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Brief Report

An Unusual Cause of Recurrent Chorea

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Summary: Recurrent chorea is described in a 61-year-old woman who had had chorea gravidarum when she was younger. The recurrent chorea appeared to be induced by a topical vaginal cream that contained conjugated estrogen. This case is consistent with the existence of a recurrent syndrome of hormone-induced chorea. The effect of estrogen on the basal ganglia is complex and not fully understood. **Key Words:** Estrogen—Chorea gravidarum—Hormone-induced chorea—Vaginal creams containing estrogen—Drug-induced chorea—Neurologic complications of pregnancy.

The incidence of chorea gravidarum has decreased during the last half of this century. The decreased incidence has been attributed to the decreased incidence of rheumatic fever, which in turn has been attributed to the introduction of penicillin (1–4). Rheumatic fever, with or without Sydenham's chorea, may predispose women to a hormone-induced chorea during pregnancy (5,6). More recently, hormone-induced chorea is more commonly associated with ingestion of contraceptive pills that contain estrogen (7–16). We describe a case in which a 61-year-old woman had chorea that was apparently induced by a topical vaginal cream that contained estrogen.

CASE REPORT

The patient was pregnant for the first time at the age of 21 years. The pregnancy was uneventful and the baby was delivered without problems. No chorea occurred. One year later, after being pregnant for 2 months, she had the subacute onset of generalized chorea that prevented her from functioning normally. Six weeks after the onset of chorea, she had a miscarriage. A few weeks after the miscarriage, the chorea remitted. The next year she was pregnant again, and by the 2nd month, she again had generalized chorea. The chorea was self-limited and lasted only a few weeks. The rest of the pregnancy was uneventful.

In April 1955, she appeared at the Mayo Clinic with a mild right hemichorea that lasted about 6 weeks. An electroencephalogram was unremarkable. She had normal menstrual periods, she was apparently not pregnant, and she was not receiving estrogen treatment. The next year, after being pregnant 2–3 months, she had a mild right hemichorea that remitted about 4 weeks postpartum. A few years later, after being pregnant 2–3 months, she again developed disabling generalized chorea. The chorea persisted until about 4 weeks postpartum. She had no other pregnancies.

In October 1988, the patient was diagnosed as having atrophic vaginitis. She was given a vaginal cream that contained conjugated estrogen at a concentration of 0.625 mg/g; the daily dosage was 4 g of cream (at bedtime) for a total of 2.5 mg of estrogen, the highest recommended dose for atrophic vaginitis. Within 3 weeks, she began to have generalized choreic movements of the limbs and face. Also, she noticed uterine bleeding, which had not occurred for 13 years. The chorea was moderately severe and generalized. There was no right-sided predominance. While sitting, she was in constant motion and unable to perform manual motor tasks well. She could eat only with assistance. She could walk, but her gait was hyperkinetic. Hypotonia and pendular reflexes were not present.

She appeared at the Mayo Clinic in December 1988. The pelvic examination, blood cell count, general blood chemistry values, antinuclear antibody test result, antistreptolysin-O test result, and sedimentation rate were all within the normal range. Activated partial thromboplastin time (APTT), anticardiolipin antibodies of the IgG and IgM subclasses, and antibodies to the extractable nuclear antigens SSA, SSB, RNP, and SM were negative. Magnetic resonance imaging showed a 0.6-cm infarct at the

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upper lateral aspect of the head of the left caudate nucleus that extended into the adjacent periventricular white matter.

The vaginal cream therapy was discontinued, and the movements improved markedly within 2–4 weeks. During the ensuing 2 months, the improvement was much more gradual until the movements ceased. This time course of improvement was similar to that of her previous chorea episodes.

There was no history of rheumatic fever, heart murmur, or rheumatism. The patient's brother had Sydenham's chorea at age 7. There was no other relevant personal or family history, including no history of other movement disorders, hyperthyroidism, or autoimmune diseases. She reported no hypersensitivity to decongestants or other medicines. She had never taken dopaminergic agonists or antagonists, lithium, phenytoin, stimulants, isoniazid, or hormonal preparations.

DISCUSSION

Several aspects of our patient's history of chorea gravidarum are typical, and a few are atypical (Table 1). Chorea gravidarum has been reviewed both in classic works and in recent articles (1,5,16–23). Its exact pathophysiology has been elusive. Most authors believe that it is part of a syndrome of "hormone-induced chorea" that occurs after a previous static lesion (such as rheumatic fever) in the basal ganglia (1,4–7,16,24,25). Some authors believe that an inflammatory process in the brain could also play a role in the development of chorea gravidarum (26). Differential diagnostic considerations in a young woman include systemic lupus erythematosus, reaction to drugs, Wilson's disease, acute rheumatic fever, polycythemia, hyperthyroidism, hypoparathyroidism, and any focal cerebral process affecting the basal ganglia (5).

To the best of our knowledge, this is the first case of chorea, recurrent or otherwise, caused by a topically applied cream that contained conjugated estrogen. Cases of recurrent chorea have been reported in individuals more than 50 years of age. In some of these cases the chorea was attributed to the ingestion of certain drugs and in other cases there was no apparent cause (27). The recurrence of chorea after the application of the vaginal cream in our patient is consistent with a syndrome of estrogen-induced recurrent chorea. There was no evidence of an inflammatory process or any other coincident disease process. There was no laboratory test evidence for an underlying chronic or recurrent autoimmune disease. The exact age of the small left caudate infarct is unknown. Because there was no apoplectic onset and because the chorea was generalized, it seems unlikely that the chorea would have been caused by the small caudate infarct. However, it is possible that the infarct (if it was present) predisposed the patient to the two previous episodes of right hemichorea. Conjugated estrogen from the vaginal cream may have been absorbed into the bloodstream, causing both the uterine bleeding and the chorea. Likewise, the estrogen component of oral contraceptive pills is believed to be responsible for the development of chorea (7,8).

TABLE 1. *Typical and atypical features of a patient with chorea gravidarum compared to cases compiled in the literature*

Typical	First onset at a young age
	Chorea began in first half of the pregnancy
	Episodes of chorea abated within 4 months
	Chorea persisted until after delivery
Commonly occur but not typical	No previous history of chorea or rheumatic fever
	Chorea recurred in a later pregnancy and with greater severity
	One episode of chorea was self-limited within a pregnancy
Atypical	First episode occurred in second pregnancy
	Chorea occurred between pregnancies without an apparent exacerbating factor

The effect of estrogen on the basal ganglia is complex and may be indirect (25,28–30). Animal studies have shown that estrogen can up-regulate dopamine receptors, inhibit enzymes that degrade dopamine, and modulate dopamine-dependent behavior (8,28). In contrast, oral conjugated estrogens (Premarin) can exacerbate parkinsonism as well as decrease L-dopa-induced dyskinesias in humans (25,31).

The case discussed illustrates the importance of taking a detailed neurologic history before prescribing estrogens in any form. Also, this case was consistent with the existence of a recurrent syndrome of estrogen-induced chorea.

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