Non-autoimmune overt hypothyroidism in the early stages of nephrotic syndrome: A case report from Somalia

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Case Report

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Abstract

Nephrotic syndrome (NS) was first characterized in 1827 as the occurrence of proteinuria greater than or equal to 3.5 g/24 hours, hypoalbuminemia (albumin less than or equal to 3.0 g/dl), peripheral edema, hyperlipidemia, lipiduria caused by increased permeability of the renal glomerulus. In the early stage of NS the loss of thyroid hormones rarely leads to hypothyroidism and euthyroid state is expected. However, persistent proteinuria will eventually lead to hypothyroidism. Non-autoimmune hypothyroidism due to NS which presents at an early stage of NS is quite rare and cases reporting it are very scarce in the literature. In the presenting case, we reported a 26-year-old male patient with no known history of chronic disease who presented to the emergency department with a complaint of one-week generalized edema, nausea, fatigue, and generalized ache in the extremities. He was diagnosed with nephrotic syndrome complicated by hypothyroidism and was hospitalized for 3 weeks. After 3 weeks of treatment and close monitoring, the patient's clinical condition and laboratory investigations were improved and was discharged in good health.

Introduction

Nephrotic syndrome (NS) was first characterized in 1827 as the occurrence of proteinuria greater than or equal to 3.5 g/24 hours, hypoalbuminemia (albumin less than or equal to 3.0 g/dl), peripheral edema, hyperlipidemia, lipiduria caused by increased permeability of the renal glomerulus (1). The estimated population incidence of NS is roughly 3 per 100,000 people per year (2). The increased permeability of the glomerulus can be due to primary causes which include focal segmental glomerulosclerosis (FSGS), membranous nephropyathy (MN), and minimal change disease (MCD), and secondary causes which comprise of diabetes, systemic lupus erythematos, multiple myeloma, amyloidosis, and infections (1). Although, albumin is the major protein which will be lost in the urine in case of NS, some other binding proteins like thyroxine binding globulin and transthyretin, and thyroid hormones itself will be lost resulting hypothyroidism (3). In the early stage of NS the loss of thyroid hormones rarely leads to hypothyroidism and euthyroid state is expected. However, persistent proteinuria will eventually lead to hypothyroidism (4). Non-autoimmune hypothyroidism due to NS which presents at an early stage of NS is quite rare and cases reporting it are very scarce in the literature. Here we report a case of a 26-year-old male presented with both nephrotic syndrome and hypothyroidism at an early stage.

Case Report

A 26-year-old, previously healthy man with no known history of chronic disease presented to the emergency department with a complaint of one-week generalized edema, nausea, fatigue, and generalized ache in the extremities. The patient has no family history of autoimmune diseases. On examination, he looked ill and distressful, and he had a puffy face. His vital signs showed a pulse of 88 bpm, blood pressure of 110/80, a temperature of 36.7°C, and a respiratory rate of 18. Head and neck examinations were normal. Neurological examinations including motor, sensory, and cranial nerves were unremarkable. The cardiovascular examination was also normal. The abdomen was soft with no
tenderness and no evidence of organomegaly. He had bilateral grade 3 pitting lower limb edema up to the thighs. He also had sacral and face edema. Laboratory investigations revealed a hemoglobin level of 14 g/dl, Glucose 99 mg/dl, AST 43 U/L, ALT 35 U/L, urea of 56 mg/dl, creatinine of 0.7 mg/dl, serum sodium 134 mmol/l, and serum potassium of 3.98 mmol/l, total protein 4.7 g/dl, and albumin level of 2.1 g/dl. Regarding the lipid profile, triglyceride was 380 mg/dL, LDL was 290 mg/dL, and total cholesterol was measured at 400 mg/dL. Protein was positive in urinalysis, and the urine protein-to-creatinine ratio resulted 7.27 g of protein per day. (Table 1)

A chest X-ray showed mild pleural effusion on both sides of the lungs. Echocardiography and electrocardiogram were both demonstrated normal results. Abdominal ultrasound revealed bilateral normal kidney anatomy with normal parenchyma and mild ascites.

The patient was immediately admitted to the internal medicine unit under the diagnosis of newly onset nephrotic syndrome and was started on ramipril, methylprednisolone, furosemide, aspirin, and atorvastatin. On routine blood tests the day after hospitalization, we incidentally revealed hypothyroidism with TSH measuring 37 mIU/L and T4 0.4 ng/dL. The anti-thyroid peroxidase and anti-thyroglobulin antibody tests were negative. The thyroid ultrasound examination was ordered and came back normal. A diagnosis of non-autoimmune overt hypothyroidism due to nephrotic syndrome was considered, and levothyroxine treatment was started immediately. After 3 weeks of hospitalization, the patient improved very well and his symptoms subsided. Lower limb edema was decreased drastically, proteinuria was decreased to 3.9 g/day, and his lipid profile and albumin levels were almost at normal levels. TSH level was also decreased to 9 mIU/L. He was discharged on oral prednisolone, atorvastatin, aspirin, and levothyroxine. After 1 month, the patient came to our clinic for routine follow-up. His TSH level was 3.56 mIU/L, there was no protein in the urine and his albumin and lipid profiles were returned to normal levels.

Discussion

Second only to diabetes mellitus in terms of endocrine illnesses, particularly in Africa, thyroid disease is the most prevalent endocrine disorder worldwide (5). Although nephrotic syndrome has long been a known cause of hypothyroidism in adults and in children, it was associated to cause hypothyroidism in patients with long-standing proteinuria, patients with heavy proteinuria, and patients with steroid resistant nephrotic syndrome. In 2021, Kwong and coworkers concluded in a large retrospective cohort study between 1979 and 2015, that the risk of hypothyroidism was directly related to the severity of proteinuria (6). Moreover, a study from 2019 which evaluated 317 NS patients stated that patients with thyroid dysfunction expressed a higher levels of proteinuria compared to NS patients with normal thyroid function (7). In 2014, a study from a teaching hospital in New Delhi, India, which evaluated 20 children with steroid resistant NS (SRNS) and 20 healthy controls done by Kapoor and coworkers, concluded that a large portion of SRNS children had subclinical non-autoimmune hypothyroidism (8). It has been known that the ultimate treatment of non-autoimmune hypothyroidism due to NS with no other cause is bilateral nephrectomy, which will stop the loss of thyroid hormones in the urine and thus normalize the thyroid function test (9).
This presented case of an unusual early stage combination of hypothyroidism and nephrotic syndrome with no background of previous nephrotic syndrome or proteinuria and no previous history of thyroid disorder is the first of its kind reported from Somalia. Our patient’s lower limb edema, along with proteinuria and low level of albumin were suggestive of NS. His thyroid function tests along with generalized muscle ache on admission were also suggestive of overt hypothyroidism due to NS. The patient was hospitalized on the background of nephrotic syndrome and hypothyroidism, and after administering ramipril, methylprednisolone, furosemide, aspirin, and atorvastatin and thyroid replacement therapy with close monitoring for 3 weeks, the patient’s clinical condition improved drastically and he was discharged from the hospital.

In 2008, Chandurkar and colleagues reported a case of a 44-year-old woman with long-standing hypothyroidism and heavy proteinuria (10). They described that the patient lost a significant amount of T4 in the urine which subsequently caused to increase her levothyroxine treatment dose. In contrast, our patient had no history of long-standing hypothyroidism and his proteinuria was less compared to their patient. In 2015, Benvenga et al. described 2 case reports in which previously known hypothyroidism patients had required higher doses of levothyroxine treatment to maintain euthyroid state (11). They concluded that digestive diseases alone should not be focused in case of increased requirement levothyroxine doses in hypothyroidism patients who previously maintain euthyroid state and NS should also be suspected and included in the workup.

In 2021, Silva and colleagues described a 23-year-old male patient with severe nephrotic syndrome and subsequent complicated with overt hypothyroidism which required thyroid hormone replacement. They stated that after bilateral nephrectomy the patient’s thyroid function tests improved and levothyroxine medication was discontinued (4).

**Conclusion**

Hypothyroidism in NS is a common entity and it has been encountered in many clinical practices. However hypothyroidism in early stages of NS is a rare entity which may be encountered and physicians should be aware that hypothyroidism can be seen at any stage of nephrotic syndrome.

**Abbreviations**

FSGS
Focal segmental glomerulosclerosis
MCD
Minimal change disease
MN
Membranous nephropathy
NS
nephrotic syndrome
SRNS
Steroid resistant nephrotic syndrome

Declarations

Data Availability:
The data is available from the corresponding author and can be accessed if requested.

Ethics Committee approval and consent for publication:
Mogadishu-Somali Turkish Training and Research Hospital ethics committee waived approval for this case report. Written informed consent was obtained from the patient.

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References


Table
<table>
<thead>
<tr>
<th>Lab results</th>
<th>Normal range</th>
<th>On admission</th>
<th>Discharge day (3 weeks later)</th>
<th>1 month after discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (HB)</td>
<td>13-17 g/dl</td>
<td>14</td>
<td>14.6</td>
<td>14</td>
</tr>
<tr>
<td>Glucose</td>
<td>60/110 mg/dl</td>
<td>99</td>
<td>112</td>
<td>100</td>
</tr>
<tr>
<td>Urea</td>
<td>10-45 mg/dl</td>
<td>56</td>
<td>35</td>
<td>22</td>
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<tr>
<td>Creatinine</td>
<td>0.6-1.35 mg/dl</td>
<td>0.7</td>
<td>0.66</td>
<td>0.63</td>
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<tr>
<td>Aspartate aminotransferase (AST)</td>
<td>0-35 U/L</td>
<td>43</td>
<td>14</td>
<td>20</td>
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<tr>
<td>Alanine aminotransferase (ALT)</td>
<td>0-45 U/L</td>
<td>35</td>
<td>28</td>
<td>25</td>
</tr>
<tr>
<td>Sodium (Na)</td>
<td>135-145 meq/L</td>
<td>134</td>
<td>139</td>
<td>141</td>
</tr>
<tr>
<td>Potassium (K)</td>
<td>3.5-5.5 meq/L</td>
<td>3.98</td>
<td>4.87</td>
<td>4.56</td>
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<tr>
<td>Total cholesterol</td>
<td>40-200 mg/dL</td>
<td>400</td>
<td>290</td>
<td>180</td>
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<tr>
<td>LDL</td>
<td>40 – 130 mg/dL</td>
<td>290</td>
<td>180</td>
<td>112</td>
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<tr>
<td>HDL</td>
<td>30-70 mg/dL</td>
<td>35</td>
<td>46</td>
<td>60</td>
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<tr>
<td>Triglyceride</td>
<td>50-200 mg/dL</td>
<td>380</td>
<td>230</td>
<td>198</td>
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<tr>
<td>Total protein</td>
<td>6.4 – 8.3 g/dL</td>
<td>4.7</td>
<td>7</td>
<td>7.5</td>
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<tr>
<td>Albumin</td>
<td>3.5 – 5.5 g/dL</td>
<td>2.1</td>
<td>3.9</td>
<td>4.2</td>
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<td>Thyroid Stimulating Hormone (TSH)</td>
<td>0.6 - 5.5 mIU/L</td>
<td>37</td>
<td>9</td>
<td>3.56</td>
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<td>T4</td>
<td>0.7-2.1 ng/mL</td>
<td>0.4</td>
<td>0.78</td>
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<td>T3</td>
<td>2.4-4.2 pg/mL</td>
<td>2</td>
<td>2.5</td>
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<td>Spot urine protein: creatinine ratio</td>
<td>0 – 3.5 g/day</td>
<td>7.27</td>
<td>3.9</td>
<td>1.5</td>
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