Table 1. Clinical data in 4 patients with confirmed diagnosis of MSA

	Cases			
	Case 1	Case 2	Case 3	Case 4
Age at death (y)	61	72	55	64
Sex	M	F	M	M
Clinical diagnosis	MSA-P	Unclassifiable Parkinsonism	MSA-C	PAF
MSA criteria	Probable	Not fulfilled	Probable	Not fulfilled
Pathological diagnosis	MSA	MSA	MSA	Minimal change MSA
Additional pathology	No	Pathological aging	No	No
Smoking	Ex-smoker	Never smoked	Ex-smoker	Never smoked
Disease duration (y)	9	8	8	5.1
First symptom	Erectile dysfunction	Tremor	Erectile dysfunction	Pain on exertion
Postural ↓BP[a]	Yes	No	No	Yes
Urinary incontinence	Yes	Yes	Yes	Yes
Parkinsonism	Yes	Yes	Yes	No
Cerebellar signs	Yes	No	Yes	No
Treatment	Levodopa, Pergolide, Amantadine, Oxybutynin, Desmopressin, Imipramine	Levodopa, Amantadine, Thyroxine, Atropine, Dothiepin, Tolterodine	Macrogol, Amantadine, Riluzole, Desmopressin	Midodrine, Desmopressin
UPSIT score	28/40 (aged 60 y)	29/40 (aged 66 y)	32/40 (aged 55 y)	30/40 (aged 64 y)
Percentile in relation to UK control population	50th percentile of 65 men aged 55–75 y	43th percentile of 58 women aged 55–75 y	79th percentile of 65 men aged 55–75 y	63rd percentile of 65 men aged 55–75 y
Percentile in relation to PD patients from the UK	95th percentile of 77 men aged 55–75 y	94th percentile of 53 women aged 55–75 y	97th percentile of 77 men aged 55–75 y	96th percentile of 77 men aged 55–75 y
Interval between smell test and death (y)	1	6	<1	<1

[a]Postural ↓BP refers to the orthostatic decrease of blood pressure being ≥30 mmHg systolic or 15 mmHg diastolic.BP = blood pressure; F = female; M = male; MSA = multiple system atrophy; MSA-C = multiple system atrophy with predominant cerebellar signs; MSA-P = multiple system atrophy with predominant parkinsonian signs; PAF = pure autonomic failure; PD = Parkinson's disease; UPSIT = University of Pennsylvania Smell Identification Test.

Painless Legs and Moving Toes: Symptom Reduction During Pregnancy

Painless legs and moving toes[1] is a rare variant of painful legs and moving toes, itself a very rare movement disorder.[2] Both conditions cause semicontinuous movements of the toes, and sometimes of fingers, jaw, and tongue.[3] We describe a woman with painless legs and moving toes, whose symptoms dramatically varied in relation to her menstrual cycle, oral hormone use, and pregnancy.

The patient developed, at age 26 years, small involuntary movements of her toes and fingers without associated limb pain. She also had childhood tics involving face and shoulders, previous minor dance-related foot injuries, a right lateral meniscus tear, and bilateral carpal tunnel syndrome (onset age 27 years). Examination revealed small, multidirectional, nearly continuous, involuntary movements of the toes (Video), and less frequent similar finger movements. The movements were not accompanied by a preceding urge or subsequent relief, and they were only briefly suppressible. They worsened for a few days before menses and during use of oral progesterone. During the course of 2 pregnancies, the toe movements considerably decreased in frequency and amplitude (Video). They remained nearly absent throughout each pregnancy and postpartum amenorrheic lactation period, after which they returned to their original severity (Video).

Serum studies, including complete blood count, electrolytes, blood urea nitrogen, creatine, glucose, creatine kinase, thyroid function tests, liver function tests, erythrocyte sedimentation rate, and rheumatoid factor, were within normal limits. Antinuclear antibodies were absent. Electromyography and nerve conduction studies revealed only mild bilateral carpal tunnel syndrome. There was no conduction abnormality or evidence of denervation in the lower extremities. Polysomnography with surface electromyography revealed that the toe movements persisted through all stages of sleep. Magnetic resonance imaging of the brain and cervical spine were normal.

Fluctuation of symptom severity has not been previously described for painless legs and moving toes. Our patient's movements nearly disappeared during 2 pregnancies and subsequent lactation periods, and worsened during her menstrual cycle and

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Additional Supporting Information may be found in the online version of this article.

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oral progesterone use. Progesterone and estrogen levels are high during pregnancy, normal during lactation, and low before menses.[4] Thus, the observed movement fluctuations do not simply relate to the levels of these hormones. The original description of the related syndrome, painful legs and moving toes, listed alleviating and aggravating factors, such as hot water, stress, and pain.[2] However, these affected the movements only briefly. The frequency of multiple sclerosis exacerbations and of migraines without aura is reduced during pregnancy, but is increased in the puerperium,[5,6] unlike the movements described here. Restless leg syndrome can appear or worsen during pregnancy, but there is no clear change in the lactation period.[7]

The mysterious nature of painless legs and moving toes further complicates the interpretation of our observation, given the variety of conditions that have been associated with this syndrome.[3] Painful legs and moving toes is commonly associated with peripheral nervous system lesions. However, peripheral nerve symptoms are only known to worsen (e.g., carpal tunnel syndrome), not improve, with pregnancy. We are thus at a loss to explain this remarkable phenomenon—movement reduction during pregnancy and puerperium—but we hope it might stimulate future ideas on this disorder's pathophysiology and treatment.

Legend to the Video

Video. Effect of pregnancy on toe movements in a patient with painless legs and moving toes. Before pregnancy, the toes move involuntarily in various directions, mostly laterally. The movements are slow and include very brief sustaining of laterally stretched postures. During the third trimester of pregnancy, the toe movements have nearly disappeared: 2 movements of the right second toe are seen, as is a barely visible small movement of the left second toe. After pregnancy and after the end of the lactation period, the toe movements have returned to similar frequency and intensity.

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Serum Levels of N-Acetylaspartate in Huntington's Disease: Preliminary Results

Magnetic resonance spectroscopy (MRS) studies have described lower levels of N-acetylaspartate (NAA) in the left putamen of premanifest and early Huntington's disease (HD) patients compared to controls, suggesting NAA as a novel biomarker of this neurodegenerative disorder.[1] A gas chromatography–mass spectrometry (GC-MS) method demonstrated the validity of NAA measurements in biological fluids in patients with neurological diseases.[2] Very recently, our group found that serum NAA, measured by liquid chromatography–MS (LC-MS), was significantly reduced in healthy controls with advancing age[3] and was increased in neurodegenerative and demyelinating diseases such as amyotrophic lateral sclerosis and multiple sclerosis.[4,5] The aim of our study was to evaluate NAA serum levels in a cohort of genetically confirmed HD patients.

Twenty-two consecutive outpatients affected by genetically confirmed HD were enrolled. The clinical features are summarized in Table 1. All patients underwent the motor section of Unified Huntington's Disease Rating Scales (UHDRSM) and the Total Functional Capacity Scale (TFC).[6] Twenty-one age- and sex-matched controls (10 females, age 36–62, mean 47.57 ± 7.68: *t* test 0.23; not significant [n.s.]) were also included. All subjects and controls gave their informed consent to the study, which was approved by the local Ethics Committee. Exclusion criteria were any general medical and central peripheral nervous system diseases.

Serum was stored at −80°C. Quantification of NAA was achieved by the standard addition approach and analysis were performed with the LC-MS technique.[3]

NAA serum levels were on average 0.084 ± 0.013 μmol/L in controls and 0.65 ± 0.15 μmol/L in HD (*t* test: 5, $P = .00001$). Patients taking drugs did not display different NAA levels compared to drug-free patients (*t* test: 0.65, n.s.). NAA levels displayed a positive correlation with the global motor impairment, expressed by the total UHDRSM scores (Spearman correlation test, $r = 0.45$, $P = .032$), including subitems such as finger tapping ($r = 0.46$, $P = .029$), ocular pursuit ($r = 0.55$, $P = .007$), saccadic initiation ($r = 0.46$, $P = .29$), and velocity ($r = 0.49$, $P = .029$), pronate-supinate

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