Case Report

An Unusual Cause of Hematuria

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Abstract

Hematuria is a cardinal manifestation of renal disease and forms a cornerstone of nephrologic diagnosis. A systemic approach is required to delineate the source of hematuria to the kidney or urinary tract. We present the case of a 14 years old boy who presented to us with history of passing red colour urine since 3 months associated with pain who was subsequently diagnosed to have of Thin Basement Membrane Disease.

Introduction

Microscopic hematuria, a common clinical problem has been reported to affect 4% of 13% of the adults population and more than half of these patients have no detectable urologic disease. IgA Nephropathy is considered to be the most common cause of idiopathic glomerulonephritis and glomerular hematuria. However recent studies suggests that Thin glomerular Basement Membrane Nephropathy (TBMN) may equal or exceed IgA Nephropathy as the leading cause of glomerular hematuria. Persistent hematuria is commonly defined as hematuria that is observed on at least 2 occasions. According to Wangard Savige, persistent hematuria occurs consistently in as much as 6% of both children and adults. On the basis of both direct and indirect approaches the overall prevalence of TBMN in population has been estimated to be 1%. We report a case of Thin Basement Membrane Nephropathy in a young boy of 14 years who presented to us with intermittent painless hematuria.

Case Report

A 14 year old boy presented to our OPD with history of passing red coloured urine intermittently since last 3 months. This was not associated with pain. He did not give history of edema feet, oliguria or puffiness of face. There was no history suggestive of preceding respiratory infection and any food or drug history. He also gave history of being admitted in private hospital for similar complaints and discharged without further investigations as urine routine microscopy showed no significant RBCs in the urine (urine RBC 3-4/hpf). There was no history of passing red coloured urine in the early morning. There was no history suggestive of hearing loss.

On examination he was averagely built, pulse rate was normal with normal blood pressure (BP -110/70mmHg). General examination and systemic examination was essentially normal. On investigations Hb was 12.3 gm% with normal ESR, WBC and platelets count. BUN was 11mg/dl and serum creatinine of 0.7mg/dl. Urine analysis showed presence of 4-6 RBCs per high power field in repeated samples when it was done during asymptomatic period. There were no pus cells, casts or proteinuria on routine urine examination. Patient had two episodes of macroscopic hematuria during hospital stay. Immune work up included ANA, ANCA, anti-GBM were all negative. There was no hypocomplementemia. Flow cytometry was done which ruled out evidence of Paroxysmal Nocturnal Hemoglobinuria. Ultrasound of kidney, ureter and bladder as well as intravenous pyelogram was done which ruled out any obstructive cause or renal calculus disease. ENT reference ruled out hearing loss. Hence we went ahead with a renal biopsy to rule out any familial causes. Histopathology and Immunofluorescence of kidney biopsy was normal, but the electron microscopy revealed normal glomeruli, diffuse thinning of GBM and thickness of GBM was varying but less than 250 nm in the glomeruli that were observed, which was consistent with thin basement membrane disease.

Thus the final diagnosis of Thin Basement Membrane Nephropathy was made and the patient and relatives were assured of its benign course in future.

Discussion

TBMN nephropathy is a familial disorder with autosomal dominant pattern of inheritance, characterized histologically by diffuse thinning of GBM and clinically by microscopic hematuria. It has also been termed as Benign Familial Hematuria. Patients with benign familial hematuria usually have persistent hematuria, although intermittent hematuria does occur in some patients. Episodic gross hematuria is rare. Also proteinuria, progression to renal failure, or extrarenal symptoms such as hearing loss are not present.

On histological evaluation of TBMN, light microscopy and immunofluorescence microscopy of renal parenchyma are typically unremarkable. Thinning of the glomerular basement membrane (GBM) on electron microscopy the hallmark of disease, is usually uniform, but focal alteration involving at least 30% of the GBM may occur. The lamina densa width of the GBM varies with the laboratory technique used to measure it, and also with the age and gender of the patient. Thus the definition of what constitute “thin” GBM has not been consistent in the literature. Generally the GBM diameter of less than 250nm in adults and 200-250 nm in the children has been suggested as indicative of Thin GBM nephropathy.

Thin GBM disease begs for a molecular explanation as thinning and attenuation of the GBM may also be seen in the early course of Alport Syndrome which is another glomerular disorder associated with hematuria. However in our patient chromosomal studies were not done to rule out Alport Syndrome. Our patient did not have family history of hematuria or renal failure. Patient also did not have any hearing loss suggestive of

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Alport syndrome.

It has been still a major clinical challenge to differentiate between TBMN characterised by non-progressive renal failure and Alport syndrome with progressive renal failure because these conditions can have a very similar appearance, especially in children. However a kidney biopsy should be able to show normal results for type IV collagen chains (COL4A3, COL4A4, COL4A5) indicating a diagnosis of thin basement Membrane Nephropathy.6

If diagnosis remains doubtful after kidney biopsy screening for genetic mutations be considered however the screening for COL4A3, COL4A4, COL4A5 is widely available. In addition, the current detection rate of COL4A5 mutations in relatives is only about 50%.7 Thus genetic testing should be limited to prenatal diagnosis or when uncertainty about diagnosis or mode of inheritance of Alport syndrome exists.

Isolated microscopic hematuria that begins in childhood and is of glomerular origin has a rather limited differential diagnosis, with Alport Syndrome, IgA nephropathy and benign familial hematuria as the most prevalent condition. Thin GBM disease may present as early as 1 year or upto 86 years. Atleast a single episode of macroscopic hematuria is observed in 5-22% of patients typically manifesting after exercise or during infection.8 Despite hematuria, individuals usually do not have proteinuria or only minimally so, indicating that the podocyte slit diaphragm is not really affected.

Generally the prognosis for the nephropathy in the TBMN is excellent. In the absence of significant proteinuria and renal dysfunction, patients can be reassured and safely followed up for periodic measurements of blood pressure, urine protein excretion and renal function.

References