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Inflammation and infection

Is corona virus infection a risk factor for hematuria in secondary bladder amyloidosis? The first case report

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ABSTRACT

Urogenital amyloidosis is a rare disease that involved every site of the urogenital system. Involvement of bladder developed with gross hematuria, and any intrinsic or extrinsic stresses exacerbate hematuria. We reported a secondary bladder amyloidosis case that presented with gross hematuria without any risk factor except COVID-19 infection.

Introduction

Amyloidosis is a disease characterized by the extracellular deposition of amyloidal material in various organs. It is categorized as localized and systemic amyloidosis based on location and primary and secondary based on its pathology.[1]

Genitourinary amyloidosis, especially primary amyloidosis, is a rare condition. Its location in the genitourinary system is variable and can occur anywhere: kidneys, pelvis, ureters, bladder, urethra, or even penis.[2]

Renal involvement usually leads to renal failure, and lower urinary tract involvement presented with gross hematuria (GH) with or without irritative voiding symptoms and any underlying factor can exacerbate the symptoms. In such a situation, cystoscopy, biopsy, and histopathological tests are necessary to confirm the diagnosis.[2]

For the first time, we report a COVID-19 positive patient with a history of rheumatoid arthritis (RA) and proven renal amyloidosis who developed spontaneous hematuria without any underlying risk factors except COVID-19 infection, that a cold cup biopsy of the bladder revealed the amyloidosis.

Case presentation

We document a case of a 68-year-old woman known case of RA since 15 years ago and amyloidosis since 6 years ago with kidney involvement (confirmed by renal biopsy) who developed dyspnea and fever 10 days before admission.

The patient was receiving immunosuppressive drugs (Methotrexate, Prednisolone, Entracept) for more than 10 years.

The patient has admitted to the hospital, and laboratory tests revealed that COVID-19 infected her. Other lab tests showed the high creatinine level (Cr: 4.7 mg/dl) and bicytopenia (RBC: 2 million/UL, Plt: 77000/UL) and microscopic hematuria (RBC: 40–50) with negative urine culture and normal coagulation test (PT:13, INR:1).

Ultrasound sonography of the kidney, ureters, and bladder revealed a normal size of both kidneys and no hydroureteronephrosis, but bilaterally increase in cortical echogenicity and decrease of corticomedullary differentiation and abdominopelvic CT was normal.

During hospitalization, the patient developed GH that was not stopped with conservative management (bladder irrigation, platelet, and packed cell transfusion). A clot passage was added, so she referred to the urology department underwent cystoscopy that revealed a slather organized blood clot in the bladder. Clots were irrigated. A large diverticulum without any malignant portion was seen in the right lateral wall. A 2 cm linear ulcerated area with hyperemia without active bleeding in the posterior bladder wall was seen (Fig. 1). A cold cup biopsy was performed. After cystoscopy, her hematuria was stopped with bladder irrigation solely, but after 2 days, the patient developed GH

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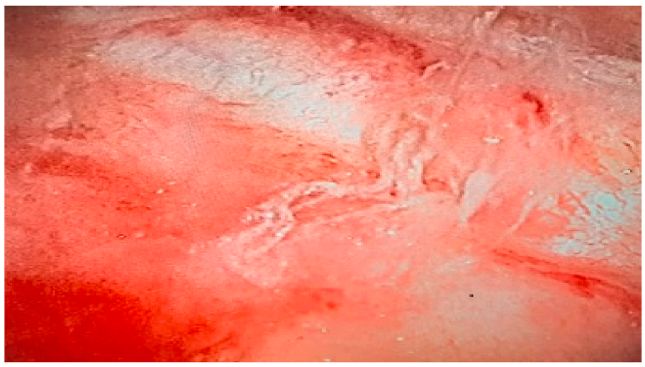

Fig. 1. An ulcerated area measuring approximately 2 cm in size with hyperemia without active bleeding.

again; due to her unstable condition and respiratory problem, the patient was not a candidate for the operation, and bladder irrigation was the only intervention that was done for her. Unfortunately, the patient died because of cardiac arrest due to respiratory failure.

Her histopathological findings were consistent with amyloidosis and were confirmed using special stains such as Congo red and Haematoxylin & Eosin (Fig. 2a and b,c).

Discussion

Primary isolated amyloidosis of the urinary bladder is a rare disease with 160 cases reported by Malek et al.[1] In primary amyloidosis, there is no underlying pathology except multiple myeloma, and cardiovascular, gastrointestinal, and respiratory systems are most affected (1), but secondary amyloidosis is related to a chronic inflammatory disease, specially RA, and genitourinary and lymphatic systems are most affected.[1] Renal involvement is always occurred in secondary amyloidosis and caused renal insufficiency. Still, the urinary bladder is involved in primary type and presented with GH that is due to amyloid deposition in the wall of vessels and impairment of arterioles contractility, so any stress caused vessels rupture and massive hematuria, that can mimic the urothelial carcinoma symptoms.[3]

Secondary amyloidosis of the bladder is more common in females and mainly secondary to rheumatoid arthritis and ankylosing spondylitis, and long-standing chronic inflammatory conditions. There have only been a few reports published so far on vesical amyloidosis in patients with RA. However, 5 of 10 patients (50%) with vesical amyloidosis died because of continuous massive hematuria, which induced disseminated intravascular coagulation and multiple organ failure[4] and any additional stress increase the hematuria and mortality rate like our case that was COVID-19 positive and after intubation without any urological intervention her hematuria (that was stopped after cystoscopy and biopsy) recurred.

Multiple studies revealed that COVID-19 infection caused hematoma (retroperitoneal, psoas) especially in patients who received anticoagulant agents and have abnormal coagulation tests [5] but our patient did not receive an anticoagulant agent, and her coagulation tests were normal, and she did not have any risk factors for bleeding. Nevertheless, she developed gross hematuria, so we should keep in mind that COVID-19 infection can increase hemorrhage risk.

Diagnosis of amyloidosis is based on radiologic (contrast-enhanced CT scan) and cystoscopic evaluation, but bladder amyloidosis can mimic bladder cancer radiologically and clinically[2] so pathologic confirmation is needed for proving the diagnosis and apple-green birefringence under the polarized microscope is characteristic for it.[2]

Management of bladder amyloidosis is based on controlling hematuria. A wide range of surgical interventions including coagulation, temporary urinary diversion, partial and total cystectomy and nonsurgical like bladder irrigation and dimethyl sulfoxide instillation were introduced[1,2] and also some case of spontaneous regression were reported so management of bladder amyloidosis should be the individualized base of the severity of symptoms, location, and size of lesion and type of amyloidosis.[3]

In conclusion, this case highlights the importance of urologists to appreciate alternative diagnoses in patients with RA who have had GH. Nowadays, COVID-19 is a risk factor that exacerbates hematuria in these patients.

Ethics approval and consent to participate

The ethical committees of the Shaheed Beheshti University of Medical Sciences approved this study and permitted us to review patients' medical data.

Consent for publication

Verbal consent was obtained from husband of patient.

Availability of data and material

None.

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None.

Author contribution

AAD: Conception and design, Critical revision of the manuscript for important intellectual content, Supervision
KH: Drafting of the manuscript
HM: Administrative, technical or material support, Supervision
MA: Drafting of the manuscript
MD: Acquisition of data

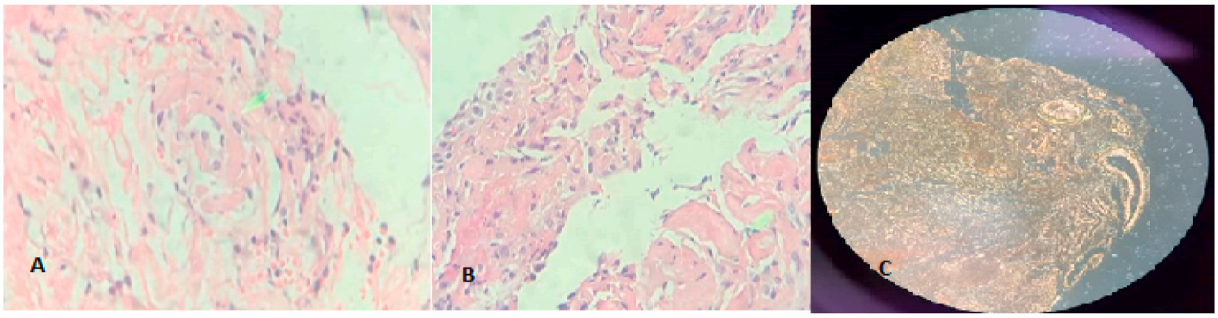

Fig. 2. A, B: sections show bladder mucosa amorphous and global eosinophilic material/C: Congo red staining reveals "apple green" birefringence with a polarized microscope. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

AR: Conception and design, Critical revision of the manuscript for important intellectual content, Administrative, technical or material support Supervision

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Declaration of competing interest

None.

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