SHORT REPORT

Oral contraceptive induced chorea: another condition associated with anti-basal ganglia antibodies

M Miranda, F Cardoso, G Giovannoni, A Church

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Use of oral contraceptives is a recognised but infrequent cause of chorea. This type of chorea has usually been considered a reactivation of Sydenham's chorea by an unknown mechanism. A patient developed a chorea triggered by the use of oral contraceptives with no definite evidence of previous Sydenham's chorea or recent streptococcal infections. However, the patient had positive anti-basal ganglia antibodies, which supports an immunological basis for the pathophysiology of this chorea.

Use of oral contraceptives is a well known but uncommon cause of chorea .[1 2] It has been hypothesised that this condition is due to reactivation of Sydenham's chorea but this antecedent has been absent in some patients, whereas other cases have been related to the development of other autoimmune disorders such as systemic lupus erythematosus.[3] To our knowledge, there have been no reports of an association of this form of chorea with the presence of anti-basal ganglia antibodies, a condition that would support an immunological mechanism for the pathogenesis of this disorder.

CASE REPORT

In March 2001, a 19 year old female college student, who was previously healthy, developed abnormal facial grimacing and writhing movements of her left hand. These abnormal movements came on insidiously and followed a stable course over a year with neither exacerbation nor remission. She did not describe premonitory urges and could not control these movements at will. Her college performance was unaffected and there was no evidence of cognitive or psychiatric manifestations; specifically there was no obsessive-compulsive behaviour. One year prior to the onset of these movements she had begun taking an oral contraceptive (OC), which contained ciproterona 2 mg and ethinylestradiol 0.035 mg, for a menstrual irregularity. She had never been pregnant. There was no personal or family history of abnormal movements and no previous history of rheumatic fever. There was no history of an antecedent streptococcal or other infection.

General medical examination was normal. Specifically, cardiac auscultation revealed no abnormalities. On neurological examination, the most relevant finding was the presence of facial grimacing, mainly affecting her lower face, and choreiform movements of the left hand. Neurological examination revealed no cognitive, pyramidal, sensory, cerebellar, or gait abnormalities. She complained that these abnormal movements, in spite of being mild, impaired her social functioning.

The laboratory evaluation revealed a raised anti-streptolysin-O titre of 287 IU/ml (normal <200 IU/ml). However, the anti-DNAase B titre of 120 IU/ml was normal (normal <340 IU/ml). Throat cultures did not detect streptococcus. Her full blood count, erythrocyte sedimentation rate, C-reactive protein, thyroid function, plasma amino acids, ceruloplasmin, antinuclear antibodies, and antiphospholipid antibodies were either normal or negative. Magnetic resonance imaging of the brain was normal. Echocardiogram showed no alterations. Anti-basal ganglia antibodies were positive by Western immunoblotting and revealed reactivity against antigens of 40 and 45 kDa in size. The antibody assay method has been described previously.[4] The patient's serum was also screened against a liver antigen preparation to exclude non-specific binding as a result of antinuclear factors or other auto-antibodies. These specific 40 and 45 kDa bands appear to be relatively specific for the group of disorders associated with anti-basal ganglia antibodies.[4]

Her neurological symptoms gradually subsided 2 months after initiating treatment with sulpiride 300 mg daily and the withdrawal of the OCP. Neurological examination 2 months after stopping the sulpiride therapy was normal.

DISCUSSION

In 1966, Fernando reported the first description of chorea associated with use of OCs.[1] Subsequently, reports by Lewis,[5] Gamboa,[6] and Nausieda[2] established OCs as a cause of chorea, although this association is uncommon. Table 1 reviews the clinical features of the cases reported in the literature over the last 23 years. Some cases have been considered to be caused by reactivation of Sydenham's chorea,[2 7 8] while in others no clear relationship with Sydenham's chorea or streptococcal infection has been established.[9 10] The recurrence of chorea during pregnancy in some of these cases suggests a role of oestrogens in these disorders.[11] However, immunologically mediated disorders such as systemic lupus erythematosus and antiphospholipid antibody syndrome must be ruled out in these patients even in the presence of a past history of chorea induced by OCs.[3 12] None of these disorders was detected in our patient. The asymmetrical features at presentation in our patient is not unusual and has been reported in other cases of OCP associated chorea[2] and in patients with Sydenham's chorea.[13]

To the best of our knowledge, this is the first report of a case of chorea associated with the use of the OCs in which anti-basal ganglia antibodies have also been detected. This suggests that there may be an immunological basis in the pathogenesis of this disorder. The hypothesis of an immune reaction associated with this condition is not new; in fact Gamboa *et al* in 1971[6] were the first to postulate an immunological mechanism in the pathogenesis of this condition. An immunological reaction associated with the

Abbreviations: OC, oral contraceptive

Table 1 Clinical features of patients with chorea associated with the use of oral contraceptives in the last 23 years

Reference	Patient age (years)	Time of use	Duration of chorea (weeks)	Clinical presentation/ onset	Medical history	Comments
Nausieda[2]	20	12 weeks	1	Hemichorea/ insidious	Congenital cardiopathy	
	17	2 weeks	2	Bilateral/ insidious	Sydenham's chorea	
	18	8 weeks	3	Bilateral/ insidious	Sydenham's chorea	
	21	2 weeks	2	Bilateral/ insidious	Congenital cardiopathy	
	20	11 weeks	2	Hemichorea/ insidious	Purpura	Normal pregnancy
Dove[7]	20	8 months	8	Hemichorea/ insidious	Rheumatic fever	2 normal pregnancies
Greene[8]	16	2 months	8	Bilateral/ insidious	Sydenham's chorea	Chorea gravidarum
Buge[9]	26	2 months	6	Hemichorea/ insidious	None	
	23	8 years	2	Hemichorea/ insidious		Normal pregnancy
Berger[10]	21	4 years	4	Hemichorea/ insidious	None	Normal pregnancy
Vela[16]	27	Not specified	16	Hemichorea/ insidious	None	PET with FDG showed increased glucose metabolism in contralateral caudate nucleus
Present case	19	2 years	57	Hemichorea/ insidious	None	Presence of anti-basal ganglia antibodies

PET, Positron emission tomography; FDG, ^{18}F-fluorodeoxyglucose.

use of OCs has also been proposed as an explanation for the cases of chorea as the initial manifestation of systemic lupus erythematosus,[3] or antiphospholipid antibody syndrome.[12]

We acknowledge that to have circulating antibodies does not necessarily imply causation; these antibodies have been described in several conditions such as Sydenham's chorea and rheumatic fever,[4] acute disseminated encephalomyelitis,[14] and in a subgroup of Tourette syndrome patients,[15] and therefore they could represent an epiphenomenon. Their pathophysiological role remains uncertain.

Recently Vela *et al*, using positron emission tomography with ^{18}F-fluorodeoxyglucose, reported increased glucose metabolism in the caudate nucleus of a patient with hemichorea induced by the OCs.[16] This supports the direct involvement of basal ganglia circuits as part of the pathological process in these patients.

Our patient had a weakly positive ASO, but negative anti-DNAse B, indicating the possibility of a recent streptococcal infection. It has been hypothesised that streptococcal infection triggers the production of anti-basal ganglia antibodies by the process of molecular mimicry.[4] In our patient, a previous streptococcal infection probably induced the formation of these antibodies, which could have rendered the basal ganglia more vulnerable, and when exposed to hormones the patient developed chorea. The oestrogenic component of OCs is most likely the causative factor in the chorea induced by these agents. Oestrogens do have a definite but very complex modulatory action in dopaminergic systems, and this has been well established, for example in chorea gravidarum.[11]

The presence of an immunological reaction directed at the basal ganglia in this particular disorder may not have therapeutic implications. This is a very benign condition; most cases have a remission after withdrawal of the pill, usually in a period of 2–3 months.

Whether or not chorea occurring in association with pregnancy, systemic lupus erythematosus, or the antiphospholipid antibody syndrome is associated with anti-basal ganglia antibodies is unknown and requires further study.

Authors' affiliations

M Miranda, Department of Neurology, University of Chile, Chile
F Cardoso, Department of Neurology, The Federal University of Minas Gerais, Brazil
G Giovannoni, A Church, Department of Neuroinflammation, Institute of Neurology, Queen Square, London WC1N 3BG, UK

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Correspondence to: Dr M Miranda, Department of Neurology, University of Chile, Llewellyn Jones 1530, Suite 201, Santiago, Chile; e-mail: marcelomiranda@terra.cl

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