High-grade microscopic hematuria in adult men can predict urothelial malignancy

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Abstract

Introduction: Microscopic hematuria in men younger than 40 is a confusing issue to urologists, especially when these men have normal radiological findings. We report our experience in looking for urologic malignancy in this group of patients.

Methods: We conducted a prospective study for men with vague urological symptoms. We included men under 40 years old, men with microscopic hematuria greater than 25 red blood cells/high power field in 2 properly collected mid-stream urine samples, and men with free urine culture and normal multiphasic computed tomography abdomen and pelvis studies. All patients underwent diagnostic cystoscurethroscopy. If there were no lesions, multiple random biopsies were taken. In cases of apparently normal cystoscopic findings and associated renal colic, uretroscopy was done to the suspected side.

Results: Only 20 patients fulfilled our inclusion criteria. The mean age of the patients were 34; 2 patients presented with pain. The other 18 patients were presenting with mild recurrent lower urinary tract symptoms. Cystoscopy showed small papillary low-grade tumour in 3 patients. All random biopsies were free of malignancy. Unilateral uretroscopy for the 2 cases presented with pain detected carcinoma in situ in one of them.

Conclusion: Cystoscopy is highly recommended for young adult men, with significant levels of microscopic hematuria, due to the 20% incidence rate of associated urological malignancy. Random bladder biopsies, in the absence of suspicious lesions, have no diagnostic role, and should not be done. Uretroscopy is advised for patients with microscopic hematuria and loin pain, even in the absence of suspicious radiological findings.

Introduction

Microscopic hematuria is defined as 3 red blood cells (RBC)/high power field (HPF) on microscopic examination of the centrifuged urine specimen, in 2 of 3 freshly voided, clean catch, mid-stream urine samples.[1]

Causes of microscopic hematuria are variable and include urinary stones, infection and genitourinary malignancy.[2] Jung and colleagues[3] conducted a large retrospective study on 156 691 patients with hematuria and the authors wanted to assess its association with urological cancer. They found that older age groups, male sex and hematuria greater than 25 RBC/HPF was significantly associated with a higher risk of urological malignancy.

Many authors recommend doing ultrasound and diagnostic cystoscopy, with or without contrast studies, as initial diagnostic studies for microscopic hematuria.[4,5] Many studies[6,7] have shown that computed tomography (CT) urography, very frequently, miss lesions smaller than 1 cm, that is why cystoscopy should be a part of the initial diagnostic algorithm.

We report our experience with a highly selected group of men, presenting to our outpatient clinic with vague urology symptoms. In the end, they had microscopic hematuria as the only positive finding.

Methods

We conducted a prospective study for men, presented to our outpatient clinic, with vague urological symptoms. We included men under 40 years old, men with microscopic hematuria greater than 25 RBC/HPF in 2 properly collected mid-stream urine samples, and men with free urine culture and normal multiphasic computed tomography abdomen and pelvis studies. Patients with gross hematuria were excluded from the study. The study was done prospectively for a period of 6 months.

All included patients were admitted for diagnostic cystoscurethroscopy. Urine for cytology study was collected during cystoscopy. If there were no lesions, multiple random biopsies were taken. In cases of apparently normal cysto-

scopic findings and associated renal colic, uretroscopy was done to the suspected side.

Results

During the 6 months of urology outpatient clinic visits, 60 male patients under 40 presented with either vague abdominal pain or lower urinary tract symptoms (LUTS), in association with microscopic hematuria more than 25 RBC/HPF. After a urine culture and multiphasic CT of the abdomen and pelvis, 40 patients were excluded from the study due to either documented infection or detection of urinary stones. Only 20 patients fulfilled our inclusion criteria. The mean age was 34 years; 2 patients presented with pain; one of them had left loin pain and the other one presented with right iliac pain, for which he had his appendix removed, with no resolution of pain. The other 18 patients were presenting with mild recurrent LUTS, mostly in the form of dysuria. Urine cytology was free in all of them. Cystoscopy showed small, solitary papillary lesions in 3 cases, which were easily resected and turned to be low-grade superficial bladder tumour.

For the remaining 17 patients, random biopsies were taken from the bladder and prostatic urethra. For the patient with left loin pain, a left uretroscopy was done showing no abnormalities and selective urine cytology was negative for malignancy. A right uretroscopy was done for the man with right iliac pain and marked erythema was found in the ureteric wall in many areas along its length. Selective urine cytology and multiple biopsies were taken from the ureteric wall (Fig. 1, Fig. 2, Fig. 3, Fig. 4, Fig. 5). Pathology showed positive urine cytology and CIS of the ureter. Right nephrouretrectomy was done, with excision of bladder cuff. The final pathology confirmed the diagnosis of carcinoma in situ (CIS) of the whole ureter, extending from the pelviureteric junction to the distal part of the ureter. The removed bladder cuff showed marked dysplastic changes. All random biopsies taken from the cases were free of malignancy.

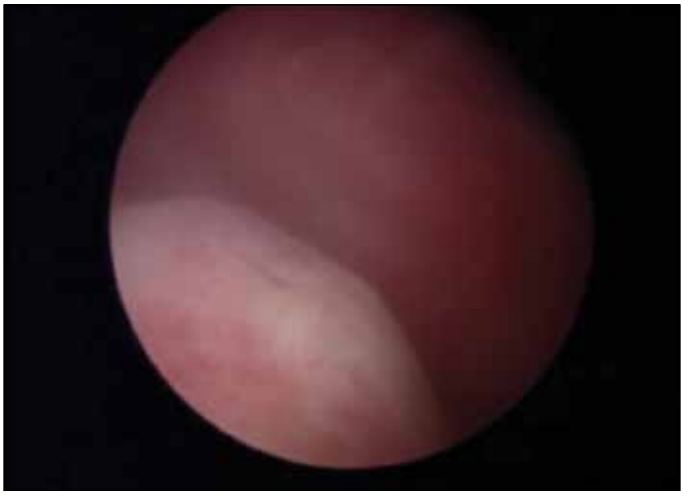

Fig. 1. Cystoscopy showing normal right ureteric orifice.

Discussion

Microscopic hematuria is especially challenging in patients under 40, when the incidence of associated urological malignancy is really low. Most of the available studies have shown low risk of urological malignancy for patients presenting with microscopic hematuria (less than 1%).[8,9] Moreover, Edwards and colleagues[2] studied 4020 patients of different age groups, and concluded that patients under 40 years of age, presenting with microscopic hematuria, can be safely first assessed by a nephrologist, due to the low risk of malig-

Fig. 2. Ureteric catheter directed to the right ureteric orifice, aiming to guide the introduction of guide wire.

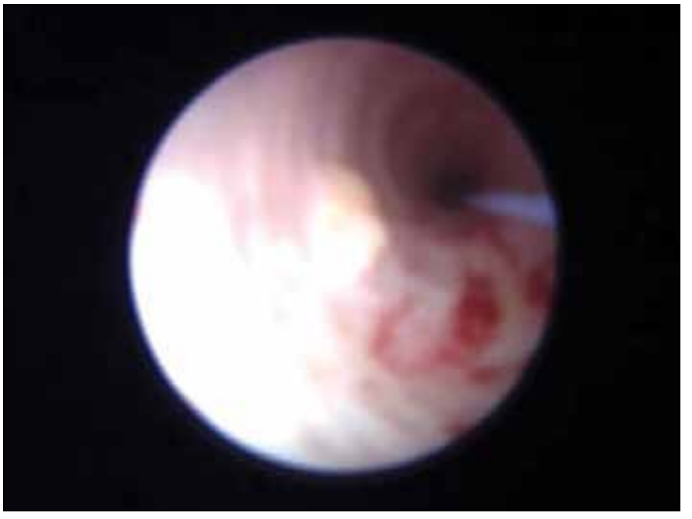

Fig. 3. Right uretroscopy showing erythematous wall and suspicious elevated areas.

Fig. 4. Introducing a forceps through the uretroscope, aiming to take a biopsy from the suspicious ureteric wall.

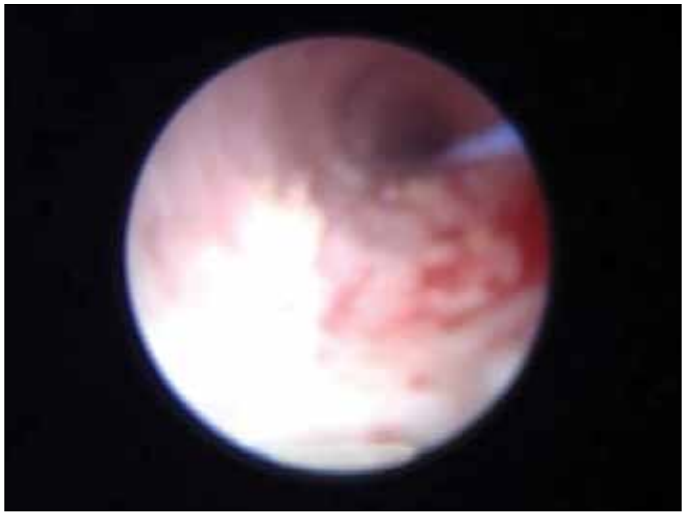

Fig. 4. Introducing a forceps through the uretroscope, aiming to take a biopsy from the suspicious ureteric wall.

nancy in such an age group. Jung and colleagues[3] conducted a retrospective study to correlate microscopic hematuria with the possibility of having urological malignancy. They concluded that male patients over 40 with a microscopic hematuria exceeding 25 RBC/HPF are at a higher risk of malignancy. Our study used the definition criteria of the above study, except that we included men under 40. Another issue, in our study, was that all of our patients had some symptoms at presentation, in the form of mild LUTS or pain.

Via cystoscopy, we were able to define 3 cases with bladder cancer that was easily resected. Uretroscopy was only done to symptomatic patients and directed only to the symptomatic side. One case during uretroscopy had suspicious lesions that were resected and ultimately were urothelial tumours. Random ureteric biopsy from the other case and random bladder biopsies from 17 cases were all negative for malignancy. Urine cytology for these cases was also negative for malignancy. These findings are in line with recent publications confirming the absent or low role of random biopsies from a normal appearing urothelium.[10,11]

Our study is unique in its selective criteria. We only included adult men under 40, with some symptoms and a considerable degree of microscopic hematuria. In our cohort, 20% of cases were diagnosed as having urological malignancy. The incidence of cancer in our cohort correlates with published data for cases presenting with gross hematuria.[12,13] That may mean that young adult men presenting with high-grade microscopic hematuria should be dealt with in the same way as patients presenting with gross hematuria, and that these men are carrying the same risk of having urological malignancy.

Although there are no current recommendations for such cases, our plan is to do annual cystoscopic screening for the remaining cases diagnosed as free of malignancy. One patient managed by transurethral resection of bladder tumour received a second cystoscopy 3 months later and was ultimately free of tumour.

Conclusion

Cystoscopy is highly recommended for young adult men presenting with significant levels of microscopic hematuria; there is a 20% incidence rate of associated urological malignancy in these patients. Random bladder biopsies, in the absence of suspicious lesions, have no diagnostic role, and should not be done. Uretroscopy is advised for cases with microscopic hematuria and loin pain, even in the absence of suspicious radiological findings.

Competing interests: Dr. Kotb and Dr. Attia declare no competing financial or personal interests.

This paper has been peer-reviewed.

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