Cureus
Part of SPRINGER NATURE

Open Access Case Report

Published via Wayne State University Department of Urology

The Apple Green Birefringence Blockade: Extensive Localized Amyloidosis of the Bladder and Ureter Requiring Cystectomy and Urinary Diversion

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Received 09/05/2026
Review began 09/11/2026
Review ended 10/06/2026
Published 10/22/2026

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DOI: 10.7759/cureus.118379

Abstract

Localized amyloidosis of the urinary bladder is a rare condition that can mimic urothelial carcinoma and may cause significant urinary tract morbidity. We report a 55-year-old woman with progressive urinary symptoms, hematuria, bladder wall thickening, and left obstructive uropathy. Biopsy demonstrated amyloid light-chain (AL) lambda-type amyloidosis with Congo red positivity and apple-green birefringence. Systemic evaluation showed no monoclonal protein, supporting localized disease. Extensive involvement of the bladder and distal ureters caused persistent obstruction and was not amenable to endoscopic resection. The patient ultimately underwent cystectomy with ileal conduit urinary diversion.

Categories: Urology
Keywords: amyloidosis, bladder, cystectomy, ureter, uropathy

Introduction

Amyloidosis is a heterogeneous protein-folding disorder that causes the aggregation and deposition of insoluble amyloid fibrils throughout the body. Amyloid is formed by misfolded proteins arranged in antiparallel β-pleated sheets, often secondary to acquired or hereditary causes [1]. The most common form is amyloid light-chain (AL) amyloidosis, making up 70-80% of all amyloid diagnoses [2]. AL amyloidosis consists of immunoglobulin light chains and is most often associated with plasma cell dyscrasias, such as multiple myeloma and Waldenström macroglobulinemia [3].

Amyloid proteins can deposit systemically or be localized within the body, including the heart, kidneys, nerves, and vasculature, leading to cardiomyopathy, nephropathy, neuropathy, and hemorrhage [4]. Involvement of the lower genitourinary tract is uncommon, and localized bladder amyloidosis is a rare manifestation that can occasionally extend beyond the bladder to involve the ureters [5,6]. With fewer than 400 cases reported in the literature, the most frequently involved site was the bladder, which comprised 71% of the cases, while ureteral involvement occurred in about 12% [7]. The median age at diagnosis is 57 years, and it occurs with a male predominance. Patients may present with painless hematuria, urinary obstruction, or irritative urinary symptoms [5]. Cystoscopy and radiographic imaging of bladder amyloidosis may closely mimic bladder malignancy, making diagnosis dependent on histopathologic examination [8].

Here, we present an unusually extensive case of localized AL amyloidosis involving the bladder and distal ureter, causing progressive obstructive uropathy that was not amenable to endoscopic resection and ultimately required cystectomy with ileal conduit urinary diversion.

Case Presentation

A 55-year-old female presented with years of progressive urologic symptoms including urinary frequency, urinary retention, intermittent gross hematuria, and bladder prolapse. CT showed mild left obstructive uropathy, most likely based on delayed left nephrogram and a distal ureteral stricture with urothelial neoplasm not excluded, as well as nonspecific bladder wall thickening. (Figure *1*).

How to cite this article
Chalom T, Juliette K, Ross E, et al. (October 22, 2026) The Apple Green Birefringence Blockade: Extensive Localized Amyloidosis of the Bladder and Ureter Requiring Cystectomy and Urinary Diversion. Cureus 18(10): e118379. DOI 10.7759/cureus.118379

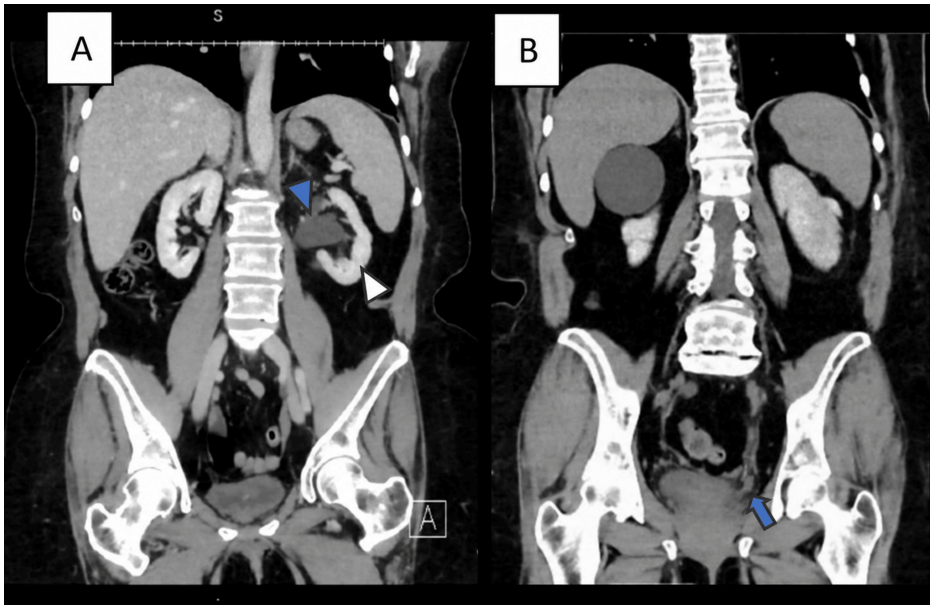


FIGURE 1: CT-abdomen/pelvis with IV contrast prior to stent or PCN

Panel A demonstrates mild left hydronephrosis (white arrow head) and hydroureter (blue arrow head). Panel B demonstrates hyperdense filling defect in the distal ureter over a long segment favored to reflect a distal ureteral stricture (blue arrow). Additional significant bladder wall thickening consistent with amyloidosis of the bladder.
PCN: percutaneous nephrostomy.

She underwent a cystoscopy and transurethral resection of a bladder tumor (TURBT) for presumed urothelial carcinoma, which instead showed extensive bladder amyloid deposits. Tissue biopsy revealed urothelial and squamous mucosa with masses of eosinophilic proteinaceous material in the lamina propria. Congo red special stain of the tissue was positive for apple-green birefringence under polarized light, and amyloid subtyping confirmed AL lambda-type amyloidosis involving the bladder (Figures *2*, *3*, *4*). Due to distal left ureter involvement, it was determined that disease burden was too extensive for complete endoscopic resection, with a plan for possible left percutaneous nephrostomy (PCN) placement if symptoms progressed.

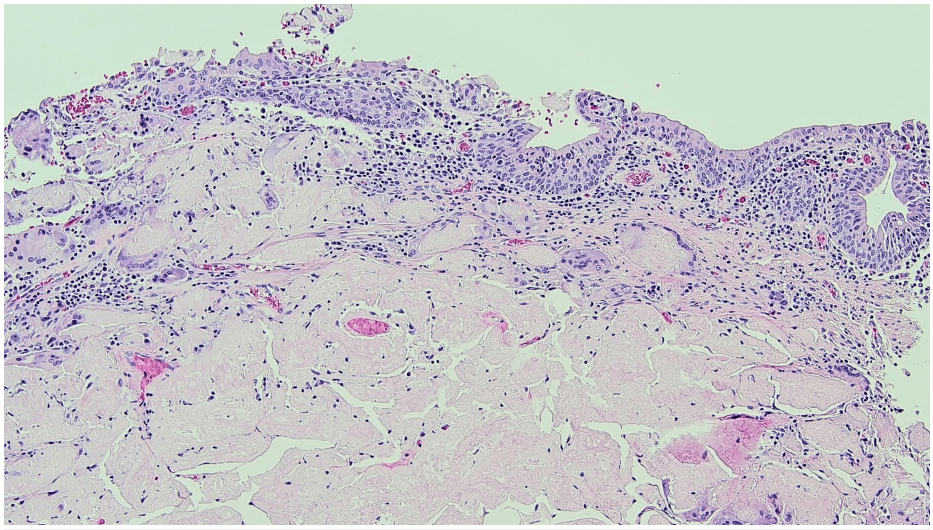


FIGURE 2: Bladder wall displaying deposition of eosinophilic amorphous material in lamina propria (H&E, 100x total magnification)

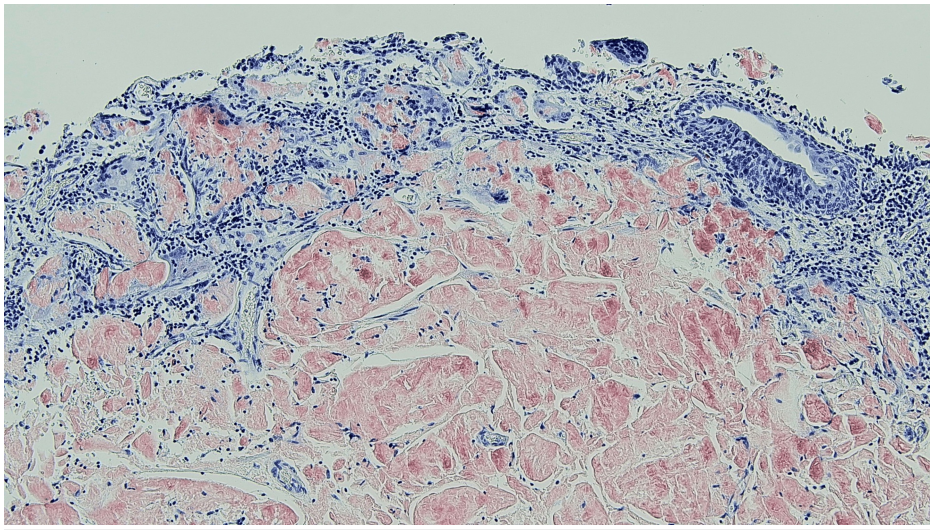


FIGURE 3: Bladder wall amorphous material is congophilic (red) when stained with Congo Red (Congo Red, 100x total magnification)

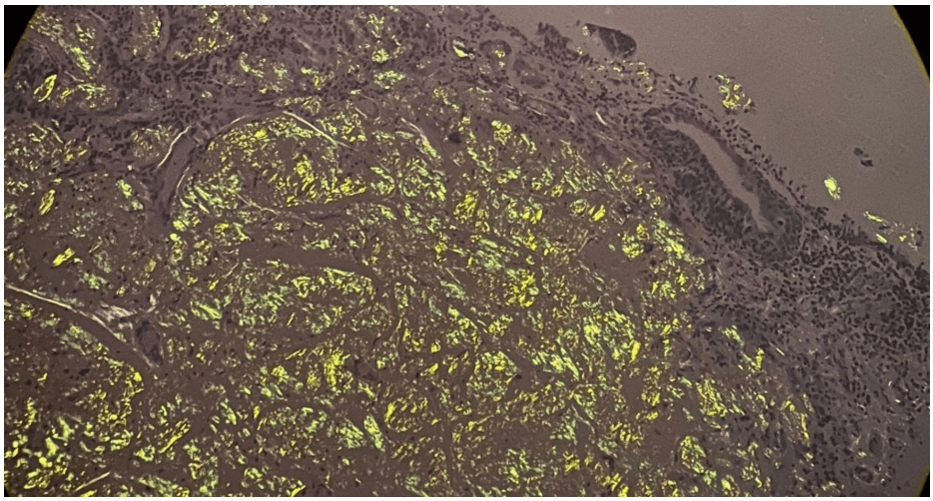


FIGURE 4: Bladder wall congophilic material demonstrates characteristic apple-green birefringence under polarized light (Congo Red with polarized light, 40x total magnification).

Three months later, the patient presented to the emergency department (ED) with decreased urinary output and flank pain. Further CT imaging demonstrated extensive bladder involvement with amyloid deposits, as well as persistent left hydroureteronephrosis with a hyperdense filling defect extending along a long segment of the distal left ureter, concerning for distal ureteral involvement (Figure *5*). A PCN tube was placed to decompress the obstructed collecting system, restore urinary drainage, and prevent further renal injury from persistent hydronephrosis. Renal function remained preserved despite the obstruction, with creatinine 0.90 mg/dL at the time of PCN placement and 0.83 mg/dL following decompression. Local resection remained infeasible given the extent of involvement. Given her progressively symptomatic disease, persistent urinary obstruction, and extensive localized involvement not amenable to endoscopic resection, cystectomy was discussed as a definitive treatment option.

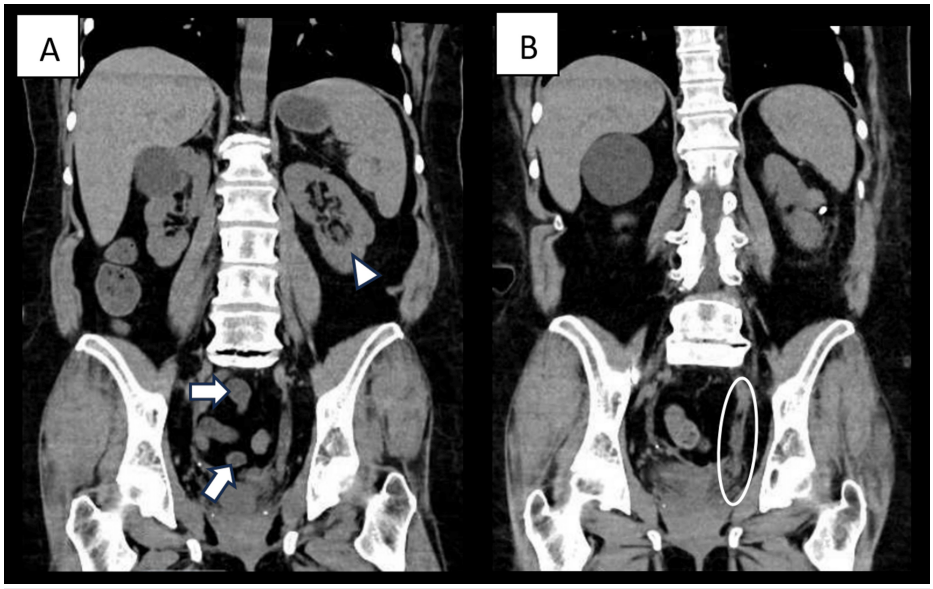


FIGURE 5: CT-abdomen/pelvis without contrast after PCN tube placement

Panel A demonstrates a urinary bladder filled with amyloid deposits (white arrows) and mild left hydroureteronephrosis (white arrowhead). Panel B demonstrates a filling defect in the distal left ureter over a long segment (white circle), with PCN visualized in the left kidney. PCN: percutaneous nephrostomy

The patient also met with medical oncology to clarify whether her bladder AL amyloidosis represented isolated localized disease or was part of a systemic plasma cell disorder. Evaluation for an underlying systemic plasma cell disorder and secondary organ infiltration was negative, with normal serum free light chain ratios, absent monoclonal bands on serum and urine immunofixation, an unrevealing bone marrow biopsy, and no biochemical evidence of cardiac or renal parenchymal amyloid involvement (normal cardiac biomarkers and absent proteinuria). Due to the extent of disease, the patient underwent robotic-assisted laparoscopic cystectomy and open ileal loop urinary diversion. Intraoperatively, both ureters were mobilized proximally and frozen sections were obtained bilaterally. The right ureter was unremarkable, while the remaining distal left ureter was excised before anastomosis to the ileal loop. Prior to cystectomy, creatinine was 0.91 mg/dL and remained stable postoperatively at 0.72-0.81 mg/dL. Final pathology confirmed extensive amyloid involvement of the bladder and left ureter, including the detrusor muscle and periureteral tissues.

Postoperatively, the left PCN was removed, and the patient was discharged on postoperative day four with a functioning ileal conduit. At two-week follow-up, wound evaluation and bilateral ureteral stent removal were uncomplicated. At two months postoperatively, creatinine remained at her baseline (0.72 mg/dL). At three-month follow-up, she denied new urinary symptoms or ileal conduit-related complications.

Discussion

Amyloidosis is a rare disorder, with approximately 3,000-4,500 new cases of AL amyloidosis diagnosed per year in the United States [9]. Different presentations of amyloidosis can make diagnosis difficult. In this case, a 55-year-old woman was found to have extensive AL amyloid deposition throughout the bladder and distal left ureter. The extent of infiltration made localized transurethral resection (TUR) an unsuitable option and led to obstructive uropathy requiring percutaneous nephrostomy placement, highlighting the significant morbidity of this presentation.

Understanding the common manifestations of bladder amyloidosis may broaden the differential diagnosis and enable earlier identification of the disease. The most common symptom is painless hematuria, documented in over 65% of patients [7]. Additional presenting symptoms may include irritative lower urinary tract symptoms such as urinary frequency, urgency, and dysuria [10]. Patients may also experience obstructive symptoms, like urinary retention, suprapubic pain, pelvic discomfort, and recurrent urinary tract infections; however, these are less frequently reported [11]. In our case, the patient exhibited several typical features, including gross hematuria and increased urinary frequency, in addition to urinary retention and obstruction, secondary to suspected distal ureteral extension.

Primary amyloidosis of the urinary bladder can closely mimic urothelial carcinoma of the bladder in both presentation and appearance. On cystoscopy, mucosal changes may appear as erythematous, nodular, and

hemorrhagic lesions within the bladder wall [11]. Imaging studies, such as CT and ultrasound, may also reveal findings suggestive of urothelial cancer, such as bladder wall thickening or filling defects [12]. Due to the overlapping presentation, histopathologic evaluation is required for definitive diagnosis. TUR can be performed to extract the lesion, reducing hematuria symptoms and retrieving tissue for examination [11]. Tissue biopsy demonstrating amorphous eosinophilic material on Hematoxylin and Eosin (H&E) stain, and apple-green birefringence of the amyloid on Congo red staining is pathognomonic for the diagnosis of amyloidosis [13]. Subtyping allows for amyloid type differentiation, which is used to determine the need for systemic workup and treatment [14]. The primary subtypes found in the bladder include AL (immunoglobulin light chain) and amyloid transthyretin (ATTR), with AL lambda light chain reported to be most common in localized bladder amyloidosis [10].

Management of these cases varies depending on the extent of disease and associated symptoms. Localized lesions can be treated with TUR or laser ablation, which can reduce disease burden [10,15]. However, recurrence following endoscopic treatment is common, occurring in over 50% of patients treated with transurethral resection [16]. Intravesical dimethyl sulfoxide (DMSO) has been used as a conservative treatment to reduce clinical symptoms due to its anti-inflammatory properties, but it should be used as an adjunct to resection [17]. Therefore, patients require long-term surveillance. In extreme cases, more invasive procedures may be required, such as partial or total cystectomy. In the literature, this is a rare occurrence and has been documented in only a few cases [18]. In the case of our patient, given the extensive obstructive nature of disease progression, cystectomy and urinary diversion were necessary.

Conclusions

Bladder amyloidosis is a rare disease that should be considered in the differential diagnosis in patients presenting with hematuria and bladder lesions on imaging. In these patients, accurate diagnosis relies on histological evaluation of the tissue, due to symptomatic overlap with urothelial bladder carcinoma. Additionally, distinguishing localized from systemic amyloidosis is required to direct management. This case highlights the potential for bladder amyloidosis to present with extensive localized disease resulting in obstructive complications, resulting in cystectomy with urinary diversion, underscoring the importance of thorough diagnostic workup.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Timothy Chalom, Kendra Juliette

Acquisition, analysis, or interpretation of data: Timothy Chalom, Kendra Juliette, Emma Ross, Hillary Smith, Michael Cher

Drafting of the manuscript: Timothy Chalom, Kendra Juliette

Critical review of the manuscript for important intellectual content: Emma Ross, Hillary Smith, Michael Cher

Supervision: Emma Ross, Michael Cher

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Acknowledgements

Timothy Chalom and Kendra Juliette contributed equally to the work and should be considered co-first authors.

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