injuries are not really urethral strictures, and thus minimally invasive methods and “cut to the light” procedures do not have any durable success.

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PATHOLOGY

Prognostic and predictive factors and reporting of prostate carcinoma in prostate needle biopsy specimens

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The information provided in the surgical pathology report of a prostate needle biopsy of carcinoma has become critical in the subsequent management and prognostication of the cancer. The surgical pathology report should thus be comprehensive and yet succinct in providing relevant information consistently to urologists, radiation oncologists and oncologists and, thereby, to the patient. This paper reflects the current recommendations of the 2004 World Health Organization-sponsored International Consultation, which was co-sponsored by the College of American Pathologists. It builds on the existing work of several organizations, including the College of American Pathologists, the Association of Directors of Anatomic and Surgical Pathologists, the Royal Society of Pathologists, the European Society of Urologic Pathology and the European Randomized Study of Screening for Prostate Cancer.

Editorial Comment

This consensus meeting was held in Stockholm in 2004 and sponsored by the World Health Organization. I will emphasize some topics of interest for the urologist.

1. Histopathologic type: greater than 99% of all carcinomas are acinar. The remain types include urothelial, ductal (endometrioid), mucinous, signet ring cell, adenosquamous, small cell carcinoma and sarcomatoid carcinoma. Although uncommon, the aggregate data on these variants suggest that they may have diagnostic, prognostic or therapeutic importance. Urothelial carcinoma is not hormone dependent. Small cell carcinoma (with or without neuroendocrine differentiation) is usually associated with widespread, often concurrent, metastasis (frequently to unusual locations) and rapid acceleration of clinical course. Sarcomatoid carcinoma (carcinosarcoma) of the prostate, like small cell carcinoma, has an extremely poor prognosis with a median survival of 3 years.

2. Gleason score: it predicts findings in radical prostatectomy (pathologic stage), biochemical progression, local recurrences, and lymph node or distant metastasis. The most significant recommendation is to separately report the Gleason score for each recognizable core irrespective of whether the cores are individually submitted (in individual container signifying specific anatomic location), or submitted together. Another important change is the recognition and reporting of the tertiary pattern of higher grade in needle biopsies. A case with primary pattern 3, secondary pattern 4, and tertiary pattern 5 should be assigned a Gleason score 3 + 5 = 8.

3. Extent of involvement of needle core: there is lack of consensus in the literature and, hence, to some extent in clinical practice as to the best method of reporting the extent of tumor involvement. It is recommended that the report should provide the number of involved cores, the percentage estimate of involvement of each of the cores derived by visual estimation and the linear length in increments of 0.5 mm.

4. Local invasion: the prostate has not a true fibrous capsule. Terms such as "capsular invasion" or "capsular penetration" should not be used. The proper term is extraprostatic extension. Only exceptionally rarely is fat present within the normal prostate. Hence, tumor in adipose tissue in a needle biopsy specimen can safely be interpreted as extraprostatic extension.

5. Perineural invasion: although perineural invasion in needle biopsy specimens is not an independent predictor of prognosis when Gleason score, serum PSA and extent of cancer are factored in, some studies indicate that its presence correlates with extraprostatic extension. The data are conflicting. Clinicians should be aware that all cases of perineural invasion on needle biopsy would not necessarily have extraprostatic extension.

6. Reporting of atypical foci suspicious but not diagnostic of malignancy: atypical small acinar proliferation (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 pathologists' threshold required for the diagnosis of cancer. The term ASAP may be confusing for the urologist. The committee members recommended designating atypical biopsies as either suspicious or highly suspicious for cancer. These patients should have a close clinical follow-up and re-biopsied.

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Prognostic factors and reporting of prostate carcinoma in radical prostatectomy and pelvic lymphadenectomy specimens

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This paper, based on the activity of the Morphology-Based Prognostic Factors Committee of the 2004 World Health Organization-sponsored International Consultation, describes various methods of handling radical prostatectomy specimens for both routine clinical use and research purposes. The correlation between radical prostatectomy findings and postoperative failure is discussed in detail. This includes issues relating to pelvic lymph node involvement, detected both at the time of frozen section and in permanent sections. Issues of seminal vesicle invasion, including its definition, routes of invasion and relationship to prognosis, are covered in detail. The definition, terminology and incidence of extra-prostatic extension are elucidated, along with its prognostic significance relating to location and extent. Margins of resection are covered in terms of their definition, the etiology, incidence and sites of positive margins, the use of frozen sections to assess the margins and the relationship between margin positivity and prognosis. Issues relating to grade within the radical prostatectomy specimen are covered in depth, including novel ways of reporting Gleason grade and the concept of tertiary Gleason patterns. Tumor volume, tumor location, vascular invasion and perineural invasion are the final variables discussed relating to the prognosis of radical prostatectomy specimens. The use of multivariate

analysis to predict progression is discussed, together with proposed modifications to the TNM system. Finally, biomarkers to predict progression following radical prostatectomy are described, including DNA ploidy, microvessel density, Ki-67, neuroendocrine differentiation, p53, p21, p27, Bcl-2, Her-2/neu, E-cadherin, CD44, retinoblastoma proteins, apoptotic index, androgen receptor status, expression of prostate-specific antigen and prostatic-specific acid phosphatase and nuclear morphometry.

Editorial Comment

This is a long paper of the Consensus meeting held in Stockholm in 2004 and sponsored by the World Health Organization. I will emphasize only some of the topics of interest for the urologist.

1. Seminal vesicle invasion: this finding in a radical prostatectomy specimen markedly diminishes the likelihood of cure. In contemporary series of men with positive seminal vesicles and negative pelvic lymph nodes, 5-year biochemical progression-free rates range from 5% to 60%. The diagnosis of invasion should be restricted to invasion of the muscle layer of the seminal vesicle that is a structure exterior to the prostate. Cases that some have diagnosed as invasion of the "intraprostatic portion" of the seminal vesicle should be regarded as invasion of the ejaculatory duct. Possible routes of seminal vesicle invasion are: 1) extension into soft tissue adjacent to the seminal vesicle and then into the muscle layer; 2) invasion via the sheath of the ejaculatory duct and extending up into the seminal vesicle muscle layer; and 3) discontinuous metastases. There are conflicting studies as to whether the first or second method is most common. Metastases are the least common mode of spread.

2. Extraprostatic extension: because the prostate lacks a discrete capsule, the term extraprostatic extension should be used instead of "capsular" penetration to describe tumor that has extended out of the prostate into periprostatic soft tissue. Prognosis has relation to extraprostatic extent. This evaluation, however, is controversial. Unfortunately, the most prognostic method to substratify the degree of extraprostatic extent remains the subjective designation of focal versus nonfocal.

3. Margins of resection: the pathological definition of positive margins of resection is "tumor extending to the inked surface of the prostatectomy specimen which the surgeon has cut across". There are two causes for positive margins: transection of intraprostatic tumor (iatrogenic incision) and non-iatrogenic. Tumors in stage T2 with positive surgical margins are designated stage T2+. This is because the pathologist cannot evaluate if the tumor in the area with positive margin is confined to the gland or has extraprostatic extension. The pathology report should also indicate the presence of normal prostate tissue at the resection margin level. This might help the urologist explain why the serum PSA in patients with such a feature remains detectable after radical prostatectomy. In fact, the serum PSA value, even though very low, is not linked to tumor recurrence and persistence, but to incomplete resection of the prostate gland.

4. Gleason score: is a very powerful predictor of progression following radical prostatectomy. Gleason scores 2-4 are rarely seen. Most of the cases were tumors incidentally found on transurethral resection (stages T1a and T1b). All men with only Gleason scores 2-4 tumor at radical prostatectomy are cured. The prognosis of Gleason scores 5-6 shows a spectrum in its biologic behavior depending on other variables such as margin status and organ-confined status. Gleason score of 7 have a significantly worse prognosis than those with Gleason score 6. It is controversial the prognostic significance of Gleason score 3 + 4 versus Gleason score 4 + 3. Gleason scores 8-10 account for only 7% of the grades seen at radical prostatectomy. Typically, these tumors are highly aggressive and present at an advanced stage such that are not amenable to localized therapy.

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