Autoimmune Hypothyroidism and Nephrotic Syndrome

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History
• Submission Date: 14-10-16
• Revised Date: 24-03-17
• Accepted Date: 11-04-17

DOI : 10.5530/ijmedph.2017.2.25

ABSTRACT

The association of autoimmune hypothyroidism with Nephrotic syndrome is a rare but significant since it is amenable to Levothyroxine therapy with a good prognosis. It is suspected in patients presenting with overlapping features of both disease conditions with supportive laboratory parameters. We describe the case of a 25 year old individual who presented with nephrotic syndrome associated with underlying autoimmune thyroiditis and was successfully treated with Levothyroxine to attain long lasting remission.

Keywords: Nephrotic Syndrome, Hypothyroidism, Levothyroxine Therapy, Autoimmune disorder, Prednisone therapy.

INTRODUCTION

Autoimmune disorders can present as single organ pathology or be associated with multiple organ system involvement.1-3 Autoimmune thyroiditis resulting in hypothyroidism (Hashimoto’s) can rarely be associated with concomitant autoimmune glomerular involvement resulting in the development of Nephrotic syndrome.2 The development of overt proteinuria results in loss of thyroid hormones bound to its carrier proteins.3 This results in hypothyroidism in a patient with a compromised thyroid gland. This is one of the rare reversible association between autoimmune hypothyroidism and Nephrotic syndrome which is amenable to Levothyroxine therapy and carries a good prognosis. Very few cases showing the association of hypothyroidism and Nephrotic syndrome have been reported so far.4-9 The clinician should have a high index of suspicion in patients presenting with overlapping features of both hypothyroidism & Nephrotic syndrome and order necessary investigations to rule out underlying hypothyroidism as a treatable cause of Nephrotic syndrome.

CASE SUMMARY

A 25 year old businessman visited the medicine outpatient department with complaints of generalised body swelling since last 6 months. Initially he experienced prominent facial puffiness which seemed more prominent in the early morning hours. His symptoms followed a gradually progressive course over the next 6 months finally resulting in generalised oedema. Besides he also experienced fatigue and lethargy, associated with cold intolerance, which occasionally interfered with his daily activities. He denied any history of breathlessness, cough, decreased urine output, change in voice or neck swelling. Family and medication history was unrewarding.

On examination his vitals were stable with pulse rate of 68/min and respiratory rate of 18/min. He had diastolic hypertension (blood pressure = 130/100 mmHg) with no postural variation. He weighed 76 kg and his height was 165 cm; hence his BMI was 27.92 kg/m². He did not appear pale, although facial and periorbital swelling was prominent with bilateral pedal oedema. There were no signs of goitre or engorgement of neck veins; JVP was within normal limits. We also noticed prominent swelling in bilateral calf regions which was firm and non-tender (Pseudo-hypertrophy). Abdominal examination revealed no hepato-splenomegaly with mild ascites as perceived by percussion over bilateral flank regions. Higher mental functions and nervous system examination was mostly normal save for the delayed relaxation of ankle reflex bilaterally (grade 1+). Examination of the cardiovascular and respiratory systems did not reveal any significant abnormality.

On further investigating, his Haemoglobin was 10.5 g/dl with normocytic normochromic peripheral blood picture. Serum electrolytes and creatinine were within normal limits while liver function tests showed reduced total protein (4.7 g/dl) and albumin (2.2 g/dl) values. He had deranged fasting lipid profile (total cholesterol = 380 mg/dl, LDL = 180 mg/dl, HDL = 36 mg/dl) while his random blood glucose level was 76 mg/dl. Urine routine examination revealed significant proteinuria (3+) without any RBC casts or pus cells. 24 h urinary protein excretion was 6000 mg. We ordered a thyroid function test and obtained results concordant with primary hypothyroidism (T3 = 45 ng/dl, T4 = 3.8 µg/dl, TSH > 100 µIU/ml). Anti TPO antibodies were positive. Kidney biopsy before the start of treatment showed Glomeruli having mesangio-capsillary proliferation with oedematous tubules filled with proteinaceous material (Figure 1 and 2).

On investigation of his thyroid function tests, his serum TSH levels were high, going up to 85.4 µIU/ml while his serum free T3 and T4 levels were low. His T3 and T4 levels were replaced with Levothyroxine and his signs and symptoms of hypothyroidism were resolved within a month.

DISCUSSION

Autoimmune hypothyroidism is the commonest cause of hypothyroidism in iodine-sufficient regions of the world. It generally causes autoimmune thyroid destruction, goitre and a variety of systemic manifestations. Renal involvement as isolated proteinuria is commonly seen in 10-30% of hypothyroid individuals. Glomerular involvement with autoimmune thyroiditis is a rare entity. Studies have revealed that the lesion most commonly associated is Membranous Glomerulonephritis (MGN) followed by Focal Segmental Glomerulosclerosis (FSGS) and Minimal Change Disease (MCD).

Several mechanisms have been proposed to explain these associations. Features suggesting a common autoimmune disorder are immune-complex deposition in the glomerular and thyroid basement membrane and association with other autoimmune diseases like type 1 diabetes mellitus. The development of nephrotic syndrome results in urinary loss of thyroid hormones bound to its binding proteins like TBG, transthyretin, prealbumin and albumin. Normal thyroid compensates for these changes by increasing synthesis of thyroid hormones. Patients with com-
promised thyroid functions may subsequently develop hypothyroidism due to urinary loss of thyroid hormones. Primary hypothyroidism has also been reported to occur in association with congenital nephrotic syndrome.8

Thyroid function tests reveal variable results in the nephrotic syndrome, primarily depending upon the level of protein losses in the urine. In addition, other factors that are frequently present in patients with the nephrotic syndrome, such as hypoalbuminemia, increased serum free fatty acid concentrations, and furosemide administration, can also affect thyroid function tests.9,10 Urinary losses of thyroxine (T4)-binding globulin (TBG) and other thyroid hormone-binding proteins (transthyretin and albumin) and the T4 bound to them result in a low total T4 concentrations in approximately 50 percent of nephrotic patients with a relatively normal glomerular filtration rate (GFR).9,10 Serum triiodothyronine (T3) concentrations may also be low due also to decreased binding. There is often a good correlation between the serum T4 and T3 and the serum albumin concentration.9,12 Serum reverse T3 (rT3) concentrations are also low. Similar mechanism also seen in patient with metabolic syndrome associated with thyroid dysfunction.14

The association of nephrotic syndrome with hypothyroidism is a rare entity with only a few cases reported so far in medical literature. A 63 year old Japanese man had co-existent minimal change disease and autoimmune hypothyroidism which was proven by biopsy and the presence of anti-microsomal and anti-thyroid peroxidase autoantibodies.7 Similarly a Turkish individual was reported to have co-existent autoimmune hypothyroidism and membranoproliferative glomerulonephritis.9 Nephrotic syndrome associated with autoimmune hypothyroidism is a treatable and reversible condition with a good prognosis, hence clinicians must rule out hypothyroidism when any patient with Nephrotic syndrome presents with compatible clinical features.

CONCLUSION

Un-treated Hypothyroidism is a rare but reversible cause of Nephrotic Syndrome which is amenable to treatment with Levothyroxine and has an overall good prognosis. The clinician should have a high index of suspicion in patients presenting with overlapping features of both hypothyroidism and Nephrotic syndrome and order necessary investigations to rule out underlying hypothyroidism as a treatable cause of Nephrotic syndrome.

ACKNOWLEDGEMENT

We owe thanks to the patient and her relatives for having patience and their contribution to this undertaking.

CONFLICT OF INTEREST

None

ABBREVIATION USED

Hb: Haemoglobin; TLC: Total Leucocyte Count; TSH: Thyroid-stimulating hormone; S.CHO: Serum cholesterol; TG: Triglycerides; S.HDL: High density lipoprotein; S.LDL: Low-density lipoprotein; S.VLDL: Very-low-density lipoprotein; SGOT: Serum glutamic oxaloacetic transaminases, SGPT: Serum glutamic pyruvic transaminases, SALP: Serum alkaline phosphatase, Anti TPO: Anti-Thyroid Peroxidase

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