

DOPA-SENSITIVE PROGRESSIVE DYSTONIA OF CHILDHOOD WITH DIURNAL FLUCTUATIONS OF SYMPTOMS

A CASE REPORT

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SUMMARY - Progressive dystonia with diurnal fluctuations sensitive to levodopa, also known as Segawa's disease, is a rare form of autosomal dominant extrapyramidal disease in the pediatric age group. The dystonic and Parkinson-like symptoms are the main clinical features of the disease and, characteristically but not in all cases, show a diurnal variation. They are absent or present to a lesser extent in the morning, worsening during the day. Treatment with small doses of levodopa results in remission or marked improvement of the symptomatology. We present the case of a 11 years old female patient that developed a dystonic posture in her feet that led her to a tip-toe walking pattern, since the age of 2. Diurnal fluctuations of the symptomatology were noticed by her mother. At 7 years of age she developed a left deviation of the head and an abnormal flexor posture of the left arm. In the next years the symptoms progressed and the fluctuations became less evident. At the age of 10, they were present soon after she woke up in the morning. The neurological examination disclosed a dystonic posturing of the head and left arm, a generalized rigidity of the extremities and a palpebral tremor. Laboratory examinations, including copper and ceruloplasmin, and neuro-imaging studies were negative. She was started on levodopa 150 mg/day with prompt disappearance of the symptomatology. After one-year follow-up she is symptom-free with only 100 mg/day of levodopa. No adverse effect was observed so far.

KEY WORDS: dystonia, Segawa's disease, fluctuating dystonia, levodopa.

Distonia progressiva da infância com flutuação sintomatológica diurna sensível a levodopa: relato de caso

RESUMO - A distonia progressiva da infância responsiva à levodopa, também conhecida como doença de Segawa, é uma forma rara de doença extrapiramidal de herança autossômica dominante na faixa etária pediátrica. As principais características clínicas da doença são as manifestações distônicas e parkinsonianas que, na maioria dos casos, apresentam variação diurna, sendo ausentes ou de pequena magnitude pela manhã e piorando com o transcorrer do dia. O tratamento com pequenas doses de levodopa resulta na melhora completa ou significativa da sintomatologia. Relata-se o caso de uma criança de 11 anos de idade, do sexo feminino, que a partir dos 2 anos de idade apresentava postura distônica dos pés levando a assumir posição equina à marcha. A flutuação da postura durante o decorrer do dia foi observada pela mãe desde o início. Aos 7 anos, ela desenvolveu desvio lateral da cabeça para a esquerda associado a postura flexora do membro superior ipsolateral. Houve piora progressiva dos sintomas até que aos 10 anos de idade a sintomatologia era observada ao despertar. O exame neurológico permitiu detectar postura distônica da cabeça e do membro superior esquerdo, rigidez generalizada nas extremidades e leve tremor palpebral. Os exames laboratoriais, incluindo dosagens de cobre e ceruloplasmina, foram normais ou negativos, bem como os exames de neuro-imagem. O tratamento com levodopa foi iniciado com dosagem de 150 mg/dia, com melhora completa e imediata da sintomatologia. Após 1 ano de seguimento,

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ela está assintomática, tomando levodopa na dose de 100 mg/dia. Nenhum efeito colateral devido à terapêutica foi observado nesse período.

PALAVRAS-CHAVE: distonia, doença de Segawa, distonia flutuante, levopa.

Segawa¹⁵, in 1976, described cases of children and adults with progressive dystonia and two striking features: fluctuation of symptoms during the day and relief or complete normalization of symptoms with low doses of L-DOPA. An autosomic dominant inheritance with variable penetrance was proposed whereas other authors proposed a recessive mode of inheritance^{4, 7, 11, 15}. The clinical picture is characterized by dystonic and Parkinson-like symptoms. Fluctuation of symptoms during the day, when present, strongly supports the diagnosis but this is not considered obligatory since there are several reports of compromised siblings where the fluctuating pattern is not observed^{3, 11}. In other cases, the diagnosis was probably made before the appearance of the diurnal variation^{3, 11}. The response to L-DOPA treatment and the poverty of side effects have encouraged authors to propose a drug trial in selected cases of dystonic patients with uncertain etiology⁴.

This is the first case of Segawa's disease with symptoms starting in infancy reported in our country to our knowledge; the other¹, had symptoms present from the age of 18 years on.

CASE REPORT

JS is a 11 years old girl, born after an uneventful gestation and delivery with a birthweight of 3,200 g, of non-consanguineous parents. Several relatives on her mother's side had history of walking difficulties, with possible dystonic symptoms starting during childhood or infancy, but were unaccessible for examination. She



Fig1. Images obtained through video-recording of the patient while walking. On the left side, recorded before treatment with levodopa was begun, the dystonic features are easily observed and, on the right, we can easily notice the resolution of the abnormal posture after levodopa therapy.

walked at 2 years of age and at that time a tip-toe walking pattern was already noticed with frequent falls and a diurnal fluctuation was observed by her mother. At 7 years of age, she developed a left deviation of her head with abnormal flexor posturing of her left arm that worsened at the end of the day. The symptoms worsened earlier in the day whenever her sleeping time was diminished during the night. After 10 years of age, the symptoms were already present in the morning, soon after she woke up. The neurological examination disclosed a dystonic posturing of the head and left arm with generalized rigidity of the extremities, no cogwheel sign was noticed, myotatic reflexes were hyperactive, a bilateral flexor plantar response was obtained and a slight palpebral tremor noticed. She had a thoracic scoliosis and a lumbar lordosis. Ophthalmologic examination was normal. Laboratory examination revealed normal serum levels of copper ($140\mu\text{g/dL}$) and ceruloplasmin (30 mg/dL). CT-scan, MRI, EEG and CSF examination were normal. She was started on levodopa (50 mg t.i.d)

with marked improvement immediately after the first dose (Fig 1). After 1 year of follow-up, she is symptom-free, with a smaller dosage of levodopa (50 b.i.d).

COMMENTS

DOPA responsive dystonia (Segawa's disease) is a disease characterized by dystonic symptoms that respond markedly to L-DOPA treatment. The clinical picture however is variable concerning aspects as age of onset, clinical symptoms, severity and inheritance.

Our case had dystonic symptoms beginning in infancy with a fluctuating pattern, and responded markedly to low dosage L-DOPA, being symptom-free after treatment, 1 year of follow-up. The age of onset was during infancy. This is in accordance with other reports that found a lower age at onset in the female sex, girls being more commonly and severely affected than boys^{3, 10, 11}.

Our patient had rigidity present during the whole day, worsening during the afternoon, and was unable to walk in the evening at the time of diagnosis. Since the early stages of the disease, the fluctuating pattern was observed in our patient. The fluctuation of symptoms observed during the day is a hallmark of Segawa's disease although not obligatory. There are several reports of patients that did not show this symptom fluctuation, even in the same family^{3, 4, 11}. Others were so severely affected that their symptomatology no longer showed any variation of intensity. On the other hand, some patients that did not show diurnal fluctuation probably were diagnosed early on the course of the disease, before the fluctuating pattern appeared.

The dystonic posturing in Segawa's disease is mainly observed in the extremities, with descriptions of mild axial involvement in the advanced stages of the disease^{2, 4, 9, 10, 13, 17, 18}. Our case presented with axial symptoms characterized by trunk scoliosis and tonic head tilt. The axial involvement occurred late in the disease evolution.

Although we were unable to examine our patient's relatives, definitely there was a positive family history of progressive motor symptoms starting in childhood that interfered with walking abilities in several relatives on the mother side, thus suggesting a dominant mode of inheritance for our case. The autosomic dominant with variable penetrance genetic origin of Segawa's disease was proposed in the first reports¹⁵, although there are reports of several sporadic cases in the literature^{3, 4, 11, 15}.

Treatment response in our case was excellent and observed just after the beginning of levodopa introduction. During the follow-up period no side effects were observed. The successful therapeutic response with low doses of levodopa is in accordance with the literature and one of the main criteria for diagnosis. Dyskinesia, nausea, vomiting, behavioral disturbances and mood abnormalities were reported and are easily controlled with dosage reduction^{6, 12, 14}. The "on-off" phenomena observed in parkinsonism are not observed in patients with Segawa's disease and are the main feature in the differential diagnosis with the juvenile form of Parkinson disease^{5, 16, 18}. Attempts to discontinue levodopa have always ended in symptom recurrence in Segawa's disease patients^{3, 10, 12, 14}.

Segawa's disease was diagnosed in several patients thought to have a static or progressive neurological disease, such as cerebral palsy or spastic paraparesis^{1, 2, 6, 8, 11, 13}. Therapeutic trial with low doses of levodopa is recommended in selected cases with dystonic symptoms even without diurnal fluctuation of uncertain etiology in view of the diagnostic value of the positive response and the benefits that treatment can offer to the patients.

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