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Localised amyloidosis of the bladder: A rare mimic of urinary tract malignancy (case report and literature review)

N. Mayor^{a,*}, A.S.J. Coppola^{b,1}, Harry Knights^a, T. Nazar^c, H. Hunter^a, H. Mostafid^a^a Stokes Centre for Urology, Royal Surrey NHS Foundation Trust, United Kingdom^b Guy's and St Thomas' NHS Foundation Trust, United Kingdom^c Cambridge University Hospitals NHS Foundation Trust, United Kingdom

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ABSTRACT

INTRODUCTION: Localised amyloidosis of the urinary tract is rare and often presents with haematuria.**PRESENTATION OF CASE:** A 59 year old male presented with recurrent episodes of frank haematuria exacerbated by anticoagulation after a minor stroke. He had a background of hypertension, hypercholesterolaemia, and Parkinson's disease. Initial investigations did not reveal a cause, but eventual cystoscopic biopsy showed bladder mucosa expanded by deposits of amorphous, pale, eosinophilic, proteinaceous material and immunohistochemical staining revealed the presence of amyloid deposition. Workup for systemic amyloidosis was negative. A diagnosis of primary localised amyloidosis of the bladder was made. Trans-urethral resection was performed and annual cystoscopic surveillance was commenced. He was followed up for 11 years without recurrence.**DISCUSSION:** A comprehensive literature review revealed 349 published cases of localised amyloidosis of the urinary tract, with a median age of 57 (interquartile range 49–69), and a male preponderance (1.5 to 1). Painless visible haematuria (65%) was the most frequent presenting complaint and the bladder was the most common site of involvement (71%). Transurethral resection was the most common form of management (42%) but a proportion of patients underwent more radical surgery (nephroureterectomy/nephrectomy 9%, cystectomy 1%). Median follow up was 33 months (interquartile range 12–108) and 35% of patients had recurrent disease. This patient represents a typical case of localised amyloidosis of the urinary tract.**CONCLUSION:** This is the most up to date review of the literature describing localised amyloidosis of the urinary tract. The disease is rare, but salient to the urologist as it invariably mimics urinary tract malignancy.© 2020 Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Amyloidosis is a group of disorders characterised by the deposition of misfolded proteins known as amyloid fibrils in tissues throughout the body [1]. Systemic amyloidosis can result from an underlying abnormality such as a plasma cell dyscrasia [2], or can be associated with chronic inflammatory disease [3]. It is the commonest and most severe subtype and causes progressive multiple organ dysfunction [2]. Localised amyloidosis is a much rarer form, with all evidence derived from individual case reports and small case series [4]. Reported sites of involvement include respiratory, gastrointestinal, cutaneous, and within the urogenital tract. Localised amyloidosis of the urinary tract was first described by Solomin in

1897 in a series of autopsies [5]. Clinical presentation and investigation invariably mimics urinary tract malignancy which can lead to misdiagnosis and radical surgical intervention that is associated with considerable and unnecessary morbidity. Here, we report a typical case of localised amyloidosis of the bladder. This case has been reported in line with the SCARE criteria [6].

2. Consent

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

3. Presentation of case

A 59 year old male office worker who had never smoked and with no previous chemical exposure presented to our centre with a single episode of frank painless haematuria. He had a background of hypertension, hypercholesterolaemia, and Parkinson's disease.

* Corresponding author at: Stokes Centre for Urology, Royal Surrey NHS Foundation Trust, Egerton Road Guildford Surrey, GU2 7XX, United Kingdom.

E-mail address: nikhil.mayor@nhs.net (N. Mayor).

¹ Joint first authors.

Prostate specific antigen was 0.5 ng/mL and International Prostate Symptoms Score (IPSS) was 7, with a normal digital rectal examination. Initial flexible cystoscopy was performed as per the suspected bladder cancer pathway, identifying generalised bladder mucosa inflammation but no discrete mass. Six months later the patient had an acute ischaemic lacunar infarct and was diagnosed with atrial fibrillation for which he was placed on oral anticoagulation with warfarin. This precipitated an emergency admission for torrential haematuria with clot retention. Follow up rigid cystoscopy showed prominent blood vessels around the bladder neck and within the prostatic urethra, again without an obvious tumour. Neither a CT scan of the urinary tract, nor an intravenous urogram, identified a lesion or filling defect. A diagnosis of prostatic bleeding was made and finasteride was commenced. The patient continued to experience recurrent episodes of haematuria over the next one year, prompting a further rigid cystoscopy identifying an area suspicious for carcinoma in situ (CIS). Histology showed bladder mucosa expanded by deposits of amorphous, pale, eosinophilic, proteinaceous material and immunohistochemical staining revealed the presence of amyloid deposition. He was referred to a quaternary centre for amyloidosis to assess for systemic amyloid deposition. Laboratory tests for IgA, IgG, IgM, serum paraprotein, serum free light chains, and urinary Bence-Jones protein to rule out an underlying plasma cell dyscrasia were performed and were all normal. Serum amyloid P (SAP) scintigraphy, a non-invasive and quantitative method for measuring amyloid deposits, was negative for visceral amyloid deposition outside of the bladder. A diagnosis of primary localised amyloidosis of the bladder was made. Trans-urethral resection was performed by a consultant urologist experienced in endourology and annual cystoscopic surveillance was commenced. He was followed up for 11 years with no evidence of recurrence under direct cystoscopic vision.

4. Literature review

We performed a comprehensive review of the literature by searching MEDLINE® and Embase® using a combination of the terms “primary”; “localised”; “amyloidosis”; “bladder”; and “urinary tract”. The objective of the literature review was to identify all published cases of amyloidosis localised to the urinary tract. After removal of articles describing renal parenchymal, systemic, or secondary amyloidosis, 349 cases were identified from years 1932–2019 and 23 different countries. Median age at diagnosis was 57 years (interquartile range 49–69) and male to female ratio was 1.53 to 1. The commonest presenting complaints were painless haematuria (65%), lower urinary tract symptoms (29%), and abdominal pain (15%). The bladder was the most common site of involvement (71%) followed by the ureter (12%), urethra (5%), and renal pelvis (4%), with 8% of cases involving multiple sites within the urinary tract. The majority of cases underwent some form of surgical management: transurethral resection (42%); nephroureterectomy/nephrectomy (9%); cystectomy (1%). Few patients were managed with dimethylsulfoxide (DMSO) (5%) or colchicine (2%). Median follow up was 33 months (interquartile range 12–108) and 35% of patients had recurrent disease. This literature review was limited by the heterogeneity in reporting of cases.

5. Discussion

This patient represents a typical case of localised amyloidosis of the urinary tract. He was a gentleman in his sixth decade of life presenting with painless haematuria and was investigated extensively for the presence of an underlying urinary tract malignancy. However, neither IV urogram, CT, nor cystoscopy and biopsy were able to identify a urothelial carcinoma. Whilst rare, our literature

review indicates that localised amyloidosis of the urinary tract is more common than previously described. Therefore, in the absence of a definitive diagnosis, alternative causes for haematuria must be considered and immunohistochemical staining should be performed. Furthermore, our literature review identified that multiple patients underwent life-changing and high risk procedures such as radical cystectomy, the extent of which may not have been required to treat the disease. This case followed the benign course described in the literature, with transurethral resection performed without recurrence for over 10 years. Where possible, transurethral resection and regular cystoscopic surveillance should form the mainstay of management. Localised amyloidosis of the urinary tract carries an excellent prognosis and systemic transformation is yet to be described. However, given the serious implications of systemic amyloidosis, investigation to rule out systemic disease at time of diagnosis must always be performed and patients referred to specialist centres where possible.

What does this case add to the existing literature?

- Our comprehensive literature review indicates that there are more cases of localised amyloidosis of the urinary tract published than previously described
- We confirm that the disease tends to carry a benign course, and radical surgery can often be avoided
- No cases of systemic transformation have been described in the literature, but the authors recommend referral to a specialist centre for investigation of systemic disease given the serious implications of systemic-type amyloidosis

Declaration of competing interest

None declared.

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Ethical approval

Nil required – case report (as per MRC research tool).

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

NM was study lead, involved in all aspects of the study, and acts as guarantor. HM was involved in conceptualisation, manuscript preparation, and supervision. ASJC, HK, TN, HH were involved in data collection and manuscript preparation and final revisions.

Registration of research studies

N/A.

Guarantor

Dr Nikhil Mayor.

Provenance and peer review

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