## PATHOLOGY

### Urothelial neoplasms in patients 20 years or younger: a clinicopathological analysis using the World Health Organization 2004 bladder consensus classification

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Purpose: Urothelial neoplasms in patients younger than 20 years are rare, with conflicting data regarding clinical outcomes.

Materials and Methods: We identified 23 patients 4 to 20 years old with urothelial neoplasms, reclassified the microscopic diagnoses using the 2004 WHO/International Society of Urologic Pathology grading classification and collected data on presentation, risk factors and outcomes.

Results: Pathological grading revealed 2 urothelial papillomas, 10 papillary urothelial neoplasms of low malignant potential (PUNLMPs), and 8 low grade and 3 high grade papillary urothelial cancers, all without invasion. Mean patient age was 13.2 years (range 4 to 20), 19 patients were male and 19 presented with gross hematuria. All lesions were solitary and measured 0.1 to 6 cm. One patient had a history of smoking and 1 had parents who smoked. Three patients (13%) had recurrences classified as either urothelial papilloma (1) or PUNLMP (2). All patients were alive with no evidence of disease after a mean followup of 4.5 years (range 6 months to 13 years).

Conclusions: Urothelial neoplasms in individuals younger than 20 years more commonly occur in males and are predominantly low grade with a favorable clinical outcome. Before the current classification system the 10 patients with a diagnosis of PUNLMP would have been classified as having papillary carcinoma. Thus, the diagnostic category of PUNLMP allowed 43.5% of patients in this series to avoid being labeled with "cancer" at a young age.

**Editorial Comment**

In 1998, the International Society of Urologic Pathology (ISUP) proposed a new classification for urothelial neoplasms (1). The new classification included the so-called superficial papillary urothelial neoplasms of low malignant potential (PUNLMP). These tumors correspond to papillary urothelial carcinomas, grade 1, pTa in the traditional classification. One of the reasons for this new nomenclature is shown in the present article. Ten patients younger than 20 years had the diagnosis of PUNLMP. Two of these patients had recurrence but all were alive with no evidence of disease after a mean follow-up of 4.5 years (range 6 months to 13 years). Thus, the diagnostic category of PUNLMP allowed 43.5% of patients in the series to avoid being labeled with "cancer" at a young age. This is also valid for patients older than 20 years of age due to the low recurrence rate of these tumors.

Considering that many urologists are unaware (or do not agree with this new classification), I have recommended to the pathologists to use both nomenclatures. PUNLMP is a papillary urothelial lesion with an orderly arrangement of cells within papillae with minimal architectural abnormalities and minimal nuclear atypia irrespective of cell thickness. In general, the major distinction from papilloma (a rare lesion), is that in papillary urothelial neoplasm of low malignant potential the urothelium is much thicker and/or nuclei are significantly enlarged. The urothelial papilloma, in contrast, has no architectural or cytologic atypia.

Because urologists should not minimize the significance of this diagnosis, pathologists are encouraged to include the following note in cases diagnosed as papillary urothelial neoplasm of low malignant potential (PUNLMP): "Patients with these tumors are at risk of developing new bladder tumors ("recurrence"), usually

of a similar histology. However, occasionally, these subsequent lesions manifest as urothelial carcinoma, such that follow-up of the patients is warranted."

As for the flat lesions, the ISUP recommends a new nomenclature: intraurothelial neoplasia instead of the term dysplasia/flat carcinoma in situ of the traditional classification. Grade 2 dysplasia corresponds to low-grade intraurothelial neoplasia and grade 3/flat carcinoma in situ (pTis) to high-grade intraurothelial neoplasia. ISUP recommends not to include in the pathology report dysplasia grade 1.

For grading of urothelial papillary carcinomas, ISUP recommends call low-grade to carcinomas grade 1, and high-grade to carcinomas grade 2 or 3.

**References**

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**Patient and urologist driven second opinion of prostate needle biopsies**

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Purpose: We reviewed second opinion prostate needle biopsies that were patient and urologist driven to determine how often an expert opinion resulted in a different diagnosis.

Materials and Methods: Of 3,155 prostate needle biopsy consultations received during a 6-month interval 684 were sent at the request of the patient or urologist. A significant change in outside diagnosis was one that could potentially result in a change in therapy or prognosis.

Results: The second opinion was requested by patients (21.6%), urologist (63.9%) and patients plus urologists (14.5%). The distribution of the 684 outside diagnoses was benign in 6.1%, HGPIN in 7.6%, atypical (ATYP) in 29.8% and cancer in 56.5%. In 241 cases (35.2%), a change in diagnosis was rendered upon expert review. We agreed with the majority of outside cancer, benign and HGPIN diagnoses, in contrast to only 36.8% of outside ATYP cases ($p < 0.0001$). Uncommonly did a cancer diagnosis become a benign one or vice versa. Of changes affecting outside cancer diagnoses 73.5% were due to changes in Gleason score. The diagnosis was more likely to be changed when the consultation was requested by the urologist rather than by the patient (41.4% vs 25%, $p < 0.0001$).

Conclusions: Cases diagnosed as ATYP have the highest likelihood of being changed upon expert review. Urologists should consider sending such cases for consultation to attempt to resolve the diagnosis as definitively benign or malignant before subjecting the patient to repeat biopsy.

**Editorial Comment**

It is a common practice in the United States a second opinion related to pathology reports. In Brazil, is not a common practice but definitely increasing in relation to prostatic needle biopsies. It is worth noting that

the diagnosis was more likely to be changed when consultation was requested by the urologist rather than by the patient (41.4% vs 25%, $p < 0.0001$). Many patients, due to lack of symptoms or for other reasons, ask a second opinion because do not accept or doubt the diagnosis but uncommonly a cancer diagnosis become a benign one after a review.

A special issue is related to Gleason score. Urologists should be careful with low Gleason scores. A Gleason score of 2 + 2 = 4 in a needle biopsy, frequently corresponds to a Gleason score of 4 + 4 = 8. The reason is that well circumscribed tumors not always correspond to low-grade carcinoma. The pathologist must be aware if there is either invasion of the stroma or fused glands in the middle of the lesion.

In a consensus conference on Gleason grading of prostatic carcinoma, the International Society of Urological Pathology (ISUP) recommended that the diagnosis of Gleason score 4 on needle biopsy should be made "rarely, if ever" (1). The consensus conference cautioned that, although the potential exists for rendering a diagnosis of Gleason score 4 on needle biopsy, it is a diagnosis that general pathologists should almost never make without consultation. Even when that exceedingly rare Gleason score 4 cancer is diagnosed on needle biopsy by an expert, a note should be added that almost always a higher grade cancer would be seen in the corresponding prostate (if examined at radical prostatectomy).

There was only a 36.8% of agreement when the consultation referred to atypical lesions. This lesion is also known as ASAP (atypical small acinar proliferation). It is important for the urologist to know that ASAP is not a diagnostic entity and is not synonymous with high-grade prostatic intraepithelial neoplasia (HGPIN). It represents descriptive diagnostic terminology in which there is architectural and/or cytologic atypia that does not reach an individual pathologist's threshold required for the diagnosis of cancer. In a consensus conference sponsored by the World Health Organization, the committee members recommended designating atypical biopsies as either "suspicious" or "highly suspicious for cancer" (2). The reasons for this, include the equation by some urologists of the term ASAP with HGPIN and because all of the atypical foci are not always "small" acinar but may include glands with larger diameter (such as pseudohyperplastic pattern of cancer or adenocarcinoma with ductal features).

The conclusion of the paper surveyed is that atypical lesions ("suspicious for cancer") have the highest likelihood of being changed upon expert review and that urologists should consider sending such cases for consultation to attempt to resolve the diagnosis as definitively benign or malignant before subjecting the patient to repeat biopsy.

**References**

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