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SÍNDROME DE GILLES DE LA TOURETTE E ABUSO DE SUBSTÂNCIAS: RELATO DE UM CASO

SÍNDROME DE GILLES DE LA TOURETTE Y ABUSO DE SUSTANCIAS: REPORTE DE UN CASO

GILLES DE LA TOURETTE SYNDROME AND SUBSTANCE ABUSE: A CASE REPORT

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RESUMO

INTRODUÇÃO: O Síndrome Gilles de La Tourette (SGT) é uma perturbação neuropsiquiátrica complexa caracterizada por tiques motores e vocais, com impacto significativo na qualidade de vida dos doentes. A sobreposição entre os mecanismos neurobiológicos, as comorbilidades e a procura do alívio dos sintomas estão entre os fatores que vulnerabilizam estes doentes para o uso de substâncias.

OBJETIVOS: A propósito da descrição detalhada de um caso clínico, realizar uma revisão e reflexão acerca das possíveis relações entre o SGT e o uso de substâncias.

MÉTODOS: Descrição de um caso clínico de um doente diagnosticado com SGT e uso comórbido de substâncias. Foi realizada uma revisão não sistemática da literatura através de pesquisa bibliográfica nas bases de dados – *Pubmed e Clinical Key – utilizando as palavras-chave: "Tourette Syndrome"; "Substance Abuse"; "Cocaine Abuse" e "Cannabinoid Abuse"*. Não foram aplicadas quaisquer restrições à data de publicação dos artigos pesquisados.

RESULTADOS: Reporta-se um caso clínico de uma doente com SGT diagnosticado aos 11 anos. Um quadro de sintomatologia grave e refratária, caracterizado por tiques motores e vocais, sintomas obsessivo-compulsivos e défice atencional. Um percurso pautado por inúmeros internamentos e abordagens farmacológicas sem resultado, tendo sido necessário o recurso a estratégias de neuromodulação. Em concomitância com o quadro descrito, regista-se um início de consumo de Canabinóides aos 25 anos, descrito pela doente como automedicação e posteriormente de cocaína, aos 29 anos, consumo que mantém até hoje. Os doentes com SGT possuem uma particular vulnerabilidade para o consumo de substâncias, tendo estas efeitos deletérios sobre a sua sintomatologia, nomeadamente a cocaína, anfetaminas e heroína. Contudo, substâncias como os canabinóides, usados frequentemente como automedicação, são reportados pelos doentes como tendo um efeito benéfico sobre os tiques motores e vocais, sendo atualmente propostos como uma possível terapêutica no SGT.

DISCUSSÃO E CONCLUSÃO: A vulnerabilidade para o consumo nos doentes com SGT e ao seu efeito deletério sobre os sintomas, junta-se o efeito positivo descrito em relação a algumas substâncias, tais como os canabinóides. Perante um caso desta complexidade, reveste-se de particular importância uma abordagem holística, atendendo não só aos riscos do consumo, mas também aos possíveis efeitos benéficos, podendo deste modo contribuir para o desenvolvimento de novas vias terapêuticas.

Palavras-Chave: Tourette Syndrome; Substance Abuse; Cocaine Abuse; Cannabinoid Abuse.

RESUMEN

INTRODUCCIÓN: El síndrome de Gilles de La Tourette (SGT) es un trastorno neuropsiquiátrico complejo caracterizado por tics motores y vocales, con un impacto significativo en la calidad de vida de los pacientes. La superposición entre los mecanismos neurobiológicos, las comorbilidades y la búsqueda de alivio de los síntomas son algunos de los factores que hacen que estos pacientes sean vulnerables al consumo de sustancias.

METAS: Con el fin de proporcionar una descripción detallada de un caso clínico, realizar una revisión y reflexión sobre las posibles relaciones entre el SGT y el uso de sustancias.

MÉTODOS: Descripción de un caso clínico de un paciente diagnosticado de SGT y consumo comórbido de sustancias. Se realizó una revisión no sistemática de la literatura mediante la búsqueda bibliográfica en las bases de datos Pubmed y Clinical Key utilizando las palabras clave: "Síndrome de Tourette"; "Abuso de sustancias"; "Abuso de cocaína" y "Abuso de cannabinoides". No se aplicaron restricciones a la fecha de publicación de los artículos investigados.

RESULTADOS: Se reporta un caso clínico de un paciente con SGT diagnosticado a los 11 años. Afección de sintomatología severa y refractaria, caracterizada por tics motores y vocales, síntomas obsesivo-compulsivos y déficit de atención. Un camino marcado por numerosas hospitalizaciones y abordajes farmacológicos sin resultados, requiriendo el uso de estrategias de neuromodulación. Concomitantemente con el cuadro descrito, se inicia el consumo de cannabinoides a los 25 años, descrito por la paciente como automedicación y posteriormente cocaína, a los 29 años, consumo que continúa hasta el día de hoy. Los pacientes con SGT son particularmente vulnerables al uso de sustancias, que tienen efectos nocivos sobre sus síntomas, a saber, cocaína, anfetaminas y heroína. Sin embargo, los pacientes informan que sustancias como los cannabinoides, a menudo utilizados como automedicación, tienen un efecto beneficioso sobre los tics motores y vocales, y actualmente se proponen como una posible terapia en SGT.

DISCUSIÓN Y CONCLUSIÓN: Además de la vulnerabilidad al consumo en pacientes con SGT y su efecto deletéreo sobre los síntomas, también está el efecto positivo descrito en relación a algunas sustancias, como los cannabinoides. En un caso de esta complejidad cobra especial importancia un abordaje holístico, teniendo en cuenta no solo los riesgos del consumo, sino también los posibles efectos beneficiosos, pudiendo así contribuir al desarrollo de nuevas vías terapéuticas.

Palabras clave: Síndrome de Tourette; Abuso de sustancias; Abuso de cocaína, Abuso de cannabinoides.

ABSTRACT

INTRODUCTION: Gilles de La Tourette Syndrome (GTS) is a complex neuropsychiatric disorder characterized by motor and vocal tics, with a significant impact on patient's quality of life. The overlap between the neurobiological mechanisms, comorbidities and the search for a symptom relief are among the factors that make these patients vulnerable for the use of substances.

OBJECTIVES: Regarding a detailed description of a clinical case, to carry out a review and reflection on the possible relationships between the GTS and substance use.

METHODS: Description of a clinical case of a patient diagnosed with GTS and comorbid substance use. A non-systematic literature review was carried out through bibliographical research in the databases – Pubmed and Clinical Key – using the keywords: "Tourette Syndrome"; "Substance Abuse"; "Cocaine Abuse" and "Cannabinoid Abuse". No restrictions were applied to the publication date of the researched articles.

RESULTS: A clinical case of a patient with GTS diagnosed at age 11 is reported. A condition of severe and refractory symptomatology, characterized by motor and vocal tics, obsessive-compulsive symptoms and attention deficit. A path marked by countless hospitalizations and pharmacological approaches without results, requiring the use of neuromodulation strategies. Concomitantly with the picture described, there is a beginning of cannabinoid use at 25 years old, described by the patient as self-medication and later cocaine, at 29 years old, a consumption that she continues to this day. Patients with GTS are particularly vulnerable to substance use, which have deleterious effects on their symptoms, namely cocaine, amphetamines and heroin. However, substances such as cannabinoids, often used as self-medication, are reported by patients as having a beneficial effect on motor and vocal tics and are currently proposed as a possible therapy in GTS.

DISCUSSION AND CONCLUSION: The tendency for using substances in GTS patients and its negative effect on symptoms, joins the positive effect described in relation with substances such as cannabinoids. Regarding a complex clinical case, a holistic approach becomes demanding, in which the risk of consumption should be kept in mind, but also the possible positive effects regarding some substances. These considerations can contribute to the development of new therapeutics in GTS syndrome.

Keywords: Tourette Syndrome; Substance Abuse; Cocaine Abuse; Cannabinoid Abuse.

INTRODUCTION

Gilles de La Tourette Syndrome (GTS) is a complex neuropsychiatric disorder that begins in childhood and has a significant impact on patient's functionality and quality of life. It is characterized by motor and vocal tics, with pathognomonic signs such as coprolalia and ecophenomena being described. The overlapping of neurobiological mechanisms, comorbidities and the search for symptomatic relief are among the factors that make these patients vulnerable to substance abuse.

OBJECTIVES

Regarding a detailed description of a clinical case, to carry out a review and reflection on the relationship between the GTS and substance use.

METHODS

Description of a clinical case of a patient diagnosed with GTS and comorbid substance use. A non-systematic literature review was carried out through bibliographical research in the databases – Pubmed and Clinical Key – using the keywords: "Tourette Syndrome"; "Substance Abuse"; "Cocaine Abuse" and "Cannabinoid Abuse". No restrictions were applied to the publication date of the researched articles.

RESULTS

1 CASE REPORT

We present the case of a 31-year-old female patient diagnosed with GTS at the age of 11 years. At the time of diagnosis, difficulties of school performance, reduced attention span and impulsivity predominated, to which the onset of vocal and light motor tics was associated. Over the following years, there was a continuous worsening of the symptoms, with the number of hospital admissions multiplied and several therapeutic adjustments were made, without any result. There was a predominance of severe and refractory symptoms, characterized by intense and complex motor and vocal tics,

obsessive-compulsive symptoms and a relevant attention deficit. In this context, and given the refractoriness of the symptoms, in 2012, when the patient was 23 years old, an intracranial neurostimulator for deep brain stimulation (DBS) was implanted. Due to repeated self-harm, the patient developed a traumatic cataract, which led to the need for evisceration of the right eye in 2013. Despite all the approaches described, the clinical picture remained refractory, leading to a marked functional incapacity.

In 2014, when she was 25 years old, the patient started using Cannabinoids. This was initially carried out in a social context, and later began to consume alone. The patient reported feeling relief from the tics with the consumption, which was carried out for several years as self-medication. Currently, only a sporadic consumption was described.

In 2018, at the age of 29, the patient started using cocaine. Just as Cannabinoids she described a beginning based on sporadic consumption in a social context, having aggravated consumption for about 1 year. At the time of the interview, she referred consuming about 3 times a week. The patient reports an improvement in tics at an early stage of cocaine use, however, she describes a later worsening with chronic use.

This is a patient with no history of GTS in her family, although there is a history of substance use. As a previous personality, a behavior based on impulsiveness, intolerance to frustration, affective flattening and little reflection on the consequences of their acts was found, traits that fit into a Cluster B personality. Various pharmacological therapies were attempted such as Aripiprazole, Haloperidol, Fluvoxamine, Clonidine and Clomipramine. At the time of the interview, she was medicated with Haloperidol Decanoate 50 mg IM every 20 days, Amisulpride 50 mg/10 ml – oral solution twice a day and Anafranil 50 mg once a day.

Due to the continued use of substances, the patient was referred for consultation at the "Equipa Técnica Especializada de Tratamento de Coimbra", held on July 9, 2020. Upon examination of her mental status, the patient had a poorly cared appearance, initially showing little cooperation with the interview. She walked into the room, immediately kicking the air. Afterwards, she sat in the chair, restless, trying unsuccessfully to control her body, which manifested itself with repeated sudden movements of the upper limbs and head. She presented an attentional pattern guided by successive distractions during the interview, with attention being recurrently captured by secondary stimuli. During the interview, several simple and complex motor tics were visible, such as blowing, cervical flexion, extension and elevation of the upper limb and tongue protrusion. An increase was observed when themes considered uncomfortable by the patient were addressed. During the interview, some affective superficiality became evident. She had a sub depressed mood, feeling sad about the maintenance of the described consumptions. She was conscious of the negative impact of consumption, as well as the need to stop them.

As a therapeutic proposal, a psychotherapeutic intervention directed at the suspension of substance use was carried out, as well as an intervention from an occupational point of view, in order to arrange an occupational activity for the patient. A psychoeducational intervention that included the family was carried out. From a psychopharmacological point of view, Haloperidol and Amisulpride were discontinued, and Methylphenidate 8 mg once daily, Haloperidol 5 mg once daily and Levomepromazine 25 once daily were introduced. The patient started psychotherapeutic appointments at the same institution.

After the institution of therapy, the patient showed a significant improvement in symptoms, namely the motor and vocal tics. She suspended the use of cocaine, maintaining only the sporadic use of cannabinoids. However, after about 1 year, she started to relapse into cocaine consumption, and with it, a new worsening of the symptoms.

Despite an evident affective indifference objectified throughout the successive observations, the patient expressed having an empathetic and warm relationship with animals. In this sense, measures were taken for the patient to integrate occupational and professional activities that involved contact with animals, however, this was never accepted by the patient. Due to the maintenance of consumption, despite the various approaches at a pharmacological, psychotherapeutic, family, social and occupational level, the patient was referred for integration in a therapeutic community.

2 GILLES DE LA TOURETTE SYNDROME

2.1 Historical Aspects

Various historical figures, such as Napoleon Bonaparte, Peter "The Great" of Russia, and King William III of England, are described in some literary works as having symptoms compatible with the GTS. Lev Tolstoy's brother is believed to have suffered from the disease, and he describes in his

works several symptoms that are now attributable to GTS. In a letter he writes to a family member, he describes his brother's behavior - "he looked at me intently, made that head and neck movement you know and screamed" (Hurst, 1994). Other examples are found in his well-known work Anna Karenina, published in 1877 - "...convulsive movement with her head and neck, so familiar to Levin" (Tolstoy, 1997) and "I took her to a prostitute's house! – He said, at the same time that her neck twisted" (Tolstoy, 1997), referring to motor tics and coprolalia.

In 1885, George Gilles de la Tourette published the article "Étude sur une affection nerveuse charactérisée par de l'incoordination motrice accompagnée d'écholalie et de coprolalie" (Robertson, 2017). This article describes 9 cases of patients with a disorder characterized by loss of motor coordination, echolalia and coprolalia. The syndrome that came to earn its name was described for the first time (Robertson, 2017). Between 1886 and 1907, Gilles de la Tourette and other authors began to describe aspects of objectified psychopathology in patients with tics, namely the presence of obsessions and phobias. During this period, there was a prevalence of the psychoanalytic theory, with tics being conceptualized as a functional disease.

In 1952, the first edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM) appeared, which included the presence of tics as a possible diagnosis, however, the GTS was not yet considered (Robertson, 2017). In 1972 the first association dedicated to the GTS is created and in 1978 the first book describing the GTS is published. In 1980 the SGT is included for the first time in a classification system, namely in the third edition of the DSM. In 1985, the first study to suggest a genetic component of the disease appeared and, in 1990, obsessive-compulsive behavior began to be considered as an alternative GTS phenotype. In 2001 the first study on quality of life in the GTS appeared and from 2009 onwards a structured behavioral treatment started being used for GTS. Currently, several meta-analyses and randomized controlled trials contribute to constant advances in diagnosis, treatment and improvement in the quality of life of these patients.

2.2 Epidemiology

The prevalence of GTS varies between 0.5 to 1% depending on the methodology (Robertson, 2008). GTS is more common in males, with a 3-4/1 ratio (Robertson, 2017; Robertson, 2008). Tics generally appear between 4 and 6 years of age, peaking between 11 and 12 years of age and decreasing from adolescence onwards (Robertson, 2008). In some cases, tics can persist into adulthood, constituting more debilitating cases (Robertson, 2017). In 4 to 5% there is a more severe symptomatic condition, which is called malignant tics (Robertson, 2017).

2.3 Etiology and Pathogenesis

Genetics

GTS is one of the most heritable non-mendelian neuropsychiatric diseases, with a 15-fold increase in the probability of diagnosis of tic disorder in siblings of patients with GTS being reported (Robertson, 2017). No gene has yet been identified as a risk factor for GTS (Robertson, 2017). A polygenic inheritance is assumed (Robertson, 2017).

Several studies point to a genetic inheritance shared with other neuropsychiatric diseases, namely Obsessive-Compulsive Disorder (OCD) and Attention Deficit Hyperactivity Disorder (ADHD). OCD represents the neuropsychiatric disorder whose etiology is most closely related to GTS (Robertson, 2017). Several studies point to a genetic overlap between these two neuropsychiatric disorders that are considered to be phenotypically similar (Davis, 2013). Other studies also point to a polygenic heritability shared between ADHD and SGT (Hirschtritt, 2015; Antilla, 2018).

Neurobiology

Cortico-striatum-thalamus-cortical circuits (CCTC) that link specific structures in the frontal cortex to subcortical structures, including the basal ganglia and thalamus, provide a framework for understanding GTS. These circuits are involved in regulating complex behaviors, integrating movement and regulating emotions. Three circuits are considered to be primarily involved in GTS: a behavioral circuit (involving a circuit between the premotor cortex and the putamen); a goal-directed circuit (involving a circuit between the ventromedial prefrontal cortex and the caudate nucleus) and an emotion-related limbic circuit (involving the hippocampus, amygdala, prefrontal cortex, anterior cingulate gyrus, and ventral striatum). Dopamine plays a major role in the neurobiology of GTS. This fact was addressed through the observation of the increase in tics after the use of amphetamines and their suppression through the use of dopamine antagonists. A role for noradrenaline is also considered by

the tic-suppressing effect of alpha-2 antagonists such as clonidine (Robertson, 2017). Several studies have shown a possible relationship between the endogenous cannabinoid system and GTS neurobiology (Robertson, 2017). Several case reports and two controlled studies suggest that cannabinoids, namely smoked marijuana and oral THC have a beneficial effect on tics in patients with SGT (Whiting, 2015).

2.4 Clinical Characteristics

Tics represent one of the main diagnostic aspects of GTS, being defined as sudden, repetitive and involuntary movements, in the case of motor tics, or in the form of sounds, vocalizations or words, in the case of vocal tics. These generally mimic an everyday behavior and last less than 1 to 2 seconds and can be simple or complex. For the diagnosis of GTS, the occurrence of several motor tics and one or more vocal tics, with a duration of at least 1 year is necessary. These can be exacerbated by stress, fatigue and high temperatures, with reports of improvement when the individual focuses his attention on certain activities. In most individuals, there is a premonitory sensation, characterized by tension, tightness, or discomfort, which is relieved after the tic is performed. Most individuals are able to suppress tics for a short period of time. Other symptoms, considered pathognomonic signs of the disease, include coprolalia and ecophenomena. GTS is a clinical condition with a significant impact on the patient's functionality and quality of life.

Regarding the course of the disease, tics typically start in the first decade of life, usually in the form of simple motor tics, with vocal tics having a later onset. There is usually an increase in intensity up to 10 to 12 years of age, with a progressive decrease with advancing into adulthood. In 4 to 5% of cases (Robertson, 2017), self-mutilating behaviors occur, with repeated head and eye injuries, often resulting in blindness. This is a serious clinical condition, which is called malignant tics. These cases are associated with greater severity of motor symptoms, comorbid OCD, complex vocal tics, mood disturbances and a poor response to therapy.

In 90% of patients with SGT, comorbid disorders are registered, namely: OCD (in 40 to 60% of patients); Obsessive-compulsive behaviors (in 60 to 80% of patients); ADHD (in 60% of patients) and Autism Spectrum Disorders (ASP) (Robertson, 2017). Other coexisting disorders include: Depression; Anxiety; Substance abuse; Conduct disorder; Personality Disorders and Learning Disorders.

Table 1. DSM-5 Diagnostic Criteria for GTS (APA, 2013)

307.23 (F95.2) –Tourette's Disorder – Diagnostic Criteria According to DSM-5
A. Both multiple motor and one or more vocal tics have been present at some time during the illness, although not necessarily concurrently.
B. The tics may wax and wane in frequency but have persisted for more than 1 year since first tic onset.
C. Onset is before age 18 years.
D. The disturbance is not attributable to the physiological effects of a substance (e.g., cocaine) or another medical condition (e.g., Huntington's disease, post viral encephalitis).

2.5 Diagnosis

The 10th Edition of the International Classification of Diseases (ICD-10) considers the existence of GTS as a syndrome since 1993, appearing in the category of "Tic Disorders" with the name "Disorders of combined multiple motor and vocal tics" (WHO, 1992). It is defined as a form of tic disturbance in which there are multiple motor tics and one or more vocal tics, which do not have to occur simultaneously (WHO, 1992). The 11th Edition of the International Classification of Diseases (ICD-11) considers the existence of the "Tourette's Syndrome". In this classification, it is defined as a chronic tic disorder characterized by the presence of chronic motor and vocal tics, with an onset during the developmental period (WHO, 2018).

In the first edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM I) only tics were recognized, and it was in 1980, in DSM III, that the GTS was mentioned for the first time. Currently, DSM 5, based on clinical criteria, defines GTS as the occurrence of several simple motor tics and one or more vocal tics (APA, 2013). GTS is included in the Tic Disturbance Spectrum, which includes: Temporary Tic Disorder; Chronic Motor Tic Disorder and Chronic Vocal Tic Disorder. The DSM-5 diagnostic criteria for the GTS are described in Table 1.

2.6 Treatment

Haloperidol was the first drug to be used to control tics, in 1961 (Roberston, 2017). In 1988, Behavioral Therapy began to be used for the treatment of GTS, and in 1999, Deep Brain Stimulation (DBS) was used for the first time (Robertson, 2017).

Currently, the first-line treatment in the GTS includes support therapy, in the form of Psychoeducation and Behavioral Therapy. As a second line of therapy, pharmacological therapy is recommended. First-generation antipsychotics such as Haloperidol and Pimozide are used, while second-generation antipsychotics such as Risperidone and Aripiprazole are preferred. Alpha-2 agonists such as Clonidine are also used. Deep Brain Stimulation (DBS) is used in cases of refractory symptomatology.

3 GILLES DE LA TOURETTE SYNDROME AND SUBSTANCE ABUSE

3.1 Introduction

Despite the little evidence, it is suggested that individuals with GTS are vulnerable to impulsive, obsessive and addictive behaviors. One of the possible explanations is related to the fact that corticolimbic structures linked to addiction are also important in the formation of tics and obsessive-compulsive symptoms. In addition, the use of some substances for self-medication in patients with GTS is frequent, such as cannabinoids, with an increased risk of substance use in these patients (Robertson, 2017). Studies show that 6 to 6.9% of patients with SGT develop addictive disorders and that 4.5% of patients with SGT initiate alcohol abuse (Hirschtritt, 2015). There is a more prevalent relationship when there is psychiatric comorbidity, with 10.3% of patients with GTS and OCD developing addictive disorders (Hirschtritt, 2015). Several case reports and small observational studies reveal data on the possible toxicity of substances of abuse in the form of behavioral changes (Hirschtritt, 2015).

3.2 Cocaine

From a neurobiological point of view, Cocaine blocks the dopamine transporter (DAT), being responsible for the increase of Dopamine in the mesolimbic pathway. The dopaminergic system is responsible for controlling reward, movement and cognition. By decreasing the inhibition in the excitatory pathways of the Ventral Tegmental Area and Nucleus Accumbens, its consumption can generate tics, dystonia and chorea. (Cardoso, 1993)

Several studies reveal that cocaine use, whether first use or in situations of chronic use, is associated with the appearance of de novo motor and vocal tics, such as symptomatic exacerbations in patients with SGT (Cardoso et al, 1993). Several case reports show the appearance of multifocal tics after de novo cocaine use, crack use, and dose escalation in a habitual user (Pascual-Leone, 1990). Consumption is rarely associated with symptoms of transient chorea, called "Crack Dancing" and oromandibular dyskinesias, called "Boca Torcida" (Narula et al, 2017). In patients with chronic consumption, abstinence is also associated with changes in movement, namely parkinsonian symptoms (Cardoso et al, 1993).

3.3 Cannabinoids

Cannabinoid use is not generally associated with movement disorders (Whiting et al, 2015). These are often used as self-medication in patients with GTS, with reports of improvement in symptoms in 85% of cases (Whiting et al, 2015). Several case reports and two controlled studies suggest that cannabinoids, namely smoked marijuana and oral THC have a beneficial effect on tics in patients with SGT (Whiting et al, 2015). In a randomized and controlled study, treatment with THC was carried out for 6 weeks in patients with GTS, with efficacy and safety being reported (Müller-Vahl et al, 2003). A recent retrospective study reinforced the safety and efficacy of cannabinoid-based drugs in treating tics in at least a subgroup of patients with GTS (Milosev et al, 2019).

3.4 Heroin

There are few data on the effect of heroin on motor symptoms (Marcelo et al, 2003). Sporadic and chronic opioid use is associated with exacerbation of tics (Marcelo et al, 2003; Cardoso et al, 1993). Continued consumption is also associated with rare episodes of uncontrollable coprolalia (Cardoso et al, 1993). A case report describes the development of coprolalia and intense tics in a patient with GTS with chronic heroin use (Marcelo et al, 2003). Elevation of dopamine levels through GABA inhibition in the Ventral Tegmental Area interneurons can lead to myoclonus, hiccups, parkinsonism or chorea (Cardoso et al, 1993).

3.5. Amphetamines

Amphetamine use, through the DAT, can give rise to agitation, tremor, ataxia and convulsions. Its consumption is associated with an increase in tics (Cardoso et al, 1993).

DISCUSSION AND CONCLUSION

We presented a case of a 31-year-old female patient diagnosed with GTS at the age of 11. A path characterized by symptom refractoriness, with reference to motor tics, vocal tics, obsessive-compulsive symptomatology and a pattern of inattention. Multiple hospital admissions, with different pharmacological strategies and electrode placement for DBS at 23 years of age. A patient with personality traits marked by intolerance to frustration and impulsiveness, demonstrating low adherence to therapy throughout the disease. There is an onset of cannabinoid use at 25 years old, used as self-medication, with a current sporadic use and a start of Cocaine

use at 29 years old, with a reported improvement in tics at an early stage and a worsening after chronic use. Due to the maintenance of consumption, despite the various approaches at a pharmacological, psychotherapeutic, familiar, social and occupational level, the patient was referred for integration in a therapeutic community.

GTS represents a complex neuropsychiatric disorder, with multiple comorbidities and an enormous impact on patient's lives. The clinical case described is marked by symptomatic refractoriness, with a significant functional impact, leading to the use of substances as self-medication.

Patients with GTS are particularly vulnerable to substance use, which have deleterious effects on their symptoms, namely cocaine, amphetamines and heroin. However, substances such as Cannabinoids are often used as self-medication and are reported by patients as having a beneficial effect on motor and vocal tics and are currently proposed as a possible therapeutic route in GTS.

The vulnerability to consumption in patients with GTS and its deleterious effect on the symptoms is added to the positive effect described in relation to some substances, such as Cannabinoids. In a case of this complexity, a holistic approach is of particular importance, taking into account not only the risks of substance use, but also the possible beneficial effects, thus being able to contribute to the development of new therapeutic approaches. When approaching these patients, symptomatology, comorbidities and vulnerability should be taken into account, with a special emphasis on improving quality of life.

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