African Journal of Tropical Medicine and Biomedical Research (AJTMBR)

The Journal is the Official Publication of the College of Health Sciences, Delta State University, Abraka, Nigeria.

ISSN: 2141-6397

Vol. 8, No. 1, June 2025

Gilles De La Tourette syndrome in one of a set of phenotypically identical twins- a case report with literature review.

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ABSTRACT

Introduction: Gilles de la Tourette's syndrome (GTS) or Tourette's syndrome (TS) is a neurodevelopmental/ neuropsychiatric movement disorder that is characterised by one or more vocal/phonic tics and multiple motor tics. It has a childhood onset and a diagnosis is usually made when symptoms have been present for greater than a year.

Case presentation: We report a 24year old female, one of a pair of phenotypically identical twins who presented with history of verbal and motor tics with associated history of social difficulties and obsessive compulsory disorder. Symptoms were first noticed at the age of nine. There is no known family history of tics and none of these symptoms were present in her twin sister.

Discussion: Aetiopathogenesis of GTS include genetic factors as well as environmental factors such as infections, neuro-immunological factors, and prenatal/ peri-natal difficulties. A younger age of onset is associated with a greater severity of symptoms, while females with GTS are less likely to undergo remission of tics during adolescence, and may experience greater functional interference from tics than males

Conclusion: Persons with GTS may experience learning and cognitive impairments, hence patients presenting with tics should be adequately evaluated for this condition as this will help bridge the gap in delay of diagnosis and management.

Key words: Tourette Syndrome, Tics, Neuropsychiatry, Neurodevelopmental, Phenotypically Identical Twins.

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INTRODUCTION

Gilles de la Tourette's syndrome (GTS) or Tourette's syndrome (TS) is a neurodevelopmental/ neuropsychiatric movement disorder that is characterised by multiple motor and one or more vocal/phonic tics. It has a childhood onset and a diagnosis is usually made when symptoms have been present for greater than a year.[1-3] The condition is named after a French doctor, Georges Gilles de la Tourette, who in an 1884 article described several movement disorders that he believed were similar to each other but different from chorea. In another article in 1885, he further identified 9

subjects who suffered from a disorder distinguished by involuntary movements, strange uncontrollable sounds, echolalia, echopraxia, and coprolalia.[4]

Tics describe brief, sudden and repetitive sounds or movements which are similar to voluntary actions and belong to the spectrum of hyperkinetic movement disorders. Tics also include more complex repetitive behaviours such as echolalia, palilalia, and coprolalia.[5] Tics have been defined as involuntary, recurrent, sudden, rapid, non-rhythmic movements (motor tics) or vocalizations (vocal/phonic tics).[6] Tics are the most common type of movement disorder in children and may occur in bouts up to many times in a single day. The prevalence may range from 1-29% of the population based on the diagnostic criteria, study population, study design and methodology. Some studies give a range of 0.3-1%.[7,8] Tics are often preceded by a subjective unpleasant feeling of 'inner tension of wanting to move' which is temporarily relieved by the appearance of tics. The presence of these sensory symptoms or 'premonitory urges' to tic is important in differentiating tics from other repetitive behaviours such as functional jerks, myoclonus, mannerisms and stereotypies.[6]

The diagnosis of GTS is often straight forward, however the condition is usually not recognised with many patients not correctly diagnosed for many years after the onset of symptoms. Delayed access to standard treatment for the tics and comorbidities such as obsessive-compulsive disorder (OCD) and attention deficit/ hyperactivity disorder (ADHD) may negatively impact quality of life and hamper psychosocial development. Hence, early recognition of tics as well as neuropsychiatric comorbidities are mandatory in the treatment of these patients.[8-12]

GTS is believed to be inherited in most cases, however the genetic mechanisms are complex. It is believed that brain development is affected by general neurodevelopmental genes following which specific GTS gene/genes further affect the phenotype. Other aetiopathogenetic postulations may include environmental factors such as infections, prenatal and peri-natal difficulties including hypoxia/ischaemia, androgen influences, exposure to heat and fatigue, maternal smoking and neuro-immunological factors.[3,13,14]

GTS is a complex heterogenous disease and several studies have demonstrated genetics in its aetiology and its comorbidity with disorders such as ADHD, autism spectrum disorder (ASD) and OCD, however the results have not been consistent. The phenotypic expression in GTS is affected by environmental factors and immune responses. GTS has a complex inheritance pattern in which several genes and loci have been correlated with it such as the Slit and Trk-like 1 (SLITRK 1) and histidine decarboxylase (HDC) which have been identified in Genome-wide linkage studies (GWLSs). Copy number variations are considered another significant source of mutation in GTS and may result from chromosomal deletions or duplications due to polymorphisms.[13-15]

Studies have demonstrated that GTS is familial. A twin study by Price et al. comprised of 43 pairs of same-sex twins, in which at least one co-twin had GTS, 30 pairs were likely monozygotic and 13 were likely dizygotic. Concordances for TS were 53% for monozygotic and 8% for dizygotic pairs. These concordances were consistent with genetic aetiology. Considering that only 53% of the monozygotic twins were fully concordant indicates other nongenetic factors affect expression of GTS. The study was inconclusive on whether some monozygotic twins with concordant co-twins are etiologically different

from those who are discordant. Segregation analysis studies in affected families have shown that GTS is manifested in an autosomal dominant pattern with variable phenotypes, including chronic tic disorders, and OCD. More recent studies indicate polygenic or oligogentic inheritance models.[13,16,17]

Neuroanatomical and brain circuitry have been implicated in GTS with most evidence being that of cortical thinning and a reduction in the size of the caudate nucleus.[3] It is generally believed that patients with GTS have cortical–striatal–thalamic–cortical (CSTC) circuits dysfunction with specific basal ganglia dysregulation. Matrisomes which are subsets of striatal neurones are thought to become abnormally active in inappropriate contexts, resulting in the disinhibition of thalamo-cortical projections that in turn lead to tics. Activity leading to stereotyped repetition of behaviour is inappropriately reinforced by activity-dependent dopamine.[7,18]

Worbe et al. in a study on distinct structural changes which underpin clinical phenotypes in patients with GTS demonstrated that these patients had reduced cortical thickness in their premotor, motor, prefrontal and lateral orbitofrontal cortical areas. The Yale Global Tic Severity Scale was used to assess the severity of tics and these correlated negatively with cortical thinning in these regions, as well as in temporal and parietal cortices. The pattern of cortical thinning was found to differ among the clinical subgroups of patients. Cortical thinning was mostly found in primary motor regions in patients with simple tics, while the thinning extended into larger prefrontal, premotor and parietal regions in patients with simple and complex tics. Patients with associated obsessive–compulsive disorders had reduced cortical thickness in the anterior cingulate cortex with altered hippocampal morphology.[19] GTS is a unique condition that is usually under-recognized and/ or misdiagnosed. There is paucity of reports of this condition especially in sub-Saharan Africa, hence we present this case presentation with discussion.

CASE REPORT

A case of a 24- year old female, one of a phenotypically identical set of twins, who presented at our neurology clinic with history of repetitive abnormal production of sounds and occasional utterances from the age of 9 years (15 years duration). There was associated history of abnormal body movements over which she had no control. Abnormal sounds were said to range from incomprehensible sounds to repetition of nearby conversations. Mother claimed these symptoms were present at the age of 3 years but were mild. The production of sounds occurs at any time of the day but were worse when she was angry or hungry. Abnormal movements involved all limbs but were more associated with the upper limbs and were small range movements. She had also noted facial grimacing. The sounds and movements were said to resolve spontaneously. There was no history suggestive of seizures or tremors nor history suggestive of head injury prior to onset of symptoms. She gradually learnt to control her symptoms over the years by staying in a quiet environment. Attempts to contain the movements or sounds made her uncomfortable, however she was relieved after performing the movements or utterances.

Symptoms worsened over the years making her to seek treatment at different health facilities with psychiatrists and neurologists, however the treatments were not satisfactory. There was history of sleep disturbances, patient said she was not happy with state of her health status. She couldn't understand how she had these symptoms and her phenotypically identical twin sister had

none. Furthermore, there was no family history of similar symptoms. She had been high performing in primary and secondary school but finished her Ordinary National Diploma (OND) with a third class. While at the tertiary institution, she found herself reluctant to go for classes due to her symptoms. Recently she had learnt to control some of the symptoms to an extent. She was placed on Tab Haloperidol 5mg daily in the past but currently on Tab Olanzepine 5mg daily.

Her blood investigations did not reveal any abnormalties. A brain computed tomography (CT) scan done in the past was normal and a brain magnetic resonance image (MRI) requested for was normal. A diagnosis of Gills de la Tourette's syndrome was made based on her motor and vocal tics. She was counselled along with family members on the diagnosis. She was maintained on Tab Olanzepine 2.5mg daily, was subsequently referred to the psychiatrist for co-management. She is currently on follow up and has been stable.

DISCUSSION

Psychopathology of GTS

GTS is described as a neurodevelopmental disorder with childhood-onset characterized by tics that are usually associated with psychiatric co-morbidities.[19] Enhanced structural connectivity in the white matter tracts linking the thalamus and striatum with cortical structures, including primary motor cortex, primary somatosensory cortex, and supplementary motor area have been demonstrated in patients with GTS and was positively associated with increased motor tic severity.[19,20] In childhood and adolescence, the ratio of boys to girls is typically 4:1, but in adulthood, the ratio of males to females is closer to parity. Hence, this childhood gender bias for boys is attenuated in adulthood. This suggests that females with GTS are less likely to undergo remission of tics during adolescence, and may experience greater functional interference from tics than males. It has been demonstrated that females, when compared to males with GTS, have increased connectivity in CSTC pathways which may result in increased tic severity.[19-21]

GTS is associated with a variety of mental illnesses including OCD, ADHD, sleep abnormalities, learning difficulties, or other behavioural problems. The mechanism by which these other neurological conditions are linked to GTS remains unclear. These comorbid conditions are more likely to cause harm than the tics and will need treatment. ADHD occurs in about 50–75% of children with GTS, this suggests that both may share a common pathophysiology in the basal ganglia circuitry.[12] Anxiety, mood disorders, and other emotional symptoms have long been described in patients with TS or ADHD. Recently, there is increased awareness of the clinical and scientific significance of TS or ADHD combined with anxiety, mood, emotional and behavioural disorders. The occurence of mood and anxiety disorders being high among these patients makes them more susceptible to poor school performance, and delayed socio-psychological development.[13,22]

Clinical features/ Diagnosis

A diagnosis of GTS requires the presence of multiple motor tics such as blinking, mouth pouting, mouth opening, head nodding, and one or more vocal tics which include throat clearing, sniffing, and coughing to be present for greater than a year. The frequently reported mean age of onset of GTS is 7 years, but may range from 2-21 years. The onset of phonic tics usually starts at 11 years. Tics may be classified as simple or complex and may have associated premonitory sensations.

Characteristic features of GTS also include palilalia (repetition of what oneself says), Coprolalia (the involuntary and inappropriate use of obscenities), echolalia (repetition of what others say), echopraxia (repetition of someone else's movements) or echomimia (repetition of someone else's facial expressions) occur in patients usually starting from the age of 15 years, however a younger age of onset is associated with a more severe GTS. Coprolalia occurs in 10-15% of patients, however echophenomena (echolalia, echomimia and echopraxia) and palilalia are fairly common and very characteristic.[23,24]

Tic symptoms, the hallmark of Tourette's syndrome (TS), may simply be fragments of innate behaviour. Hence, the sensory urges that precede tics may explain some of the normal internal cues that are intimately involved in the behavioural sequences. The fractal characteristics of tics which occur over time may be responsible for the waxing and waning course of these disorders. Although tics markedly decline during adolescence, GTS may be associated with emotional, social, and academic difficulties in early adulthood. Long-term adaptive outcomes of individuals with GTS may likely be influenced by co-morbid conditions like OCD and ADHD.[25] Affective disorders are common in patients with GTS, with a lifetime risk of 10%, and a prevalence of 1.8–8.9%. Depressive symptomatology was found to occur in between 13% and 76% of cases of GTS seen at specialist clinics.[26] Other issues associated with tics are those of orderliness, symmetry, counting, repetitive checking, aggression, inappropriate sexual behaviours and religiousity.[1,25]

Management

Symptom reduction, management of precipitants and comorbidities is the primary aim of management of GTS. Pharmacological management mainly involves antipsychotics (haloperidol, risperidone, aripiprazole, quetiapine, pimozide, etc.), benzodiazepine (clonazepam, etc.) and alpha agonists (clonidine, guanfacin). The typical antipsychotics (dopamine receptor antagonists) remain the drugs of choice for the treatment of tics with marked improvement in symptoms. GTS patients may also see improvements in their tics with drugs that have partial dopamine receptor agonist activity such as the new generation of antipsychotics.[1,27]

The presence of OCD as a comorbid condition in GTS may require the use of Selective Serotonin Reuptake Inhibitors (SSRI). Other medications that may be used include oxcarbazepine, tetrahydrocannabinol, atomoxetine, and botulinum toxin. Deep brain stimulation may also be used as a means of treatment. Behavioral management primarily includes desensitization techniques, habit reversal, and relaxation exercises.[1,27]

CONCLUSION

GTS is a heterogenous disease with a combination of varied neurological and psychiatric symptoms. Patients presenting with tics should be adequately evaluated for this condition as this will help bridge the gap in delay of diagnosis and management. Learning and cognitive impairments should be identified early to assist with academic progress and social adjustments.

Author's contribution: OEM is responsible for the conceptualization of the case report and literature review, OEM, AOW, OBN and AEB developed, read, and approved the manuscript.

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Ogbimi EM, Agboro OW, Ogbimi BN, Anyanwu EB . Gilles De La Tourette syndrome in one of a set of phenotypically identical twins- a case report with literature review. Afr. J. Trop. Med. & Biomed. Res. 2025; 8(1) 116-122
https://doi.org/10.4314/ ajtmbr.v8i1.12