A 39-Year-Old Man With Microscopic Hematuria

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A 39-year-old man attended a "screening day" sponsored by his workplace. At the event, a nurse practitioner took his medical history; performed a physical examination; drew blood for lipid studies, a complete blood cell panel, and metabolic panel; collected a stool sample for occult blood screening; collected a urine sample for a urinalysis; and conducted an electrocardiography scan.

The man's history was wonderfully negative for serious illness. He had no major medical diagnoses or surgical history. He had an administrative white-collar job, regularly went to the gym, and was in good physical shape. His examination findings were entirely within normal limits, including blood pressure (110/70 mmHg) and BMI (22 kg/m^2).

However, the next day he was given a report and summary of his findings that demonstrated the urinalysis dipstick stained faintly positive for blood. A microscopic urine examination revealed 3 to 5 red blood cells per high power field (RBC/HPF). Everything else was nonremarkable and within normal limits. The summary prompted him to see a physician for further evaluation of the urine abnormality.

Which of the following statements most accurately describes the approach and management pertaining to the case presented?

A. If a decision for further evaluation is made, initial optimal studies are ultrasonography and cystoscopy.
B. The routine screening for urinary tract cancers via urinalysis the patient had received has been validated as an effective genitourinary tract cancer screening method.
C. The finding of microscopic hematuria as described in our patient requires obligatory and prompt urologic/radiologic follow-up.
D. Both microscopic and gross hematuria in adults carries high and equivalent cancer risk.

Correct Answer: A

The patient presented was found to have microscopic hematuria at one of the ever-increasing screening opportunities available today to screen everyone for just about everything. Thus, a routine urinalysis was found to have very small numbers of red blood cells and the question thus raised in what to do about it. A related subissue is whether urinalysis to screen for blood is an effective maneuver in the first place. Both these issues will be discussed with below. But before that, the more specific definitions of "hematuria" must be considered.

A very effective and simple subclassification of hematuria is to divide gross (visible) hematuria and microscopic hematuria and proceed from there. Gross or visible hematuria is enough blood in the urine to change the yellow/amber hue into a more pink/red/purple color. Traditional estimates of extent describe "rose wine color" as roughly a 1% hematocrit, a more frank "red" as 1% to 3%, and "port wine purple" as more than 3% hematocrit values. The good news is that translating these values into actual blood loss results in approximately 10 cc/L of urine, 20 to 30 cc/L urine, and perhaps 30 to 50 cc/L urine, respectively. This means that as alarming as passing such bloody urine appears, usually the value of blood loss is not great, and there is more time to arrive at a diagnosis in an orderly manner in comparison, for example, to the passage of bright red blood or melena from a gastrointestinal bleed. And the accuracy of differential diagnosis with gross hematuria as a rule will be prompt using age, history, and a few relatively "easy" studies to arrive at a diagnosis (eg, severe flank pain of renal colic, indicating kidney stones, and painless gross hematuria in a smoker > 50

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years, often indicating bladder cancer). The genitourinary cancer risk of painless gross hematuria is high, up to 8% in the DETECT I prospective observational trial.[1] There is both adequate data and general agreement that the finding of painless gross hematuria in an adult is a strong indication for a consultation with a urologist for cystoscopy and ultrasonography, at minimum, for investigation of potential genitourinary tract cancer.

But our patient presents not with gross hematuria, but rather microscopic hematuria, which has a broader differential. And unlike the situation with visible hematuria most causes of microscopic hematuria are nonmalignant.[2] This fact makes Answer D an incorrect one. Microscopic hematuria brings into play glomerular disease, urinary tract infections, neoplasms, and, in at least half of cases, no identifiable cause.[2] The initial evaluation for microscopic hematuria is careful, professional urine sediment examination including absolute red blood cell count, red blood cell morphology, and presence of proteinuria. The latter 2 items—dysmorphic/deformed red blood cell and positive proteinuria—are major indicators of significant glomerular disease and further studies in that direction. A recently published risk stratification study showed that in nonsmokers younger than 40 to 50 years, a single urinalysis result showing 3 to 10 RBC/HPF is low risk, a level higher than 11 to 25 RBC/HPF is moderate-risk criteria, and higher than 25 RBC/HPF is high-risk criteria.[2] Our patient's demographics and findings—younger than 40 years, less than 10 RBC/HPF, and nonsmoker status—place him at low risk for glomerular disease. And what to do in such cases is where a lot of disagreement is encountered.

One of the confounding issues is the conflicting data showing a relatively high incidence of genitourinary cancers in the general population, with the American Cancer Society reporting more than 150,000 renal and bladder cancer cases per year.[2] That nonetheless is coupled with a very low yield rate in the diagnosis of 0.7% genitourinary cancer incidence at 3 years after initial discovery of microscopic hematuria.[3] Not surprisingly, the American Urology Association (AUA) released aggressive guidelines in 2012, partially data-driven and partially opinion-driven, recommending evaluation in microhematuria cases without "obvious" cause.[4] The evaluation suggested is a step beyond the usual cystoscopy and ultrasonography, substituting computed tomography scanning as the imaging test.[4] In the past decade, this very aggressive stance has been questioned such that updated AUA guidelines using the aforementioned risk scheme[5] now take into account the reasonably low incidence of cancer in the lower-risk microhematuria population, the costs and risks associated with a more invasive strategy, and thus arrive at the ever more common "shared decision-making plan between patient and clinician."[6] This often means attentive monitoring and follow-up when the clinician involved in the decision is an internist, generalist, or family practitioner and immediate cystoscopy and imaging when the clinician is a urologist. There is more general agreement that when a decision is made to pursue microhematuria, cystoscopy, and ultrasonography as the studies of choice, which makes Answer A the correct one here. The patient's data put him firmly in the low-risk category by age younger than 40 years, nonsmoker status, and number of RBC in the urinalysis. These criteria do not make immediate and aggressive invasive follow-up necessary, and Answer C overstates the risk.

TAKE-HOME MESSAGE

Hematuria is a hallmark symptom of disease in the genitourinary tract. A useful initial division is between gross, visible hematuria and microscopic hematuria. The latter can cause positive dipstick results (which chemically detects oxidant in blood) but not an actual tint to the urine. Painless gross hematuria is a frequent herald symptom of urinary tract cancer, bladder more so than kidney. Although there are other differential diagnoses such as kidney stones (which frequently is accompanied by renal colic), the incidence and association of genitourinary cancer is high such that any episode is a strong indication of immediate urologic consultation or cystoscopy and imaging with ultrasonography or computed tomography scanning. Microscopic hematuria conversely is more often caused by nonmalignant causation including glomerular diseases, with immunoglobulin A nephropathy being most frequent. Additionally, in many cases, no definitive diagnosis is ever confirmed. A very important initial maneuver in microscopic hematuria is to perform a professional sediment examination. However, there is enough of an association with malignant causation to create a degree of controversy regarding how aggressive an evaluation should be pursued. Schemes have been formulated to adjudicate a risk stratification (eg, age, sex, number of RBC/HPF, smoking status, and occupational exposures), which can help define which patients need prompt and aggressive evaluation and who can be more conservatively followed. The usual "shared decision-making plan between patient and clinician"[2] is commonly mentioned with microhematuria. An additional note is that many professional societies and the US Preventive Services Task Force do not recommend routine screening with urinalysis for genitourinary cancer screening.

Finally, 2 issues require further comment. First, as previously stated, unlike gross hematuria, microhematuria has more nonmalignant causation than malignant ones. What are these? Glomerular disease, kidney stones, and inflammatory disorders of the urethra, bladder, or prostate are the bulk of diagnoses found with immunoglobulin A nephropathy, likely the most common in younger patients. And a number of large studies have found, even with thorough and long-term follow-up, a large proportion of microhematuria cases result in no diagnosis ever being made.[7,8]

Lastly, what is the role of routine screening in asymptomatic individuals? The one-time obligatory urinalysis as part of every "yearly checkup"? The answer is likely "none." Both the American College of Physicians and US Preventive Services Task Force do not recommend routine screening in asymptomatic individuals for the presence of microhematuria, citing inadequate risk/benefit data, making Answer B incorrect.[9]

Patient Follow-Up

The patient promptly made an appointment with his family physician. He was seen within a week. A battery of tests, including complete blood cell count, metabolic panels, and creatinine, returned results within normal limits. The urinalysis chemical was within normal limits, but a sediment examination was ordered, results of which showed 3 to 5 RBC/HPF. The patient's demographics and low number of RBC/HPF categorized him as "low risk" for bladder cancer, and the decision was made to carefully monitor the patient for now with a repeat urinalysis and sediment evaluation in 3 months and proceed from there.

What's the Take Home?

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