



RESEARCH ARTICLE

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PISA SYNDROME IN THE EVOLUTION OF PARKINSON'S DISEASE: A CASE REPORT

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ARTICLE INFO

Article History:

Received 17th September, 2020
Received in revised form
29th October, 2020
Accepted 10th November, 2020
Published online 30th December, 2020

Key Words:

Parkinson's disease; Pisa Syndrome;
Postural Balance; Pathophysiology.

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ABSTRACT

Parkinson's disease (PD) is characterized as a neurodegenerative disease marked by motor and non-motor signals. Due to the advancement of motor symptoms, a patient with PD may develop postural abnormalities, such as Pisa Syndrome. Little is known about the pathophysiological mechanisms that cause such complications, however, theories about the etiology are now consolidated in the exploratory field of neuroscience. **Objective:** The objective of the present work is to elucidate the clinical aspects, as well as theories about the pathophysiology of Pisa Syndrome in patients with Parkinson's disease, through a case report. **Discussion:** Patients with Parkinson's disease usually present postural changes resulting from the balance element - detriment of postural reflexes, and from the postural orientation element, in view of what occurs in Pisa Syndrome. There is no agreement on the diagnostic criteria for Pisa Syndrome, however, the criterion most frequently used for diagnosis is based on a lateral flexion of the trunk of at least 10°. There are many hypotheses that contribute to the pathophysiology of Pisa Syndrome, however, the exact mechanisms have not yet been elucidated. **Conclusion:** Studies on Pisa Syndrome found that although the abnormality affects the quality of life of patients who have it, they remain functionally active and partially independent. Even so, it is conjectured that the Syndrome for generating greater dynamic postural instability is responsible for a greater risk of falling. Such information points to the importance of early diagnosis and intervention.

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Citation: Marco Orsini, Henry Pereira-Silva, Jacqueline Stephanie Fernandes do Nascimento, Thais de Rezende Bessa Guerra, Nicolle dos Santos Moraes Nune et al., 2020. "Pisa syndrome in the evolution of parkinson's disease: A case report", *International Journal of Development Research*, 10, (12), 42656-42658.

INTRODUCTION

Parkinson's disease (PD) is characterized as a neurodegenerative disease marked by motor and non-motor signals. With regard to motor signals, four are considered cardinal signals: bradykinesia, tremble, stiffness and postural instability, which derive especially from the loss of dopaminergic neurons from the substantia nigra pars compacta (Kalia, 2015 and Schirinz, 2016). Due to the advancement of motor symptoms, patients with PD may develop postural abnormalities, such as dropped head Syndrome, Camptocormia and especially Pisa Syndrome (Villarejo, 2003).

Little is known about the pathophysiological mechanisms that cause such complications, however, theories about the etiology are now consolidated in the exploratory field of neuroscience (Kalia, 2015). Studies show that Pisa Syndrome can be found in several neurological diseases, however, it was only in 2003 that it was reported in patients with Parkinson's disease (Villarejo, 2003). The Pisa Syndrome, also known as pleurothotonus, is a peculiar and rare postural complication, which is characterized by tonic truncal dystonia with lateral flexion of more than 10° and slight rotation of the axial axis backwards without presenting dystonia in other regions of the body, which can be totally relieved by passive mobilization or by adopting the supine position (Barone, 2016 and Tinazzi,

2016). A postural change in Parkinson's disease represents a sign of extrapyramidal involvement, considering that it can occur in untreated patients and without a defined clinical diagnosis of PD.⁶ The theory of postural change being a genuine symptom of Parkinson's disease is based on clinical evidence of an association of risk factors and severity with the symptoms and evolution of the disease, such as increased axial stiffness, high daily dose of levodopa, dementia associated and constant motor fluctuations (Lepoutre, 2006). The Pisa Syndrome is considered an incapacitating and imminently reversible symptom, which has a strong impact on the quality of life of these patients. In addition, it was found that the Syndrome is more common in patients with advanced age and more severe stage with a long period of presentation of Parkinson's disease and consequent motor deficiencies (Barone, 2016 and Tinazzi, 2016). The aim of the present study is to elucidate the clinical aspects, as well as theories about the pathophysiology of Pisa Syndrome in patients with Parkinson's Disease, through a case report.

Case Report

Male, 63-year-old, has been diagnosed with Parkinson's disease since 2012. About six months ago (05/2020), a picture of paravertebral muscle dystonia with trunk deviation to the left with rotation emerged (Figure 1).



Figure 1. Dystonia of the paravertebral musculature with trunk deviation to the left with rotation

The condition was initially considered to be light and fluctuating, however over time it became progressive followed by more intense episodes, making it hard for him in walking patterns and in basic and instrumental activities of daily life. He had been evaluated about 1 month ago (09/2020), with a suggestion of gradual withdrawal of 0.375mg pramipexole (dosage at the time of the first consultation) - 1 tablet every 8 hours. Weaning started with the removal of 1 tablet every four days, suspending the medication completely after 15 days. After about two weeks of the complete withdrawal of the medication, there was considerable improvement in posture, although he still has mild dystonia (Figure 2). It is a case of Pisa Syndrome induced by dopaminergic agonists. The thoracic and lumbar computed tomography exam showed only

scoliotic deviation with tiny disc protrusions. He is undergoing clinical treatment and rehabilitation.



Figure 2. Considerable improvement in posture, however, still presents mild dystonia

DISCUSSION

Patients with Parkinson's disease usually present postural changes resulting from the balance element - detriment of postural reflexes, and the postural orientation element, in view of what occurs in Pisa syndrome (Alwardat, 2018; Doherty, 2011). Risk factors for the development of Pisa Syndrome are considered to be advanced age, a longer duration of Parkinson's disease, although it may occur throughout the course of the disease, use of medications such as neuroleptics, cholinesterase inhibitors, levodopa, female sex and presence of organic brain disorders (Doherty, 2011). It is also suggested that the imbalance between neurotransmitters, with attenuation of dopaminergic stimuli and too much cholinergic stimuli, neurochemical instability in basal ganglia homeostasis, peripheral involvement with myopathy and other musculoskeletal diseases, understanding of the unusual body scheme and aberrant sensory-motor integration, contribute to the pathophysiology of Pisa Syndrome, however, the exact mechanisms have not yet been elucidated (Fife, 2017 and Colebatch, 1994). Recently, the vestibular system has been linked to the pathophysiology of Pisa Syndrome, as well as falls and motor complications of advanced Parkinson's disease,¹² for this reason, current studies have focused on vestibular evoked myogenic potentials, used to assess the descending vestibular-colic system (Rosengren, 2010). In particular, cervical vestibular evoked myogenic potentials portray the response of the sternocleidomastoid muscle when subjected to the saccule's sound activation and signal transmission through the vestibulospinal tract (Seidel, 2015 and Vitale, 2011). The upward accumulation of the so-called Lewy bodies composed mainly of α -synuclein immunoreactive and other brain stem structures for upper brain regions is considered the neuropathological mark of Parkinson's

disease, however, it was observed that the Lewy body accumulation occurred in all tracts of brain stem fibers and cranial nerve nuclei, comprising the vestibular system.¹⁶ In addition, drugs that affect dopamine metabolism in the central nervous system are associated with Pisa Syndrome. Likewise, neurodegenerative diseases can also cause the syndrome, especially Parkinson's disease. The therapy with dopaminergic drugs by activating the basal ganglia circuit promotes the development of the syndrome. Priming is a pharmacological event whereby hypersensitivity of dopaminergic receptors occurs following the denervation of the nigrostriatal pathway, as occurs in Parkinson's disease. The more exposed to dopamine, the more sensitive the response in the affected striatum will be, causing the appearance of Pisa Syndrome (Olsson, 2014). There is no agreement on the diagnostic criteria for Pisa Syndrome, however, the criterion most frequently used for diagnosis is based on a lateral flexion of the trunk of at least 10° (Ye, 2017). Furthermore, the syndrome can be divided into mild when the flexion is less than 20° or severe, when the flexion is greater than 20° according to the lateral flexion angle of the trunk (Broussolle, 2007). Research reveals that patients with Parkinson's disease and postural deformities had a previous history of degenerative diseases of the spine, in addition to pathologies related to the senescence process, such as osteoporosis and arthrosis, and these relations were corroborated in the Pisa Syndrome. It is assumed that older patients with Parkinson's disease have a high risk of developing osteoarthropathies, such as those mentioned, and consequently these comorbidities make the patient with Parkinson's disease more susceptible to developing Pisa Syndrome. In addition, pathologies of the musculoskeletal system may be involved in the peripheral mechanism of the pathophysiology of the syndrome (Fife, 2017 and Alwardat, 2018). The most important differential diagnosis for Pisa Syndrome is scoliosis, which it is not attenuated in the supine position. Furthermore, logistic regression showed that motor disability is an impartial risk factor related to the syndrome. Rigidity, one of the essential manifestations of Parkinson's disease, has been mentioned as a cause of postural deformity. In advanced stages of the disease, the striatum is denervated so the patients may develop more serious motor deficiencies, such as stiffness and abnormal postures, including Pisa Syndrome (Castrìo, 2014).

Conclusion

Studies on the Pisa Syndrome have found that although the abnormality affects the quality of life of patients who have it, they remain functionally active and partially independent. Even so, it is conjectured that the syndrome for generating greater dynamic postural instability is responsible for a higher risk of falling, which becomes worrying since this abnormality is associated with advanced age, as well as a longer time of installation of Parkinson's disease. Such information points to the importance of early diagnosis and intervention.

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