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Management of Microscopic Hematuria

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Speaker Disclosures | Alan So

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- Advisory Boards: None

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- Members of the SPC committee (Alan Bell, Peter Lin, and Arthur Kushner) received honorarium from the Canadian Urological Association.
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Mitigating Potential Bias

The scientific planning committee of this program have complete control over the content of this program.

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Learning Objectives

Upon completion of this program, participants will be able to:

- 1. Define clinically significant hematuria
- 2. Describe the differential diagnoses of hematuria
- 3. Recognize the appropriate investigation and management of hematuria
- 4. Determine when to refer a patient with hematuria to a urologist

Definitions

- Microscopic hematuria is defined as the presence of 3 or more red blood cells (≥ 3 RBC) per high power field (hpf) on a urine microscopy evaluation

- Clinical Pearl: Positive urine 'dipstick' may indicate hemoglobinuria, hematuria, or both and requires confirmation on urine microscopy investigation.

Barocas DA, Boorjian SA, Alvarez RD et al: Microhematuria: AUA/SUFU guideline. J Urol 2020; 204: 778.

Definitions - classification

- Classification of hematuria can help provide clues of the etiology and aid diagnostic approach

- Hematuria is classified as:
  - 1. visible or non-visible hematuria (gross or macroscopic hematuria vs microscopic)
  - 2. symptomatic or asymptomatic
  - 3. glomerular or non-glomerular

Assess symptoms and risk factors with a good history

- 1. Localizing signs or symptoms:
  - Flank/abdominal pain to suggest colic
  - Lower urinary tract symptoms such as:
    - dysuria to suggest UTI
    - frequency to suggest carcinoma-in-situ
- 2. Systemic symptoms
  - Signs of infection: fever, chills, back pain
  - Signs of coagulopathy: epistaxis, etc.
  - Signs of malignancy: weight loss, anorexia, cachexia

  - Clinical pearls: ensure UA done when women are non-menstruating, and only do UA 4-6 weeks after a UTI (ie, if signs of infection, repeat UA 4-6 weeks after)

Assess Risk Factors for Bladder Cancer

- History of smoking is the strongest risk factor
- Other risk factors include:
  - Occupational exposure to chemicals or dyes (e.g. benzenes or aromatic amines)
  - Exposure to certain drugs (phenacetin, cyclophosphamide)
  - Exposure to pelvic radiation
  - Specific occupations at risk: tobacco workers, dye & textile workers, chimney sweeps, rubber workers, waiters, metal workers, firemen/women, painters, printers, seafarers

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Rule out other non-urologic etiologies

- 1.Rule out infection (WBCs, nitrates, positive urine culture)

- 2. Isolated hemoglobinuria may suggest hematologic problems such as paroxysmal nocturnal hemaglobinuria (PNH) that may require expedited referral to hematology
  - PNH symptoms: Intermittent and morning ‘dark’ and ‘discolored’ urine, anemia, abdominal pain

Rule-out non-urologic entities

- 3. Assess for renal causes (dysmorphic RBCs, proteinuria, cellular casts, renal insufficiency or any suspicion of renal parenchymal disease) that may warrant nephrologic workup.

- 4. Clinicians should perform the same evaluation of patients with microhematuria who are taking DOACs or other anticoagulants (regardless of the type or level of therapy) as patients not on these agents. Do not assume hematuria is ‘due to anticoagulation’

Initial Evaluation

- 1. Microscopic evaluation to confirm positive dip test
  - Confirm presence of RBCs (3 or more /HPF)
  - Assess for isolated hemoglobinuria or signs of glomerular causes that may prompt hematology / nephrology referral
- 2. Urine cytology and urinary markers are poor screening tests and are **not recommended** in the initial workup
- 3. Measure Serum creatinine, Urine albumin-to-creatinine ratio (ACR) and blood pressure
  - Proteinuria, dysmorphic RBCs, casts, abnormal ACR, reduced GFR, new onset hypertension suggests renal parenchymal disease prompting nephrology referral

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Indications for Urology Referral

- SINGLE episode of **visible** hematuria (any age)
- SINGLE episode of **symptomatic** hematuria not associated with infection
- SINGLE episode of isolated microscopic hematuria (3 or more RBCs/ HPF) **aged ≥ 40 years**
- Microscopic hematuria and aged < 40 years AND perceived high risk factors, including:
  - Current or past tobacco use
  - History of pelvic irradiation
  - Cyclophosphamide or other carcinogenic alkylating agent exposure
  - Exposure to occupational hazards such as dyes, benzenes, and aromatic amines

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Urologic Assessment

- Lower tract assessed by cystoscopy (over 98% sensitive for cancer)
- There is limited evidence to strongly recommend one modality.
    A. Ultrasound, CT, MRi, retrograde pyelogram are acceptable

    B. Taking patient safety (ionizing radiation and exposure to i.v. contrast), availability, and cost into consideration, it is recommended that ultrasound be used as the imaging test of first choice for asymptomatic microhematuria
- In those with visible hematuria and/or strong risk factors, CT-Urography or MR-Urography are better to assess for upper tract urothelial abnormalities

Follow up:

- No cause will be found for microscopic hematuria in many cases (up to 50%).

- When no specific cause for microscopic hematuria is found, the patient should be followed annually with:
  - Urine microscopy
  - Creatinine/eGFR with ACR
  - Blood pressure
  - Urine cytology (only in patients with risk factors for urothelial cancer)

Follow-up: (American Urologic Assoc. Guildelines)

- If patients develop new visible hematuria, new urinary symptoms, or increasing degree of microscopic hematuria, proteinuria, or declining renal function, re-investigation (i.e. re-referral to Urology) should be undertaken.
- If, after initial investigation, the degree of microscopic hematuria persists unchanged on annual follow-up, repeat investigation within 3-5 years should be considered.
- If three consecutive annual urine microscopies are negative, follow-up testing can be discontinued.

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Summary:

- 1. Evaluation of hematuria starts with a good history and proper classification

- 2. Although not all episodes of hematuria are clinically significant, many may prompt referral to either Urology or Nephrology even after a single episode

- 3. Initial negative work-up in those with hematuria still require follow up, usually with continued annual assessment especially in those with risk factors for bladder cancer

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