walk (UPDRS motor score: 54 of 108). During 60 Hz STN alone/off-drug condition, he was able to walk unaided in open space without initiation akinesia and with only two FOG episodes during a half-turn (Segment 1: UPDRS III, item 30: 2 of 4). During the PPN-DBS alone/off-drug condition, the patient was unable to walk unaided because of severe gait initiation failure and severe half-turn FOG (Segment 2: UPDRS III, item 30: 3 of 4).

Author Roles: C. Moreau, A. Peppe, D. Devos, and F. Marchetti participated in design of the study and acquisition of the data. C. Moreau, D. Devos, L. Defebvre, A. Destée, A. Stefani and A. Peppe participated in the drafting and critical revision of all the submitted material and made a major intellectual contribution.

Caroline Moreau, MD*
Luc Defebvre, MD, PhD
David Devos, MD, PhD
Department of Neurology and Movement Disorders
Roger Salengro Hospital
Lille University Medical Center
Lille, France
**E-mail: c-moreau@chru-lille.fr*

Fabio Marchetti, PhD
Neurological Department
IRCCS Fondazione St. Lucia
Rome, Italy

Alain Destée, MD
Department of Neurology and Movement Disorders
Roger Salengro Hospital
Lille University Medical Center
Lille, France

Alessandro Stefani, MD, PhD
Movement Disorder Centre
University of Tor Vergata
Rome, Italy

Antonella Peppe, MD, PhD
Neurological Department
IRCCS Fondazione St. Lucia
Rome, Italy

References

1. Stefani A, Lozano AM, Peppe A, et al. Bilateral deep brain stimulation of the pedonculopontine nucleus and subthalamic nuclei in severe Parkinson's disease. Brain 2007;130:1596–1607.
2. Yelnik J. PPN or PPD what is the target for deep brain stimulation in Parkinson's disease? Brain 2007;130:79.
3. Zrinzo L, Hariz M. The pedunculopontine and peripeduncular nuclei: a tale of two structures. Brain 2007;130:1596–1607.
4. Mazzone P, Sposato S, Insola A, Dilazzaro V, Scarnati E. Stereotactic surgery of nucleus tegmenti pedunculopontine. Br J Neurosurg. 2008;22(Suppl 1):S33–S40.
5. Moreau C, Defebvre L, Destée A, et al. STN-DBS frequency effects on freezing of gait in advances Parkinson's disease. Neurology 2008;71:80–84.
6. Peppe A, Chiavalon C, Pasqualetti P, Crovato D, Caltagirone C. Does gait analysis quantify motor rehabilitation efficacy in Parkinson's disease? Gait Posture 2007;26:452–462

Catamenial and Oral Contraceptive-Induced Exacerbation of Chorea in Chorea-Acanthocytosis: Case Report

Autosomal recessive chorea-acanthocytosis (ChAc) is a neurodegenerative disorder with diverse neuropsychiatric presentations including behavioral, cognitive, and movement manifestations, the latter typically chorea and oroligual dyskinesias.[1]

Several endocrine and hormonal disturbances, especially those linked to estrogen, can influence the occurrence and severity of movement disorders including Parkinsonism, chorea, dystonia, tics, and myoclonus.[2,3] We report for the first time the exacerbation of chorea in ChAc during treatment with an oral contraceptive (OC).

The patient is a 38-year-old woman with no medical history until 18 years of age when the occurrence of secondary generalized seizures brought her to neurologic evaluation. Investigations with EEG tracing, brain CT and MRI scans were unremarkable. She was started on phenytoin 100 mg bid, soon switched to phenobarbital 100 mg qd because of hirsutism. She remained stable until the age of 33 when she experienced the onset of mild upper extremities chorea. One year later, overt chorea became evident, including orolingual dyskinesias with lip and tongue biting. At this point obsessive-compulsive behavior, depression and motor tics (eye blinking and lip smacking) were noticed. She was the first of four siblings, parents had remote consanguinity (forth cousins). One of her two sisters had obsessive-compulsive disorder, and her brother had epilepsy. Peripheral red-blood cell analysis revealed acanthocytes; serum transaminase levels were mildly elevated [GOT 42 U/L (5–36), GPT 60 U/L (5–52)]. Serum creatine kinase was 700 U/l (1-75) and aldolase was 9.5 U/l (<6). ESR, C-reactive protein level, rheumatoid factor assay, antiphospholipid antibodies, ANA test, and antistreptolysin O were negative or absent. Electromyography with nerve conduction studies of the upper and lower limbs were normal. Western blot analysis of erythrocyte membrane preparations using anti-chor1 antiserum was performed at the Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK, as previously described,[4] revealing markedly reduced levels of chorein in the proband and her brother. She was started on quetiapine 50 mg bid, paroxetin 20 mg qd, clonazepan 2 mg qd, and tetrabenazine 25 mg tid with satisfactory response of both movement and behavioral disorders. After 6 months, during a routine gynecologic evaluation, she complained of exacerbation of chorea during 3 to 4 days that preceded her menses. This catamenial worsening was noted in the four latest

Published online 4 September 2009 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/mds.22730

cycles. Continuous oral desogestrel 75 μg/day was started. During the initial days on this medication, she experienced an abrupt and dramatic worsening of involuntary movements, which became generalized, significantly more severe, interfering with daily activities and feeding. Hormonal treatment was withdrawn after 1 week and abnormal movements gradually returned to baseline. During follow-up, slow and insidious progression of symptoms occurred, partially controlled with changes in drug regimen.

Since the first description of the association of OCs and chorea by Fernando,[5] clinical data have grown considerably, usually in the form of case reports illustrating this phenomenon from diverse standpoints. One of the earliest reports describe five cases of chorea related to OCs, one with probable basal ganglia vasculopathy leading to acute hemichorea, and four cases in women with a history of Sydenham's chorea (SC).[3] Riddoch et al.[6] reported six additional cases, one with a history of SC. Finally, menopause and hormone replacement therapy have also been implicated in the occurrence of chorea, reinforcing the association between female hormones and this movement disorder.[3,6,7]

Although most of such cases have been hypothesized to be related to reactivation of SC, this antecedent is not found in some patients. Other immunological bases have been mentioned in the literature such as SLE, antiphospholipid or anti-basal ganglia antibodies syndromes.[2,7]

This is the first case of a patient with ChAc presenting with catamenial worsening of chorea and its' even more dramatic exacerbation after starting an OC. Of importance, the case presented here had no history of SC. These observations differ from the cases described earlier mainly because the movement disorder, present for almost 2 years, was exacerbated, not triggered by the hormonal treatment. This also implies that additional mechanisms, other than a purely immunological, may have played roles in this case. Catamenial exacerbation of chorea may be explained by the reduction of endogenous progesterone levels. Recent studies have shown that progesterone and its metabolites have GABA(A)/NMDA modulatory effects on an animal model of tardive dyskinesia.[8] Although progesterone and allopregnanolone seem to have mainly an inhibitory net effect through positive GABA and negative NMDA modulation, pregnenolone has the opposite net effect. These variable effects of different progestogens may also explain the apparently paradoxical worsening of chorea when desogestrel (a synthetic progesterone analog) was initiated. Another example is a previous case of generalized chorea after treatment with medroxyprogesterone acetate.[9] Finally, induction of quetiapine or tetrabenazine metabolism, leading to a reduction in the dopamine D_1/D_2 blockage or an increase in synaptic dopamine, could explain the exacerbation of chorea. However, so far no known interaction between these two drugs and desogestrel has been described, although all three are substrates of the cytochrome P450 3A4.[10]

Author Roles: R.P. Munhoz: Organization, execution, review, writing of the first draft; P.A. Kowacs: Conception, organization, execution, review, writing of the first draft; M.G. Sória: Execution, writing of the first draft; R.D.-P. Ducci: Execution, review and critique; S. Raskin: Execution, review and critique; H.A.G. Teive: Conception, organization, execution, review and critique.

Renato Puppi Munhoz, MD
Department of Neurology
Federal University of Paraná
Curitiba, Brazil

Pedro André Kowacs, MD*
Marília Grando Sória, MD
Renata Dal-Prá Ducci, MD
Department of Neurology
Federal University of Paraná
Curitiba, Brazil
Instituto de Neurologia de Curitiba
Curitiba, Brazil
**E-mail: pkowacs@gmail.com*

Salmo Raskin, MD
Department of Molecular Genetics
Genética Laboratory
Curitiba, Brazil

Helio Afonso Ghizoni Teive, MD, PhD
Department of Neurology
Federal University of Paraná
Curitiba, Brazil

References

1. Walker RH, Jung HH, Dobson-Stone C, et al. Neurologic phenotypes associated with acanthocytosis. Neurology 2007;68:92–98.
2. Miranda M, Cardoso F, Giovannoni G, Church A. Oral contraceptive induced chorea: another condition associated with anti-basal ganglia antibodies. J Neurol Neurosurg Psychiatry 2004;75:327–328.
3. Lewis PD, Harrison MJ. Involuntary movements in patients taking oral contraceptives. Br Med J 1969;15:404–405.
4. Dobson-Stone C, Velayos-Baeza A, Filippone LA, et al. Chorein detection for the diagnosis of chorea-acanthocytosis. Ann Neurol 2004;56:299–302.
5. Fernando SJ. An attack of chorea complicating oral contraceptive therapy. Practitioner 1966;197:210–211.
6. Riddoch D, Jefferson M, Bickerstaff ER. Chorea and the oral contraceptives. Br Med J 1971;4:217–218.
7. Steiger MJ, Quinn NP. Hormone replacement therapy induced chorea. Br Med J 1991;302:762.
8. Bishnoi M, Chopra K, Kulkarni SK. Modulatory effect of neurosteroids in haloperidol-induced vacuous chewing movements and related behaviors. Psychopharmacology 2008;196:243–254.
9. Knoblich OE, Witt TN, Meyendorf R, Spatz R. Choreic syndrome following intramuscular exhibition of a contraceptive preparation. Nervenarzt 1981;52:239–242.
10. Newcomer JW. Second-generation (atypical) antipsychotics and metabolic effects: a comprehensive literature review. CNS Drugs 2005;19 (Suppl 1):1–93.