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Original contribution

Vasitis nodosa and related lesions: a modern immunohistochemical staining profile with special emphasis on novel diagnostic dilemmas☆

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Summary Vasitis nodosa is a benign proliferation of vas deferens epithelium, thought to be a response to trauma or obstruction, usually vasectomy. Although histologic features mimic malignancy, diagnosis is usually straightforward due to the clinical context. We analyzed 21 specimens with vasitis or epididymitis nodosa with antibodies to PAX8, CD10, p63, α-methyl-acyl-coA-racemase (AMACR), GATA3, prostein, NKX3.1, and prostate-specific antigen (PSA). Two diagnostically problematic cases included (1) florid bladder muscle involvement after prostatectomy and (2) involvement of the ampulla and ejaculatory duct in a radical prostatectomy specimen. Vasitis nodosa was excluded in 3 additional histologic mimics (2 post-treatment prostate cancers and 1 bladder cancer). PAX8 yielded consistent positive (100%) nuclear staining in the proliferative glands of vasitis nodosa, often stronger and more uniform than native vas deferens. CD10 labeling was common but also labeled secretions and other structures. Labeling for p63 was often basally located in glands with a multilayered appearance, but often markedly attenuated or lacking in the proliferative glands compared to native epithelium. AMACR positivity was variable but often present (19/21). PSA, prostein, and NKX3.1 were consistently negative. Rare problematic cases of vasitis nodosa include "invasion" of the ejaculatory duct at the prostate and involvement of bladder muscle after prostatectomy. The proliferative vasitis nodosa glands often have a prostate cancer–like staining pattern with variable AMACR positivity and negative or patchy p63. However, reliable positivity for PAX8, patchy GATA3, and negative staining for PSA, NKX3.1, and prostein aid in distinguishing from prostate cancer and tubular variants of bladder cancer.

1. Introduction

Vasitis nodosa is a benign proliferation of vas deferens epithelium, thought to occur as a response to mechanical obstruction or traumatic injury. It is hypothesized that mechanical obstruction leads to increased intraluminal

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pressure and resulting spermatic fluid leakage. This extravasation of fluid is thought to result in subsequent inflammation and glandular proliferation. Vasitis nodosa typically occurs in the setting of prior vasectomy, but has been reported in other clinical scenarios, such as trauma, primary infertility, cystitis, or surgery. Clinical findings can include palpable nodules, scrotal pain, or swelling [1-4].

In the usual clinical context (characteristically post-vasectomy), vasitis nodosa is a relatively straightforward diagnosis, despite that it is known to have worrisome histologic characteristics, such as prominent nucleoli, pseudoinvasive growth pattern, and vascular and perineural invasion [5-8]. However, we have encountered rare clinical scenarios in which vasitis nodosa presented a diagnostic challenge, including occurrence at the ampulla of the vas deferens (the tortuous and dilated segment at the junction with the prostate and ejaculatory duct) in a prostate cancer specimen and in the wall of a cystectomy specimen after radical prostatectomy. Conversely, we have encountered occasional cancers that raised morphologic consideration of vasitis nodosa in these sites. Although a few immunohistochemical markers have been previously studied in vasitis nodosa, we sought to characterize the immunohistochemical staining pattern of vasitis nodosa with a modern antibody panel to aid in such scenarios.

2. Materials and methods

After approval by the institutional review board of the Henry Ford Health System, we queried the databases at two academic health systems (Indiana University Health and Henry Ford Health System) for cases of vasitis nodosa, epididymitis nodosa, and sperm granuloma, yielding 29 specimens. These cases were reviewed, of which 21 from 18 patients were ultimately confirmed to have vasitis or epididymitis nodosa and were included in the final cohort.

The specimens were from primarily vasectomy, vasovasostomy, or excisional biopsy samples, whereas 2 of the problematic diagnoses were found in resection specimens (1 radical prostatectomy and 1 cystectomy). Three cancer specimens (2 prostate cancers and 1 bladder cancer) for which morphology raised consideration of vasitis nodosa were also studied. Each specimen was fixed in 10% formalin solution and embedded in paraffin wax. Sections of 4-micron thickness were cut, stained with hematoxylin and eosin, and microscopically examined.

Each specimen was scored for presence or absence pseudoinvasive growth pattern, perineural invasion, vascular invasion, and prominent nucleoli. Clinical parameters, including age, reason for surgery, history of obstructive event, and history of previous chemotherapy or radiation were gathered. Using 4-μm-thick tissue sections, immunohistochemistry was performed using the Dako Link Autostainer automated system (Dako Corp, Carpinteria CA). Immunohistochemical stains were performed using anti-GATA3 monoclonal mouse antibody (1:200; Biocare, Concord, CA), anti-PAX8 monoclonal mouse antibody (1:50; Biocare), anti-CD10 monoclonal mouse antibody (1:75; Dako), anti-prostein (p501s) monoclonal mouse antibody (1:1000; Dako), anti–prostate-specific antigen monoclonal rabbit antibody (1:6000; Dako), anti-NKX3.1 polyclonal rabbit antibody (1:50, Biocare); and a PIN cocktail consisting of anti-p63 and α-methylacyl-CoA racemase (AMACR), monoclonal mouse antibodies (Biocare). Hematoxylin was used as a counterstain. Strength and pattern of staining, in addition to percentage of lesional tissue staining positive were recorded.

3. Results

Proliferative glands with prominent nucleoli were commonly present, in 19 of 21 cases, with infrequent perineural localization (3/21 cases). In the vasitis nodosa tissues (Figs. 1 and 2), PAX8 yielded consistent positive (100%) nuclear staining in the lesional glands, often stronger and more uniform than native vas deferens, and GATA3 was often positive (10/18). CD10 staining was consistently positive (21/21 cases), but in addition to the proliferative glands, this staining also labeled luminal and extra cellular secretions, and the basement membranes and apical surfaces of native and proliferative glands. Labeling for p63 was often basally located, resembling the basal cell pattern expected of prostate glandular tissue, but often markedly attenuated or lacking in the proliferative glands compared to the native epithelium. Labeling for GATA3 largely corresponded to the same areas as p63 positivity, preferentially glands with a more multilayered appearance. Overall, 12/21 cases demonstrated p63-positive basally located cells, although this was variable within a given specimen, ranging from 10% to 80% of glands positive (median 28%). Specimens without any p63-positive cells primarily corresponded to small foci of vasitis nodosa with only a few monolayered-appearing glands. AMACR positivity was variable but often present (18/21), ranging from weak to strong staining. No example of vasitis nodosa included in this study was positive for PSA, prostein, or NKX3.1 (0/20).

Two diagnostically challenging scenarios included (1) a radical prostatectomy specimen from a 74-year-old man, performed for Gleason 3 + 4 = 7 prostate cancer (Fig. 3A-D), and (2) a cystectomy specimen from a 70-year-old man, performed for severe radiation cystitis after prostatectomy (Fig. 3E and F). The cystectomy specimen demonstrated bladder muscle and florid soft tissue involvement by proliferative glands, mimicking recurrent prostate cancer invading the bladder wall. The radical prostatectomy specimen showed involvement of the ampulla and ejaculatory duct, mimicking seminal vesicle invasion (Table).

3.1. Vasitis nodosa mimics

Three cancers for which vasitis nodosa was considered in the differential diagnosis were also studied, including 2 post-