Autoimmune Polyglandular Syndrome Presenting with Jaundice and Thrombocytopenia

A.W. Norasyikin a M. Rozita a M.J. Mohd Johan b Z. Suehazlyn a

a Pusat Perubatan Universiti Kebangsaan Malaysia (PPUKM), and b Hospital Angkatan Tentera Tuanku Mizan, Kuala Lumpur, Malaysia

Introduction

Autoimmune polyglandular syndrome (APS) is a rare form of autoimmune disorder involving at least two glandular autoimmune-mediated diseases [1]. It is a combination of endocrine and non-endocrine autoimmune disorders [2]. In APS type III, there is an association between autoimmune thyroid disorders and other autoimmune diseases with an absence of Addison’s disease and/or hypoparathyroidism [2]. The exact prevalence is unknown. APS type III can be further classified into 4 subcategories, i.e. a through d. The presence of autoimmune thyroiditis is a prerequisite for all categories as shown in table 1 [2, 3]. Here we report a rare case of APS type IIIb in an elderly woman.

Case Report

A 62-year-old hypertensive woman presented with anaemic symptoms and jaundice. Blood tests showed macrocytic anaemia due to vitamin B₁₂ deficiency with Coombs negative haemolysis. A thyroid function test was consistent with hypothyroidism. Autoimmune antibody assays were positive for anti-parietal cell, anti-intrinsic factor and anti-thyroid peroxidase antibodies. A final diagnosis of autoimmune thyroiditis with pernicious anaemia, which constituted autoimmune polyglandular syndrome type IIIb, was made and the patient was treated with L-thyroxine, vitamin B₁₂ injection and a blood transfusion. She was discharged uneventfully after a week of hospitalization.
tures with polychromasia and ovalostomatocytosis. The total serum bilirubin level was elevated at 45 μmol/l, with predominantly unconjugated forms and normal liver enzymes. Serum lactate dehydrogenase was elevated at 3,778 U/l but Coombs tests were negative. Her bone marrow aspirates and trephine biopsy showed severe megaloblastic anaemia without excess blast cells. Her thyroid profile revealed a free T4 level of 8.48 pmol/l (normal range 9.0–24) and the thyroid-stimulating hormone level was 83.96 IU/ml (normal range 0.3–5). The serum vitamin B12 concentration was less than 44 pmol/l (normal range 145–637), with normal serum folate levels. The morning serum cortisol level was 445 nmol/l and after 250 μg Synacthen the cortisol level increased to 798 nmol/l at 30 min, representing an adequate response.

Her oesophagoduodenoscopy showed atrophic gastritis at the antrum. Both of her anti-gastric parietal cell and anti-intrinsic factor antibodies were positive. The anti-thyroid peroxidase level was more than 1,000 IU/ml. Her fasting serum gastrin level was more than 1,000 pg/ml (normal range <101). Thus, she had both anti-gastric parietal cell and anti-intrinsic factor antibodies. She also had hypergastrinaemia which is a known complication of long-standing achlorhydria due to a lack of acid secretion by the parietal cells of the stomach. The pronounced hypergastrinaemia (>1,000 pg/ml) likely leads to subsequent hyperplasia of gastric enterochromaffin-like cells which predisposes to gastric malignancy [7].

The treatment of APS depends on the organ involved and the accompanying hormonal deficiencies. This patient was treated with L-thyroxine replacement as well as intramuscular vitamin B12 injection which she will require as lifelong therapy. However, it is important to highlight that autoimmune adrenalitis with accompanying adrenal insufficiency must be excluded before commencement of treatment with L-thyroxine.

APS is often preceded by an asymptomatic latency period of months or years following positive detection of

| Table 1. APS type III and subcategories |
|---------------------------------------|
| **Autoimmune thyroid disease**         |
| APS IIIa                              |
| Hashimoto’s thyroiditis               |
| Idiopathic myo-oedema                 |
| Asymptomatic thyroiditis              |
| Endocrine diseases                    |
| Type 1 diabetes mellitus              |
| Premature ovarian failure             |
| Lymphocytic hypophysitis              |
| Neurohypophysitis                     |
| Gastrointestinal apparatus diseases   |
| Atrophic gastritis                    |
| Pernicious anaemia                    |
| Coeliac disease                       |
| Chronic inflammatory bowel disease    |
| Autoimmune hepatitis                  |
| Primary biliary hepatitis             |
| Sclerosing cholangitis                |
| Skin/haemopoietic system/ nervous system diseases |
| Vitiligo                              |
| Alopecia                              |
| Autoimmune                            |
| thrombocytopenia                      |
| Autoimmune haemolytic anaemia         |
| Anti-phospholipid syndrome            |
| Myasthenia gravis                     |
| Stiff man syndrome                    |
| Multiple sclerosis                    |
| Collagen diseases/ vasculitis          |
| Systemic lupus                        |
| Erythematous                          |
| Mixed connectivitis                   |
| Rheumatoid arthritis                  |
| Reactive arthritis                    |
| Scleroderma                           |
| Sjögren’s syndrome                    |
| Vasculitis                            |

Discussion

Our patient fulfilled the criteria for APS type IIIb, i.e. autoimmune thyroiditis due to Hashimoto’s thyroiditis and pernicious anaemia. It occurs more frequently among middle-aged women [4, 5]. In its early stages, destruction of the thyroid gland gives rise to transient hyperthyroidism referred to as Hashitoxicosis [5]. However, once the process is complete, it leads to hypothyroidism as was seen in our patient.

Pernicious anaemia is a sequel of autoimmune chronic atrophic gastritis that involves the fundic glands and is characterized by severe gland atrophy [6]. Almost 90% of patients have antibodies directed against the parietal cells [6]. As a result, pernicious anaemia leads to vitamin B12 malabsorption and subsequently B12 deficiency. This patient had both anti-gastric parietal cell and anti-intrinsic factor antibodies. She also had hypergastrinaemia which is a known complication of long-standing achlorhydria due to a lack of acid secretion by the parietal cells of the stomach. The pronounced hypergastrinaemia (>1,000 pg/ml) likely leads to subsequent hyperplasia of gastric enterochromaffin-like cells which predisposes to gastric malignancy [7].
antibodies [8]. It is characterized by the presence of circulating disease-associated antibodies which are useful markers for future organ failure [8]. Thus, regular and long-term glandular function monitoring seems necessary. This is important because early recognition and replacement therapy can be life saving, particularly when the glandular failure involves the adrenal glands. Although the gland involvement in APS type III is usually limited to 2 or 3 glands, extensive involvement of up to 7 autoimmune diseases with extensive circulating antibodies including anti-glutamic acid decarboxylase antibodies and islet cell antibodies has been reported [9].

Hence, long-term follow-up and screening for other possible glandular involvements is necessary for our patient. Surveillance monitoring for gastric carcinoma tumours, which have been reported in 3–5% of patients with hyperplasia of gastric enterochromaffin-like cells, should also be performed [7]. Furthermore, pernicious anaemia is also associated with an increased risk of gastric cancer [10].

**Conclusion**

This case showed that the presence of one autoimmune endocrine disease should prompt clinicians to look for other coexisting autoimmune diseases which may be asymptomatic despite positive autoantibodies. This is especially important in patients with autoimmune hypothyroidism and undetected adrenal insufficiency because corticosteroid replacement before thyroxine therapy is mandatory to avoid an adrenal crisis.

**References**

1. Kahaly GJ: Polyglandular autoimmune syndromes. Eur J Endocrinol 2009;161:11–20.
2. Betterle C, Zanchetta R: Update on autoimmune polyendocrine syndromes (APS). Acta Biomed 2003;74:9–33.
3. Arya RK, Gupta DK, Chaudhary SC, et al: A rare case of autoimmune polyglandular syndrome type IIIc. Indian J Endocrinol Metab 2012;16:480.
4. Jain J, Banait S, Jajoo UN, et al: Polyglandular autoimmune syndrome: we should entertain this possibility more than often. Thyroid Res Pract 2012;9:93–95.
5. Fatourechi V, McConahey WM, Woolner LB, et al: Hyperthyroidism associated with histologic Hashimoto’s thyroiditis. Mayo Clin Proc 1971;46:682–689.
6. Davidson RJ, Atrah HI, Sewell HF, et al: Longitudinal study of circulating gastric antibodies in pernicious anaemia. J Clin Pathol 1989;42:1092–1095.
7. Harvey RF, Bradshaw MJ, Davidson CM, et al: Multifocal gastric carcinoid tumours, achlorhydria, and hypergastrinaemia. Lancet 1985;1:951–954.
8. Dittmar M, Kahaly GJ: Polyglandular autoimmune syndromes: immunogenetics and long-term follow-up. J Clin Endocrinol Metab 2003;88:2983–2992.
9. Shimomura H, Nakase Y, Furuta H, et al: A rare case of autoimmune polyglandular syndrome type 3. Diabetes Res Clin Pract 2003;61:103–108.
10. Ahn MJ, Han D, Park YJ, et al: A case of type IIa early gastric cancer developed in pernicious anemia. J Korean Med Sci 1998;13:81–84.