RESEARCH COMMUNICATION

Assessment and Clinical Significance of Haematuria in Malaysian Patients - Relevance to Early Cancer Diagnosis

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Abstract

Aim: To study the causes and significance of both microscopic and macroscopic haematuria in adult patients and assess possible relevance to early detection of urological cancers. Methods: 417 patients presenting with haematuria were assessed in our Urology Unit. Following confirmation of haematuria, these patients were subjected to imaging techniques and flexible cystoscopy. Parameters analysed included clinical characteristics, imaging results, flexible cystoscopy findings, time delay to diagnoses and eventual treatment and final diagnoses of all cases. Results: 390 haematuria cases were analysed from 417 consecutive patients with haematuria. After 27 cases were excluded as they had previous history, 245 microscopic and 145 macroscopic. Age range was 17 to 95 years old with predominance of 152 females to 239 males. The racial distribution included 180 Chinese, 100 Indians,95 Malays and 15 other races. The final diagnoses were benign prostatic hyperplasia (22.6%), no cause found (22.3%), other causes (18.7%), urolithiasis (11.5%), urinary tract infection UTI (10.8%), non specific cystitis (10.3%), bladder tumours (2.8%) and other genitourinary tumours (1%). 11 new cases (2.8%) of bladder cancers were diagnosed, with a mean age of 59 years. Only 3 of 245 (1.2%) patients with microscopic haematuria had newly diagnosed bladder tumour compared with 8 of 145 (5.5%) patients with frank haematuria (p=0.016). Mean time taken from onset of symptoms to diagnosis of bladder cancer was 53.3 days with definitive treatment (TURBT) in 20.1 days from diagnosis. Conclusion:- This study has highlighted the common causes of haematuria in our local setting. We recommend that full and appropriate investigations be carried out on patients with frank haematuria especially those above 50 years old in order to provide earlier detection and prompt management of bladder diseases especially tumours.

Keywords: Haematuria - underlying disease - bladder tumours - diagnosis - Malaysia

Asian Pacific J Cancer Prev, **13**, 2515-2518

Introduction

Haematuria, both microscopic and macroscopic is a common presenting symptom among patients seen in a urology clinic. These symptoms, especially macroscopic haematuria causes a lot of anxiety and distress to patients.. The causes of haematuria can originate from any site along the genitourinary tract. Neoplasms of the genitourinary tract needs to be ruled out in most patients who present with haematuria (Carrol, 2000)

A complete urological assessment of haematuria would include relevant history and physical examination, blood and urine investigations, radiological imaging and flexible cystoscopy. Study by Khadra et al in a review of 1930 patients, provided the commonly accepted diagnostic algorithm for haematuria which include intravenous urography (IVP), Xray KUB, ultrasound (U/S) and flexible cystoscopy (Khadra et al., 2001).

Lately, specialised haematuria clinics have paved the way for appropriate radiological imaging and flexible cystoscopy in a single clinic visit to facilitate early diagnosis and treatment for significant urological diseases. The aim of this study was to identify the various causes of micro and macroscopic haematuria in our local setting. A secondary endpoint was the time taken from presentation to diagnosis and definitive treatment of bladder tumours.

Materials and Methods

Study population

All consecutive patients who presented with haematuria to University Malaya Medical Centre (UMMC) from June 2005 to May 2006. The presence of haematuria was confirmed by urine microscopy before subjecting these patients for further tests. All patients had either ultrasound or IVU as the primary imaging. Further imaging depended on the findings of Ultrasound or IVU. All patients were subjected to flexible cystoscopy. After confirmation of diagnosis, appropriate treatment was carried out. Patients who defaulted the investigative workup or subsequent treatment were excluded from this study.

Data analysis

Data collected were analysed with SPSS 13th edition.

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The data collected were: age, gender, race, occupation, type of haematuria, smoking, previous UTI or stone disease, family history, comorbid illnesses, medications, previous genitourinary tract tumours, presence of lower urinary tract symptoms, radiological findings cystoscopy and histopathology examination (HPE).

Results

Total of 390 cases were reviewed with 245 patients (62.8%) presented with microscopic haematuria and 145 had macroscopic haematuria (37.2%). Age range was from 17 years to 95 years old; with mean age 59 years old. There were more Chinese patients (180 cases; 46.2%) compared to Indians (100 cases, 25.6%); Malays (95 cases, 24.4%); and others (15 cases, 3.8%).

There were 238 males (61%) studied and females accounted for 152 cases (39%). Causes of haematuria found were benign prostatic hyperplasia (22.6%), no cause found (22.3%), other causes (18.7%), urolithiasis (11.5%), urinary tract infection UTI (10.8%), non specific cystitis (10.3%), bladder tumours (2.8%) and other genitourinary tumours (1%) (Figure 1a). There were differences in the causes for micro and macroscopic haematuria. In microscopic haematuria group, the causes are:- no cause found (27.8%); BPH (22.9%); other causes(21.2%); UTI (10.6%); non specific cystitis (9.8%); urolithiasis (6.5%); bladder tumours (1.2%) (Figure 1b).

In macroscopic haematuria, BPH was the most common cause (22.1%), followed by urolithiasis (20%); other causes (14.5%),no cause found (13.1%), urinary tract infection (11%); non specific cystitis(11%); bladder tumours (5.5%) and other genitourinary tumours (2.8%) (Figure 1c)

There were also variations in causes of haematuria for different age groups. For patients between 51 years to 70 years; the most common cause will be BPH, while those between 31 years to 50 years had no cause found and UTI as the main causes. The incidences of bladder tumours were highest in the >70years group (7 patients), followed by 51-70years group (3patients) and only one patient <50 years old. 11patients (6 males and 5 females) were newly diagnosed with bladder tumours which accounted for 2. 8% and majority (82%) had transitional cell carcinoma of bladder. Of these newly diagnosed bladder tumours, 3 cases had microscopic haematuria while the other 8 cases had macroscopic haematuria. Odds ratio of macroscopic haematuria leading to bladder tumours compared to odds ratio of microscopic haematuria is 4.52. 1.2% of patients who presented with microscopic haematuria had newly diagnosed bladder tumour whilst 5.5% of patients with macroscopic haematuria had bladder tumour There were also 2 new cases of newly diagnosed prostate cancer and 2 cases of renal tumours (1 renal cell carcinoma and 1 TCC renal pelvis).

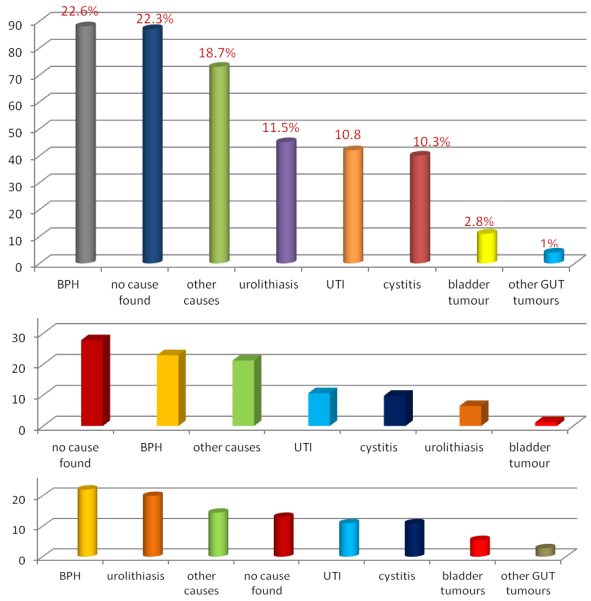

Figure 1. Causes of Haematuria. a) Overall; b) Microscopic; c) Macroscopic

There was no significant relationship between various risk factors for bladder tumours in this study as none of the patients had significant smoking history, previous exposure to dye, family history of genitourinary tumours, or previous radiation history. However, this review of 11 newly diagnosed patients with bladder tumours is too small to establish a relationship with the above mentioned risk factors. The mean age of patients diagnosed with bladder tumours was 59 years of age with all aged above 49 years. The average time taken from onset of symptoms until referral to our department was 38 days while the time to diagnosis was achieved in 15.3 days following referral. Definitive therapy for these patients was 20.1 days following diagnoses.

Some 76 cases (31%) cases of microscopic haematuria were referred as asymptomatic microscopic haematuria(AMH) with 75 % of them had no cause found at the end of the assessment.

Discussion

This study in our local hospital setting has highlighted the various common causes for both microscopic and macroscopic haematuria. There were more microscopic haematuria cases referred compared frank haematuria as many cases of microscopic haematuria are being identified incidentally through increasing usage of urine dipstick tests in primary care settings.

However, only microscopic haematuria confirmed on urine microscopy (3 or more than 3 RBC /high power field) were subjected to further investigations in our hospital.

In fact, with increasing usage of urine dipstick tests, there will be more referrals to urologists and thus leading to overuse of urological services which may delay treatment to patients who have serious urological diseases. Single detection of microscopic haematuria cannot be considered a useful guide to the presence or absence of bladder cancer and thus the potential use of dipsticks to diagnose haematuria is of limited clinical value. Similarly, the absence of haematuria on a single dipstick test cannot reasonably be used to exclude symptomatic patients from further tests (Rodgers 2006)

The main causes of haematuria as shown above, identified BPH (22.6%) as the most common cause followed by no significant cause found (22.3%). The third

commonest cause for haematuria was grouped as 'other causes' (18.7%) and these included:- urethral stricture, renal cysts, angiomyolipoma, glomerular disease, fistula into bladder, uterovaginal prolapse etc. In a Singaporean study of integrated haematuria clinic, they found 50% of patients with haematuria harboured urological disease, with 20.4% of cases were due to urolithiasis, while urological malignancy made up 14.2%; and most common malignancy diagnosed was TCC bladder at 8% (Tan 1998)

In our study, the urological malignancy rate is 3.8% (bladder tumour rate 2.8% with other genitourinary tract tumour rate 1%).Our study figures of BPH and no cause found as causes of haematuria were similar to the study by Paul et al where 22% of their patients had BPH as cause for haematuria, 7.2% had urolithiasis and 2.3% were due to urethral stricture; and they found no cause for hematuria in 20% of cases with UTI as the commonest cause at 25% (Paul et al., 1993).

It is not surprising that when the various causes of haematuria were divided into microscopic haematuria and macroscopic haematuria, the underlying causes were different in both groups. In cases of microscopic haematuria, no cause was found in 27.8% of cases, followed closely by BPH (22.9%), with bladder tumours at 1.2%. For frank haematuria, BPH (22.1%) was the most common cause followed by urolithiasis (20%)and bladder tumours were noted in 5.5% cases and other genitourinary tumours at 2.8%. In a study of 1046 patients in the United Kingdom, no malignancy was found in patients < 50 years old with microscopic haematuria. 25% of patients presenting with frank haematuria had malignancy as compared to 3.7% of patients with microscopic haematuria (Alishah 2002).

In our study, in the age group of <30 years old, no cause found (61%) was the most common cause as compared to patients above the age of 50,where BPH (24.7%) was the most common cause. The rates of bladder tumours was highest in >70 years group (63.6% of the 11 patients) followed by 51-70 years group at 27.3 % (3 patients) and 1 patient (9.1%) was aged 49 years old.

Sultana et al showed in a study in UK that no malignancy was found in those < 50 years old who presented with microscopic haematuria when compared to 7.5% in those > 50 years of age (Sultana and Baxby, 1996). The authors argued that the investigations of older patients with microscopic haematuria (and all those with frank haematuria) is well justified, as malignancy will be found in a significant proportion even if they are asymptomatic. The benefit of full urological investigation of younger patients with microscopic haematuria is debatable.

As noted above, there were 11 new cases of bladder tumours reviewed in this study; with majority coming from the frank haematuria group. There were 3 out of 245 patients (1.2%) from the microscopic haematuria group as compared to 8 out of 145 patients (5.5%) from the frank haematuria group. This was also agreed by Edwards et al where for any given age range, prevalence of malignancy was significantly higher in patients presenting with macroscopic than microscopic haematuria. In this study, transtitional cell carcinoma (TCC) of the bladder is the commonest diagnosis in 82% of cases and this is echoed by a similar study, where they noted TCC to be the commonest malignancy (75%). Asymptomatic microscopic haematuria (AMH) cases amounted to 31% of patients with microscopic haematuria reviewed in this study. AMH is defined as patients with confirmed microscopic haematuria but were identified incidentally as they had no urinary symptoms. In our study, the majority of AMH had no cause found (75%) and only one patient was diagnosed with bladder tumour (1.3%).Population based studies to determine the prevalence of AMH in the general public are scarce but studies suggest a prevalence of 2.5% to 20% (Mohr et al., 1986). Previous studies have shown that patients with AMH have incidences of malignancy ranging from 2% to 22% (Greene et al., 1956).

Majority of our bladder cancers diagnosed were found to be in early stage and this is also reflected in a study by Carrol et al that at time of diagnosis, 85% of tumours were localised to bladder whereas 15% have spread to regional lymph nodes or distant metastases (Carrol, 2000). In our study, of the newly diagnosed cases of bladder tumours, only one case had distant metastases (lymph nodes and liver). All but one of our 11 patients of newly diagnosed bladder tumours were aged 49 years and above and this is consistent with review of literature where most bladder tumours have peak incidences at age 50 years and above. However, Khadra et al (2001) have shown that patients below age 40 with microscopic haematuria can still present as bladder tumour.

The average time taken from the onset of haematuria to being seen at urology department UMMC is 38 days. Total time taken to diagnosis after referral to urology department is another 15.3 days and then another 20.1 days to definitive urological intervention or surgery for these patients with bladder tumours. As shown by a study in Edinburgh, the delay between referral and TURBT (transurethral resection of bladder tumour) was reduced from a mean of 60 days to a mean of 33 days by the institution of the haematuria clinics. ($p<0.001$). Therefore they concluded that the integration of investigations in a single day decreases delays in diagnosis and management (Paul et al., 1993)

All 390 patients underwent flexible cystoscopy which led to positive findings in 240 patients (61.%) and the remainder yielded normal findings. These positive findings prove that flexible cystoscopy is an essential part of the diagnostic algorithm for haematuria. Another study earlier also showed that cystoscopy led to positive findings in 46% of cases (Kumar et al., 2004). There is definitely a role in providing rapid service for patients with haematuria clinics where imaging techniques and flexible cystoscopy are performed on the first visit. This will in turn lead to earlier detection of significant urological pathologies and more efficient approach to treatment of the underlying causes of haematuria.

In conclusion, this study has highlighted the most common cause of haematuria is benign prostatic enlargement with bladder cancer forming 1.2% of patients with microscopic haematuria and 5.5% in macroscopic patients. Mean time taken from diagnosis to definitive TURBT in newly diagnosed bladder tumour cases was less than 3 weeks. As shown in this study, full urological

investigations of patients with both microscopic and macroscopic haematuria is important in the assessment of haematuria especially in patients above 49 years old presenting with frank haematuria. The aim of management should be the prompt detection and treatment of serious underlying causes of haematuria, while minimising the number of tests conducted in asymptomatic patients with benign causes.

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