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Samuel B. Reynolds BS USF MCOM- LVHN Campus, samuel.reynolds@lvhn.org

Ryan Lutz USF MCOM-LVHN Campus, ryan.lutz@lvhn.org

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# Diagnosis and management of nephrotic syndrome in an adult patient: A case report

#### Samuel B. Reynolds, Ryan W. Lutz

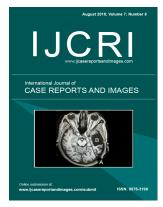
#### **ABSTRACT**

**Introduction:** Nephrotic syndrome is a disorder characterized by proteinuria >3.5 g/24 hr, hypoalbuminemia <3 g/dL, and peripheral edema. The underlying etiology of the condition is influenced in large part by the age of the patient. In children under the age of 16, a large majority of cases are secondary to minimal change disease, whereas in adults the causes are more varied to include focal segmental glomerulosclerosis and membranous nephropathy. **Case Report:** A 68-year-old male with nephrotic range proteinuria who required workup with laboratory studies, immunological screening, and both light microscopy as well as electron microscopy to arrive at a diagnosis of minimal change disease.

**Conclusion:** Also included is a review of previously published studies regarding minimal change disease and its association with non-Hodgkin lymphoma in the adult population, along with a discussion of current treatment approaches and a comparison of their efficacies.



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#### ABSTRACT

Introduction: Nephrotic syndrome is a disorder characterized by proteinuria >3.5 g/24 hr, hypoalbuminemia <3 g/dL, and peripheral The underlying etiology of the condition is influenced in large part by the age of the patient. In children under the age of 16, a large majority of cases are secondary to minimal change disease, whereas in adults the causes are more varied to include focal segmental glomerulosclerosis and membranous nephropathy. Case Report: A 68-year-old male with nephrotic range proteinuria who required workup with laboratory studies, immunological screening, and both light microscopy as well as electron microscopy to arrive at a diagnosis of minimal change disease. Conclusion: Also included is a review of previously published studies regarding minimal change disease and its association with non-Hodgkin lymphoma in the adult population, along with a discussion of current treatment approaches and a comparison of their efficacies.

Keywords: Adult, Change, Minimal, Nephrotic, **Proteinuria** 

Samuel B. Reynolds<sup>1</sup>, Ryan W. Lutz<sup>1</sup>

Affiliations: 1Medical Student, Department of Education. Lehigh Valley Health Network, Allentown, PA, USA.

Corresponding Author: Samuel Benjamin Reynolds 3711 Allen Street, Apt 4, Allentown, PA, USA, 18104; Email: Samuel.Reynolds@lvhn.org

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#### INTRODUCTION

Nephrotic syndrome is a disorder characterized by proteinuria >3.5 g/24 hr, hypoalbuminemia <3 g/dL, and peripheral edema [1]. The underlying etiology of the condition is influenced in large part by the age of the patient. In children under the age of 16, a large majority of cases (76.6%) are due to minimal change disease (MCD) [2]. However, in adults aged 15-65 the cause of nephrotic syndrome becomes more varied to include primary kidney pathologies such as focal segmental glomerulosclerosis, membranous nephropathy, or less commonly minimal change disease. In addition, nephrotic syndrome can manifest itself secondary to a host of underlying conditions such as diabetes, amyloidosis, or systemic lupus erythematosus. This case in particular highlights the importance of determining the underlying etiology in patients with nephrotic-range proteinuria, which will guide future management and prognosis.

#### CASE REPORT

A 68-year-old male with a past medical history of hypothyroidism and urinary tract obstruction presented



to the Emergency Department with chief complaints of mild dyspnea on exertion, increasing abdominal girth, and weight gain over a period of 2-3 weeks. On arrival to the emergency room, the patient was found to have bilateral edema involving both the upper and lower extremities. He recalled a prior episode four months earlier, which prompted his primary care physician (PCP) to begin furosemide at 80 mg daily. He initially responded well to this treatment which was discontinued when his symptoms resolved. At the onset of this episode, his PCP re-started 80 mg furosemide, but this time with no therapeutic benefit. Given his worsening fluid retention and past history of urinary tract obstruction, the patient was admitted for further evaluation.

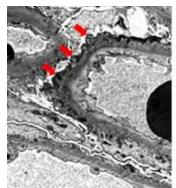
laboratory studies revealed glucosuria, microscopic hematuria, proteinuria and an elevated urine protein to creatinine ratio of 12.16 mg/mmol. Patient was also found to have hyperlipidemia, with LDL and triglyceride levels of 355 and 238 mg/dL, respectively. An initial workup for adult onset nephrotic syndrome included measurements of ANA, ANCA, anti-DNA, C3 and C4 complement levels, free light chains, and anti-GBM as well as anti-streptolysin antibodies, which all came back negative. He was refractory to IV furosemide and had an improved diuretic response to intravenous torsemide. Blood pressure throughout admission ranged from 132-152 mmHg systolic and 75-90 mmHg diastolic.

Since his initial laboratory studies did not elucidate an etiology, the patient underwent an ultrasoundguided percutaneous needle biopsy of the patient's left native kidney. Pathological examination of this sample by light microscopy revealed normal-appearing glomeruli without any evidence of segmental sclerosis, endocapillary proliferation, crescents, or necrotizing lesions. More specialized testing also showed an absence of tram-tracking or spikes on silver stain and negative immunofluorescent studies. Renal vasculature was unremarkable for signs of thrombotic microangiopathy, micro-emboli, or vasculitis. Despite these negative findings, ultrastructural examination of several glomeruli revealed severe, widespread effacement of foot processes, a finding consistent with minimal change disease (MCD) (Figure 1).

For treatment of his MCD, he was started on prednisone 20 mg PO t.i.d. and his intravenous torsemide was continued. The patient responded to this regimen with a decrease in lower extremity edema as well as a drop in weight from 115.8 kg to 107.8 kg, during his hospital stay. The patient was discharged on hospital day eight on prednisone (60 mg total per day) and torsemide 40 mg PO b.i.d.

#### **DISCUSSION**

Minimal change disease occurs most often in children, and nephrotic syndrome in adults is more commonly attributed to focal segmental glomerulosclerosis or



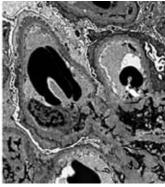


Figure 1: Two separate EM images of sample from patient's left kidney obtained via ultrasound-guided percutaneous needle biopsy, each showing notable podocyte effacement (demonstrated by red arrows) consistent with minimal change disease (Source: Health Network Laboratories).

membranous nephropathy and not often included in the differential diagnosis of adult onset nephrotic syndrome. A Brazilian study explored this topic by looking at the changing incidence of glomerular disease among 2068 adults from 1999-2005. The data obtained found the most common cause of primary glomerular disease to be focal-segmental glomerulosclerosis (29.7%), followed by membranous nephropathy (20.7%), IgA nephropathy (17.8%), and minimal change disease (9.1%) [3]. Similar results were found in a 2006 study out of Minnesota examining the incidence of glomerular disease among 208 patients [4]. It is important for clinicians to include variant presentations of nephrotic syndrome, particularly minimal change disease when evaluating a patient. As the treatment of nephrotic syndrome varies based on the specific etiology, the recognition and diagnosis of MCD is particularly important in the adult population.

Adult cases of minimal change disease, though less common than cases in children, are documented, specifically in patients actively diagnosed with or suspected of having non-Hodgkin lymphoma (NHL). A 2014 retrospective study examined this association in a series of 18 patients with established diagnoses of concurrent MCD and NHL. Researchers reported that, of these patients, 33.3% had Waldenström macroglobulinemia, 27.7% marginal zone B cell lymphoma and 22.2% chronic lymphocytic leukemia. Further investigation into the timing of disease presentation in this population, revealed four patients in whom MCD presented prior to NHL (with an average delay of 15 months), ten patients who were diagnosed simultaneously, and four who were found to have MCD after their NHL presented (average delay 25 months). Regarding management of the two conditions, reappearance of MCD was more likely in patients who had received only steroid therapy versus those who had been given steroids along with chemotherapy (77.8% and 25%, respectively). The authors concluded that MCD is most likely to appear in patients with NHL's of B cell origin,

and that the nephrotic syndrome is best managed with a combination of steroids and chemotherapy [5]. These conclusions are relevant to the patient described earlier, as he had been worked up for MCD but demonstrated no signs or symptoms consistent with NHL at the time. Since the latter condition confers a graver prognosis, the patient should have close monitoring for NHL going forward. However, if he were to be diagnosed with cancer and subsequently receive chemotherapy, he could be at increased risk for nephrotic syndrome depending on which medication he receives. A recently-published case described this risk, citing a 57-year-old female being treated with gefitinib for lung adenocarcinoma who was diagnosed with minimal change nephrotic syndrome, prompting her care providers to switch to erlotinib [6]. Awareness of this potential complication and consideration of minimal change nephrotic syndrome as a disease continuum will be also be important components of outpatient care.

Treatment for minimal change disease in adults has largely been accomplished by an approach with nonimmunosuppressive in addition to immunosuppressive therapies. Non-immunosuppressive therapy is commonly instituted regardless of the etiology of nephrotic syndrome and typically consists of an angiotensinconverting enzyme inhibitor in order to preserve renal function. Immunosuppressive therapy is much more individualized to the underlying etiology of the nephrotic syndrome. Treatment of minimal change disease primarily employs glucocorticoids. In a study, Nolasco, et al. examined the efficacy of corticosteroid treatment in adult-onset minimal change disease. Researchers analyzed 75 patients who were treated with an initial dose of prednisone of 60 mg/day. 58 patients (81%) achieved complete remission [7]. A similar study out of Japan by Nakayama et al., found 38 out of 62 patients achieved remission within eight weeks of starting glucocorticoid therapy, and another 15 patients after eight weeks [8]. Although glucocorticoid therapy leads to a transient remission in 80-95% of adults with minimal change disease, approximately 50-75% of glucocorticoidresponsive patients will have a relapse at some point [9]. In patients with recurrent relapses, it is recommended to look at additional therapies, including cyclophosphamide, cyclosporine, tacrolimus, or rituximab.

#### **CONCLUSION**

Although uncommon in the adult population, minimal change disease carries a favorable response to glucocorticoid treatment, with 80-90% of patients achieving complete remission. It is important, therefore, for providers to maintain a broad differential when considering the underlying etiology of nephrotic syndrome in adults, as minimal change disease is treatable with a timely diagnosis and early intervention. In addition, it is prudent to look for secondary diagnoses in an adult

patient with MCD for hematologic malignancies as they can be present upon initial diagnosis or appear at a later

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#### **Author Contributions**

Samuel B. Reynolds – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Ryan W. Lutz – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

#### Guarantor

The corresponding author is the guarantor of submission.

#### **Conflict of Interest**

Authors declare no conflict of interest.

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