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CASE REPORT

Gross hematuria, irritative lower urinary tract symptoms, and bilateral hydroureteronephrosis: A concerning presentation of an ultimately benign case of concurrent nephrogenic adenoma and eosinophilic cystitis

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Abbreviations used: CT, computed tomography; NA, nephrogenic adenoma; EC, eosinophilic cystitis

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ABSTRACT

Nephrogenic adenoma and eosinophilic cystitis are well-known, distinct pathologic bladder diagnoses that rarely occur concurrently in the published literature. We present the first adult case, and second reported case, of these two disease processes occurring synchronously. Our patient's initial complaints were the characteristic symptoms of gross hematuria and urinary urgency, which were primarily worrisome for malignancy. She had no prior genitourinary history, whereas these two diagnoses are commonly associated with chronic bladder irritation, instrumentation, and trauma. Our patient did not respond to conservative management with prophylactic antibiotics and antihistamines, however experienced full resolution of her symptoms following resection of the lesions.

Keywords: benign neoplasm, eosinophilic cystitis, hydronephrosis, nephrogenic adenoma, urinary bladder neoplasm

A 79 year-old female was referred to the urogynecology clinic after complaining to her internist of a one year history of intermittent, new onset urinary urgency and urge incontinence associated with vulvar burning, itching, and pressure. On presentation she also reported new onset gross hematuria within the past month. A one week trial of estrogen cream did not relieve the symptoms.

She had no prior medical or surgical genitourinary history and no family history of genitourinary disorders or malignancies. She denied any tobacco or chemical exposures, was married, and had delivered two children vaginally.

Her physical exam was unremarkable except for posterior forchette tenderness to palpation. Her urinalysis revealed microscopic hematuria with pyuria and no urinary eosinophils. A urine culture was negative. Her laboratory assessment revealed no abnormalities in her complete blood cell count with differential, serum chemistries, liver or renal function.

An in-office cystoscopy revealed an approximately 1cm papillary, bullous bladder lesion near the right ureteral orifice. The tumor was friable with a small amount of bleeding. Catheterized cytology was benign. A CT Urogram revealed moderate bilateral hydroureteronephrosis with distal ureteral and asymmetric bladder wall thickening (**Fig. 1**). The combination of the patient's symptoms and the radiographic and cystoscopic findings was highly concerning for muscle-invasive bladder cancer.

The patient underwent an operative cystoscopy and transurethral resection of the bladder tumor with intra-operative findings of diffusely erythematous urothelium with small papillary masses on the right posterior and lateral bladder walls. Upper tract endoscopy was delayed as there was concern for possible upper tract seeding if the lesions were malignant.

Pathology revealed multiple papillary structures lined by cuboidal epithelium consistent with nephrogenic adenoma (NA), as well as abundant eosinophils in clusters within the lamina propria and the deep muscle diagnostic of eosinophilic cystitis (EC) (**Fig. 2**). The patient was treated with a one month course of daily anti-histamines and prophylactic dose trimethoprim-sulfamethoxazole.

At follow-up four months later, the patient's symptoms were unchanged. On repeat in-office cystoscopy her urothelium had normalized, except for frond-like, ulcerated lesions on the right-lateral bladder wall and superior to the trigone. She had bloody ureteral efflux bilaterally, prompting subsequent operative cystoscopy. Bladder biopsies, lesion fulguration, right renal pelvis washing and retrograde pyelogram were performed which demonstrated hydroureteronephrosis to the level of the bladder with no filling defects, and a stent was placed. Left retrograde pyelogram was attempted, but the left ureteral orifice was unable to be cannulated due to edema. The right upper-tract cytology was benign, and bladder biopsies demonstrated persistent NA. Following this procedure, her urinary symptoms resolved. She was seen in follow-up two months later and remained asymptomatic. Left antegrade pyelogram was performed with interventional radiology and demonstrated no hydroureteronephrosis or filling defects, and contrast flowed distally

into the bladder. Left retrograde endoscopy, selective cytology, and stent placement one month later, to complete the hematuria work-up, revealed a minute papillary neoplasm of low malignant potential with no invasion in the left distal ureter, which was completely resected. Follow-up in-office cystoscopy and left ureteral stent removal two weeks later demonstrated no erythematous bladder mucosa, bladder lesions, or bloody ureteral efflux.

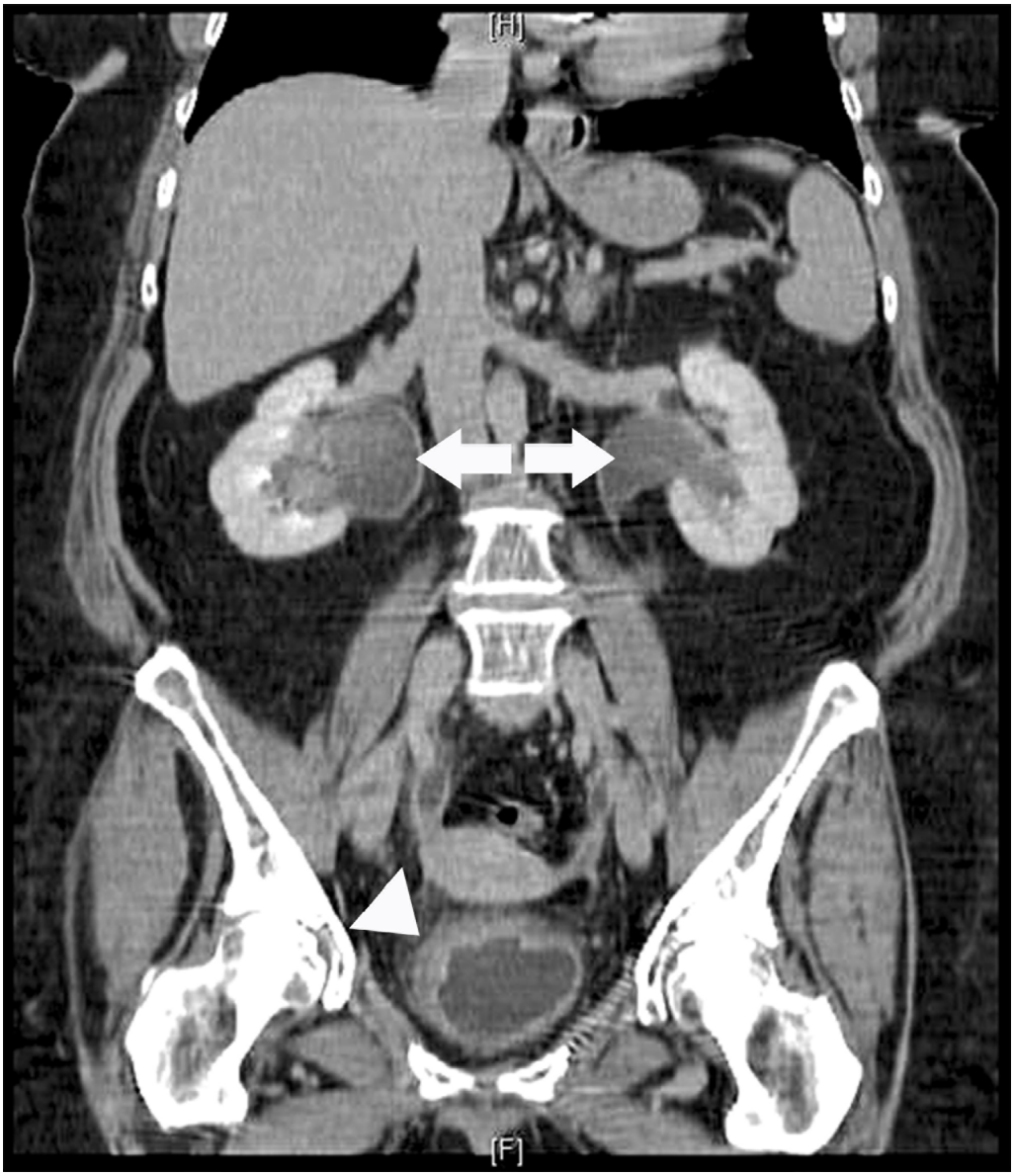

Figure 1. Delayed intravenous contrast CT scan demonstrates bladder wall thickening (white arrowhead) and bilateral hydroureteronephrosis (white arrows).

This patient represents a unique case of concurrent NA and EC, which are typically diagnosed as distinct entities. NA is a benign, reactive lesion common to patients with chronic bladder irritation, instrumentation, or trauma. The etiology of EC is unknown, but thought to be either immunologic or allergic in nature [1]. Though the coexistence of these two disease processes may be immunologic, as the patient had no history of chronic irritation, instrumentation, or trauma, given that the symptoms resolved following diagnostic evaluation and resection of all lesions, no further diagnostic evaluation of possible immunologic sources, nor additional treatments, were pursued.

In 2011, Rossi et al. published the only other case of concurrent NA and EC to date in an 8-year-old boy who was diagnosed after complaining of sudden onset left flank pain [2]. Both this patient and our patient were found to have hydronephrosis on presentation, which may have been due to an obstructing lesion but has also been shown to occur in the fibrotic stage of EC, where the bladder is small and contracted [3,4].

Treatment for both conditions includes transurethral resection and long-term prophylactic antibiotics, while antihistamines may also be used for EC [1,5]. Though these lesions are thought to be benign, they frequently recur. Concurrent NA and adenocarcinoma and EC and urothelial carcinoma have been reported, therefore surveillance cystoscopy is recommended given the unknown long-term prognosis [4,6].

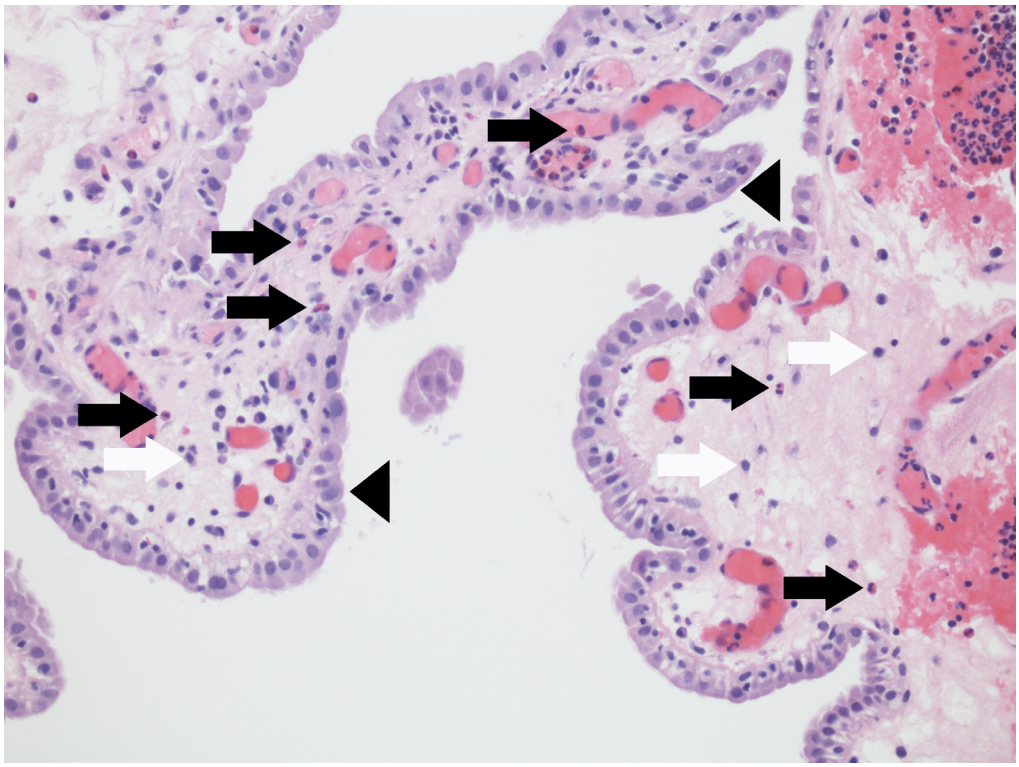

Figure 2. Cuboidal epithelium-lined papillary structures (black arrowheads) diagnostic of NA and numerous eosinophils (black arrows) and lymphocytes (white arrows) in the lamina propria and throughout deep muscle of the bladder wall (not shown) diagnostic of EC (hematoxylin and eosin stain).

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