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Graves' Thyrotoxicosis Presenting as Schizophreniform Psychosis: A Case Report and Literature Review

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Abstract

Psychosis, as the first presentation of thyrotoxicosis, is extremely rare. Consequently, it is often misdiagnosed as a primary psychiatric disorder, especially in developing countries with poor healthcare facilities. Owing to the high level of illiteracy and lack of knowledge, it is fairly common to ascribe many illnesses to spiritual attacks in Nigeria and other African countries, especially when the disease is rarely seen or is associated with psychiatric manifestations. Herein, we present the case of a teenage female Nigerian and review the literature on this subject.

Keywords: Case report, Graves' Disease, Thyrotoxicosis, Hyperthyroidism, Psychosis, Nigeria

1. Introduction

Similar to other parts of the world, Graves' disease is the most common cause of thyrotoxicosis in Nigeria (1). Subtle neuropsychological symptoms such as anxiety, irritability, tremor, and insomnia are not uncommon in severe thyrotoxicosis, regardless of the cause. However, psychosis, as the first clinical presentation of Graves' disease, is extremely rare. The first case of thyrotoxic psychosis was described over a century ago (2). Since then, many other cases have been reported, mostly from developed countries (3-5), while only one case of psychosis associated with Graves' disease has been reported in Nigeria (6).

Superstitious beliefs about the causes of psychiatric disorders abound in Nigeria and other developing countries (7, 8). Mental diseases are often wrongly ascribed to witchcraft, evil spirits/demons, and nemesis. Consequently, treatment of most psychiatric disorders is first sought in unorthodox centers, such as herbal homes and prayer houses, leading to delayed patient admission and management with poor outcomes.

Herein, we report an unusual case of a 16-year-old female Nigerian with schizophreniform psychotic disorder, associated with Graves' disease, who was believed to be possessed by demonic spirits and was kept in a prayer house ostensibly for "spiritual deliverance".

2. Case Presentation

A 16-year-old female student was admitted to the hospital with a two-month history of increasing irritability and insomnia and a three-week history of aggressive behaviors, irrational talking, and poor personal hygiene. She was said to have become unfriendly, verbally abusive, and physically aggressive, resulting in her withdrawal from school. She had no prior history of psychoactive substance abuse and had never been diagnosed with mental disorders in the past. A history of excessive sweating was reported in the patient, while no weight loss, fever, or sore throat was notable.

The patient's condition had worsened over time, and she was said to have started seeing strange figures and hearing strange voices about two weeks prior to presentation. She reportedly said that some white-clad people were mocking her, saying that she was ugly and threatening to kill her. It was reported that she was screaming constantly, rebuking her "assailants" and invoking the "holy ghost fire" upon them. Following this development, she was labeled as being possessed by demonic spirits by her family and relatives and was taken to a prayer home, ostensibly for "spiritual deliverance".

It was reported that she had been repeatedly beaten by the priest, presumably to drive away the demon(s), but all to no avail. She was the third child in a monogamous family of seven children. She lived with her parents and siblings in a rural settlement, and there was no family history of psychiatric diseases; it should be mentioned that

the family was deeply religious.

Physical examination revealed an unkempt, diaphoretic, young female with bilateral exophthalmos and lid retraction (Figure 1). She had a soft, diffuse, smooth, and non-tender goiter, warm moist palms, regular tachycardia (112 beats/min), and normal blood pressure. Mental state examination revealed a restless and uncooperative patient with poor eye contact. Also, speech was coherent but irrelevant. Perception examination revealed visual hallucinations, auditory hallucinations (in the second person), and persecutory delusions. Cognitive assessment was unremarkable, except that she had no insight of her circumstances.

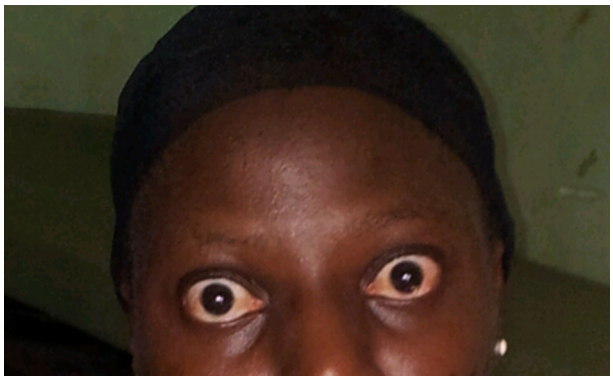

Figure 1. Bilateral Proptosis and Lid Retraction in the Index Patient

A provisional diagnosis of schizophreniform psychosis, secondary to Graves' disease with thyrotoxicosis was established. She was admitted to the hospital and was administered intramuscular haloperidol for one week (10 mg daily), followed by haloperidol (5 mg nocte, discontinued after 10 days), propranolol (80 mg b.i.d.), carbimazole (15 mg t.i.d.), prednisolone (20 mg daily), and folic acid (5 mg daily) tablets after collecting blood specimens for hematological and thyroid function tests. Neck ultrasonography and electrocardiogram (ECG) were deferred until the patient was calm.

The investigation results showed markedly elevated thyroid hormone and suppressed thyroid-stimulating hormone (TSH) levels in keeping with primary thyrotoxicosis (Table 1). Thyroid auto-antibody assay could not be performed due to financial constraints. Neck ultrasonography revealed a non-nodular bilobar goiter (right: 4.3 × 3.0 cm, left: 3.5 × 2.4 cm). Hematological investigations did not reveal any abnormalities, while ECG showed sinus tachycardia.

The patient showed marked improvement in psychotic symptoms within two weeks of therapy and complete resolution in the fourth week. She was discharged for follow-ups at both endocrine and psychiatric outpatient clinics. Repeat thyroid function tests within eight weeks showed a remarkable improvement in the hormonal profile (Table 1), and her medications were then adjusted accordingly. No re-emergence of psychotic features was reported in her last clinic visit (one year after hospital discharge), and she is euthyroid at present.

3. Discussion and Literature Review

Graves' disease is an autoimmune disorder of the thyroid gland, typically characterized by a diffuse goiter, hyperthyroidism, and circulating thyroid auto-antibodies in the blood. Although thyroid auto-antibody assay could not be carried out in our index case due to financial constraints, diagnosis of Graves' thyrotoxicosis was supported by the patient's young age, female sex, diffuse non-nodular goiter, bilateral exophthalmos, and markedly elevated level of free thyroid hormones.

In Nigeria, Graves' disease accounts for over 80% of all cases of thyrotoxicosis, with a male-to-female ratio of 1:5 (1). Other relatively common causes of thyrotoxicosis, such as subacute thyroiditis and nodular goiters, were also considered in the index patient. However, the patient did not have any constitutional symptoms (i.e., fever, malaise, and myalgia), sore throat, or tenderness of the thyroid gland, which are the hallmark of subacute granulomatous thyroiditis (9).

Moreover, the present case had no leukocytosis or elevated inflammatory markers. Distinction between subacute lymphocytic thyroiditis (painless) and other types of autoimmune thyroiditis such as Graves' disease can be difficult in the absence of radio-iodine uptake test, which could not be carried out in our index case. However, the presence of proptosis, which was observed in our patient, is exclusively described and considered pathognomonic in Graves' disease (10).

3.1. Epidemiology of Psychiatric Disorders in Graves' Disease

Not uncommonly, patients suffering from Graves' disease and other forms of thyrotoxicosis exhibit subtle neuropsychiatric abnormalities, including irritability, anxiety, sleep disturbances, confusion, mood changes, and memory deficits. However, psychosis, as the first presenting feature of thyrotoxicosis, is extremely rare. Since Von Basedow described the first case of manic psychosis in a patient with exophthalmic goiter over a century ago (2), a few cases have been reported, including major depressive (11), manic (12), paranoid (3), and schizophreniform disorders (4-6). Indeed, thyrotoxicosis is now a recognized cause of organic psychosis. However, only one case of thyrotoxic psychosis has been reported in Nigeria (6).

Table 1. Hormonal Profile of the Patient at Presentation and Follow-Up

Hormones	Test Results			Reference Range
	At Presentation	At 8 weeks	At 9 months	
Free T3, pmol/L	19.4	11.4	5.5	3.8 - 6.0
Free T4, pmol/L	33.1	24.7	11.0	7.2 - 16.0
TSH, mIU/L	< 0.05	0.1	1.3	0.37 - 3.50

Abbreviations: TSH, Thyroid-stimulating hormone; T3, Tri-iodothyronine; T4, Thyroxine.

Psychosis generally occurs in less than 1% of patients with thyrotoxicosis, and the majority of patients have a previous diagnosis of one or more mental disorders, unlike our index case (13). The duration and severity of thyrotoxicosis, as well as the patient's susceptibility to psychiatric disorders, are the main determinants of the development of psychosis. Most cases have been reported in thyrotoxicosis due to Graves' disease and multi-nodular goiter. Overall, only one case of psychosis has been reported in subacute thyroiditis (14) and postpartum thyroiditis (15). The severity of psychiatric manifestations often reflects the severity of thyroxinemia; also, these manifestations typically remit with successful treatment of the thyrotoxic state (13).

3.2. Pathophysiology of Psychiatric Manifestations in Thyrotoxicosis

The exact mechanism underlying the development of psychosis in Graves' disease and other causes of hyperthyroidism is not well understood. However, a large number of thyroid hormone receptors are localized in the brain, especially in the limbic system (hippocampus and amygdala). These receptors affect a variety of functions including behavior, mood, and long-term memory (16). It is speculated that excess thyroid hormones affect the activities of neurotransmitters such as serotonin and dopamine in this area of the brain and possibly account for the neuropsychiatric abnormalities in thyrotoxicosis. Thyroid hormones also modulate the beta-adrenergic response to catecholamines in the central nervous system and may contribute to psychotic behaviors in thyrotoxic patients (17).

It is noteworthy that hyperthyroxinemia can be also a consequence of psychiatric disorders. In a study on 1,584 psychiatric outpatients in Kaduna, Nigeria, Obembe and Abengowe (18) reported 0.6% prevalence of hyperthyroxinemia. This type of hyperthyroxinemia is characterized by a modest and often transient elevation of thyroid hormones and TSH in the upper range of normal (19). This alteration in thyroid function can occur in other non-thyroidal disorders and has been termed as "euthyroid sick syndrome".

3.3. Treatment of Thyrotoxic Psychosis

In thyrotoxic psychosis, improvement of neuropsychiatric symptoms generally parallels the amelioration of thyrotoxicosis through standard methods, including the administration of anti-thyroid drugs and beta-adrenergic blockers (5). Psychotropic drugs such as lithium, antidepressants, benzodiazepines, and antipsychotics are usually not indicated as the primary treatment option for thyrotoxic psychosis. However, in patients who are severely psychotic, dopamine receptor blockers or phenothiazines may be employed for a short period and discontinued following the resolution of symptoms. In our patient, the presence of psychomotor agitation necessitated the administration of haloperidol. More radical approaches, such as radioactive ablation and surgery, may be required if resolution of thyrotoxicosis is not achieved with medical management alone.

3.4. Conclusions

We presented a rare case of secondary psychosis due to unrecognized Graves' thyrotoxicosis in a female teenager. To the best of our knowledge, this is the first reported case of thyrotoxic psychosis in a teenage Nigerian. Although medical attention was sought considering the more dramatic psychotic manifestations, presence of classical features, such as exophthalmos, diffuse goiter, and features of hypermetabolic rate, heightened the clinical suspicion of Graves' disease, while hyperthyroxinemia was confirmed biochemically. Absence of a prior history of psychiatric disorders and quick resolution of psychotic features following treatment for thyrotoxicosis supported the diagnosis of thyrotoxic psychosis.

There were obvious challenges in the management of the present case, which are worth mentioning. First, it should be noted that Graves' disease remains only a clinical diagnosis in this patient, as thyroid auto-antibody assay could not be performed due to financial constraints.

Secondly, besides the severity and probably long duration of thyrotoxicosis, the cause of psychotic manifestations in this patient remains unknown in the absence of any identifiable underlying predisposition to psychiatric diseases. Thirdly, this case greatly underscores the negative impact of ignorance and superstitious beliefs on health. Our patient suffered from a purely organic and highly treatable condition, but became a victim of superstitious beliefs; therefore, both poverty and ignorance were prominently influential in this case. Overall, our index case highlighted the need for improved public health education on good health-seeking behaviors, especially in rural communities of Nigeria.

Footnote

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