

PedsCases Podcast Scripts

This is a text version of a podcast from PedsCases.com on "Evaluation of Hematuria." These podcasts are designed to give medical students an overview of key topics in pediatrics. The audio versions are accessible on iTunes or at www.pedscases.com/podcasts.

Evaluation of Hematuria

This podcast was written by Peter Gill and Dr. Verna Yiu. Peter is a medical student at the University of Alberta. Dr. Yiu is a pediatric nephrologist at the Stollery Children's Hospital in Edmonton, Alberta, Canada.

Preamble

Let's start with a scenario. After sending off the urine of a 2 year old with a fever in clinic, you get the dipstick results stating 1+ hematuria. What the heck does that mean? What do you need to do with that information?

Introduction

This podcast provides an overview to the evaluation of hematuria in children. Hematuria is a common finding on urinalysis in children. Depending on the study, the prevalence in children ranges from 0.5-2%.

In the first part of this podcast, we will help you develop an approach to the evaluation of hematuria. We will then go through a brief overview of some of the common causes of hematuria in children.

Definition

To start, what is hematuria? Microscopic hematuria is defined as greater than 5 red blood cells per high power field. Gross hematuria is urine that is pink, red or brown in color. The colour is visible to the naked eye and the hematuria is confirmed by dipstick and sediment exam.

Red blood cells in the urine may be a normal finding but it is usually not detectable due to the minute amounts in normal individuals. The red blood cells may originate anywhere from the renal artery to the tip of the urethra and the hematuria can result from a leakage through the capillary bed or the mucosal bed of the gut. There can be several underlying causes of hematuria; therefore it is essential to have an organized approach to evaluate the patient.

History

Evaluation consists of a thorough history and physical examination. The history will focus on any associated symptoms and a review of systems. It is crucial to ask about any recent infections, including upper respiratory tract, skin or GI. Ask if there is a history of skin rash, abdominal pain, bloody diarrhea and joint pains to look for evidence of Henoch-Schönlein purpura or lupus. Ask about specific urinary tract symptoms such as fever, dysuria, urinary frequency, gross hematuria or suprapubic pain as a urinary tract infection is an important cause of hematuria.

Attempt to determine if there is a history of vigorous exercise, bruising or recent injuries. If the patient is a female and depending on age, ask about menses. Attempt to determine if there is a particular pattern of hematuria and to describe the urine. Is it visibly red or tea colored?

Lastly, do not forget to ask about a family history of renal conditions, such as any family members that needed dialysis or a kidney transplant, or specific diseases like polycystic kidney disease, collagen vascular diseases like lupus or Alport Syndrome. Obtain a medication history, particularly if the patient has started any new medications.

Physical Examination

Your physical examination will focus on the key physical aspects of patients with kidney diseases. Accurate height, weight and blood pressure are essential. Assess the patients' fluid status and look for evidence of edema in the peripheral extremities or of ascites. An abdominal exam will look for evidence of a palpable kidney. The physical examination will also look for other signs of skin and joint involvement. Do not forget to examine the genitalia.

Investigations

When considering investigations, it's really all in the urine. The amount of information gathered from a urine sample is vast. It is worthwhile to know some causes of colored urine and of a false positive and negative dipstick. Colored urine can be due to beets, lead, rifampin, nitrofurantoin and ibuprofen. The previous examples will lead to a negative dipstick for hemoglobin. On the other hand, false positive dipsticks can arise if there is myoglobinuria or hemoglobinuria. In these cases, no red blood cells will be seen on microscopic exam.

So, to review, if the dipstick is negative, then there is no hematuria.

However, a positive dipstick could be due to red blood cells, myoglobin or hemoglobin.

Once the sediment is spun down, it can be reviewed under a microscope. As mentioned previously, hematuria is defined as greater than 5 red blood cells per high power field. It

is also very important to look at the morphology of the RBCs to see if they are dysmorphic as well as to determine if there are any casts.

Evaluation

Now that you have gathered all the pertinent and important information, what do you do next? Evaluation can be divided into phases based on the initial results.

Here's the first phase and the one that is most important for you to know. Repeat the urinalysis and examine the urine sediment for casts. Send the urine for culture and sensitivity. Additionally, if the child is of African ethnicity, consider sending a Sickle screen. One might also consider ordering urine Calcium to Creatinine ratio to rule out normocalcemic hypercalciuria.

If all the above investigations return normal, move on to the second phase. You don't need to know all of these as a medical student, but here they are for completeness: Test the urine of first degree relatives. Send off blood work with the appropriate investigations. These include CBC, electrolytes, Blood urea nitrogen, Creatinine, C3, C4, ANA, antistreptolysin O test, IgA, PT, and PTT. An abdominal ultrasound to visualize the kidneys would be indicated to rule out any morphologic abnormalities.

If no definitive solution arises from the investigations, your next step depends on the presence or absence of symptoms. If the patient is asymptomatic, simple observation with recheck in 6-12 months time may be appropriate. Alternatively, if the patient is symptomatic with hypertension, edema, and/or rash, the patient should get a renal biopsy to rule out a glomerulonephritis.

Differential Diagnosis

Having an organized differential diagnosis is very important. With hematuria, it is easiest to classify the etiologies as non-renal, lower tract, glomerular and non-glomerular.

In terms of nonrenal causes, the most common culprits are drugs, fever, coagulopathy, exercise, or menses.

Lower Tract causes include infection, trauma, stones, vascular anomalies, cysts, foreign body and tumors.

There are a large number of possible glomerular causes of hematuria. These can be because of primary or secondary glomerulonephritides or glomerular basement membrane abnormalities.

There are also several non-glomerular pathologies. These include renal cysts, arteriovenous malformation, tumor, pyelonephritis, renovascular obstruction, papillary necrosis, sickle cell trait and anemia, trauma, hypercalciuria and stones.

Common Causes of Hematuria

Often times, the clinical picture will lead you to the likely cause of hematuria in patients. However, other times the etiology may be more insidious. The following are common causes of hematuria in children.

Benign Familial Hematuria

The first common condition that we will discuss is thin-basement membrane nephropathy, otherwise known as benign familial hematuria, an autosomal dominant disease. In these patients, microscopic hematuria is due to an abnormally thin glomerular basement membrane. To make this diagnosis, you need evidence of hematuria in 3 generations with no family history of renal failure, dialysis and/or transplantation.

Alport syndrome

Another inherited cause of hematuria is Alport syndrome, which is characterized by the triad of glomerulonephritis, end-stage kidney disease, and hearing loss. This X-linked disorder is caused by heterogeneous defects in collagen. Hematuria is usually discovered in childhood in boys with Alport syndrome. Proteinuria develops later in childhood and 90% will reach end-stage renal failure by the age of 40. Hearing loss and ocular abnormalities become apparent by late childhood or early adolescence.

Normocalcemic Hypercalciuria

One-third of children with asymptomatic isolated microscopic hematuria have a condition called normocalcemic hypercalciuria. This means patients have high levels of urinary Calcium but normal serum Calcium. Usually normocalcemic hypercalciuria is asymptomatic, but occasionally patients have dysuria. A classic feature is a history of "sandy urine." An abnormal spot urine calcium-to-creatinine ratio above 0.2 is considered abnormal. Patients should be instructed to reduce excessive Calcium intake and ensure adequate hydration. If this fails, thiazide diuretics are indicated.

IgA nephropathy

The most common cause of chronic glomerulonephritis is Berger disease, also known as IgA nephropathy. The classic history includes gross hematuria that is painless and intermittent, followed by on-going microscopic hematuria. Often an upper respiratory tract infection will precede gross hematuria. Around one-third of patients have elevated serum IgA levels but this is not used as part of the diagnostic criteria. A renal biopsy is diagnostic but often not necessary unless the patient has aggressive disease. Unfortunately, there is no effective treatment strategy although immunosuppressive agents can be used in the severe cases with equivocal results.

Henoch-Schönlein purpura

Henoch-Schönlein Purpura (HSP) classically presents acutely with acute joint swelling, abdominal pain and a purpuric rash. Around 40% of patients will have renal involvement, ranging from asymptomatic hematuria and/or proteinuria to acute kidney

injury, renal failure and nephritis. HSP is an IgA-mediated vasculitis, is common in children and usually occurs after a viral infection. In general, HSP is a self-limited disease and does not require treatment.

Hemolytic uremic syndrome

Hemolytic uremic syndrome, while leading to hematuria, is more importantly the most common paediatric cause of acute kidney injury. A classic history includes abdominal pain and bloody diarrhea followed by acute renal failure and evidence of hemolysis. The triad of HUS consists of uremia, thrombocytopenia and microangiopathic hemolytic anemia. HUS is caused by shigatoxin positive *Escherichia coli* O157:H7. The most common source is from undercooked ground beef or any conditions with farm animals. The toxin binds to, attaches to and injures endothelial cells, especially in the kidney, leading to the release of endothelial products. This leads to a cascade of platelet thrombi resulting in thrombocytopenia from platelet consumption and shearing of red blood cells leading to hemolytic anemia. Treatment is mainly supportive. Antibiotics to treat the *E. coli* are contraindicated as they lead to increased bacterial lysis and worsen the disease.

Postinfectious glomerulonephritis

Postinfectious glomerulonephritis is frequently precipitated by a recent *Streptococcal* pharyngitis or skin infection. These patients can develop gross hematuria, along with other features of nephritis such as edema, hypertension and oliguria. RBC casts are common as is proteinuria. Elevation of antistreptolysin (ASO) serum levels and low C3 levels assist in diagnosis. Treatment is mainly supportive. Prognosis is excellent with >95% complete recovery.

Other

Lastly, there are several temporary or transient causes that can lead to hematuria such as fever, rigorous exercise, trauma, foreign bodies, urinary tract infections or menses in girls.

When to refer

An important learning objective is to determine when it is appropriate to refer to a pediatric nephrologist. The following are situations where a referral is warranted:

- 1) Recurrent episodes of gross hematuria.
- 2) Systemic complaints suggestive of connective tissue disease.
- 3) Coexistent heavy proteinuria in the absence of gross bleeding.
- 4) An elevated BUN and Cr.
- 5) Increased parental anxiety.
- 6) Nephritic picture with or without hypertension.
- 7) A family history of glomerulonephritis, nerve deafness, chronic renal failure, or transplantation.

If all investigations are negative, the patient will need to be followed yearly.

Summary

Hematuria is a common urinary finding that is usually first identified with a urine dipstick test. It may be painless or painful, temporary or persistent, and associated with other renal or urinary abnormalities such as proteinuria, edema or hypertension. You should be more concerned if there are associated symptoms and/or the co-existence of proteinuria. In this podcast, we reviewed the evaluation of hematuria, outline the various investigative steps, identified common causes and listed the criteria for referral to a specialist.

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