# Síndrome Cerebelar Rapidamente Progressiva: Um Caso Clínico

## *Rapidly Progressive Cerebellar Syndrome: A Case Report*

**Leticia Santos, Filipa Monteiro, Maria Inês Marquês, Catarina Valadão, Francisca Delerue**

## Resumo:

A síndrome cerebelar rapidamente progressiva é a segunda apresentação neurológica paraneoplásica mais frequente e a elevada suspeita clínica e a exclusão de outras etiologias é essencial no diagnóstico. Este pode preceder o da neoplasia e apresentar efeitos dramáticos, independentemente do estadiamento da neoplasia.

É apresentado o caso de uma mulher de 69 anos foi hospitalizada por quadro com algumas semanas de evolução de vertigem e marcha instável. Ao exame objetivo destaca-se disfagia, disartria, nistagmo patológico e ataxia da marcha e membros. A investigação analítica revelou elevação de parâmetros inflamatórios e de marcadores tumorais e positividade dos anticorpos anti-Yo. Foi diagnosticada neoplasia do ovário com metastização peritoneal após exclusão de outras etiologias.

Apesar de ser uma condição rara, é crucial que todos os médicos reconheçam o síndrome cerebelar rapidamente progressiva e a possibilidade de uma doença neoplásica subjacente.

**Palavras-chave:** Degeneração Paraneoplásica Cerebelar; Neoplasias Cerebelares; Neoplasias do Ovário; Síndromes Paraneoplásicas.

## *Abstract:*

*Rapidly progressive cerebellar syndrome is the second most frequent paraneoplastic neurological syndrome and its diagnosis requires the exclusion of other entities. The syndrome can precede the malignancy diagnosis and present with dramatic effects, regardless of malignancy stage.*

*We present a case of a 69-year-old female who was hospitalized due to vertigo and gait ataxia that started a few weeks before. Physical examination revealed dysphagia, dysarthria, pathological nystagmus and gait and limb ataxia. The blood analysis revealed elevated inflammatory parameters and tumor markers and positivity to anti-Yo antibodies. The patient was diagnosed with ovarian cancer with peritoneal metastasis after other conditions were excluded.*

*Even though it is a rare condition, it is important that all physicians recognize rapidly progressive cerebellar syndrome given the possibility of an underlying neoplastic disease.*

[1]Serviço de Medicina Interna, Hospital Garcia de Orta, Almada, Portugal

***Keywords:*** *Cerebellar Neoplasms; Ovarian Neoplasms; Paraneoplastic Cerebellar Degeneration; Paraneoplastic Syndromes.*

## Introduction

Paraneoplastic syndromes refer to clinical disorders that cannot be directly attributed to the physical effects of the primary tumor or metastasis and were first reported in 1888.[1]

The paraneoplastic neurologic syndromes are described as neurologic disorders that occur due to the remote effect of a malignancy. They are thought to have an autoimmune pathogenesis and they have no pathognomonic presentation, only "high-risk" phenotypes.[2] The diagnosis if often difficult and requires a high clinical suspicion since these syndromes can affect any part of the nervous system, its symptoms may develop over a variable period of time and diagnostic tests (imaging exams, cerebrospinal fluid analysis among others) may be normal.[3]

The paraneoplastic cerebellar degeneration was first described in 1919 in a patient with an ovarian tumor, however it is now know that it may affect patients with gynecologic malignancies, lung cancer, Hodgkin's disease and others.[4] In the updated diagnostic criteria, the syndrome is now referred to as rapidly progressive cerebellar syndrome and usually presents with rapidly and severe cerebellar syndrome progressing in less than 3 months.[2,4] Paraneoplastic neurological syndromes are rare (1 in 300 patients with a cancer diagnosis) and rapidly progressive cerebellar syndrome is the second most frequent presentation.[5]

## Case Report

We present a 69-year-old female patient with a medical history of hypertension, dyslipidemia, asthma, glaucoma, unquantified smoking habits and social ethanolic consumption. There was no relevant family history and no regular gynecological follow-up. The patient presented in the emergency department with vertigo not tolerating upright position due to gait ataxia. She also complained of nausea for a few weeks. No other symptoms were reported.

The neurological examination showed multiple impairments regarding the cranial nerves and the cerebellum. On the evaluation of eye movements, she presented horizontal nystagmus bilaterally. She also presented hypoacusis on the left, hypophonia, dysarthria and dysphagia. Asymmetrical ataxia was also observed, mainly on the superior limbs with

bilateral intention tremor. As referred previously, gait ataxia was observed as well as axial stiffness.

Blood tests revealed elevated erythrocyte sedimentation rate (97 mm in the first hour), C-reactive protein (1.2 mg/dL) and lactate dehydrogenase (758 IU/L).

The patient was admitted with the diagnosis hypothesis of stroke in the posterior arterial basilar territory.

A brain magnetic resonance imaging (MRI) scan was performed, excluding vascular injury and revealing no other changes. Biochemical and urine analysis, including metabolic and toxicological panels, revealed no abnormalities and the HIV serology was negative. Tumor markers were measured revealing an elevated CA-125 (11296 U/mL; normal range: 0–35U/mL) and CA-15.3 (405 U/mL; normal range: 0–25U/mL). Other tumor markers (such as NSE and CEA) were within normal range. Antineuronal antibody testing was performed (such as anti-Yo, anti-Ri and anti-Hu) and was only positive for anti-Yo. The cerebrospinal fluid analysis revealed mild pleocytosis and protein elevation and the direct and cultural examination were both negative.

Given the negative results to vascular, infectious, metabolic and toxicological causes and taking into account the elevated neoplastic markers, an investigation of paraneoplastic syndrome was warranted. An abdominal and pelvic MRI scan was performed, identifying an ovarian neoplasia and peritoneal implants.

The patient was diagnosed with paraneoplastic cerebellar degeneration and ovarian neoplasia with peritoneal carcinomatosis. Chemotherapy was initiated, although no neurological improvement was observed. The patient was informed about the poor prognosis and irreversibility of the condition and was referred to palliative care.

## Discussion

Rapidly progressive cerebellar syndrome may present initially with isolated gait ataxia, but truncal and limb involvement are needed to define it as rapidly progressive cerebellar syndrome and extracerebellar dysfunction may be associated.[2]

Many neuronal antibodies are found to be associated and to be important markers and may provide a clue to the specific type of underlying cancer.[2,4,5] In almost 80% of patients, the syndrome may precede the diagnosis of the tumor by months or years (but most frequently by 4 to 6 months).[6]

Anti Yo-antibodies, or Purkinje cell cytoplasmic antibody type 1, target the Purkinje cells of the cerebellum resulting in their death and were first described in 1983.[7] It is hypothesized to exist an immunological response to cerebellar degeneration-related protein 2, which is ectopically expressed by tumor cells.[8] Anti-Yo can be synchronous or precede (sometimes by years) the diagnosis of the tumor.[9,10] These markers are mostly frequently associated with gynecological tumours, affecting women between 60 and 80 years of age and are usually associated with poor prognosis.[3,5,9]

Cerebrospinal fluid may reveal the presence of white blood cells, an increased protein count and oligoclonal bands.[3,10] CT and MRI are initially normal, but may show cerebellar atrophy later in the course of the disease.[6]

In the presence of clinical suspicion, treatment should be initiated as soon as possible with acute immunotherapy, oncologic treatment and maintenance immunotherapy.[11] Outcome is typically poor since neurological symptoms are due to neuronal damage, but some patients with antibodies may respond well to immunotherapy.[3,6,11]

In the case described, the clinical suspicion was essential to the initial directed blood tests which revealed the presence of anti-Yo antibodies and elevated CA-125. These results guided the investigations towards the underlying tumor. Rapidly progressive cerebellar syndrome is a rare but important neurological disorder that might precede the diagnosis of the primary malignancy and increase the burden of the disease. For this reason, it is important that all clinicians take this syndrome into consideration when evaluating their patients. ■

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LS, FM, MIM – Contribuição intelectual e redação do artigo
CV, FD – Contribuição intelectual e revisão do artigo
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**Correspondence / Correspondência:**
Leticia Santos – leticia.santos@hgo.min-saude.pt
Serviço de Medicina Interna, Hospital Garcia de Orta, Almada, Portugal
Av. Torrado da Silva, 2805-267, Almada, Portugal

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