HIDDEN IN PLAIN SIGHT: HYPERTHYROIDISM SHROUDED AS GASTROINTESTINAL DISTRESS IN A DIABETIC PATIENT.

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Abstract

Thyroid hyperfunction usually manifests with typical symptoms such as palpitations, fatigue, heat intolerance, excessive sweating and polydipsia. Atypical presentation with gastrointestinal disorders in a known diabetic patient in a resource-poor environment could lead to misdiagnosis. Delay in diagnosis and treatment may occur due to a lack of classical symptoms of hyperthyroidism occurring on a background of immunosuppression due to diabetes mellitus (DM) in an environment where infectious causes of gastrointestinal symptoms abound. We report a case of a 53-year-old, known DM patient with no prior history of hyperthyroidism, who presented with spurious diarrhoea that eventually led to the diagnosis of hyperthyroidism.

The report highlighted the importance of recognition of thyroid disorder in DM in the midst of confounding symptoms. It further emphasized that diarrhoea can present as a lone clinical feature of thyroid hyperfunction in some patients. Furthermore, it underscored the need for TSH levels monitoring after commencement of metformin therapy in diabetic patients.

Keywords: Hyperthyroidism, Diabetes Mellitus, diarrhoea, Type 2 Diabetes Mellitus, metformin

Introduction

Thyroid disorders(TD) often coexist with a certain degree of insulin resistance and hyperglycaemia. DM and TD are two closely associated disorders. Hence, TD is more common in patients with Type 2 diabetes mellitus (T2DM) than in the general population, a bi-directional relationship exists between them,each exacerbating the other's clinical courses. A higher prevalence of TD was observed in the United States among DM compared with those without, especially in patients with positive anti-thyroperoxidase antibodies [1]. On the other hand, few studies assessed the prevalence of TD among T2DM patients in Nigeria. In a recent study, 21.4% patients with T2DM in a rural health facility in Nigeria had abnormal thyroid function profiles[1]. The increasing incidence of T2DM may likely be compounded by reports of the coexistence of TD with DM [2].

Diarrhoea may be a symptom of a systemic disease, like diabetes or hyperthyroidism [3], and both conditions are risk factors for diarrhoea[4]. This study reports a case of a 53-year-old, known DM patient without a prior history of hyperthyroidism, who presented with non-specific gastrointestinal symptoms that eventually led to the diagnosis of hyperthyroidism. This aims to illustrate the non-specific presentation of hyperthyroidism and the need for high index of suspicion by clinician.

Case Presentation

A 53-year-old black woman known hypertensive for two- years and diabetic for one-year who presented with passage of loose stool of 5 days duration. The stool was non-bloody, non-mucoid and there was no associated tenesmus. The average number of bowel movements was four times per day over the period. She also had generalized body weakness and progressive unintentional weight loss of over 6 months duration prior to presentation . Her previous body weight of 98 kg against her current weight of 70 kg. She is a teacher, uses a reading glass,and has no other past medical history of note. She had no history of cough, breathlessness, chest pain, vomiting, or swelling on any part of the body. Also, there was no dysuria, anorexia, polyuria nor polyphagia, but she had blurred vision. There was no neck swelling, no bulging eyes nor excessive sweating. Physical examination revealed no notable findings except for a reduced muscle bulk and a regularly, irregular heart rate. An impression of acute gastroenteritis of an unknown cause was made and she was admitted for resuscitation and management.

Serum samples for urea and creatinine, as well as stool samples for routine rapid test for cholera, were collected and sent for analysis but the results were unremarkable. ECG showed a pulse rate of 107bpm, sinus rhythm, Left axis deviation, normal QRS, P wave and T wave, and no bundle branch block.

Initially, oral hypoglycemics and antihypertensives were administered, but upon reassessment three hours later, antihypertensives were halted due to low blood pressure (100/50 mmHg) and bradycardia (PR 20 cpm). Intravenous Ringer's lactate was switched to normal saline every six hours. Despite discontinuing antihypertensives, the patient's blood pressure dropped further to 80/40 mmHg the next day, with persistent diarrhoea and palpitations, raising concern for hypovolemic shock and hyperthyroidism. Thyroid function tests confirmed hyperthyroidism, leading to the initiation of Carbimazole 5 mg daily alongside continued IV fluid monitoring. Third day into the admission, diarrhoea resolved, blood pressure normalized to 110/80 mmHg, patient was discharged with ongoing management for hyperthyroidism and DM as an outpatient and on follow up.

Table 1: Thyroid function tests

	TSH (IU/ml)	Free T4 (µg/dl)	Free T3 (ng/ml)	FBG	Chol	TG	HDL-c	LDL-c	Carbimazole (dose)
Normal range	(0.4-7.0)	(0.8-2.0)	(1.4-4.2)		< 5.14	< 2.26	≥ 0.91	< 3.36	
Day 3	0.1	9.2	8.8	5.4	3.05	0.84	1.54	1.12	5mg o.d
12 weeks	0.0	3.3	6.3						10mg b.d
52 weeks	0.0	2.0	4.6						10mg o.d

Discussion:

Thyroid hormones play a major role in regulating metabolism, impacting carbohydrate metabolism and pancreatic function. However, the release of thyroid hormones, primarily controlled by the thyroid itself, is significantly influenced by DM at the hypothalamic level[5]. This influence extends to the conversion of T4 to the biologically active T3 form in peripheral organs. Patients with DM often exhibit reduced T4-to-T3 conversion due to impaired TSH response to TRH stimulation. It is important to recognize the interdependence between TD and DM which is crucial for clinicians to guide optimal screening and management of these conditions.

Hyperthyroidism has long been recognized as a cause of hyperglycaemia. The prevalence of TD in patients with DM in studies from Europe and Saudi Arabia ranges from 4% to 20%[6]. Recent findings indicate a higher incidence of severe hyperthyroidism in newly diagnosed cases among females compared to males, with females exhibiting a significantly elevated relative risk [6].

Regarding screening protocols, the American Thyroid Association recommends initiating serum TSH assessment at age 35 and repeating every five years thereafter [7]. However, establishing a screening program for TD in patients with T2DM remains controversial due to insufficient evidence regarding the specific screening tests, screening intervals, and cost-effectiveness ratios. Despite this, the American Diabetes Association recommends thyroid palpation for all diabetic patients and serum TSH evaluation in adults over 50 years of age and those with dyslipidemia[8]. Conversely, the British Thyroid Association, recommends thyroid function tests in type 1 diabetes mellitus (T1DM) only when there is a suspicion of an autoimmune thyroid diseases [9], with routine annual testing not recommended for patients with T2DM [9]. However, in the Nigerian context where health expenses are often paid out of pocket, implementing such policies may be challenging due to limited funds.

Despite these differing recommendations, the benefits of a screening program for thyroid dysfunction in patients with T2DM are evident. Asymptomatic TD is commonly observed in these patients and can compromise metabolic control, increasing the risk of cardiovascular events[10]. Timely screening could mitigate these risks and prevent the progression of mild subclinical TD.

Coexistence of TD and T2DM has been attributed to many factors some of which has made the diagnosis of TD in patients with T2DM difficult. Some oral antidiabetic drugs can interfere with the evaluation of serum TSH levels, while hyperthyroidism increases the endogenous glucose production and insulin requirement, and reduces hepatic insulin sensitivity[11]. Hyperthyroidism often presents with elevated fasting or postprandial insulin and proinsulin levels, alongside increased free fatty acid concentrations. For instance, patients with subclinical or overt hyperthyroidism expresses increased glucose and insulin responses following an oral glucose tolerance test. Furthermore, hyperthyroidism is linked to increased insulin degradation and β-cell apoptosis, contributing to glucose intolerance and hyperglycemia. Therefore, this leads to a vicious cycle, hence, peripheral glucose transport and tissue utilization are increased in hyperthyroidism with peripheral insulin resistance [11].

In patients with hyperthyroidism, the insulin-stimulated glucose oxidation rate is increased in both muscle and adipose tissue. This elevation in glucose levels within peripheral tissues prompts an augmented metabolism of glucose through the nonoxidative pathway. Specifically, due to muscle insulin resistance, glucose is primarily processed via glycolysis, resulting in the generation of lactic acid. This lactic acid is released into the circulation, ultimately returning to the liver, where it contributes to an increase in hepatic glucose production[12]. Furthermore, peripheral insulin resistance can also be due to the secretion of hyperthyroidism-induced proinflammatory mediators (IL-1, TNFa, and several adipokines) by adipocytes [13]. Therefore, hyperthyroidism is associated with increased energy expenditure and weight loss despite increased appetite and food intake, reduced cholesterol levels, increased lipolysis, and gluconeogenesis. Insulin resistance, which is associated with hyperthyroidism, can be improved with the restoration of euthyroidism. Hence, patients with hyperthyroidism can have an increased risk of severe hyperglycemia , and exacerbation of preexisting DM[14].

In the index case, there was a remarkable reduction in weight prior to presentation which occurred over the period she was diagnosed to be diabetic and probably may have had TD even before the diagnosis

of DM was made. Possibly, dysglycemia resulted from impaired thyroid function as no screening for TD was done.

Diarrhoeal symptoms are relatively common in people with diabetes yet clinical experience suggests the symptoms may often not be volunteered unless asked about specifically. Diarrhoea as the only symptoms in hyperthyroidism was reported in a case report [14]. Therefore, we suggest that diarrhea presentation in a diabetic patient should be reviewed meticulously and thyroid function be screened during clinical consultations in patients with DM. Multiple pathogenic mechanisms have been implicated including autonomic neuropathy, bacterial overgrowth, and pancreatic exocrine insufficiency being the most important underlying aberrations. However, diabetic diarrhea does not have a uniform and unequivocal pathogenesis. The diagnosis depends on judicious clinical assessment accompanied by a stepwise laboratory evaluation, which allows the differentiation of idiopathic diabetic diarrhea from the many other causes of diarrhea that can occur in diabetic and non-diabetic patients.

Consider searching for underlying reversible or treatable causes such as medications (e.g., metformin, GLP-1 agonists), foecal incontinence masquerading as diarrhea (due to decreased anorectal sensation and reduced resting sphincter tone, if there is not overflow incontinence from constipation),small intestinal bacterial overgrowth, autonomic neuropathy, or rarely pancreatic insufficiency, or in T1DM, celiac disease [15]. It is also important to rule out hyperthyroidism as a potential cause. In this case, the patient's diarrhoea only reduced following diagnosis of hyperthyroidism and treatment with carbimazole.

Some antidiabetic drugs can affect thyroid function and impact the hypothalamo-pituitary-axis. Therefore, the use of these drugs in patients with T2DM can influence the evaluation of serum TSH and thyroxine levels. Metformin, Sulfonylureas, Thiazolidinediones and insulin have been reported to have significant effect on thyroid function. Metformin which is one of the most commonly prescribed oral hypoglycaemics has TSH lowering effect which can be observed in diabetic patients with thyroid disorder. Metformin, an oral hypoglycaemic biguanide, is the first drug of choice for treatment of patients with T2DM because of its safety profile, efficacy in controlling glycaemic levels, and reasonably good compliance and tolerance. The main side effect of metformin is gastrointestinal intolerance (diarrhea, nausea, dyspepsia, and abdominal pain), which may be observed in up to 28 % of patients leading to discontinuation of therapy in < 2% of patients [16]. The index patient has been on metformin, one of the confounding factors that delayed the diagnosis. Initially, the diarrhoea was attributed to diabetic gastroenteropathy, infections or side-effects of her medication.

The initial diagnosis of hyperthyroidism is frequently overlooked, particularly in cases where DM coexists, especially if accompanied by gastrointestinal symptoms. Recognizing TD in diabetic patients is crucial to initiate early treatment and prevent the adverse synergistic effects of these two endocrine disorders on metabolic stability. Untreated TD can compromise the metabolic control of diabetics, leading to significant repercussions on both conditions' outcomes. Despite the diagnostic challenges posed by the influence of DM on evaluating concurrent TD, screening diabetic patients for TD can facilitate early diagnosis and improve treatment outcomes.

Learning Point:

a. TSH levels should be monitored after beginning metformin treatment in diabetic patients.
b. TD in patients with diabetes mellitus, should be readily recognised.
c. Diarrhoea can be a lone symptom of hyperthyroidism in a patient.

Limitations:

This case was managed in a poor resource setting ,patient could not afford to do TRAb and Thyroid stimulating immunoglobulin to confirm the subtype of hyperthyroidism.

Recommendation:

We recommend high index of suspicion of thyroid disorder in assessment of non-specific symptoms especially in gastrointestinal distress in DM and also propose that TSH should be monitored on commencement of metformin treatment .

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