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CASE REPORT

Adult minimal change disease with acute kidney injury: a case report and literature review

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ABSTRACT

Minimal Change Disease (MCD) is identified via renal biopsy as the etiology of nephrotic syndrome in a minority of adult cases; however, a significant proportion of these occurrences are accompanied by acute kidney injury (AKI). Risk factors for AKI in MCD include increased age, male sex, hypertension, and marked proteinuria and hypoalbuminemia. The etiology of AKI appears to be tubular injury as demonstrated with biomarkers, and although it is usually reversible with steroid therapy, resistance and relapses can occur and may require the use of second-line agents. We present a case of an adult patient with acute onset of biopsy-proven MCD and AKI demonstrating a partial response to corticosteroids and aggressive diuresis and later relapsing and requiring further immunosuppression with tacrolimus. Ultimately, further studies are required to determine the optimal treatment regimen for MCD to ensure remission and avoid relapse.

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1. Introduction

Minimal Change Disease (MCD) comprises the vast majority of cases of nephrotic syndrome in children but only 15% of the cases in adults [1]. The etiology can be idiopathic or secondary to medications such as NSAIDs, hematologic or solid malignancies, infections, or other renal or systemic diseases [2]. These secondary causes account for up to 15% of minimal change disease in adults [2]. Thus, it is important to collect a detailed history on adults with MCD as the prognosis and management depend on the underlying etiology.

Abrupt onset of edema and proteinuria heralds the disease. In contrast to the pediatric presentation, hypertension (25%-50%), hematuria (20%-30%), and acute kidney injury (AKI) (20%-25%) are more commonly observed in adults [3]. AKI is theorized to be hemodynamically induced, with stigmata of acute tubular necrosis noted in up to 60% of such patients [3]. Risk factors for AKI, and occasionally irreversible kidney damage, include increased age, male sex, hypertension, and marked proteinuria and hypoalbuminemia [4].

Since the signs and symptoms of MCD can be identical to other nephrotic syndrome etiologies, a renal biopsy remains the gold standard to establish the diagnosis and initiate treatment. As in children, a majority of adult MCD cases remain steroid sensitive. When steroid resistance occurs in 5%-20% of cases, this minority of patients frequently has Focal Segmental Glomerulosclerosis (FSGS) on review of the original specimen or on repeated biopsy [3,5].

2. Case description

A 75-year-old Caucasian male with hypertension and no history of diabetes presented to the hospital with a one-month history of dyspnea, lower extremity edema, 30 lb weight gain, and elevated blood pressure. Hypertension had previously been well controlled on lisinopril 5 mg daily for 10 years. Patient had a history of intermittent NSAID use with meloxicam 15 mg for headaches, but no antibiotic use, history of malignancy, or underlying CKD.

Physical exam revealed bilateral wheezes and lower extremity pitting edema. Laboratory studies were significant for creatinine of 1.69 mg/dL, which continued to climb despite furosemide diuresis. Albumin was 1.9 g/dL, liver function tests and lipid panel were both normal. Urinalysis showed nephrotic-range proteinuria with urine protein/creatinine ratio 5.41, 13 RBC/HPF, 10 WBC/HPF, and granular and hyaline casts. Ultrasound revealed a left renal cyst. Echocardiogram was unremarkable. Further serologic studies including viral hepatitis panel, HIV Ag/Ab, ANA, ANCA, and urinary eosinophils were negative. C3/C4 were normal. SPEP revealed hypogammaglobulinemia. Phospholipase A2 Receptor antibodies were negative.

Given the patient's unexplained nephrotic syndrome, renal biopsy was performed. Light microscopy exhibited glomeruli without mesangial expansion or increased cellularity (Figures 1–2). Electron microscopy revealed diffuse podocyte

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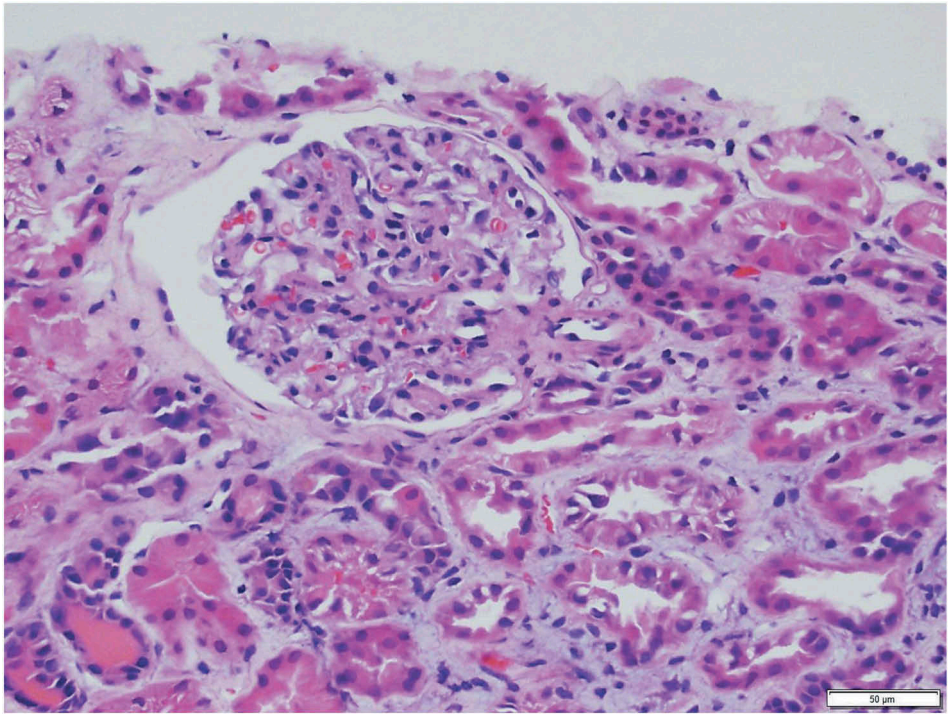

Figure 1. Glomerulus without mesangial expansion or increased cellularity H&E 20x.

effacement consistent with minimal change disease (Figure 3).

The patient's fluid overload was initially treated with furosemide administered with albumin to augment diuresis, but his kidney function continued to worsen. Following biopsy results, the patient was given 3 days of pulse steroids (Methylprednisolone 1000 mg IV daily) followed by oral prednisone 60 mg daily. However, his creatinine continued to climb during the pulse period and the following day was 7.66 mg/dL. The patient was then placed on ultrafiltration for 2 days and his kidney function began to improve. He was subsequently diuresed with Furosemide 200 mg IV BID augmented with metolazone. His creatinine eventually trended down to 3.16 mg/dL, and he was discharged in improved condition on oral prednisone 40 mg daily and no diuretics.

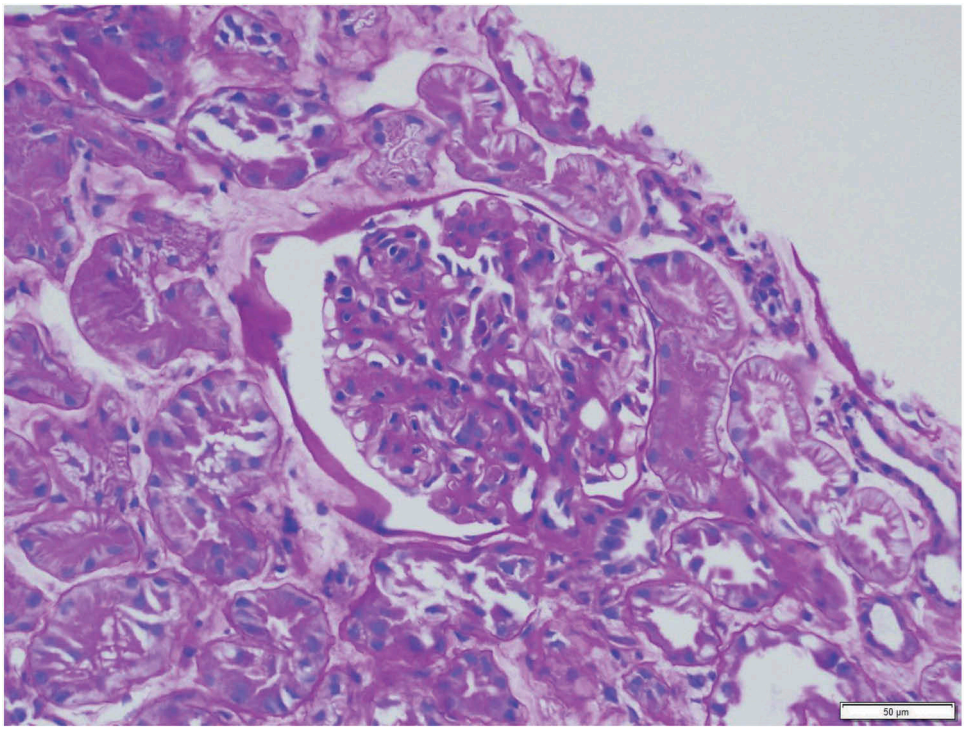

Figure 2. Glomerulus without mesangial expansion or increased cellularity PAS 20x.

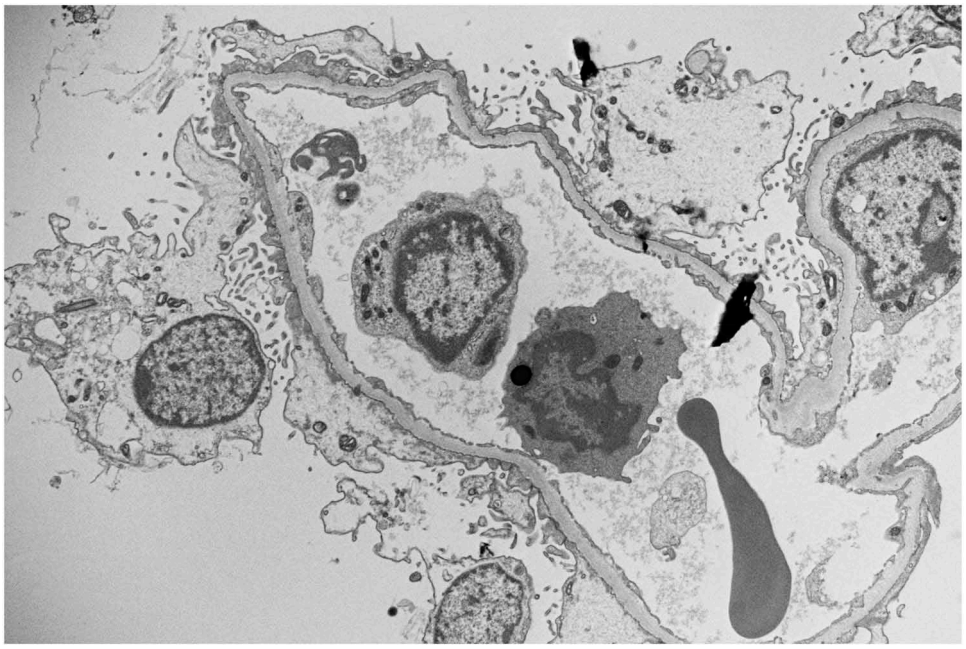

Figure 3. Glomerular capillary loop with diffuse foot process effacement and microvillous transformation. No electron-dense deposits. Transmission electron microscopy 1500x.

Six months later, the patient returned to the hospital with lower extremity edema and weight gain. He was again found to have nephrotic range proteinuria, with a urine protein/creatinine ratio 10.45, creatinine 2.15 mg/dL, and albumin 2.0 g/dL. He was seen in the nephrology office 1 month prior to this readmission, at which time his creatinine was 1.80 and urine protein/creatinine ratio was 1.84. He was diagnosed with acute kidney injury related to relapse of his MCD. His dose of prednisone was increased to 80 mg daily and he was started on tacrolimus 2 mg twice daily.

3. Discussion

There is significant morbidity observed in MCD patients due to AKI and other complications. Our patient is unique in that he presented with AKI during his initial presentation of MCD and during his relapse. Patients with AKI are more likely to be male, older, and hypertensive with lower serum albumin and greater proteinuria than those without AKI [3]. These high-risk features for AKI were all observed with our patient.

AKI is an established complication of MCD that manifests in 20%-25% of adult cases and is usually displays reversibility with steroid therapy [6]. The pathogenesis of the AKI is theorized to involve a combination of ischemic injury, tubular obstruction via interstitial edema, perfusion shifts from cortical to juxtaglomerular nephrons, and diminished capillary filtration [7,8]. Fujigaki et al. investigated the pathophysiology of AKI in adult-onset MCD through examination of biomarkers of tubular injury such as the intermediate filament vimentin and the lysosomal enzyme urinary N-acetyl-β-D-glucosaminidase (uNAG) [9]. Both Vimentin expression and increased levels of uNAG demonstrated that tubular injuries were present in both AKI and non-AKI patients with MCD, but their extent was markedly greater in the AKI group. It is additionally speculated that severe proteinuria induces particular tubular insults that predispose adult MCD patients to marked AKI [10].

A diagnosis of MCD is confirmed in patients with biopsy-proven disease that respond to corticosteroid treatment. An alternative diagnosis, FSGS, should be considered in cases of steroid resistance regardless of the number of glomeruli captured in the initial biopsy [11]. Our patient suffered disease relapse after 6 months of corticosteroid therapy; thus, FSGS could be considered as a differential diagnosis on repeat biopsy or review of the initial biopsy. Most relapses occur within 2 years with currently no reliable predictors, although younger age at onset and shorter duration of corticosteroid therapy have been proposed as risk factors [12].

In a large retrospective review of 95 adults with MCD, second-line agents including cyclosporine, cyclophosphamide, mycophenolate mofetil, and tacrolimus were utilized for cases of steroid resistance, dependence, partial response, toxicity, or contraindications as well as for frequent relapses [4]. The study classified steroid resistance as the lack of disease remission with 16 weeks of prednisone. Steroid dependence was characterized as disease relapse with either tapering or discontinuing steroids within 1 month as well as requiring chronic maintenance steroids. Waldman et al. found that no particular second-line immunosuppressant

demonstrated superiority in attaining remission. Interestingly, a statistical amalgamation of all agents' response rates revealed significantly greater remissions in steroid-dependent patients versus steroid-resistant patients [13]. Future studies should focus on delineating the corticosteroid regimens most efficient at achieving remission and further comparing second-line agents for relapsing MCD.

Acknowledgments

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Disclosure statement

No potential conflict of interest was reported by the authors.

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