Case Report

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Berger's Disease in Urgent Care: A Case Report

Urgent Message: Although urgent care providers would not be equipped to make an initial diagnosis of Berger's disease, it's important to recognize the signs that may suggest this condition and refer patients for follow-up.

Emily Pierson PA-C, Christina Gardner DHSc, MBA, PA-C

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Abstract

Introduction

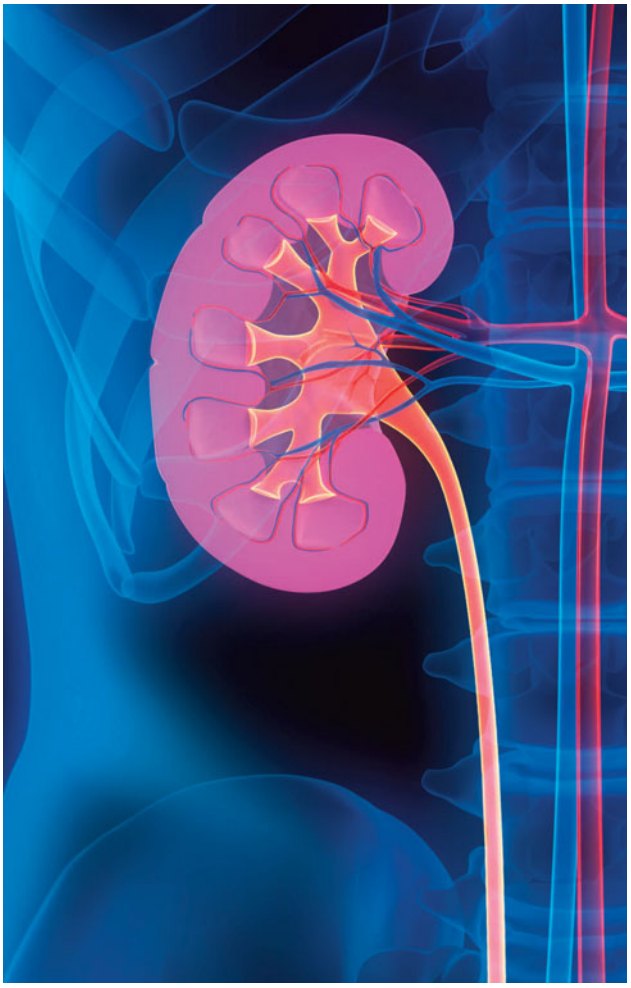
IgA nephropathy (IgAN)—sometimes known as Berger's disease—is the most common primary glomerular disease in the world. It often has delayed diagnosis since biopsy is required to confirm, but the main presenting symptom of gross hematuria may very easily be seen in an urgent care setting.

Clinical Presentation

A 22-year-old female college student presented to the urgent care with lower urinary tract symptoms and no red flags, but this was her fourth such visit in the last 8 months. On review of her chart, she had already been diagnosed with IgAN.

Physical Exam/Workup

Physical exam was unremarkable, and vitals were normal, though urinalysis showed dark red turbid urine with large bilirubin and blood, trace ketones, and large protein, as well as trace leukocyte esterase and negative nitrites. She was prescribed oral antibiotics to treat the presumed urinary tract infection, and a urine culture was sent, which later confirmed pan-sensitive *Klebsiella*.



Author Affiliations: Emily Pierson PA-C, Carilion Clinic, Roanoke, Virginia. **Christina Gardner, DHSc, MBA, PA-C,** Carilion Clinic, Roanoke, Virginia.
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Case Resolution

The patient's UA showed significantly more protein in her urine than previous visits, and she would not be able to see her hometown nephrologist for several months since she was away at college. A referral was placed to the local nephrology group, but subsequent communication with the patient was lost to follow-up.

Conclusion

While this case itself has an unsatisfactory resolution, it provides a good stage for discussion of a common disease that is just as commonly overlooked, and suggests how urgent care providers might best serve patients with this condition through recognition and referral for further workup and treatment.

Introduction

Clinical Presentation

A 22-year-old female college student presented to a local urgent care (UC) with a 1 day history of urgency, frequency, dysuria, and hematuria. She denied any abdominal pain, flank pain, fevers, chills, or gastrointestinal (GI) complaints. She also denied any recent sexual encounters or concern for sexually transmitted infection or pregnancy. She reported that she recovered from an upper respiratory infection (URI) 1 day ago and that she typically has hematuria just after URIs.

This was her fourth visit to a UC center in the last 8 months for the same set of complaints. On further questioning about this she says that she sees a "special doctor" back in her hometown because "something is wrong with my kidneys." She denies taking any medications for this condition, but reports she is supposed to be on a low sodium diet, which she admits she has not been doing since coming to college.

Physical Exam and Lab Findings

The physical exam was unremarkable, and specifically there was no abdominal or costovertebral angle tenderness. Her vitals were also normal. A urinalysis (UA) showed dark, red, turbid urine with large bilirubin and blood, trace ketones, and large protein, as well as trace leukocyte esterase and negative nitrites. Her basic metabolic panel (BMP) showed a normal creatinine and electrolyte values were also within the normal range.

Urgent Care Management and Diagnostic Assessment

On review of her chart, the patient had been seen by a nephrologist in her hometown for IgA nephropathy (IgAN) previously. She had been seen much more frequently, however, for IgAN flares in UC. The UA obtained during this UC visit showed significantly higher levels of protein than her previous visits. In reviewing the electronic medical record, there was a note from her nephrologist that if proteinuria became persistent or her kidney function declined, they would consider immunosuppressive treatments.

Due to these factors and poor adherence to a low salt diet, a BMP was obtained to assess for electrolyte abnormalities and renal function. She was referred to a local nephrology group as she could not follow up with her nephrologist until returning to her hometown at the next school break, which was over a month away. More immediately, she was prescribed an oral antibiotic to treat the presumed urinary tract infection (UTI), and her urine culture later confirmed pan-sensitive *Klebsiella spp*.

Case Conclusion

Ultimately, the patient was lost to follow-up and did not present either to the nephrologist or subsequently return to the UC.

Epidemiology

IgA nephropathy—sometimes known as Berger's disease—was first described in 1968. It is the most common primary glomerular disease in the world. It is more common in children and young adults, and slightly more common in males. There appears to be a higher prevalence in Asian countries than in the United States or Europe, but this is likely due to a higher rate of screening and of renal biopsies in those countries when compared to North America and Europe.[1] In fact, because of the higher threshold to biopsy by most North American nephrologists, true epidemiologic data is lacking. There have been some studies suggesting a genetic component, however, most data supports the theory that IgAN is a sporadic condition.[2]

Pathophisiology

IgAN is an autoimmune disease in which the immune system creates antibodies that are deposited in the basement membrane of the kidneys. These antibodies are generated in response to a mild illness like a URI or a gastrointestinal infection. IgAN can also be seen in more chronic conditions like celiac disease, cirrhosis, hepatitis, and HIV. The immune response results in inflammation and renal injury, specifically to the

semi-permeable membrane of the glomeruli.[3] This damage will mostly heal once the immune response resolves, and deficits in renal function are usually transient. However, after repeated episodes of immune response and renal damage, the glomeruli can develop scarring and permanent renal insufficiency can result. This can lead to persistent proteinuria and chronic kidney disease (CKD). Twenty years after diagnosis, up to 40% of patients will have developed end-stage-renal disease (ESRD) requiring dialysis or transplant.[2]

Presentation

The damage to the glomeruli allows red blood cells and sometimes protein to pass into the renal tubules and subsequently into the urine. If the damage is extensive enough, this will result in gross hematuria. This hematuria is often a darker red, almost brown color, giving it the classic name of "cola-colored urine."[3] It is this gross hematuria that will bring most patients to medical attention and possibly an index visit occurring in a UC setting.

Generally, the first episode of gross hematuria will occur in the second or third decade of life, though it can occur in teenagers. Painless gross hematuria should also prompt consideration for bladder or renal cancer and referral to urology for further evaluation. Nephrology referral is appropriate if there is concomitant proteinuria.[4]

Patients with IgAN will usually present with painless, gross hematuria *during* or *immediately after* a symptomatic infection of the upper respiratory tract or GI tract. Conversely, post-streptococcal glomerulonephritis typically has a 2-3 week delay between URI symptoms and hematuria.

Apart from hematuria, most patients with IgAN are asymptomatic, although mild flank/low back pain during a flare, which is thought to be due to pressure on the renal capsule caused by swelling during the immune response, can also occur.[2] Only about 5% of patients will present with signs of nephrotic syndrome during a flare, which include edema, hyperlipidemia, hypoalbuminemia, and >3g of proteinuria/day.[2] The presence of peripheral edema in a patient with hematuria and proteinuria is an indicator of more significant disease and warrants more prompt follow-up with a nephrologist.

Diagnosis

As discussed, patients are not formally diagnosed with IgAN until they have a renal biopsy, which is generally only ordered by nephrologists. Often in North America, patients are presumptively diagnosed with IgAN, either by their primary care provider (PCP) or by a nephrologist based on pattern of hematuria and/or proteinuria during or just after a respiratory/GI infection.

These patients often have a creatinine monitored regularly to evaluate for changes in renal function. Periodic 24-hour protein excretion is also obtained to assess for the extent of renal damage. If there is no persistent proteinuria between flares, these patients are generally monitored with periodic nephrology follow-up. Formal renal biopsy may be obtained before initiation of medical intervention, but this is still not always done.[3]

"The damage to the glomeruli allows red blood cells and sometimes protein to pass into the renal tubules and subsequently into the urine. If the damage is extensive enough, this will result in gross hematuria."

Treatment

Initially, patients without persistent proteinuria between flares are monitored and encouraged to make certain renal protective lifestyle changes like maintaining a low-salt diet, staying well-hydrated, and controlling blood pressure if hypertensive. If the disease progresses, patients are generally started on corticosteroids or other immunosuppressants—such as tacrolimus, cyclophosphamide, mycophenolate mofetil, or azathioprine—to mitigate autoimmune renal injury. These two classes of medications—corticosteroid and immunosuppressants—were shown to be the most effective at reducing proteinuria in a recent meta-analysis.[5] Even though UC providers are not going to be making the initial diagnosis of IgAN or initiating immunosuppressive agents, it is critical to know if a patient is taking these medications. Antibiotics according to standard treatment guidelines are appropriate when treating other urinary complaints, such as UTI.

"If able to review previous UAs in the patient's medical record, evidence of prior hematuria and/or significant proteinuria warrants an immediate nephrology referral."

Referral

UC may be the site where gross hematuria initially presents, however, specialist referral, again, is appropriate in such cases—some of which may result in a diagnosis of IgAN. All patients with painless gross hematuria (or microscopic hematuria on repeat urinalyses without UTI) should be referred back to their PCP or to nephrology or urology if available.[6] Unfortunately, the most commonly used tool to predict outcomes in IgAN, known as the MEST-C Score or the Oxford Classification, is based largely on the renal biopsies.[2,3] This makes it difficult to quickly and objectively classify patients into higher risk categories in an UC setting. However, a 2021 meta-analysis found that patients who initially present with microscopic hematuria and persistent hematuria seemed to have increased risk for poor outcomes, while those who initially presented with macroscopic hematuria tended to have a decreased risk of poorer outcomes.[7]

If able to review previous UAs in the patient's medical record, evidence of prior hematuria and/or significant proteinuria warrants an immediate nephrology referral. If this is the first episode of microscopic hematuria, the patient could be referred their PCP for repeat UA. Macroscopic hematuria could be seen by a PCP for follow-up, but patients should be informed that they will ultimately need to be referred to a specialist most likely.[6]

Discussion

Micro- and macroscopic hematuria are commonly encountered in UC in the setting of UTI and kidney stones. Painless, gross hematuria or persistent microscopic hematuria outside of these settings, however, warrant specialist referral. Urinary tract malignancy is a primary consideration, especially in older patients. If a younger patient presents with gross hematuria, especially after a recent URI, IgAN may be the culprit. While both nephrologists and urologists are equipped to evaluate patients with hematuria, the presence of proteinuria, worsening renal function, and/or peripheral edema, suggests a renal issue, and nephrologist referral is most appropriate.

Though UC providers will not be making an initial diagnosis of IgA nephropathy, it's important to recognize the signs that may suggest this condition. Furthermore, in cases with known IgAN, it is important to counsel patients on the importance of following recommended dietary modifications and renal protective measures as prescribed by their nephrologist to limit the likelihood of CKD and progression to ESRD.

Ethics Statement

An attempt was made to contact the patient to obtain informed consent to publish this case, but she was lost to follow-up and could not be reached. The patient's identifying details were changed or omitted to protect her privacy. ■

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