

# Association between Primary Hypothyroidism and Nephrotic Syndrome: A Case Report

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## Abstract

A 11-year-old girl was admitted in the Department of Paediatric Nephrology, National Institute of Kidney Diseases and Urology (NIKDU), Sher-E-Bangla Nagar, Dhaka. She was diagnosed as a case of nephrotic syndrome associated with primary hypothyroidism. She had short stature and was malnourished, but had no family history of hypothyroidism or renal diseases. She also had no consanguinity. She was treated with oral steroid and levothyroxin associated with nutritional support. Her condition improved with the treatment. At regular follow up her height and nutritional status was improved. Though hypothyroidism may be associated with nephrotic syndrome, it should be carefully evaluated.

**Key words:** Nephrotic syndrome; Hypothyroidism.

## INTRODUCTION

Nephrotic syndrome is a common renal disease among children all over the world. It results in loss of plasma proteins and various other macromolecules in the urine. Many of the physiologically important molecules which exist in the plasma, bound to plasma proteins, are also carried away and are lost in the urine.<sup>1</sup> The abnormalities arising as a result of heavy proteinuria are hypothyroidism, vitamin D deficiency, and iron deficiency. Hyperlipidaemia is a consequence of increased hepatic synthesis of cholesterol, triglycerides and lipoproteins, decreased catabolism of lipoproteins, a decreased LDL receptor activity, and an increased urinary loss of high density lipoprotein.<sup>2</sup> In nephrotic syndrome, thyroxine may be reduced due to increase loss of thyroid binding globulin. So, thyroid stimulating hormone (TSH) level in blood becomes high. Many cases of glomerular diseases have been associated with thyroid diseases, both in adults and in children.<sup>3</sup> However, TSH levels were found to be very high in nephrotic syndrome and the increase in TSH correlates well with the degree of proteinuria. This leads to the possibility that significant amounts of thyroid hormones are also lost in nephritic syndrome resulting in a total body negative balance. In situations of long standing heavy proteinuria, it results in clinically significant hypothyroidism.

Primary hypothyroidism or thyroid hormone deficiency due to abnormality in the thyroid gland is the most common endocrine disease in children. The prevalence of hypothyroidism in the general population ranges from 3.8% to 4.6%.<sup>4-7</sup> Diagnosis and treatment of hypothyroidism is often considered simple and is mostly carried out in a primary care setting. The common clinical features associated with hypothyroidism in children are short stature, tiredness, weight gain, dry

skin, cold intolerance, constipation, muscle weakness, peri-orbital swelling, hoarseness of voice, and poor memory. However, a study surveying thyroid disease in Colorado has shown that the sensitivity of individual symptoms ranges from 2.9% to 24.5%.<sup>8</sup> Although the likelihood of hypothyroidism increases with increasing numbers of symptoms,<sup>8,9</sup> absence of symptoms does not exclude the diagnosis. Because symptoms of hypothyroidism are non-specific, many patients have such symptoms without biochemical evidence of hypothyroidism.

## CASE PRESENTATION

A 11-year-old girl, first issue of non-consanguineous parents admitted in the Department of Paediatric Nephrology, National Institute of Kidney Diseases and Urology (NIKDU) presented with puffiness of face followed by generalized swelling of whole body with scanty urine. Her parents told that she developed same features 3 months back. Then she was diagnosed as a case of nephrotic syndrome and treated with steroid. She was gradually improving, but for the last 15 days her body swelling reappeared and she became puffy. On examination she was puffy, edematous, afebrile, blood pressure was 100/70 mm of Hg. Her height was 128 cm (according to 3<sup>rd</sup> centile it should be 130 cm), her nutritional status was moderate malnourished ('Z'score was -2) but her parents and another brother of her family had normal height and weight according to age and sex. Her secondary sexual characteristics (breast development, menarche, pubic hair, axillary hair) was developed. She had no oral ulceration, arthritis, joint pain, photosensitization, butterfly rash over face, or any other feature. Urinary routine microscopic examination shows albumin +++; pus cell: 0-4/hpf; RBC: nil; haemoglobin - 10.3 gm/dl; serum creatinine - 0.6 mg/dl; serum cholesterol 230 mg/dl; Serum albumin - 2.6 gm/dl; complement C3 and C4 were within normal limit, ultrasonography (USG) of kidney-ureter-bladder (KUB) shows both kidneys were normal in size, shape, and position. Serum anti nuclear antibody (ANA) was negative, T3 and T4 were low but TSH level was increased to 8.1  $\mu$ iu/ml (normal value (0.70-5.70  $\mu$ iu/ml)). USG of thyroid showed normal study of thyroid gland. X-ray chest P/A view had no abnormality. Renal biopsy shows there is mild mesangial proliferative glomerulonephritis. We treated this case with steroid and levothyroxin (50  $\mu$ g) with additional nutritional support. In follow up visit after 4 weeks of discharge from hospital her general condition improved, urine albumin was absent, serum TSH was 5.1  $\mu$ iu/ml, and her height 129 cm. After 3 months of her first

follow up she was well and her height became 131 cm and her secondary sexual character gradually developing.

## DISCUSSION

Nephrotic syndrome is accompanied by changes in the concentrations of thyroid hormone (TH).<sup>10-13</sup> In nephrotic syndrome, urinary losses of TH binding proteins occurs, such as thyroxine binding globulin (TBG), transthyretin or pre-albumin and albumin, result in a reduction in serum total thyroxine (T4) and, sometimes, in total T3 levels. These hormonal changes are related both to the degree of proteinuria and to serum albumin levels. Subclinical hypothyroidism occurred more frequently in the nephrotic syndrome patients.<sup>14</sup>

In primary hypothyroidism, there is an increase serum TSH and decrease T4 level. When there is nephrotic syndrome there is also an increase serum TSH level. This patient had increase serum TSH and low level of T4. So whenever she came with features of nephrotic syndrome, her feature of hypothyroidism subsided. But her clinical feature and short stature suggest that she had both nephrotic syndrome with primary hypothyroidism.

Girls with primary hypothyroidism may also present with abdominopelvic masses—large ovarian cysts caused by hyperstimulation.<sup>15,16</sup> Poor growth, menarche at early age and early onset of breast development, menarche before appearance of pubic or axillary hair, and delayed bone age are present in primary hypothyroidism. Although her abdominopelvic mass was absent, her menarche had started at early age before appearance of pubic or axillary hair. Resolution of pubertal changes after treatment with thyroid hormone replacement is the hallmark of primary hypothyroidism.

There is no frequency of this condition,<sup>17</sup> and there is limited information on the long-term prognosis for children with precocious puberty caused by primary hypothyroidism.<sup>18</sup> Although this is an uncommon presentation of a common disorder, this case highlights the value of regular, accurate monitoring, and recording of growth measurements during childhood. Development of body swelling caused by hypothyroidism may be prevented by observing and investigating a significant change in growth parameters. This is a relatively simple process that is essential to facilitate optimal growth during childhood. In nephrotic syndrome, features of hypothyroidism should be evaluated with other features of it and careful assessment of the features of other family members should be done. Family members of this girl were all perfect and had no feature of hypothyroidism.

She had no feature of lupus nephritis. Her menarche had started but she looked much younger than her age which she corresponds. We gave levothyroxin for the management of primary hypothyroidism as well as steroid for her nephrotic syndrome and she responded dramatically. Her general condition improved, she developed adolescent behaviour,

and her height gradually improved. Her nutritional status also improved with the administration of regular nutritional diet.

The case conveys clear, practical lessons. Preference should be given to common presentations of important rare conditions, and important unusual presentations of common problems.

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