CLINICAL VIGNETTE

Membranous Glomerulonephritis

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Case Report

A 60-year-old African American male, with no significant past medical history, presented with a one-week history of progressive lower extremity pitting edema, somnolence and polyuria. He first noticed edema when removing his socks at the end of the day. He subsequently had progressive edema to the knee with an associated 15lb weight gain. He described no new medications, no recent gastrointestinal illness, no arthralgias, and no episodes of chest pressure or pain. He had no orthopnea or dyspnea on exertion. There had been no dietary changes or recent travel. He did report increasing polyuria.

His examination was remarkable for 4 pitting edema of bilateral lower extremities to the mid calf. He had no crackles on pulmonary examination and a blood pressure of 120/80. Bilateral lower extremity duplex showed no evidence of DVT and Chest X-Ray was negative. EKG showed no acute changes. Laboratory testing included a comprehensive metabolic panel, which revealed a total protein of 4.4g/dL (previous 7.5g/dL), Albumin 2g/dL (previous 4.3g/dL). His cholesterol panel revealed an LDL of 184mg/dL (previous 71mg/dL) and his urinalysis showed protein of 1306mg/dL and albumin >3000mg/L. Serum creatinine was 1.1mg/dL. Hepatitis B antibody and antigen were negative. ANA was negative.

He subsequently underwent renal biopsy, which showed Membranous Glomerulonephritis with no significant chronic tubulointerstitial changes. IgG deposits were noted in both subepithelial and occasional subendothelial or intra-membranous locations raising the suggestion of a secondary membranous glomerulonephritis. He was placed on an Ace Inhibitor and furosemide with gradual improvement in his edema. He subsequently had a decrease in his level of proteinuria.

Discussion

Membranous Glomerulonephritis comprises 25% to 33% of all nephrotic syndrome cases, affecting males more often than females, with the greatest prevalence over 40 years of age. The cause is IgG deposition in the basement membrane, which is seen on Immunoflorescence microscopy. This can be provoked through secondary causes, such as Hepatitis B infection, autoimmune disease, malignancy or drug sensitivity (gold, penicillamine, NSAIDs)[1]. The differential would include any of the other causes of the nephrotic syndrome, including Focal Segmental Glomerulosclerosis, Membranoproliferative nephro-sclerosis, and Minimal Change Disease. These would be differentiated based on their appearance on electron micrsocopy. If none of the secondary causes can be identified and microscopic findings support the diagnosis, Idiopathic Glomerulonephritis is confirmed in 75% of cases.

The clinical presentation, as in the case discussed, includes the rapid onset of edema, polyuria, malaise and fatigue. Laboratory abnormalities include nephrotic range proteinuria with occasional blood on urinalysis. Despite these urinary abnormalities, serum creatinine is typically normal. Lipid panel can reveal a sharp rise in LDL and total cholesterol. Serum albumin is low, due to urinary protein losses. Coagulopathy from loss of coagulation factors in the urine result in abnormal prothrombin and partial thromboplastin times. Investigation for secondary causes should include Hepatitis B, C antibodies, ANA, C3, C4, RPR, and anti-TPO antibodies[2]. Routine, age appropriate cancer screening should also be undertaken[3].

The progression of the disease is gradual, with spontaneous remission occurring in 40% of patients at 5 years. With longer follow up, however, up to 40% of patients will progress to end stage renal disease at 15 years[4]. Typically, older age at presentation, higher levels of proteinuria, and elevation in creatinine at presentation are predictors of eventual renal failure. Based on these predictors, patients can be categorized into risk groups for future renal disease and thereby stratified for treatment.

Low risk patients have less than 4g of proteinuria on serial 24 hours urine measurements over a six-month period. Moderate risk patients excrete 4-8g of protein, but have manageable edema with normal creatinine clearance. High-risk patients excrete over 8 grams of protein in a 24-hour period and have abnormal creatinine clearance.

Treatment options are based on the likelihood of future renal failure. In cases of secondary membranous glomerulonephritis, treatment of the underlying cause (ie discontinuation of NSAID) will often results in remission. For idiopathic MGN, nearly all patients would benefit from ACE inhibition, blood pressure control, and cholesterol reduction. Diuretics are employed to help control edema, and in the case of hypercoagulability, anticoagulation is needed[5].

The decision to treat with immunosuppressive agents is based on the risk of progressive disease[6]. In the moderate and high-risk groups--patients with elevated creatinine at presentation, or persistent proteinuria (over 4g at 6 months), immuno-suppression may be indicated. Gluco-corticoids alone are typically not effective, but need to be paired with either cyclosporine or tacrolimus. In patients who do not respond to initial therapy, rituximab is the second line therapy of choice.

The prognosis of Idiopathic Membranous Nephropathy in patients with spontaneous or medically induced remission is excellent; with nearly all patients avoiding dialysis over long term follow up. In patients with progressive disease, immuno-suppressive therapy can still alter progression to dialysis with induction of partial remissions and thereby slow the rate of renal decline[7].

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