

# Ataxia, ophthalmoplegia and laryngeal stridor related to glutamic acid decarboxylase antibodies

## *Ataxia, oftalmoplegia e estridor laríngeo relacionados a anticorpos antidescarboxilase do ácido glutâmico*

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### ABSTRACT

Glutamic acid decarboxylase (GAD) is the enzyme responsible for the conversion of glutamate to gamma-aminobutyric acid (GABA) in the central nervous system. The presence of anti-GAD antibody in cerebrospinal fluid and high levels in blood have been described in some neurological disorders, such as stiff person syndrome and cerebellar ataxia. It is postulated that African descent with anti-GAD may exhibit more severe neurological impairment. We report a case of a young adult African descent with cerebellar syndrome associated with ophthalmoplegia and laryngeal stridor. We found in the literature relationship of ophthalmoplegia plus ataxia with anti-GAD, but no reports of these symptoms with laryngeal stridor, apparently being the first reported case.

**Keywords:** Ataxia, ophthalmoplegia, glutamic acid decarboxylase, GAD, anti-GAD, laryngeal stridor.

### RESUMO

Descarboxilase do ácido glutâmico (GAD) é a enzima responsável pela conversão do glutamato em ácido gama-aminobutírico (GABA) no sistema nervoso central. A presença do anticorpo anti-GAD no líquido cefalorraquidiano e em altos níveis no sangue tem sido descrita em alguns distúrbios neurológicos, tais como a síndrome da pessoa rígida e ataxia cerebelar. Postula-se que pacientes afrodescendentes podem apresentar comprometimento neurológico mais severo. Relatamos o caso de um adulto jovem afrodescendente com síndrome cerebelar associada a oftalmoplegia e estridor laríngeo. Encontramos na literatura relação entre a oftalmoplegia com ataxia e anti-GAD, mas nenhum relato desses sintomas com estridor laríngeo, sendo aparentemente o primeiro caso reportado.

**Palavras-chave:** Ataxia, oftalmoplegia, descarboxilase do ácido glutâmico, GAD, anti-GAD, estridor laríngeo.

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## INTRODUCTION

Glutamic acid decarboxylase (GAD) is the enzyme responsible for conversion of glutamate in gamma-aminobutyric acid in the central nervous system (CNS).<sup>1</sup> It is also found in pancreatic beta cells and type 1 diabetes mellitus (DM) that could be related to the presence of anti-glutamic acid decarboxylase (anti-GAD) antibodies.<sup>2-4</sup>

The presence of anti-GAD in cerebrospinal fluid (CSF) and high levels in blood have been described in some neurological disorders, such as stiff person syndrome and cerebellar ataxia.<sup>5-7</sup> It is postulated that African descent patients may exhibit more severe neurological impairment.<sup>8</sup>

We report a case of a young adult, African descent with progressive cerebellar syndrome associated with ophthalmoplegia and laryngeal stridor.

## CASE REPORT

A 20 years-old African-Brazilian man started four years earlier with diplopia, gait ataxia with frequent falls, impaired speech (slurred speech), and sharp sound on breathing, compatible with stridor.

The neurological examination showed intermittent stridor, severe gait ataxia with truncal titubation, head tremor (no-no), slurred speech, bilateral and complete ophthalmoparesis with non-reactive mydriatic pupils.

He denied family history of neurological conditions, use of illicit drugs, alcohol and previous exposure to toxins.

Initial investigation (blood levels of glucose, vitamins B1, B12 and E, thyroid function, and serological tests for HIV and syphilis) were within normal range/negative.

Magnetic resonance imaging (MRI) of the brain revealed cerebellar atrophy (Figure 1). Electromyography with repetitive stimulation test was normal.

Tests for spinocerebellar ataxia type 1, 2, 3, 6, 7, 10, and 12, Friedreich's ataxia, Dentatorubral-pallidoluysian atrophy (DRPLA) were all negative, as well as anti-endomysial antibodies and anti-transglutaminase.

Levels of anti-GAD were positive in blood (3,4 U/mL; normal value < 1,0 U/mL), and in CSF (1,17 U/mL; normal value < 1,0 U/ml). Oligoclonal bands were also detected in the CSF.

Methylprednisolone therapy was prescribed (1 g/day, for 5 days), without improvement, followed by two monthly courses of human immunoglobulin (400 mg/kg/day, for 5 days), with partial improvement of ataxia as well as of the laryngeal stridor. About eight months after starting treatment the patient had high fever with respiratory distress and obitus in an another institution.

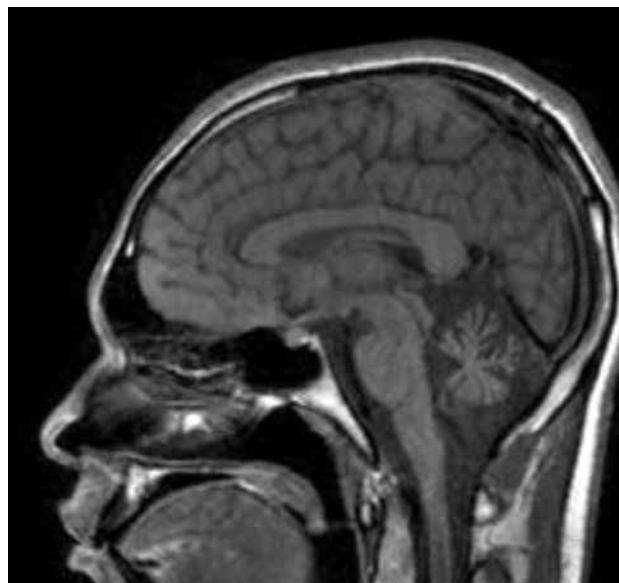


Figure 1. Brain MRI sagittal sequence revealing cerebellar atrophy.

## DISCUSSION

We present a case of a young African-Brazilian man with high levels of anti-GAD that presented insidious painless ophthalmoplegia, and developed severe ataxia with impairment of speech, and laryngeal stridor.

The MRI guided the initial research to genetic causes. Researches for hereditary ataxias were performed, but all were negative.

Levels of anti-GAD were high in the blood and present in the CSF, establishing the diagnosis of ataxia-ophthalmoplegia-laryngeal stridor due to anti-GAD.

It is known that GABAergic neurons are widely distributed in the CNS and anti-GAD disorders can produce various symptoms in the brainstem, extrapyramidal system and spinal cord. The cause of more severe symptoms in African descent is unclear.<sup>8</sup> Our patient confirmed this finding, considering that he presented a severe global ataxia with impairment of the basic activities of daily living, complete ophthalmoplegia, and laryngeal stridor.

We found in the literature reports of ophthalmoplegia plus ataxia with anti-GAD, but without the presence of laryngeal stridor, being this case, apparently, the first one reported.

The treatment is based on immunosuppressive therapy, with variable degrees of response.<sup>9,10</sup> Our patient received methylprednisolone without satisfactory results, but presented partial improvement with human immunoglobulin.

We concluded that it is important to consider this diagnosis, considering it is a treatable condition, and that African descent patients may present more severe neurological manifestations related to anti-GAD.

## CONFLICT OF INTEREST

There is no conflict of interest to declare.

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