CASE REPORT
Apathetic thyrotoxicosis presenting with diabetes mellitus

Resham R. Poudel, MBBS1*, Bipin Belbase, MBBS1, Bishal Belbase, MBBS1 and Nisha K. Kafle, BPH2

1Department of Medicine, Institute of Medicine, Kathmandu, Nepal; 2Department of Public Health, Institute of Medicine, Kathmandu, Nepal

Apathetic form of thyrotoxicosis occurs in the elderly who can present with features of hyperglycemia, hypothyroidism, depression, or an internal malignancy. A clinical suspicion and timely diagnosis of hyperthyroidism is needed to define the correct etiology of existing problems, and to prevent grave complications. We discuss an 84-year-old woman who presented with fatigue and uncontrolled diabetes due to apathetic thyrotoxicosis.

Keywords: apathetic; elderly; diabetes; hyperglycemia; thyrotoxicosis

*Correspondence to: Resham R. Poudel, Department of Medicine, Institute of Medicine, Kathmandu, Nepal, Email: poudelresham@gmail.com

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The clinical presentation of hyperthyroidism in some elderly is similar to that seen in hypothyroidism, and can be obscured by other existing diseases such as diabetes. Only a quarter of elderly hyperthyroid patients have typical symptoms and this incidence falls with increasing age (1). In 1931, Lehey described a distinct form of thyrotoxicosis characterized by lethargy as the main symptom, with tired and disinterested patients who did not react well to stress; and this presentation was termed 'apathetic thyrotoxicosis' (2). It is a unique manifestation of hyperthyroidism in which the characteristic mental and physical activation of hyperthyroidism are absent and the chief clinical features are weakness, apathy, and depression; therefore, a diagnosis of thyrotoxic crisis can be missed with consequent fatal outcome (2). The aim of this case report is to review a form of hyperthyroidism that can be confused with hypothyroidism or depression, or may be a secondary cause of diabetes.

Case presentation
An 84-year-old Asian woman with 1 year history of type 2 diabetes on metformin presented to diabetes clinic with deranged serum glucose [Fasting: 140(70–110 mg/dL) and 2-hour postprandial: 147(< 140 mg/dL)]. She complained of extreme weakness, fatigue, forgetfulness, somnolence, and a weight loss of 10 kg (22 lbs) during 1 year duration. She denied increased sweating, heat intolerance, change in bowel habits, or any other symptoms suggestive of thyrotoxicosis. She had a thin built (BMI: 16 kg/m²), and exhibited listlessness, delayed reaction, apathy, tachycardia (108/minute) and hypertension (180/90 mm Hg). She also had diffuse, waxy thickening of skin involving pretibial area and dorsum of the foot with peau d’orange appearance (Fig. 1); however, there were no signs of thyromegaly or ophthalmopathy. Biochemical evaluation revealed thyrotoxicosis [T₃: 338.59(60–181 ng/dL), T₄: 19.5(3.2–12.6 μU/dL), TSH: < 0.01(0.35–5.50 μU/ml)] and hypocholesterolemia [total Cholesterol: 135 (150–240 mg/dL), HDL: 30 (30–70 mg/dL), LDL: 65 (< 160 mg/dL)]. The liver and kidney function tests were normal. EKG showed sinus tachycardia. Treatment with carbimazole and propranolol improved her symptoms, and her glucose levels returned to normal. Metformin was gradually tapered and the result was normal glucose tolerance without any glucose-lowering therapy. Application of topical corticosteroid for the pretibial myxedema produced gradual improvement in her skin texture.

Discussion
Hyperthyroidism and diabetes can co-exist; however, hyperthyroidism itself may cause hyperglycemia in such patients. Excess thyroid hormone can induce glucose intolerance by increasing the hepatic glucose output via glycogenolysis and gluconeogenesis (3), and by lowering both insulin secretion and peripheral insulin sensitivity (4). Diabetes and hyperthyroidism can have quite similar presentation, so thyrotoxicosis can be missed unless screened for specifically. In a patient with both the
conditions concurrently, an oral glucose tolerance test should be done after correction of thyrotoxicosis, before considering a definite diagnosis of diabetes.

After considering the weight loss attributable to hyperglycemia/diabetes, the first clinical impression in this patient was hypothyroidism. However, the picture of lethargy, slowness, weight loss, and apathy combined with low TSH and high T₄ was compatible with apathetic hyperthyroidism. In this condition, the core presentation of apathy and depression is associated with severe muscle wasting and weight loss, dry skin, mild tachycardia, arrhythmias, and often congestive cardiac failure (5). Hand tremor and ophthalmopathy typical of Graves’ disease are absent, and the thyroid gland if palpable is minimally enlarged (5). Although giving every appearance of apathy, the metabolic effect of the disease from excess thyroid hormone is severe as seen in our patient: hypertension (increased β receptor synthesis, positive inotropic, and chronotropic effect on heart), hyperglycemia, and hypocholesterolemia (increased LDL receptor synthesis). Pretibial myxedema due to dermal deposition of excess glycosaminoglycans may be seen on the lower legs, feet, and particularly the shins. The psychological aspects are probably related to increased levels of thyroxine and its effect on the nervous system. The elderly might have a reduced capacity to react to elevated thyroid hormones (2).

The disease may remain atypical throughout its course; these patients under usual conditions do not appear extremely ill, but under stress may quietly sink into coma and die a relaxed death without activation, unlike the classic thyrotoxic patient who goes into crisis (1, 6). The etiology of the disease is unknown. Greater age, increased corrected calcium level, decreased TSH level, increased FT4, decreased FT3/FT4 ratio, increased bone-specific alkaline phosphatase, and increased ALT (alanine aminotransferase) may be significant in differentiating apathetic thyrotoxicosis from typical hyperthyroidism, which may aid in accurate diagnosis and treatment (7). Early detection and treatment can help in reducing morbidity and mortality (8).

**Conclusion**

Thyrotoxicosis can both co-exist with and cause diabetes. Absence of hyperkinetic motor activity, hand tremor, and ocular signs of Graves’ disease can sometimes mislead the diagnosis of hyperthyroidism. Diabetes itself requires a screening for thyroid function, and when associated with apathy, weight loss and mild tachycardia in an elderly patient gives a strong indication for thyroid function testing to look for apathetic thyrotoxicosis.

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