells in the basal layer. In basaloid PeIN the epithelium is replaced by a monotonous population of uniform, small, round, and basophilic cells. Warty PeIN is characterized by a spiky surface, prominent atypical parakeratosis, and pleomorphic koilocytosis. Warty–basaloid PeIN show features of both warty and basaloid PeIN. There is a significant association of subtypes of PeIN with specific variants of invasive SCCs. This is a simple and reproducible nomenclature for penile precancerous lesions based on cell type and differentiation. It takes into account the similarities between vulvar and penile pathology and the hypothesis of a bimodal pathway of penile cancer progression.

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The vast majority of penile carcinomas are of squamous origin.¹⁻³ Invasive squamous cell carcinomas (SCCs) of the penis are likely preceded by squamous precursor lesions.^{4,5} From a pathogenic point of view, there are 2 major morphologic groups of penile invasive carcinomas: those related to human papillomavirus (HPV) and those unrelated or rarely related to HPV.⁶⁻⁸ The former group includes basa-

loid, warty, and warty–basaloid carcinomas, and the latter group encompasses usual, verrucous, papillary, sarcomatoid, pseudohyperplastic, and cuniculatum carcinomas. Beside the subtype of penile carcinoma, an even more significant pathologic feature correlating to the presence or absence of the virus was recently found to be the predominant cell type. HPV-related tumors are partly or entirely composed of a small to intermediate basophilic, undifferentiated cell, the basaloid cell, whereas HPV-negative tumors are predominantly composed of highly keratinized, differentiated squamous cells.^{6,9} These cells are also present in noninvasive precursor lesions. Based on these findings, we constructed a simplified classification of precancerous le-

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