Minimal Change Disease and Metabolic Syndrome: A Therapeutic Challenge in a Young Adult Male

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Abstract

Minimal Change Disease (MCD) is a podocytopathy most commonly diagnosed in children and less frequently in adults, where the clinical course tends to be more complicated and variable. In adults, the disease often demonstrates delayed responsiveness to corticosteroids, higher relapse rates, and an increased likelihood of requiring alternative forms of immunosuppression to achieve remission. When MCD occurs together with metabolic syndrome—a cluster of metabolic abnormalities including central obesity, dyslipidemia, hypertension, and hepatic steatosis—the condition becomes even more challenging to manage. The combination creates a vicious cycle in which metabolic dysfunction aggravates glomerular injury while renal impairment worsens cardiometabolic status. In this case, we describe a 21-year-old male who presented with nephrotic-range proteinuria and severe metabolic derangements. Renal biopsy revealed MCD, and treatment required a highly individualized approach in

order to preserve renal function while avoiding the detrimental metabolic consequences associated with high-dose steroid therapy. Rituximab was introduced early as part of a steroid-sparing strategy, resulting in a favorable clinical response. This case highlights the significance of personalized immunosuppressive therapy, long-term metabolic control, and multidisciplinary care in preventing irreversible renal and cardiovascular outcomes in young adults living with both MCD and metabolic syndrome.

Introduction

Minimal Change Disease is characterized by the loss of podocyte foot processes, resulting in marked proteinuria and nephrotic syndrome. [1,2] However, because glomerular structure appears preserved on routine light microscopy, diagnosis often requires electron microscopy. [2] Although its precise pathogenesis remains incompletely understood, immune dysregulation affecting podocytes is strongly implicated. [3] Adults diagnosed with MCD frequently experience a clinical course that differs substantially from children, including delayed response to steroid therapy, higher likelihood of sustained proteinuria, and an increased overall burden of disease-related complications. [3,4] Metabolic syndrome, which includes obesity, elevated blood pressure, altered lipid metabolism, insulin resistance, and in many cases, non-alcoholic fatty liver disease—has become increasingly common among young adults as a result of changing dietary patterns and reduced physical activity. [5] When metabolic syndrome exists alongside kidney disease, each condition accelerates the progression of the other. [5-7] Glomerular hyperfiltration, lipid-mediated inflammatory damage, and increased oxidative stress contribute to podocyte dysfunction, raising concern that cases initially diagnosed as MCD may evolve into more severe forms of glomerulosclerosis if metabolic drivers remain uncontrolled. [5-7] The therapeutic challenge in this case lies not only in ensuring remission of proteinuria, but also in protecting metabolic health, preventing steroid-associated toxicity, and enabling long-term kidney preservation.

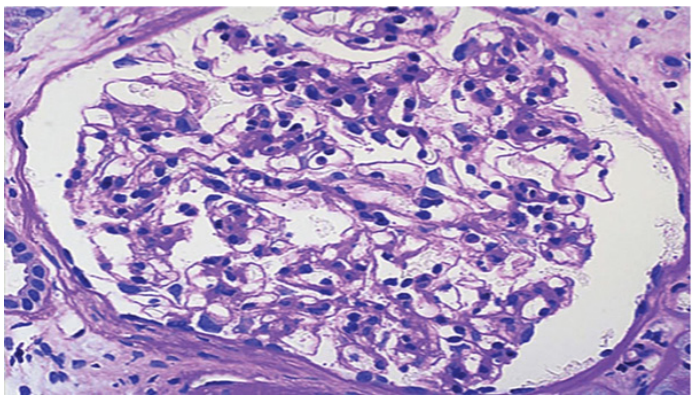
Case Presentation

A 21-year-old male presented with a gradual 5-year history of episodic occipital headaches, persistent hypertension, polyuria accompanied by excessive thirst, and chronic joint discomfort. Over this period, he gained significant body weight, particularly around the abdomen. He reported a lifestyle characterized by frequent intake of highly processed meals and the consumption of approximately two liters of sugar-sweetened beverages each day, contributing to the development of metabolic complications. He had no known family history of autoimmune disease, hereditary kidney disorders, or premature cardiovascular disease.

Initial medical evaluation in April 2024 revealed important abnormalities. Laboratory assessment showed persistent nephrotic-range proteinuria, reaching over 5 grams in 24 hours, in addition to a mildly elevated serum creatinine level that indicated an early decline in kidney function. His lipid profile demonstrated markedly elevated cholesterol and triglyceride levels, confirming severe dyslipidemia. His uric acid level was also significantly high, suggestive of metabolic overproduction or impaired renal excretion. Liver function testing detected elevations consistent with hepatocellular stress. A computed tomography scan of the abdomen confirmed Grade III hepatic steatosis, demonstrating significant fat infiltration within the liver parenchyma. At that time, however, the patient was unfortunately lost to follow-up and no specific treatment was started.

Parameter	Result	Interpretation
Urea	56 mg/dL	Mild azotemia
Creatinine	1.30–1.47 mg/dL	Early renal dysfunction
Proteinuria	4.3–5.5 g/24h	Nephrotic range
Cholesterol	264 mg/dL	Severe dyslipidemia
LDL	167 mg/dL	High cardiovascular risk
Triglycerides	360 mg/dL	Metabolic syndrome
Uric acid	12 mg/dL	Hyperuricemia
Liver enzymes	Elevated	Suggest NAFLD
Urinalysis	No hematuria	Non-inflammatory pathology

Nearly one year later, in March 2025, he returned to medical attention with visible peripheral edema, persistent hypertension, and worsening proteinuria. A renal biopsy was performed to determine the underlying cause of his nephrotic syndrome. Initially, the biopsy was mistakenly interpreted as suggesting mesangiocapillary glomerulonephritis, a condition associated with immune complex involvement. A more detailed re-evaluation, confirming Minimal Change Disease, without immune complex deposition.



Further Hospital Evaluation

He was admitted to the hospital in April 2025 due to the progression of renal dysfunction and worsening nephrotic syndrome. At that time, laboratory findings indicated proteinuria exceeding eight grams per day, accompanied by elevated urinary microalbumin levels. Kidney function remained impaired, though stable, while liver enzymes were significantly higher than before, indicating progression of hepatic steatosis. Extensive immunological testing—including markers for autoimmune, viral, and neoplastic diseases—returned negative results. Cardiac function and renal Doppler ultrasonography were normal, ruling out secondary hemodynamic causes of kidney injury.

Test	Result
Proteinuria	8.4 g/24 h
Microalbuminuria	6.6 g/24 h
Creatinine	1.27 mg/dL
Urea	49 mg/dL
Triglycerides/LDL	351/156 mg/dL
ALT/AST/GGT	141/47/209 U/L

The confirmed final diagnosis included:

- Minimal Change Disease causing severe proteinuric nephropathy
- Chronic kidney disease, stage G2/A3
- Metabolic syndrome with hypertension, dyslipidemia, hyperuricemia, and obesity
- Grade III non-alcoholic fatty liver disease

Therapeutic Intervention

Management required addressing both nephrotic syndrome and the systemic metabolic burden. To reduce glomerular pressure and protein loss, an angiotensin-converting enzyme inhibitor was initiated. In addition, an SGLT2 inhibitor was introduced to improve metabolic control by reducing glucose reabsorption and to provide additional kidney-protective benefits such as lowering intraglomerular hyperfiltration. A statin was added to attenuate lipid toxicity and reduce long-term cardiovascular risk.

For immunosuppression, a low-dose steroid regimen was started. Unlike standard recommendations, high-dose corticosteroids were intentionally avoided to prevent further deterioration of hepatic steatosis, minimize body fat accumulation, and reduce the risk of steroid-induced diabetes. Rituximab was selected as a steroid-sparing agent due to its demonstrated efficacy in achieving remission in adults with MCD. The patient received two 1-gram infusions of rituximab spaced 14 days apart. This allowed suppression of B-cell-mediated immune activity while minimizing systemic metabolic consequences.

Supportive therapy included:

- ACE inhibitor - reduction of intraglomerular hyperfiltration and proteinuria
- SGLT2 inhibitor - dual benefit in renal protection and weight/metabolic control
- Statin therapy - management of persistent dyslipidemia to reduce renal lipotoxicity
- Sodium restriction and structured weight-loss program

Immunosuppressive strategy:

- Methylprednisolone 0.5 mg/kg/day (32 mg) - lower dose to reduce metabolic toxicity
- Rituximab 1 g IV on days 1 and 14 - selected for steroid-sparing effect and durable remission potential

Clinical Progress and Follow-Up

Over the following months, the patient demonstrated noticeable improvement. His proteinuria decreased substantially, though it had not yet reached complete remission. Kidney function also stabilized, indicating a halt in the progression of chronic kidney disease. Importantly, he achieved meaningful weight loss (-10kg) through lifestyle changes and dietary counseling, which contributed to improvements in blood pressure control and liver enzyme normalization. Edema resolved completely, and his physical functioning improved.

Date	Creatinine (mg/dL)	Urea (mg/dL)	Proteinuria (g/24h)	Microalbuminuria (g/24h)
30/07/2025	1.54	86.9	2.7	2.7
21/08/2025	1.48	73.9	3.7	-
08/10/2025	1.20	78	3.1	2.7

While he did not yet reach full remission of nephrotic syndrome, his gradual progress reflected a positive response to rituximab therapy. The stabilization of renal function and slowing of proteinuria progression suggest the potential to avoid progression to more permanent glomerular scarring.

Discussion

This case illustrates several important lessons in the management of Minimal Change Disease in an adult with metabolic syndrome. First, diagnosis required careful histological review, emphasizing that MCD cannot be reliably confirmed without electron microscopy. [4,5] Second, the metabolic abnormalities present in this patient likely contributed both to the severity of his disease and to reduced responsiveness to standard steroid therapy. [3-5] Obesity and dyslipidemia are known to cause harmful mechanical and inflammatory stress on podocytes, potentially leading to more complex glomerular pathology resembling early focal segmental glomerulosclerosis — a condition that may develop if MCD is not adequately controlled. [3-5]

The avoidance of high-dose steroids in this case was crucial. [4,5] Corticosteroids, while highly effective in many patients, can worsen insulin resistance, promote visceral fat accumulation, and accelerate liver steatosis. [4,5,8] These metabolic side effects would only further impair kidney recovery. [8] Rituximab therefore represented a more appropriate immunosuppressive choice, with evidence supporting its ability to induce remission and prevent relapses while maintaining a favorable metabolic safety profile. [9-14]

Long-term monitoring remains essential. Although the patient's progress is promising, persistent proteinuria indicates ongoing podocyte vulnerability. [9,10] If remission is not achieved or if proteinuria worsens, a repeat kidney biopsy may be necessary to evaluate whether irreversible glomerulosclerosis has begun to develop. [9-14]

Conclusion

This case highlights the complex interaction between podocyte-driven renal disease and systemic metabolic dysfunction in a young adult. Early investigation, accurate renal biopsy interpretation, and rapid initiation of appropriate immunotherapy were vital to improving this patient's prognosis and preventing further kidney damage. Rituximab allowed for effective immunosuppression while reducing steroid exposure, ultimately improving both renal and metabolic outcomes.

Equally important, lifestyle modification and weight reduction provided essential support in halting disease progression. Continued follow-up is required to ensure sustained remission, prevent renal decline, and avoid severe cardiovascular and hepatic complications that often accompany metabolic syndrome.

This case demonstrates that kidney disease cannot be treated in isolation. Successful care requires a multidisciplinary approach that addresses the full spectrum of metabolic risk factors, especially in young adults whose long-term health and organ function can still be preserved through timely, coordinated intervention.

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