CLINICAL VIGNETTE

IgA Nephropathy in Primary Care

Alina Katsman, MD

Case

A 30-year old Asian American female with no significant past medical or surgical history presents to her primary care physician for an annual wellness exam. Her family history is significant for diabetes in both parents and a sister who passed away from heart failure and pulmonary hypertension. She does not smoke, drinks alcohol occasionally and does not use recreation drugs. Her only medication is combined oral contraception pills. Vitals signs are unremarkable and reveal a blood pressure of 123/86. Physical exam is unremarkable. Routine blood work reveals an elevated serum creatinine of 1.5 and glomerular filtration rate (GFR) of 46; a urinalysis reveals microscopic hematuria and presence of proteinuria. Two years prior her creatinine was normal at 0.9 (GFR 75). A repeat creatinine level done 1 month later is 1.67 (GFR 41) and urine total protein/Cr ratio is 2.8. Additional labs to evaluate for chronic kidney disease are unremarkable – ANA and rheumatoid factor negative, ANCA negative, complement levels normal, SPEP negative, acute hepatitis panel negative, antisteptolysin O screening negative, crycrit negative. She is referred to nephrology, at which time her urine total protein/Cr ratio is 3.4. Kidney biopsy reveals IgA nephropathy with advanced global and segmental glomerulosclerosis and fibrocellular crescents with extensive chronic tubulointerstitial changes and arterial/arteriolar nephrosclerosis. She is started on lisinopril 5 mg daily. Immunosuppression is not recommended at the time of the diagnosis. Six months later she is seen by another nephrologist for a second opinion who prescribed prednisone 50 mg every other day. She presents back to her primary care doctor about 1 year after initial diagnosis. She tapered prednisone 35 mg every other day and remains on lisinopril 5 mg daily. Her blood pressure is 110/73. She has gained 10 pounds, has moon facies on exam, and labs reveal new onset prediabetes and hypercholesterolemia. She continues to have significant proteinuria with urine total protein/Cr ratio of 3.1 and a low glomerular filtration rate (GFR) of 31.

Discussion

IgA nephropathy is the most common cause of primary glomerulonephritis with peak incidence in the second and third decades of life. There is approximately a 2:1 male-to-female predominance in North American and Western European populations, although the sexes are equally affected among populations in East Asia.[1] Slow progression to end-stage renal disease occurs in up to 50 percent of affected patients, often over 20 to 25 years of observation. The remaining patients enter a sustained clinical remission or have persistent low-grade hematuria and/or proteinuria.

The presence of IgA nephropathy is established only by kidney biopsy. The pathognomonic finding observed on immunofluorescence microscopy is dominant or co-dominant mesangial deposits of IgA, either alone, with IgG, with IgM, or with both IgG and IgM. More advanced clinical presentations are marked by decreased glomerular filtration rate (GFR), increased proteinuria, and features of chronic disease on renal biopsy: glomerulosclerosis, tubulointerstitial inflammation, tubular atrophy, and interstitial fibrosis.[2]

Most patients with IgA nephropathy present with either gross hematuria, usually accompanying an upper respiratory infection, or microscopic hematuria with or without mild proteinuria incidentally detected on a routine examination. Rarely, patients may develop acute kidney injury with or without oliguria, due either to crescentic IgA nephropathy or to gross hematuria causing tubular occlusion and/or damage by red cells. Kidney biopsy is usually performed for the evaluation of suspected IgA nephropathy only if there are signs suggestive of more severe or progressive disease such as urine protein excretion of at least 500 mg/day, elevated serum creatinine, or the presence of hypertension.

Treatment of IgA nephropathy depends on severity of disease. Patients with isolated hematuria, minimal to no proteinuria (less than 500 to 1000 mg/day), and a normal glomerular filtration rate (GFR) are typically not treated and often not biopsied and therefore not identified as having IgA nephropathy. However, these patients should be periodically monitored at 6- to 12-month intervals to identify progressive disease, manifested by increases in proteinuria, blood pressure, and/or serum creatinine. Patients with persistent proteinuria (above 1 g/day or perhaps above 500 mg/day), normal or only slightly reduced GFR that is not declining rapidly, and only mild to moderate histologic findings on renal biopsy are initially managed with non-immunosuppressive therapies to slow progression. Non-immunosuppressive therapy includes angiotensin inhibition with either an ACE inhibitor or angiotensin II receptor blocker (ARB) with the goal of therapy to limit urinary protein excretion below 500 mg/day or 1 g/day and maintain blood pressure below 130/80 mmHg. Another non-immunosuppressive therapy is fish oil (at 3.3g/day or more), which may have cardiovascular benefits. Although some studies suggested

a possible benefit of statin therapy on progression of chronic kidney disease, this was not seen in the meta-analysis and a subsequent large randomized trial (SHARP) that included 6247 patients with chronic kidney disease not requiring dialysis. At this time statin therapy is not recommended to slow the progression of chronic kidney disease.[3]

The indications for the use of glucocorticoids alone or in combination with other immunosuppressive drugs in patients with IgA nephropathy are not well defined. Most nephrologists do not treat mild, stable, or very slowly progressive IgA nephropathy with glucocorticoids or other immunosuppressive therapies. Most nephrologists would start treatment with glucocorticoids in patients with hematuria and one or more of the following: a progressively declining glomerular filtration rate (GFR), persistent proteinuria above 1 g/day despite use of ACE inhibitors or angiotensin II receptor blockers (ARBs) for three to six months, or morphologic evidence of active disease based upon kidney biopsy (eg, proliferative or necrotizing glomerular changes).

In summary, our patient had a classic presentation of microscopic hematuria and significant proteinuria (more than 1gm/day) with a decrease in glomerular filtration rate (GFR). She was initially started only on non-immunosuppressive therapy with an ACE inhibitor and then six months later on immunosuppressive therapy with prednisone due to her progressive disease.

REFERENCES

1. **Galla JH**. IgA nephropathy. *Kidney Int*. 1995 Feb;47(2): 377-87. Review. PubMed PMID: 7723227.
2. **Haas M**. Histologic subclassification of IgA nephropathy: a clinicopathologic study of 244 cases. *Am J Kidney Dis*. 1997 Jun;29(6):829-42. PubMed PMID: 9186068.
3. **Reith C, Staplin N, Herrington WG, Stevens W, Emberson J, Haynes R, Mafham M, Armitage J, Cass A, Craig JC, Jiang L, Pedersen T, Baigent C, Landray MJ; SHARP Collaborative Group**. Effect on non-vascular outcomes of lowering LDL cholesterol in patients with chronic kidney disease: results from the Study of Heart and Renal Protection. *BMC Nephrol*. 2017 May 1;18(1):147. doi: 10.1186/s12882-017-0545-2. PubMed PMID: 28460629; PubMed Central PMCID:PMC 5412040.

Submitted December 1, 2018