A Case of Vasitis Nodosa with Biphenotypic Differentiation

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Case Report

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Abstract

Background

Vasitis nodosa is a nodular lesion within the vas deferens that is characterized by a benign glandular proliferation of the vas deferens epithelium mixed with sperm and chronic inflammation. It is considered a reactive condition caused by increased intraluminal pressure. Problems in diagnosis can arise when atypical morphologic features are present or when vasitis nodosa is colonized by metastatic tumors.

Case presentation:

A 25-year old African American male status post vasectomy was diagnosed with obstructive azoospermia and elected to undergo a vasovasostomy. The histology of the resected specimen was consistent with vasitis nodosa, but the proliferative epithelial cells demonstrated the phenotypes of both vas deferens epithelium and mesothelium by immunohistochemistry.

Conclusion

This is the first reported case of vasitis nodosa expressing mesothelial markers, and it may therefore mimic mesothelial tumors such as mesothelioma and adenomatoid tumor.

Background

Vasitis nodosa is a terminology first used by Benjamin *et al* to describe a lesion in the vas deferens that reflects its nodular macroscopic appearance and potential inflammatory nature. The mechanism is believed to be due to increased intraluminal pressure as a result of obstruction and subsequent cascade of spermatic leakage and tubular proliferation (1). Vasitis nodosa has been most often seen in patients status post vasectomy and associated with spontaneous recanalization (2). Patients are mainly asymptomatic and require no clinical intervention (1). Although rare painful lesions have been reported (2). Vasitis nodosa may occasionally be misinterpreted as a malignant lesion or inguinal hernia clinically, and it is resected when it presents as a mass or a painful lesion (3-6).

The histology of vasitis nodosa is characterized by mural nodules composed of extravasated spermatozoa accompanied by the formation of epithelial-lined spaces (7). The lesion is usually associated with fibrosis, chronic inflammation, and sperm granulomas (8). Although it is a benign condition, vasitis nodosa demonstrates several features of malignancy (1,9,10). Overdiagnosis of malignancy may occur if one is not familiar with these variations. However, metastatic tumors can colonize vasitis nodosa, and some tumors can even mimic vasitis nodosa (11-13). Diagnosis of these tumors can be challenging especially when overwhelming tubular proliferation and inflammation are present.

The immunoprofile of these tubules are identical to the vas deferens epithelium except for the increased expression of AMACR (P504S)(11). Our case of vasitis nodosa expresses vas deferens epithelial markers as well as mesothelial markers. This knowledge will help expand the known immunoprofile and help reduce misdiagnosis of this lesion as mesothelioma or adenomatoid tumor.

Case Presentation

Clinical history

The patient is a 25-year old African American male married with two kids, who underwent a vasectomy in March of 2017. Subsequently, he and his wife desired to have children. He was counseled on options including vasovasostomy versus microsurgical epididymal sperm aspiration/testicular sperm aspiration with in vitro fertilization. The patient and his wife elected for a vasovasostomy in September of 2019. Intraoperative findings include bilateral segments of atretic vas deferens, spermatic granuloma on the left and clear fluid from the testicular end of the vas which demonstrate lack of sperm under microscope. Semen analysis was scheduled for approximately 6 weeks to 2 months post operation.

Histopathology

Histologically, the vas deferens was stenosed by multiple unencapsulated nodules with seemingly infiltrative borders. The nodules were composed of florid proliferation of anastomosing tubules centered on the lumen of vas deferens and mixed with sperm and chronic inflammation involving the muscle and adventitia. These tubules were composed of syncytial and streaming epithelial cells with clear to eosinophilic cytoplasm, monotonous nuclei, and conspicuous nucleoli with fine chromatin and a smooth nuclear membrane. The tubule cells stained positive for pancytokeratin. Occasional hyaline globules and rare mitoses were present. The tubule cells demonstrated very low proliferative index (Fig. 1). The inflammatory cells were predominantly histiocytes which were highlighted by the CD68 (KP1) antibody . Several spermatic granulomas were also identified. No lymphovascular or perineural invasion were identified.

Immunohistochemical stains were used to delineate the lineage of differentiation (Fig. 2). Similar to vas deferens epithelium, the lesional tubule cells demonstrated positive reactivity to PAX-8 antibody. As reported previously, AMACR (P504S) was overexpressed in comparison to vas deferens epithelium (which was weakly positive). WT-1 and calretinin were initially performed to rule out a mesothelial lesion such as adenomatoid tumor and mesothelioma which are common lesions in this anatomical location. Both markers were positive in the lesional cells. However, the lesion was centered on the vas deferens lumen in contrast to a mesothelial lesion in which it would extend from the mesothelial surface. The epithelium was characteristically mixed with sperms and chronic inflammation. We believed that this lesion represents vasitis nodosa with simultaneous mesothelial differentiation. Several other organ-specific markers including NKX3.1, GATA3, PLAP and synaptophysin were also performed to exclude metastatic prostatic, urothelial, germ cell, and neuroendocrine tumors and found to be negative (Fig. 3).

Discussion

Various tumor and tumor-like lesions can occur in near the testes. A few have a positive epithelial component with adenomatoid tumor being the most common (14). Unlike vasitis nodosa, the epithelium of adenomatoid tumor is flattened, and the stroma is fibrotic (14). Our case did not show these morphologic features, and the lesional cells were centered on the lumen of vas deferens.

Vasitis nodosa and its counterpart in epididymis epididymitis nodosa were named for their resemblance to salpingitis isthmica nodosa (7, 15). Vasitis nodosa is the most common asymptomatic postoperative complication of a vasectomy and is identified in 50%-66% of the patients with the obstruction of the proximal end and associated inflammation. (1, 16). Most cases of vasitis nodosa occurred within 2 months to 19 years post operation (17). It was thought to be a result of a breach in the lining epithelium due to increased intravasal pressure and subsequent epithelial regeneration (18). This could be attributed to an attempt at re-establishing the communication in an obstructed lumen and restoring the reproductive capacity of the individual (19). Recanalization has been reported in the presence of vasitis nodosa (20). Similarly, spermatic granuloma represents the body's attempt to restore fertility by allowing sperm to leak into tissue (21). This hypothesis was indirectly supported by the observation that a better surgical sealing of the cut ends lead to a decreased incidence of vasitis nodosa and spermatic granulomas (21). Vasitis nodosa has also been identified in patients status post herniorrhaphy, chronic inflammation, bladder diverticulum, torture, and trauma (1, 3, 22). Vasitis nodosa can rarely arise in patients with none of these risk factors, and these lesions usually lack inflammation (3, 17). Presence of spermatic granulomas was thought to be associated at a better chance of impregnation (23). However, the result was not successfully reproduced in a later study (1). The persistent infertility after vasectomy reversal might be attributed to the development of antisperm antibody which has been detected in 50–70% patients after vasectomy (1).

The correct diagnosis of vasitis nodosa relies on the recognition of a benign process with seemingly malignant morphologic features. The florid proliferative activity of the epithelium can be misleading and easily misinterpreted as a malignant process. Atypical cytologic features such as vesicular nuclei, prominent nucleoli and mitotic figures can occasionally be present (16). The lesion can extend to involve the muscle layer and adventitia (1, 24, 25). Benign perineural and intraneural invasions have also been reported (4, 9, 16, 26). In one study, “benign neural invasion” was identified in 16% of the vasitis nodosa cases in which one or two nerves were invaded by one to eight glands (10). This was further complicated by nerve hyperplasia and neuromas (1). The phenomenon might be due to nerve growth factor expression which has been demonstrated in the epithelium of vasitis nodosa immunohistochemically (27). The epithelium in vasitis nodosa can also invade small veins or arteries which are almost always accompanied by elastosis (28). It has been postulated that proliferating ductules in vasitis nodosa invade the blood vessels after they have become obliterated by regressive and reparative processes (28).

Tumors can also mimic or colonize vasitis nodosa. Tumors especially of adjacent organs, such as prostatic adenocarcinoma and urothelial carcinoma with glandular differentiation can mimic the

epithelial proliferation of vasitis nodosa (11). Presence of seminoma cells in the stroma or pagetoid spread inside tubules with concurrent testicular seminoma has been reported (12). Because no lymphatic, perineural, epididymis, or proximal vas deferens involvement could be demonstrated, it was hypothesized that the tumor cells may spread by shedding and subsequent arresting (12). A similar case of involvement of vasitis nodosa by germ cell tumors demonstrated unclassified germ cell neoplasia with pagetoid spread involving vasitis nodosa. The concurrent germ cell tumor was in the ipsilateral testis and contained no seminoma component (13).

Similar to the lining epithelium of vas deferens, the epithelial cells of vasitis nodosa are positive for cytokeratin 7 and 19, PAX8, CD10 and vimentin with patchy expression of GATA3 (8, 11). High-molecular-weight keratin 34betaE12 is present in the basal lining cells of the vas deferens and vasitis nodosa (8). P63 is positive in basal cells of vas deferens lining epithelium but shows patchy expression in vasitis nodosa (11). In contrast to the lining cells, some vasitis nodosa cells are also positive for CA125 and AMACR (8, 11). However, other prostate markers such as PSA, prostein and NKX3.1 are consistently negative (11).

In conclusion, we report for the first time a case of vasitis nodosa with both phenotypes of vas deferens lining epithelium and mesothelium. Electron microscopy may be useful in eliminating the possibility that the nature of the proliferating cells is truly mesothelial (17).

Declarations

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Not applicable.

Authors' contributions

B.R. diagnosed the surgical samples pathologically and wrote the manuscript.

W.L. diagnosed the surgical samples pathologically and revised the manuscript.

All authors have read and approved the final manuscript.

Availability of data and materials

The surgical materials and the datasets analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Written informed consent for publication of clinical history was obtained from the patient. A copy of the consent form is available for review by the Editor of this journal.

Ethics approval and consent to participate

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Figures

Figure 1

A (20x) and B (40x): Proliferation of epithelial cells in the vas deferens wall. The arrow depicts native vas deferens epithelium. H&E stain reveals epithelial cells form tubules mixed with inflammatory cells and sperms. C: Pancytokeratin immunostain (20x) confirms the epithelial nature of the lesional cells. D: Ki67 immunostain (20x) demonstrates very low proliferative index.

Figure 2

Lesional cells demonstrating biphenotypic differentiation. Vas deferens epithelial differentiation was evidenced by positive PAX-8 (A) and AMACR (B) immunostains; mesothelial differentiation was evidenced by positive calretinin stain (C) and WT-1 (D) stains.

Figure 3

Histologic mimickers including prostatic adenocarcinoma, urothelial carcinoma, neuroendocrine tumor and germ cell tumor were further ruled out by negativity of makers NKX3.1 (A), GATA3 (B), synaptophysin (C) and PLAP (D), respectively.