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CLINICAL VIGNETTE

A Case of Minimal Change Disease in Adulthood Presenting with Hypertensive Crisis

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Case Report

A 70-year-old female non-smoker who recently relocated from Mexico to live with her daughter presented to primary care with worsening dyspnea and edema for the past week. Her initial BP was 219/119 mmHg and she was sent to the emergency room with concern for hypertensive crisis. Her past medical history included hypertension and hypothyroidism on replacement. Her chronic medications included losartan 50 mg, levothyroxine 50 mcg/day, donepezil 5 mg qhs and prn lorazepam for anxiety. ED evaluation was remarkable for persistent hypertension and significant edema involving bilateral lower extremities, face and hands. Echocardiogram showed mild concentric left ventricular hypertrophy, and labs were remarkable for mildly elevated Cr of 1.1, elevated BNP of 193 and significant proteinuria. She was treated with furosemide and clonidine with improved BP to 150/80 and discharged on losartan/hctz (100/25) and referred to cardiology and was seen the following day. ED evaluation also included positive ANA and CT Chest which showed coronary calcifications. She brought copies of prior labs which showed creatinine of 0.6 one year prior. Repeat BP remained elevated at 170/73 with unremarkable cardiothoracic exam. Additional labs included: A1C of 7.8%. Her losartan was held due to CKD and she was started on carvedilol 3.125 mg bid, nifedipine 60 mg bid as well as resuvastatin 20 mg/day.

Carvedilol was titrated up to 25 mg bid over two weeks with improvement in BP to 130s systolic and diastolic BPs in the low 80s mmHg. Her edema also improved, but still noted "foamy" urine with 3+ proteinuria. There was no orthopnea and she had improved exercise tolerance. Creatinine also returned to baseline, and subsequently losartan 50 mg bid was restarted. She was also started on glipizide for new diagnosis of diabetes mellitus type 2.

A month later, her systolic pressures were again elevated in the 150s despite compliance with losartan and carvedilol. Carvedilol was changed to labetalol 200 mg bid and pressures improved to 130 /80 mmHg. She was also evaluated by rheumatology for possible SLE given proteinuria and positive ANA. Double stranded DNA and other rheumatological/ autoimmune labs were negative, except for positive Thyroid Peroxidase Antibody (TPO) test and the positive ANA titer was attributed to Hashimoto's thyroiditis.

The proteinuria persisted and a renal biopsy was performed about two months after initial presentation. Core biopsy showed near complete podocyte foot process effacement with normal glomeruli consistent with Minimal Change Disease (MCD). There was a comment noting minimal tubulointerstitial inflammation and nonspecific scarring that raised possibility of a secondary disease such as NSAID or other drug toxicities. However, the patient was not on any renal toxic medications and there were no eosinophils, granulomas, immune complex deposits with negative immunofluorescent staining, diabetic or hypertension changes on the biopsy. She also underwent screening with negative colonoscopy and mammogram given an association of malignancy with MCD. At cardiology follow up four months later, she had no dyspnea or edema, and her blood pressures were well controlled, at goal of < 130/80 mmHg, on labetalol 200 mg po bid, and losartan 50 mg po bid, along with life style modifications to optimize her blood pressure control. Her proteinuria improved and completely resolved after optimized BP control. Corticosteroids were not required for treatment.

Minimal Change Disease

Nephrotic syndrome is a clinical syndrome caused by damage to the glomeruli filtration barrier leading to increased permeability and significant protein loss which can include albumin, clotting factors, transferrin, Vitamin D binding protein and other hormone carrying proteins.[1,2] This may result in a constellation of symptoms including massive proteinuria, > 40 mg/kg per day, hypoalbuminemia, and significant edema[1]. Hyperlipidemia and thrombotic disease may also be present.[1,2] Other symptoms may include weight gain, fatigue, foamy urine, hypercoagulability, infection and hypertension.[1,2] Most cases of nephrotic syndrome are thought to be secondary to a number of conditions including diabetes, infection and autoimmune disease including amyloidosis and systemic lupus erythematosus.[1,3] Primary nephrotic syndrome is due to minimal change disease, focal segmental glomerulosclerosis, membranous nephropathy and membranoproliferative glomerulonephritis.[1,3]

Minimal Change Disease (MCD) is also called nil disease or lipoid nephrosis.[4] The name reflects the appearance of normal glomeruli on light microscopy with no complement or immunoglobulin deposits seen on immunofluorescence microscopy.[5] The characteristic histologic lesion of MCD is diffuse podocyte foot effacement on electron microscopy.[4,5] MCD most commonly occurs in children, with up to 70-90% cases in children >1-year.[4] MCD also occurs in adults at a much lower

prevalence of 10-15% of idiopathic nephrotic syndrome cases.[6] Most adult MCD cases are idiopathic but some are associated with drugs, malignancy, infections, allergy, other glomerular diseases, and other autoimmune conditions.[7,8] MCD presents with signs and symptoms of nephrotic syndrome, such as proteinuria, peripheral and facial edema, foamy urine, hypoalbuminemia, hyperlipidemia, and resistant hypertension. Some unique characteristics of MCD include a more sudden onset of symptoms over days to weeks after an inciting event such as infection. In contrast, other types of nephrotic syndrome such as FSGS and membranous nephropathy typically develop over weeks to months.[7] MCD may also present with a modestly elevated creatinine and acute kidney injury.[7] To diagnose MCD in adults, early renal biopsy is recommended prior to treatment. In contrast, a renal biopsy is generally not needed for pediatric patients as diagnosis can be made based on presentation and response to glucocorticoid therapy. This is because MCD is the most common cause of nephrotic syndrome in children and children's excellent response to glucocorticoid therapy. In adults, there are multiple causes of nephrotic syndrome and adults often take longer or may not respond to glucocorticoid therapy.[5]

Initial treatment for MCD includes glucocorticoids and management of associated symptoms. MCD is classically known to have an excellent response to glucocorticoids with an often-complete disappearance of proteinuria in 80-95% cases. In children, up to 50% of proteinuria cases resolve within 8 days with glucocorticoid treatment. However, in adults, the glucocorticoid treatment response is typically much slower with median response to treatment greater than two months.[5,9] Most patients are started on oral prednisone 1 mg/kg daily for 8-16 weeks. A steroid taper is recommended for durations longer than 8 weeks to sustain remission and avoid adrenal suppression.[10] In adults, remission and relapses may occur as well. Additional treatment includes management of hypertension and peripheral edema in adults with MCD. Firstline therapy include low sodium diet and diuretic usage. If blood pressure remains poorly controlled, ACE inhibitors or angiotensin II receptor blocker are initiated to help reduce blood pressure and urinary protein excretion.[10]

Conclusion

While most cases of minimal change disease occur in children, MCD can also present in adults with nephrotic range proteinuria, peripheral edema and hypoalbuminemia. Interestingly, this 70-year-old female presented with hypertensive crisis with acute kidney injury and nephrotic range proteinuria. Her persistent severe proteinuria, led to a renal biopsy with histopathology consistent with Minimal Change Disease. This is an uncommon presentation of minimal change disease in an adult. The MCD appears to be idiopathic, as there were no identified associated causes. Interestingly, her Minimal Change Disease, hypertension, acute kidney injury and proteinuria spontaneously resolved over four months with blood pressure optimization and avoiding nephrotoxic drugs. Unlike most cases of minimal change disease, she did not receive any glucocorticoid treatment.

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