Inadequate treatment in a patient with minimal change disease (MCD) nephrotic syndrome: a case report

Alifatul Maslachah1, Dana Pramudya2*, Pranawa2, Widodo2, Nunuk Mardiana2, Artaria Tjempakasari2

ABSTRACT

Introduction: Minimal change disease (MCD) is the cause of primary nephrotic syndrome in about 90% of children but is rare in adults and only found in about 10% to 15% of adults. Adequate steroid therapy can lead to complete remission in more than 80% of adults with MCD nephrotic syndrome. This study aimed to report a case of an adult patient with nephrotic syndrome with renal biopsy results of MCD and her clinical improvement after adequate therapy with glucocorticoids.

Case Presentation: We report a case of a female patient, 35 years old, who complained of swelling all over the body 3 months before admission. Previously, the patient was diagnosed with nephrotic syndrome on December 2020 and received oral steroid therapy that had been tapered down early, which caused the clinical symptoms to recur. The patient underwent a kidney biopsy, and MCD was found on histopathological examination. The patient received supportive therapy and resumed steroid therapy with adequate dosage. On the six-month follow-up, the patient was in complete remission.

Conclusion: MCD is a nephrotic syndrome with a good prognosis, and 80% of patients will respond to adequate therapy. Our patient's previous medical history was re-evaluated, and concluded that the previous patient had received inadequate therapy. The patient has now reached a state of complete remission. This case highlighted the importance of adequate therapy in managing nephrotic syndrome.

Keywords: nephrotic syndrome, minimal change disease, adequate steroid therapy.

CASE PRESENTATION

Mrs. E., aged 35, Javanese, married, a housewife who lives in Sidoarjo, East Java, presented to the nephrology clinic at Dr. Soetomo General Hospital on March 9th, 2021, with a complaint of swelling in both legs since the last 3 months, the swelling worsened and extended to the calves, thighs and abdomen and eyelid in the last 2 weeks. The patient had gained weight up to 8 kilograms in the last 3 months. Other symptoms included foamy urine. The patient has no family history or social history related to complaints that arise in her.

The patient had previously been diagnosed with NS on December 2020. At that time, the patient had received oral methylprednisolone 3x16 mg for one month, improving the symptoms. However, swelling reappeared when the dose was tapered down to methylprednisolone 3x8 mg in a week. The patient was later referred to undergo a kidney biopsy to establish the etiology of NS.

Physical examination revealed swelling on both eyelids. Abdominal examination revealed a slightly distended abdomen and shifting dullness. On examination of the extremities, pitting edema of both legs was found.

The laboratory examination on the first day of admission (Table 1 and Table 2) shows that the blood urea nitrogen (BUN) level was 44 mg/dl, serum creatinine was 0.49 mg/dL, and albumin level was 1.9 g/dl. Total cholesterol observed was 280 mg/dl, HDL 101 mg/dl, LDL 237 mg/dl, and triglycerides was 153 mg/dl. Urinalysis revealed protein 3+, erythrocytes 2+, and Esbach protein of 3.5 g/L.

The patient underwent a kidney biopsy. The histopathologic examination revealed: a glomerulus with a minimal proliferation of cells and mesangial matrix, perihilar adhesions in 3 glomeruli (<50%), The

INTRODUCTION

Nephrotic syndrome (NS) is the clinical features of a glomerular disease characterized by edema, proteinuria of >3.5 g/day, and hypoalbuminemia, and may be accompanied by hyperlipidemia.1-4 The incidence of NS in adults is about 3 cases out of 100,000 individuals.5,6 In Indonesia, the prevalence of NS was 6 instances per 100,000 children annually in children under 14, with a male preponderance.7 Primary nephrotic syndrome is caused by minimal change disease (MCD) in roughly 90% of children, whereas only 10% to 15% of adults have this condition.8 More than 80% of adults with MCD can achieve full remission with adequate glucocorticoid therapy.9

This case report aimed to discuss an adult patient with nephrotic syndrome with renal biopsy results of minimal change disease and clinical improvement after adequate glucocorticoid therapy.

Keywords: nephrotic syndrome, minimal change disease, adequate steroid therapy.


Received: 2023-05-04
Accepted: 2023-06-02
Published: 2023-06-24

Published: 2023-06-24

CASE PRESENTATION

Mrs. E., aged 35, Javanese, married, a housewife who lives in Sidoarjo, East Java, presented to the nephrology clinic at Dr. Soetomo General Hospital on March 9th, 2021, with a complaint of swelling in both legs since the last 3 months, the swelling worsened and extended to the calves, thighs and abdomen and eyelid in the last 2 weeks. The patient had gained weight up to 8 kilograms in the last 3 months. Other symptoms included foamy urine. The patient has no family history or social history related to complaints that arise in her.

The patient had previously been diagnosed with NS on December 2020. At that time, the patient had received oral methylprednisolone 3x16 mg for one month, improving the symptoms. However, swelling reappeared when the dose was tapered down to methylprednisolone 3x8 mg in a week. The patient was later referred to undergo a kidney biopsy to establish the etiology of NS.

Physical examination revealed swelling on both eyelids. Abdominal examination revealed a slightly distended abdomen and shifting dullness. On examination of the extremities, pitting edema of both legs was found.

The laboratory examination on the first day of admission (Table 1 and Table 2) shows that the blood urea nitrogen (BUN) level was 44 mg/dl, serum creatinine was 0.49 mg/dL, and albumin level was 1.9 g/dl. Total cholesterol observed was 280 mg/dl, HDL 101 mg/dl, LDL 237 mg/dl, and triglycerides was 153 mg/dl. Urinalysis revealed protein 3+, erythrocytes 2+, and Esbach protein of 3.5 g/L.

The patient underwent a kidney biopsy. The histopathologic examination revealed: a glomerulus with a minimal proliferation of cells and mesangial matrix, perihilar adhesions in 3 glomeruli (<50%), The
tubules were partially atrophic, erythrocyte cells were seen in the tubular lumen, and PMN and mononuclear inflammatory cell infiltration was seen in the tubular interstitial. On immunofluorescence examination: C1q negative, C3 negative, IgA negative, IgG negative, and IgM negative. The results match with MCD (Figure 1).

The patient had MCD. This patient was given supportive therapy by dietary management, i.v. 20% albumin 100 ml every 24 hours, i.v. furosemide 3x20mg, p.o. candesartan 1x8 mg, and p.o. Simvastatin 1x20 mg. The patient received oral methylprednisolone therapy 3x16 mg for 8 weeks and then gradually tapered within 6 months. The patient also received oral candesartan 1x8 mg. Follow-up after six months showed improved the patient improved clinical condition. Urinalysis in the 28th week showed protein-negative and negative erythrocytes. The patient was finally in complete remission without any adverse events.

**DISCUSSION**

NS is one of the clinical features of a glomerular disease characterized by edema, proteinuria of > 3.5 g/day, hypoalbumin and hyperlipidemia.\(^9,11-13\) Our patient complained of swelling all over the body 3 months before admission. On physical examination, there was edema of the eyelids, shifting dullness of the abdomen and pitting edema on the lower extremities. Edema in nephrotic syndrome is due to massive proteinuria, further decreasing oncotic plasma pressure.\(^14,15\)

![Figure 1. Histopathology result of patient’s kidney biopsy (a-c) with the conclusion of minimal change.](image)

On the laboratory investigation, there was an increased level of lipid profile. Dyslipidemia, characterized by increased cholesterol and triglycerides, can also develop in people with nephrotic syndrome. Increased lipoprotein production in the liver is assumed to be the cause, albeit the exact mechanism is still unknown.\(^16\)

NS can occur due to idiopathic (primary) glomerular disease or as a systemic consequence of disease involving the kidneys (secondary). Primary glomerular diseases include focal segmental glomerulosclerosis (FSGS), membranous nephropathy (MN), MCD, membranoproliferative glomerular disease, and other glomerular diseases.\(^17\)

Secondary diseases resulted from diabetes mellitus, systemic lupus erythematosus, amyloidosis, cancer, drugs and infections.\(^6\)

Three cases of NS occur annually for every 100,000 people. About 80% to 90% of adult instances of NS are idiopathic. MN is the most frequent cause in white people (about 30%), while FSGS is more prevalent in black people (around 35%). About 15% of those with MCD have immunoglobulin 15% of cases have nephropathy as the underlying cause. The remaining 10% were brought on by an underlying medical issue besides NS.\(^11\) In

<table>
<thead>
<tr>
<th>Blood analysis</th>
<th>Day 1</th>
<th>Day 4</th>
<th>Day 9</th>
<th>Week 6</th>
<th>Week 28</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>11.9</td>
<td>12.1</td>
<td>12.9</td>
<td>12.3</td>
<td></td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>79.1</td>
<td>79.1</td>
<td>80.1</td>
<td>87.1</td>
<td></td>
</tr>
<tr>
<td>MCH (pg)</td>
<td>24.5</td>
<td>24.5</td>
<td>25.5</td>
<td>30.5</td>
<td></td>
</tr>
<tr>
<td>MCHC (g/dL)</td>
<td>31.1</td>
<td>31.1</td>
<td>32.1</td>
<td>33.1</td>
<td></td>
</tr>
<tr>
<td>WBC (10^3/uL)</td>
<td>9,500</td>
<td>10,500</td>
<td>8,600</td>
<td>6,600</td>
<td></td>
</tr>
<tr>
<td>Neutrophil (%)</td>
<td>86</td>
<td>87</td>
<td>87</td>
<td>69.1</td>
<td></td>
</tr>
<tr>
<td>Lymphocyte (%)</td>
<td>11.2</td>
<td>10.2</td>
<td>10.2</td>
<td>23.2</td>
<td></td>
</tr>
<tr>
<td>Platelets (10^3/uL)</td>
<td>364,000</td>
<td>392,000</td>
<td>361,000</td>
<td>232,000</td>
<td></td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td>44</td>
<td>18</td>
<td>18</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Serum Creatinine (mg/dL)</td>
<td>0.49</td>
<td>0.5</td>
<td>0.6</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>1.9</td>
<td>2.3</td>
<td>2.55</td>
<td>3.9</td>
<td>3.8</td>
</tr>
<tr>
<td>PPT (second)</td>
<td>12.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>APPT (second)</td>
<td>29</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood Sugar (mg/dL)</td>
<td>112</td>
<td></td>
<td>104</td>
<td>115</td>
<td></td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>280</td>
<td></td>
<td>182</td>
<td>172</td>
<td></td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td>101</td>
<td></td>
<td>44</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td>237</td>
<td></td>
<td>114</td>
<td>110</td>
<td></td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>153</td>
<td></td>
<td>122</td>
<td>108</td>
<td></td>
</tr>
</tbody>
</table>

Note: *abnormal level
our patient, secondary causes of nephrotic syndrome were excluded.

In some cases, a kidney biopsy should be considered to determine the underlying histologic abnormality of the nephrotic syndrome.11-13 If the procedure results will influence therapy or reveal further information about the patient’s prognosis, a kidney biopsy should be considered. According to Kidney Disease Improving Global Outcomes (KDIGO), a kidney biopsy is a gold standard for diagnosing glomerular disease.14-15

From the histopathological examination, MCD is characterized by global thinning of the podocyte leg on electron microscopy and appears to be near normal (or only minimal mesangial prominence) on light microscopy and no staining on immunofluorescence microscopic (or low-intensity staining for C3 and IgM). Renal function in MCD patients is usually normal.13 As in our patient, mesangial cells and matrix had minimal proliferation and perihilar adhesions <50%. Partially atrophic tubules and erythrocyte cells were seen in the tubular lumen, and PMN and mononuclear inflammatory cell infiltration in the tubular interstitial. C1q, C3, IgA, IgG, and IgM were negative on immunofluorescence examination.

Therapy for NS consists of supportive therapy and immunosuppressants. General management includes dietary sodium restriction, diuretics and renin-angiotensin-system (RAS) inhibitor therapy. Angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, with a target systolic blood pressure of less than 120 mmHg, are the first-line treatments for proteinuria. Non-pharmacological therapy includes limiting sodium intake (<2 grams/day), normalizing body weight, regular exercise, and smoking cessation. A diet high in calories and adequate in protein (0.8 mg/kgBW/day) has been shown to reduce protein excretion in the urine without causing malnutrition in patients.9 Loop diuretics can be used as first-line therapy for treating edema. If furosemide is clinically inadequate, thiazide diuretic or 20% intravenous albumin can be added.15 Treatment of NS’s underlying disease and reducing proteinuria will eventually improve hypercholesterolemia.22 Our patient was given supportive therapy of dietary management, 20% albumin infusion, furosemide, candesartan and simvastatin.

For individuals with MCD, the KDIGO recommendations suggest using glucocorticoids to achieve remission. Prednisone or prednisolone is prescribed at a dose of 1 mg/kg per day (maximum 80 mg) or 2 mg/kg alternate days (maximum 120 mg) for 4 to 16 weeks, with a tapering period of 6 months.8,9,23 Glucocorticoid therapy results in complete remission in more than 80% of adults with MCD.16 The response rate to glucocorticoids is slower in adults than in children. In children, remission can occur on day eight to 4 weeks, but approximately 50% of adult patients need 8 weeks to reach remission and nearly 80% reach remission within 16 weeks.24

Our patient's kidney biopsy resulted in MCD, in which 80% of cases will respond to adequate glucocorticoid therapy. The patient was given oral methylprednisolone therapy of 3x16 mg in 8 weeks and then gradually tapered within 6 months. After attaining remission, KDIGO advises tapering glucocorticoids to 5-10 mg/week or fewer for a total exposure time of at least 24 weeks.9 MCD has an excellent prognosis and a good response to glucocorticoid therapy. Approximately more than 80% of adult MCD patients can go into complete remission with adequate glucocorticoid therapy. However, MCD is also a disease that often recurs. After six months of therapy, our patient showed improved the patient improved clinical condition and was finally in complete remission.

From the histopathological examination, MCD is characterized by global thinning of the podocyte leg on electron microscopy and appears to be near normal (or only minimal mesangial prominence) on light microscopy and no staining on immunofluorescence microscopic (or low-intensity staining for C3 and IgM). Renal function in MCD patients is usually normal.15 As in our patient, mesangial cells and matrix had minimal proliferation and perihilar adhesions <50%. Partially atrophic tubules and erythrocyte cells were seen in the tubular lumen, and PMN and mononuclear inflammatory cell infiltration in the tubular interstitial. C1q, C3, IgA, IgG, and IgM were negative on immunofluorescence examination.

Therapy for NS consists of supportive therapy and immunosuppressants. General management includes dietary sodium restriction, diuretics and renin-angiotensin-system (RAS) inhibitor therapy. Angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, with a target systolic blood pressure of less than 120 mmHg, are the first-line treatments for proteinuria. Non-pharmacological therapy includes limiting sodium intake (<2 grams/day), normalizing body weight, regular exercise, and smoking cessation. A diet high in calories and adequate in protein (0.8 mg/kgBW/day) has been shown to reduce protein excretion in the urine without causing malnutrition in patients.9 Loop diuretics can be used as first-line therapy for treating edema. If furosemide is clinically inadequate, thiazide diuretic or 20% intravenous albumin can be added.15 Treatment of NS’s underlying disease and reducing proteinuria will eventually improve hypercholesterolemia.22 Our patient was given supportive therapy of dietary management, 20% albumin infusion, furosemide, candesartan and simvastatin.

From the histopathological examination, MCD is characterized by global thinning of the podocyte leg on electron microscopy and appears to be near normal (or only minimal mesangial prominence) on light microscopy and no staining on immunofluorescence microscopic (or low-intensity staining for C3 and IgM). Renal function in MCD patients is usually normal.15 As in our patient, mesangial cells and matrix had minimal proliferation and perihilar adhesions <50%. Partially atrophic tubules and erythrocyte cells were seen in the tubular lumen, and PMN and mononuclear inflammatory cell infiltration in the tubular interstitial. C1q, C3, IgA, IgG, and IgM were negative on immunofluorescence examination.

Therapy for NS consists of supportive therapy and immunosuppressants. General management includes dietary sodium restriction, diuretics and renin-angiotensin-system (RAS) inhibitor

### Table 2. Patient urinalysis parameters

<table>
<thead>
<tr>
<th>Urinalysis</th>
<th>Day 1</th>
<th>Day 4</th>
<th>Day 9</th>
<th>Week 6</th>
<th>Week 28</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color</td>
<td>Yellow</td>
<td>Yellow</td>
<td>Yellow</td>
<td>Yellow</td>
<td>Yellow</td>
</tr>
<tr>
<td>Clarity</td>
<td>Clear</td>
<td>Clear</td>
<td>Clear</td>
<td>Clear</td>
<td>Clear</td>
</tr>
<tr>
<td>Specific Gravity</td>
<td>1.014</td>
<td>1.014</td>
<td>1.030</td>
<td>1.030</td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>5</td>
<td>5</td>
<td>6</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Ketone</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Protein</td>
<td>+3</td>
<td>+I</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Glucose</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Erythrocyte</td>
<td>+2</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Nitrit</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Urobilinogen (mg/dL)</td>
<td>0.2</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Leukocytes</td>
<td>+1</td>
<td>+1</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Esbach Protein (gr/L)</td>
<td>3.5</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: *abnormal level
concluded that the previous patient had received inadequate therapy. Our patient was treated with methylprednisolone of 3x16 mg for 8 weeks, and then the dose was gradually tapered within 6 months. The patient has now reached a state of complete remission. This case highlighted the importance of adequate therapy in managing nephrotic syndrome.

ACKNOWLEDGMENT
We thank Dr. Soetomo General/Teaching Hospital for supporting our research.

PATIENT’S INFORMED CONSENT
The patient has already signed a written informed consent and agreed regarding the publication of this case report.

CONFLICT OF INTEREST
All authors declare no conflict of interest.

FUNDING
There is no external funding for this study.

AUTHOR CONTRIBUTIONS
All authors contributed equally from the patient’s management until this manuscript’s preparation and publication.

REFERENCES