Pancytopenia and nephrotic syndrome related to autoimmune hypothyroidism

Manjusha S Rathi  •  Steven R Peacey
Department of Diabetes and Endocrinology, Bradford Teaching Hospitals NHS Foundation Trust, UK
Correspondence to: Manjusha S Rathi. Email: manjusharathi@hotmail.com

This case report highlights rare manifestations of hypothyroidism, its effects on the haematological and renal systems.

Case report

A 64-year-old woman presented to her general practitioner with a four-week history of progressive bilateral leg swelling, tiredness and dry skin. She had no significant past medical history. She was not taking any medication and there was no family history of thyroid or renal disorders.

On examination she had bilateral pitting oedema up to her knees, BP was 147/81 mmHg. Initial investigation showed heavy proteinuria (4+ on urinalysis), full blood count revealed pancytopenia Hb 10.2 g/dL (ref range 11.5–16) normocytic anaemia, WBC 2.9 × 10^9/L (ref range 4–11) and platelets 127 × 10^9/L (ref range 150–400); impaired renal function with serum creatinine of 129 μmol/L (ref range 70–100) and total serum cholesterol was 12.2 mmol/L. Serum B12, folate and ferritin were normal.

At this stage, the possibility of nephrotic syndrome was raised and she was referred to nephrology services. Further investigations revealed – normal serum complement levels and normal autoimmune profile (ANA, dsDNA, ANCA, Ro/SS – A, Ro/SS – B, Sm, RNP, Scl 70, Jo1). Her thyroid function was abnormal with TSH 182 miu/L (0.2–6.0) and free T4 – 2.3 pmol/L (10.0–25.0). She was referred to endocrinology for further management.

On examination, she appeared grossly hypothyroid with dry skin, typical hypothyroid facial features, hoarse voice, and delayed relaxation of deep tendon reflexes. Her thyroid peroxidase antibodies were elevated 347 iu/L (<100) confirming the diagnosis of autoimmune hypothyroidism. Her adrenal cortex, gastric parietal, mitochondrial, smooth muscle, liver/kidney microsomal antibodies were negative.

In April 2008, she was commenced on 50 μg of thyroxine o.d. and 2 weeks later the dose was increased to 100 μg o.d. Proteinuria resolved within a few weeks of thyroid hormone replacement and over the next five months, serum creatinine normalized, eGFR improved and the pancytopenia completely resolved (Table 1).

Discussion

In hypothyroidism, plasma volume and RBC mass are both diminished, and blood volume is decreased. Anaemia of a mild degree is commonly present, and the haemoglobin level may be as low as 8–9 g/dl. Characteristically, the anaemia of hypothyroidism is normochromic and normocytic. Less commonly it can be macrocytic or microcytic.

In a report looking at 202 individuals with hypothyroidism, the overall incidence of anaemia as per criteria established by the World Health Organization was slightly less than 30%. The anaemia was macrocytic in 16 cases, microcytic in nine cases, and normocytic in 32 cases.1

It is important to note that anaemia can occur due to coincident vitamin B12, folate or iron deficiency. Microcytic hypochromic anaemia in hypothyroidism can be due to iron deficiency, in women secondary to menorrhagia, or in men due to decreased iron absorption especially in those with associated achlorhydria or associated coeliac disease, but may have no obvious cause.

Hypothyroidism per se can cause anaemia. The pathogenesis of the anaemia is not precisely understood but appears to reflect a physiologic adaptation to the decreased tissue oxygen requirements resulting from a decrease in the basal oxygen uptake.
metabolic rate. Plasma erythropoietin levels have been shown to be low. This contrasts with the findings in most other cases of anaemia, in which plasma or urinary erythropoietin levels are increased as a result of tissue hypoxia. Results of ferrokinetic studies show decreased erythropoiesis, prolonged plasma iron clearance rate and decreased maximum Fe59 utilization by red blood cells suggesting that hypothyroidism per se affect cellular needs for oxygen and interfere with erythropoiesis. In some hypothyroid individuals with anaemia and normal serum iron, B12, and folate levels, an increase in haemoglobin was observed with thyroid hormone replacement alone.

The anaemia of hypothyroidism is not correlated with the severity of the hypothyroidism and typically responds more slowly following thyroid hormone therapy compared to treatment of iron deficiency anaemia with iron therapy.

The anaemia of hypothyroidism is not correlated with the severity of the hypothyroidism and typically responds more slowly following thyroid hormone therapy compared to treatment of iron deficiency anaemia with iron therapy.

Besides, pancytopenia, our patient was noted to have heavy proteinuria with no known renal problems. It is well-known that thyroid hormone is essential for adequate growth and development of the kidney and plays an important role in water and electrolyte homeostasis. Hypothyroidism can cause significant changes in kidney function with reduction in glomerular filtration rate and renal plasma flow, leading to reduced creatinine clearance and rise in serum creatinine.

About 55% of patients with primary hypothyroidism are noted to have a slight increase in the serum creatinine levels that is usually reversible upon correction of the hypothyroid state. Renal involvement in autoimmune thyroiditis is not uncommon, usually manifesting as proteinuria, seen in 11–30% of cases. The most common glomerular lesion among these reports based on renal biopsy findings is membranous glomerulonephritis. The pathogenesis of glomerular disease and proteinuria in patients with autoimmune thyroiditis is not well understood. The major proposed mechanism focuses on deposition of immune complexes in glomerular basement membranes in conjunction with derangement in renal hemodynamic and architecture secondary to hypothyroidism.

There may also be mild proteinuria, secondary to increased capillary transudation of proteins. Treatment with thyroid hormone enhances renal function and improves glomerular filtration rate, thereby normalizing these changes.

Table 1

| Laboratory results at diagnosis and during treatment with thyroid hormone | March 2008 | April 2008 | Thyroxine started | June 2008 | August 2008 | September 2008 | December 2008 |
|---------------------------------|-----------|-----------|------------------|-----------|-------------|--------------|--------------|
| Haemoglobin (11.5–16 g/dL)      | 10.4      | 10.2      | 10.6             | 11.4      | 11.6        |              |              |
| WBC (4–11 x 10⁹/L)             | 2.86      | 3.02      | 3.42             | 4.02      | 5.42        |              |              |
| Platelet (150–400 x 10⁹/L)     | 133       | 127       | 132              | 132       | 183         |              |              |
| Sodium (135–145 mmol/L)        | 141       | 139       |                  |           | 140         |              |              |
| Potassium (3.5–5.0 mmol/L)     | 4.6       | 4.0       |                  |           | 4.5         |              |              |
| Urea (2.1–8.0 mmol/L)          | 8.7       | 5.8       |                  |           | 7.2         |              |              |
| Creatinine (70–100 μmol/L)     | 129       | 123       |                  |           | 81          |              |              |
| eGFR (mL/min/1.73m²)           | 38        | 41        |                  |           | 78          |              |              |
| TSH (0.2–6.0 miu/L)            | 182       | 32        | 1.1              |           | 0.44        |              |              |
| Free T4 (10–25 pmol/L)         | 2.3       | 14        | 21.5             |           | 21.1        |              |              |
Conclusion

In summary, we have described two rare complications of hypothyroidism: renal impairment and pancytopenia. Our patient showed complete recovery of renal function as well as pancytopenia within five months of thyroid hormone replacement. Hypothyroidism should be considered in patients with unexplained kidney disease as well as in unexplained pancytopenia.

References

1 Horton L, Coburn RJ, England JM, Himsworth RL. The haematology of hypothyroidism. Q J Med 1976;45:101–23
2 Das KC, Mukherjee M, Sarkar TK, et al. Erythropoiesis and erythropoietin in hypo- and hyperthyroidism. J Clin Endocrinol Metab 1975;40:211–20
3 Fein HG, Rivlin RS. Anemia in thyroid diseases. Med Clin North Am 1975;59:1133
4 Song SH, McCallum CJ, Campbell IW. Hypoplastic anaemia complicating myxoedema coma. Scott Med J 1998;43:149–50
5 Francis DA. Pure red cell aplasia: association with systemic lupus erythematosus and primary autoimmune hypothyroidism. BMJ 1982;284:85
6 Acton L, Chakraborty A, Thompson D, et al. An unusual cause of Pancytopenia. Acute Medicine 2007;6:77–8
7 Iglesias P, Di Ez J. Thyroid dysfunction and kidney disease. Eur J Endocrinol 2009;160:505–15
8 Montenegro J, Gonzalez O, Saracho R, et al. Changes in renal function in primary hypothyroidism. Am J Kidney Dis 1996;27:195–8
9 Mooraki A, Broumand B, Neekdoost F, et al. Reversible acute renal failure associated with hypothyroidism: Report of four cases with a brief review of literature. Nephrology (Carlton) 2003;8:57–60
10 Agras PI, Kinik ST, Cengiz N, et al. Autoimmune thyroiditis with associated proteinuria: Report of two patients. J Pediatr Endocrinol Metab 2005;18:319–22
11 Suher M, Koc E, Ata N, Ensari C. Relation of thyroid dysfunction, thyroid autoantibodies, and renal function. Ren Fail 2005;27:739–42
12 Weetman AP, Tomlinson K, Amos N, et al. Proteinuria in autoimmune thyroid disease. Acta Endocrinol (Copenh) 1985;109:341–7
13 Gurkan S, Dikman S, Saland MJ. A case of autoimmune thyroiditis and membranoproliferative glomerulonephritis. Pediatr Nephrol 2009;24:193–7
14 Mahjoub S, Ben Dhia N, Achour A, et al. Hypothyidie primitive et atteinte glomérulaire [Primary hypothyroidism and glomerular involvement]. Ann Endocrinol (Paris) 1991;52:289–92

© 2011 Royal Society of Medicine Press
This is an open-access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by-nc/2.0/), which permits non-commercial use, distribution and reproduction in any medium, provided the original work is properly cited.