TABLE 1. *Pre- and posttreatment scores for patients randomized to tegaserod or placebo*

	Tegaserod		Placebo		*P* for change
	Pre	Post	Pre	Post	
Total SGA	9.1 ± 4.4	8.3 ± 4.0	6.2 ± 3.7	8.7 ± 3.9	.10
Bothersome constipation	3.3 ± 2.0	2.8 ± 1.7	2.2 ± 1.5	3.0 ± 1.5	.14
SGA of abdominal pain and discomfort	2.8 ± 1.5	2.5 ± 1.4	1.7 ± 1.9	2.7 ± 1.5	.30
SGA of satisfaction	3.1 ± 1.1	3.0 ± 1.1	2.3 ± 1.0	3.0 ± 1.1	.10
UPDRS	42.1 ± 22.5	39.8 ± 25.7	33.8 ± 10.4	37.0 ± 11.6	.32

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Suppression of Myoclonus in SCA2 by Piracetam

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Video 

Abstract: We report on a 30-year-old patient with advanced cerebellar degeneration due to SCA2. He presented with severe myoclonus, which was resistant to conventional therapy and dramatically improved after administration of 12–18 gm/die piracetam. Piracetam may be considered in the treatment of refractory myoclonus in spinocerebellar degenerations. © 2005 Movement Disorder Society

Key words: myoclonus; piracetam; SCA2; nootropic drugs

Spinocerebellar ataxia type 2 (SCA2) is one of the most frequent among the autosomal dominant cerebellar ataxias and the most common in Italy. An abnormally expanded cytosine-adenine-guanine (CAG) triplet sequence has been found within a gene encoding for ataxin-2, a protein of unknown function.[1] The main clinical features of SCA2 are gait and limb ataxia, dysarthria, supranuclear ophthalmoplegia, and peripheral neuropathy. Myoclonus is infrequent in SCA2 and usually present in late disease stages, whereas it is a typical clinical feature of other dominant ataxias such as DRPLA, SCA14, and SCA19.[2]

Piracetam (2-oxo-1-pyrrolidine-acetamide) at high doses is an effective and well-tolerated drug for treatment of myoclonus.[3,4] We describe an SCA2 patient who developed a severe

This article includes Supplementary Video, available online at http://www.interscience.wiley.com/jpages/0885-3185/suppmat

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Received 10 December 2004; Revised 2 March and 29 April 2005; Accepted 21 May 2005

Published online 7 September 2005 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/mds.20683

multifocal myoclonus in a late stage of the disease. Piracetam administration dramatically improved myoclonus.

Case Report

This 30-year-old man was affected by SCA2, confirmed by molecular diagnosis (46/22 CAG triplets). His 57-year-old father (37/22 CAG triplets) did not report any complaint but the neurological examination showed mild dysarthria as well as gait and limb ataxia. The disease onset was at 17 years of age with mild dysarthria, dizziness, gait ataxia, and clumsiness. A brain MRI showed marked atrophy of cerebellar hemispheres, vermis, and pons. The clinical picture worsened rapidly and severe dysphagia both for solids and liquids developed. The patient was admitted to our department for aspiration pneumonia and a percutaneous endoscopic gastrostomy (PEG) was performed.

Neurological examination showed mild drowsiness, impossible stance and gait, anarthria, intention tremor, dysmetria, slowness of saccadic eye movements, weakness, hypotrophy and increased tone in all limbs, reduced tendon reflexes, dystonic movements, and severe continuous multifocal myoclonus. Myoclonus was markedly worsened by movement (see Video, Segment 1), pinprick, or passive stretch. International Cooperative Ataxia Rating Scale (ICARS) score was 97/100.[5] Neuropsychological evaluation was impossible due to the severe cognitive decline.

Video polygraphic examination showed irregular high-amplitude continuous and multifocal myoclonus, more evident at the upper limbs with diffuse slowing of background activity and no paroxysmal activity at EEG. Surface EMG recording from the wrist extensor and flexor and biceps brachii revealed muscle jerks lasting approximately 40 to 60 msec with no synchronous agonist and antagonist muscle involvement. Jerk-locked back-averaging analysis did not demonstrate any EEG–EMG correlate. It was not possible to perform somatosensory evoked potentials (SEPs) and Long Loop Reflex I (C-reflex) because of the muscular artifacts and the patient's poor cooperation.

Valproate (30 mg/kg/die) and clonazepam (0.1 mg/kg/die) oral administration only resulted in partial and transient suppression of involuntary muscle jerks. Levetiracetam (60 mg/kg/die) at a daily dosage of 3,000 mg for 2 months was also ineffective. Then, we administered 12 gm of piracetam (240 mg/kg/die) by rapid intravenous bolus once a day for a week. After 1 day, we observed a dramatic reduction of myoclonus, which almost disappeared within 3 days. The patient also appeared more alert. No clinical benefit on the other neurological symptoms was obtained. The benefit lasted approximately 48 hours after drug discontinuation. The reintroduction of piracetam rapidly induced the disappearance of the myoclonus again. In concomitance of a febrile illness, we observed reappearance of myoclonus, which was successfully treated, increasing the dose to 18 gm once a day. After 3 months of IV treatment, piracetam was administered by PEG at the daily dose of 18 with no benefit loss. Due to difficulty to get drug supply, it was withdrawn on two occasions and marked myoclonus reappeared. To date, after 1 year of treatment, the patient is myoclonus-free (see Video, Segment 2) with neither side effects nor routine blood test changes.

Discussion

Myoclonus is an infrequent and usually late symptom in SCA2 patients and its origin is still unclear. Neurophysiological studies suggested that myoclonus may be of brainstem or spinal origin in SCA14,[6] whereas both cortical and spinal myoclonus have been described in SCA19.[7] In our case, the origin of myoclonus is not very clear because it was not possible to perform a complete electrophysiological study before piracetam (PIR) treatment. In cortical myoclonus, EEG recording may show variable paroxysmal abnormalities, usually consisting of multifocal or generalized spike-and-wave discharge.[8] Surface EMG recording reveals a burst duration less than 75 msec.[9] Jerk-locked back-averaging discloses a focal and central positive–negative biphasic spike that precedes the jerk onset by 10 to 40 msec.[8,9] In our patient, we did not detect paroxysmal EEG activity and surface EMG recording revealed a muscle jerk lasting 40 to 60 msec, not correlated to EEG. Stimulus sensitivity and burst duration may be consistent with cortical myoclonus, but the absence of EEG abnormalities and jerk-locked back-averaging results are against this hypothesis. The electrophysiological data may suggest a myoclonus of subcortical origin, usually characterized by burst of variable duration and no EMG–EEG correlate.[9] The disturbance seems to differ from minipolymyoclonus that is characterized by subtle and recurring twitches predominant in the fingers and hands with simultaneous discharges in antagonist muscles of the same limb and bilateral synchronous jerks of homologous muscles, correlated to bilateral synchronous frontocentral potentials.[10]

Piracetam, a low-molecular-weight derivative of γ-aminobutyric acid (GABA), has been widely used to treat cognitive disorders as nootropic agent and myoclonus.[3,4] It is traditionally considered quite safe in terms of side effects. However, gastric discomforts, diarrhea, and hematological abnormalities may sometimes occur, especially at high doses.[3,4] Piracetam is present in the polar heads of phospholipid membrane models and it is thought to alter the physical properties and the fluidity of the brain cell membranes.[11,12] In our patient, piracetam was effective on myoclonus at daily doses of 12–18 per day, whereas levetiracetam was not at the daily IV dose of 3,000 mg. This could be explained by the different mechanism of action of the drugs[12] or by the need to reach a higher levetiracetam dose.[13]

Piracetam at high dose (60 g/die) improved gait ataxia in a patient with degenerative cerebellar ataxia without myoclonus. The effect was fast and lasted approximately 1 month after discontinuation of the drug.[14] Conversely, in our case, piracetam improved only myoclonus and its effect only lasted few days after drug withdrawal. The baseline condition was much more severe and the cerebellar atrophy at a more advanced stage in our patient. We observed improved alertness, possibly due to the nootropic effect of piracetam or due to the withdrawal of clonazepam. In conclusion, the good tolerability of piracetam makes it easy to test for treatment of refractory and disabling myoclonus in SCA patients.

Legends to the Video

Segment 1. Baseline condition. Neurological examination shows diffuse, irregular, and continuous myoclonic jerks worsened by movement. Repetitive, pseudorhythmic, not voluntary movements of the fingers are also evident.

Segment 2. After 1 year of therapy with piracetam, 18 g/day, both rest and action myoclonus are clearly reduced and the patients appears more alert. Dysmetria and dystonic neck and trunk posture are evident.

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Sporadic Rapid-Onset Dystonia–Parkinsonism Presenting as Parkinson's Disease

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Video 

Abstract: We report on a 38-year-old patient with rapid-onset dystonia–parkinsonism (RDP) with a missense mutation in the Na/K-ATPase α3 subunit (ATP1A3). Asymmetrical parkinsonian symptoms evolved over a year. After a stable episode of another 2.5 years, overnight he developed oromandibular dystonia and more severe parkinsonian symptoms. We conclude that RDP should be considered as a rare cause of levodopa-unresponsive parkinsonism even if there is no family history and the classic presentation is lacking. © 2005 Movement Disorder Society

Key words: RDP; dystonia; mutation; genetic; Parkinson

Rapid-onset dystonia–parkinsonism (RDP, DYT12) was first described in 1993.[1] It is an autosomal dominantly inherited disorder, and recently, mutations in Na/K-ATPase α3 subunit (ATP1A3) on chromosome 19q13 were discovered, implicating a malfunction of the Na/K pump in familial cases.[2] One of the two sporadic cases described in that study (Patient 1 with mutation T821C and codon change 1274T) is the subject of the present study. RDP classically presents with acute-onset dystonia predominantly affecting bulbar musculature and with additional mild parkinsonian symptoms. Here, we describe a patient who presented with right-sided parkinsonism developing gradually over a year. Three and a half years after the onset of symptoms, sudden parkinsonian and subtle dystonic bulbar signs appeared.

Case Description

A 39-year-old, right-handed man presented in 1998 with dragging of the right leg and difficulties writing. The symptoms had progressed insidiously in the course of approximately a year. Some worsening of symptoms occurred in the course of

This article includes Supplementary Video, available online at http://www.interscience.wiley.com/jpages/0885-3185/suppmat.

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Received 7 April 2005; Revised 3 June 2005; Accepted 12 June 2005

Published online 13 September 2005 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/mds.20695