

Hematuria -- Preceptor Final

Educational Objectives:

- 1) Be able to define hematuria and interpret the results of urine dipstick testing.
- 2) Be able to use the patient's history and clinical context to help identify causes of microscopic hematuria.
- 3) Be able to use an algorithm when evaluating microscopic hematuria and know when to refer to urologist or nephrologist.
- 4) Know what initial imaging modalities should be ordered for the non-pregnant patient with microscopic hematuria.

CASE ONE:

Mr. H. is a 23 year old African American man who comes to your office for a physical exam as part of a requirement for his commercial truck driver's license. The nurse obtains his vitals, completes a Snellen's eye test, and obtains a urine specimen as part of the requirement for his commercial license. He is then scheduled to see you in two days for his physical exam and completion of his paper work. The results of the urine test come back the next day positive for 1+ blood. No microscopic exam of the urinalysis is reported.

QUESTIONS:

1. What is the definition of hematuria? How should a urine specimen be collected? What are the limitations of urine dipstick testing?

The American Urological Association (AUA) Best Practice Policy Panel gives the following definitions for asymptomatic hematuria:

Microhematuria is defined as > 3 RBC/HPF on two of three properly collected and performed urinalyses.

Gross hematuria is defined as visibly bloody urine or >50 RBC/HPF on a single urinalysis. (RAO, 2008)

However, new terminology to define hematuria was suggested as visible hematuria (replace macroscopic and gross hematuria), and non-visible hematuria (replace microscopic and dipstick positive hematuria (Kelly, 2009).

The specimen should be from a clean catch urine that is freshly voided and mid stream. (Proper preparation is important and the patient should be instructed to first wipe the urethral meatus with a disinfectant, followed by voiding the initial portion of urine into the toilet, and then collecting the urine.)

Urine specimens should not be collected less than 48 hours after exercise. (Patel, 2008)

Though a urine dipstick is a simple, time efficient and sensitive way to detect microscopic hematuria, false positive results can occur. A urine dipstick detects the presence of blood when hemoglobin is catalyzed by the oxidative reaction between hydrogen peroxide and a chromagen embedded on a cellulose test strip. This results in a green color change on the dipstick (refer to Table 2 of the Canadian Journal of Urology article). There are a number of conditions that can cause a false positive result. False positive results can occur with dehydration, and the presence of free hemoglobin, myoglobin or povidone-iodine in the urine. Urine microscopy is usually recommended for (+) dipstick tests to detect urinary red blood cells.

False negative results can occur if the urine has a high concentration of ascorbic acid (vitamin C), vitamin A, beta carotene (carrots), bilirubin, certain drugs, or porphyrins.

2. What are some important questions to ask in the history when a patient presents with hematuria?

Evaluate for transient or spurious causes of hematuria by asking if exercise preceded the collection of the urine specimen or if he has any symptoms of a urinary tract infection. If you are evaluating a female for hematuria be sure to ask about menstrual history or any abnormal uterine bleeding with respect to the timing of the urine specimen.

You should also obtain a detailed medication history. This is vitally important and specifically includes asking about any over the counter medications, herbal supplements, specialty teas or drinks, recent antibiotic use (for acute interstitial nephritis), or analgesic medications such as NSAIDs. These medications could place the patient at risk for papillary necrosis.

Do not forget to ask about family history. A positive family history for kidney disease raises the possibility for congenital conditions such as polycystic kidney disease or Alport syndrome (hereditary nephritis). Both sickle cell disease and diabetes increase the risk for papillary necrosis. A history of hyperparathyroidism increases the risk for stone formation, although these are usually associated with symptoms.

A brief history should be obtained. Travel abroad may raise suspicion for TB, malaria or schistosomiasis.

Finally ask about any occupational exposure to chemicals and dyes. Some of the agents that can be associated with hematuria include benzenes or PCBs/rubber.

Certain occupations can result in exposure to aromatic amines (factories, dry cleaners, car detailing businesses or other solvent exposure) that place one at higher risk for GU cancers that may present with hematuria.

Never forget to ask about tobacco use, as some GU malignancies, as well as urethral strictures with bladder outlet obstructions are seen in smokers and can present with hematuria.

A good review of systems is important to ensure that you rule out any systemic diseases such as vasculitis, Goodpasture's syndrome, Hemolytic uremic syndrome and TTP.

3. Can you think of any additional questions to ask Mr. H. that would provide clues to a specific diagnosis?

Ask questions about fever, visible blood or clots in the urine, urine discoloration, or urinary burning or frequency that might indicate a UTI or bleeding from the urinary tract.

Has Mr. H. ever had elevated blood pressure, frothy urine or leg/ facial swelling that would suggest a nephritic cause for hematuria?

- Any recent cough or sore throat to suggest a recent upper respiratory infection raising the suspicion for IgA nephropathy or a post infectious glomerulonephritis?
- Does he have flank pain with nausea/vomiting that might suggest pyelonephritis or the presence of a kidney stone?

- Any pain in the lower mid abdomen or painful tender urethral area to suggest cystitis or urethritis? If so in men, a rectal exam should be performed to evaluate the prostate as well.
- Recent rash or petechiae raise the possibility of a systemic cause or possible coagulopathy?
- For the female patient, ask questions to exclude a vaginal, cervical or uterine source of bleeding and perform a pelvic speculum exam.

CASE ONE CONTINUED:

Mr. H returns to see you for his scheduled appointment. He admits to feeling a bit tired lately since he started taking a college course in the evening while working as a construction worker during the day. He denies any medication use except for a daily multivitamin and an occasional acetaminophen for muscle aches. He has no history of tobacco smoking and rarely uses alcohol. He has been running almost daily and doing some light weight lifting while training for a local road race. He has no known family history of sickle cell disease, diabetes, or any kidney or bladder conditions in either of his parents and he is an only child.

On physical exam, he is a well-built, well-nourished man with a blood pressure of 140/86; otherwise the rest of his vitals and exam are unremarkable. You decide to obtain another urine specimen to have the urine sediment spun down and examined under the microscope.

4. What would you consider with each of the following results?

- No RBCs (**myoglobinuria**)
- Dysmorphic RBCs or RBC casts plus proteinuria (**glomerular source**)
- RBCs of uniform character or RBC clumps (**lower urinary tract bleeding**)
- WBC clumps or pyuria +/- proteinuria (**infection**)

CASE ONE CONTINUED:

His urine microscopy shows 2 RBC/HPF that are of normal morphology in a first sample of the morning mid-stream clean catch urine after not exercising for 48 hours prior to the urine collection.

5. How should this patient be evaluated?

Please see Figure 1 in the Cleveland Clinic Journal of Medicine article for an algorithm. As you can see the first step is to do a microscopic evaluation and then, given that he has <3 RBCs/HPF, to repeat his urinalysis in six months. However, some authors would recommend completing three urinalyses given that he has two RBCs/HPF as the exact number that constitutes hematuria is debated.

6. How would you approach this patient if he were an asymptomatic 45 year old smoker with BP of 140/90 and a urinalysis showing 15-20 RBC/HPF?

Infection must first be explored by history and possibly a culture if any symptoms.

It should be noted that the degrees of hematuria do not predict the likelihood of malignancy, so that four RBCs are not necessarily less concerning than 20 RBCs.

Given this patient's risk factors of age >40 and smoking, he should have a urological evaluation with imaging and a urology referral for cystoscopy.

CT urography is the best and most sensitive imaging modality to evaluate the upper genitourinary tract. It is a three-phase CT with a non-contrast phase to evaluate for stones, a contrast enhanced nephrographic phase to look for small renal masses, and delayed images of the renal collecting system and ureters for filling defects. However, a serum creatinine should be checked, and if creatinine >2.0, you should carefully think about administering IV contrast. The patient should be screened for seafood allergies or adverse reaction to contrast or multiple drug allergies. In the childbearing female patient, a screening pregnancy test should always be done before radiation exposure. If the female patient with unexplained microhematuria is found to be pregnant then renal ultrasound is usually the first test of choice.

If the patient has an iodine or seafood allergy, and MR urography could be done, which is just as accurate, though more expensive. Again, MRI is limited in patients with creatinine > 2.0.

Primary references:

1. Patel JV, Chambers CV, Gomella LG. Hematuria: etiology and evaluation for the primary care physician. The Canadian Journal of Urology. 2008; 15:54-62
2. RAO Pk, Jones JS. How to evaluate 'dipstick hematuria' what to do before you refer. Cleveland Clinic Journal of Medicine. 2008; 75(3); 227-233

Additional Reference:

1. Kelly JD, Fawcett DP, Goldberg LC. Assessment and management of non-visible hematuria in primary care. British Medical Journal. 2009; 338: 227-232

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