CLINICAL VIGNETTE

Does IgA Nephropathy Increase Risk for IgA Vasculitis? IgA Nephropathy with IgA Vasculitis

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Introduction

There is debate whether Immunoglobulin A (IgA) nephropathy and IgA vasculitis are two different diseases or are two clinical manifestations of the same disease.

IgA nephropathy, previously known as Berger's disease, is a common glomerulonephritis[1] consisting of a predominance of IgA deposits in the glomerular mesangium.[2] IgA nephropathy presents with macroscopic hematuria associated with upper respiratory or gastrointestinal illness in children and macroscopic hematuria and proteinuria in adults.[2]

IgA vasculitis, previously referred to as Henoch-Schönlein Purpura, is a common vasculitis seen in children, but can be present at any age.[3] IgA vasculitis presents with IgA-dominant immune deposits affecting small vessels that typically involves skin, gut, and glomeruli. It has associated arthralgias or arthritis.[4]

Although there are reports of IgA nephropathy and IgA vasculitis occurring in the same patient[5], some question whether IgA nephropathy and IgA vasculitis are the same disease.[6]

We present a patient with both IgA nephropathy and IgA vasculitis.

Case Presentation

A woman in her 50s presented to Nephrology for evaluation of nephrotic range proteinuria. Her past medical history includes hypertension (HTN) for 25 years, and type 2 diabetes mellitus (DM) for 10 years. She was followed by an outside nephrologist for proteinuria, which was attributed to long standing HTN and DM. The patient also reported a recent rash on her legs and watery stools for a few weeks prior to presentation.

The patient was followed by a community nephrologist for ten years, with subnephrotic range proteinuria. She had well controlled blood pressure and was compliant with her medications.

A few weeks prior to presenting to Nephrology, she was evaluated by Rheumatology for a petechial rash. The rash started in the inner upper thighs that spread to her abdomen. The rash was non painful, non-pruritic and had no crusting or bleeding. She reported increased work stress at the time of presentation of her rash. Evaluation included a punch skin biopsy of her inner thigh. Biopsy showed mild superficial perivascular lymphocytic inflammation with neutrophils, infiltration of vessel walls by neutrophils, red blood cell extravasation and leukocytoclasia. Direct immunofluorescence showed granular IgA, fibrin, and C3 in blood vessel walls. No IgG or IgM was detected. The skin biopsy findings suggested leukocytoclastic vasculitis.

She was started on a prednisone taper with resolution of her petechial rash. However, the rash recurred a few weeks later, after a fever that lasted two to three days.

The patient's chlorthalidone and allopurinol were discontinued, given concern as a possible cause of the rash. She was continued on azilsartan for blood pressure control. Eventually, she was started on spironolactone and dapagliflozin for blood pressure, diabetes, and antiproteinuric effects.

She continued to have waxing and waning petechiae and underwent renal biopsy in 2023 to evaluate other causes for the petechial rash. In the interim, the patient was restarted on prednisone taper.

The renal biopsy showed no definite sclerosis, necrotizing lesions, or crescents. There was at least mild interstitial fibrosis and tubular atrophy in the small amount of cortical tissue present. Arteries and arterioles were unremarkable. There was no vasculitis, no vascular thromboses, and no significant tubulointerstitial inflammation. Immunofluorescence showed diffuse global granular glomerular and segmental capillary wall staining with IgA (4+), IgM (1+), C3 (2-3+), kappa light chain (3+) lambda light chain (4+), and fibrinogen (3+). Tubular casts stained with IgA and equally with both light chains.

Renal biopsy suggested IgA nephropathy with at least focal mesangial proliferative glomerulonephritis. Glomerulomegaly, focal global glomerulosclerosis, moderate interstitial fibrosis/ tubular atrophy, and focal hyaline arteriolosclerosis were also seen.

Discussion

It is uncertain whether IgA vasculitis and IgA nephropathy are the same disease. Reports suggest IgA vasculitis is a systemic form of IgA nephropathy.[7] Patients with IgA nephropathy produce anti-GalNAc antibodies against a defective IgA1 molecule. This leads to formation of IgA immune complex deposits in the kidneys, leading to a type 3 hypersensitivity reaction, causing kidney damage.[8] IgA vasculitis appears to be a systemic form of IgA nephropathy, where IgA immune complexes are deposited systemically, involving small vessels of different organs including skin, joints, gastrointestinal tract, and kidneys, with multiple disease manifestations.[9]

Treatment for IgA nephropathy varies with risk factors for progression. General measures include blood pressure control and reduction of proteinuria with renin-angiotensin system inhibition[10] and lifestyle modification. Other treatments include sodium-glucose cotransporter 2 inhibitors,[11] dual endothelin angiotensin receptor antagonists,[12] or immunosuppressive therapy in patients at high risk for disease progression.

Treatment for IgA vasculitis also depends on symptom severity. Treatment typically includes supportive care such as hydration and analgesics. Immunosuppressive therapy may be indicated with organ- or life-threatening vasculitis.[13] Limited treatment guidelines for patients with IgA vasculitis nephritis follow treatment recommendations for IgA nephropathy.

Conclusion

This patient with IgA vasculitis also presented with IgA nephropathy. Given her history of proteinuria and petechial rash, she may have had long standing IGA nephropathy, alternatively her IgA vasculitis may have been precipitated from a stressor event. This is consistent with the proposed concept that IgA vasculitis is a systemic form of IgA nephropathy.[7]

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