A Patient with Antiphospholipid Syndrome and Psychotic Symptoms Misdiagnosed as Conversion Disorder

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SUMMARY

Chorea gravidarum (CG) is a rare movement disorder characterized by rapid, irregular randomly distributed involuntary movements during pregnancy. Similar to Sydenham chorea, psychiatric symptoms may be observed in cases of CG. CG may be idiopathic or secondary to an underlying cause. One of the most common causes of CG is antiphospholipid syndrome. Herein we present a case of recurrent CG that was considered to be due to antiphospholipid syndrome. The patient had a history of 3 pregnancy losses and her fourth pregnancy was treated appropriately, resulting in the birth of healthy full-term baby. During the patient's first pregnancy CG was accompanied by psychotic symptoms.

Keywords: Chorea gravidarum, psychosis, antiphospholipid syndrome, conversion disorder

INTRODUCTION

Chorea Gravidarum (CG) is a rare movement disorder characterized by rapid, irregular randomly distributed involuntary movements during pregnancy (Wild and Tabrizi 2007; Karageyim et al. 2002). The symptoms begin during the first trimester in 50% of cases, resolve spontaneously before labor in 33% of cases and in 66% post labor, but may reoccur during subsequent pregnancies. Rhabdomyolysis, hyperthermia, myoglobinuria-related disorders, and death can occur in patients with severe choreic movements (Kranick et al. 2010; Ichikawa et al. 1980). CG may accompany acute rheumatic fever, systemic lupus erythematosus, syphilis, antiphospholipid syndrome (APS), and encephalitis. Differential diagnosis should included consideration of Wilson's and Huntington's diseases, thyrotoxicosis, infarctions or hemorrhages of the basal ganglia, choreas related to toxins, and diabetic hyperosmolar non-ketotic comas.

The most frequent etiological disease is APS and it was reported that menstruation, oral contraceptives, and estrogen might cause chorea via alteration of dopamine sensitivity (Kim et al. 2009). Depression, anxiety, attention deficit-hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), tics, nervousness, personality changes, psychotic disorders, mania, cognitive disorders, dementia, suicide attempts, and other psychiatric symptoms may accompany CG. In particular, in patients with Sydenham chorea and CG these symptoms may resolve spontaneously or with treatment, but can reoccur. Primarily, dysregulation of dopamine and other neurotransmitter pathways are responsible for these symptoms (Ben-Pazi et al. 2011). On the other hand, antibodies produced against neurons primarily affect the basal ganglia and other brain regions, resulting in psychosis and other psychiatric disorders. The fluctuation in the severity of neuropsychiatric symptoms is hypothesized to be related to changes in the levels of these antibodies (Zandman-Goddard et al. 2007).

Patients with CG may also present with personality changes, nervousness, depression, Tourette's syndrome, delirium, hypnogogic and hypnopompic hallucinations, and cognitive disorders. Psychotic disorders are frequently observed and

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most resolve spontaneously, but CG and psychosis can reoccur with or without pregnancy (Brockington 2006; Ghanem 1985; Breton 1893). Treatment should focus on the underlying disease, but in patients with severe choreiform movements symptomatic treatment may be required. Low-dose haloperidol and chlorpromazine may be effective and are rarely associated with side effects; in particular, haloperidol is recommended by the American Pediatric Academy due to the low incidence of anticholinergic, hypotensive, and antihistaminergic side effects (Kranick 2010; Dike 1997).

CASE REPORT

A 19-year-old female at 13 weeks of gestation presented to our outpatient gynecology unit with a history of 3 pregnancy losses. She reported involuntary movement of the hands, feet, and face, as well as difficulty maintaining her balance, which began about the ninth week of her pregnancy and disappeared during sleep. She reported difficulty falling asleep, eating, drinking, and using a spoon and fork, as well as frequent episodes of spilling water, dropping food, and falling because of the involuntary movements.

Three years earlier during the second month of her first pregnancy involuntary movements of both hands and feet, and face began, which eventually caused difficulty eating, walking, and talking, followed by weight loss. Two weeks after the onset of these symptoms psychiatric symptoms began. She saw spiders on the wall and heard babies crying. She at times could not decide what was real or imagined, which frightened her. She was evaluated by a psychiatrist and complained about her husband's mothers bad behaviors, and her husband's lack of interest in her and her childhood problems. Based on the involuntary movements and psychiatric symptoms she was diagnosed as conversion disorder and was prescribed sertraline 50 mg d^{-1} and alprazolam 1 mg d^{-1}. After 1 month of this treatment there was no improvement in her symptoms and she stopped taking the medications. Three weeks after cessation of the medications (fourth month of the pregnancy) all symptoms resolved spontaneously. At 24 weeks of gestation she had spontaneous vaginal delivery of a dead fetus. Then, 1 year later and again the following year she became pregnant for the 2nd and 3rd time, each time aborting during the first trimester.

Anamnesis showed that she was born to a conservative family in a small city and developed normally. She reported no major illnesses and that she was a quiet and relaxed child. She had her first menstruation at age 11 years and had no academic problems at elementary school. Her father and mother died in a traffic accident when she was aged 7 years; her brother was adopted and she was raised by her grandmother and uncle. She married at age 15 years at the urging of her relatives. Family history of psychiatric disorder was negative.

Routine physical examination was normal. Neurological examination showed choreiform movements of the face, tongue, and upper and lower extremities (bilaterally, but more prominent on the left side). Mental status, speech, memory, and attention were normal. Her affect was slightly anxious and she was euthymic. She did not report any hallucinations or perception disorders. She reported no problems other than the movement disorder, and that her relationship with her husband's mother was improving and that she was not depressed.

Ocular examination was normal and gestational age of the fetus based on ultrasonography was concordant with the patient's account. Complete blood count, serum biochemistry evaluation for liver, kidney, and thyroid function, fasting glucose level, lipid profile, urine anti-streptomycin-O level, C reactive protein level, anti-nuclear anticore level, anti-double stranded DNA level, serum complement level, activated thromboplastin time, protein C and S levels, activated protein C resistance, anti-thrombin 3 activity, serum ceruloplasmin and copper levels, and HIV/AIDS and syphilis serology were normal. On the other hand, lupus anticoagulant test results were positive and the anticardiolipin IgG level was 76 U mL^{-1} (0-12). She refused evaluation via cranial MRI due to fear it may negatively affect her pregnancy. Electrocardiographic, echocardiographic, and electroencephalographic evaluations were normal. She was diagnosed as APS-related CG and recurrent pregnancy loss due to hypercoagulability; therefore, enoxaparin 100 U·kg^{-1}·d^{-1} and aspirin 100 mg d^{-1} were started, and haloperidol starting at 0.5 mg d^{-1} and increasing to 2 mg d^{-1} was prescribed.

The patient was followed-up via telephone every 3 d. She reported marked improvement with haloperidol 1.5 mg d^{-1} on d 7 of the treatment. After 2 weeks of haloperidol treatment she was re-evaluated at the outpatient unit; minor choreiform movement of the hands persisted, but all other symptoms were resolved, including those related to speech, gait, and sleep. Two months later the haloperidol dose began to decrease slowly and was stopped; after 3 months of the treatment she was again re-evaluated at the outpatient unit and observed to be psychiatrically and neurologically normal. Her anticardiolipin IgG level was 62 IU mL^{-1} and lupus anticoagulant test results were negative. She had spontaneous vaginal delivery of a healthy baby at 40 weeks of gestation, and as of 2 months post delivery the patient was symptom free.

DISCUSSION

In all, 45% of attacks of CG begin during the 1st trimester, 35% begin during the 2nd trimester, and 20% begin during the 3rd trimester (Karageyim et al. 2002). In the presented patient choreiform movements began with psychotic symptoms during the first attack and resolved spontaneously. During her fourth pregnancy only choreiform movements

occurred during the first trimester, which negatively affect her ability to eat and drink; as such, haloperidol was initiated and after 2 weeks of treatment the symptoms disappeared almost completely. The patient's first 3 pregnancies did not reach full term, whereas with anti-aggregant and anticoagulant therapy her fourth pregnancy resulted in the birth of a healthy full-term baby. Although the most frequent underlying cause of CG is APS, infections, cerebrovascular, autoimmune, and endocrinological diseases can also cause CG (Kim et al. 2009).

APS is characterized by ≥1 thrombotic attacks or loss of pregnancy, as well as moderate to high levels of antiphospholipid antibodies, and is a major cause for pregnancy morbidities and pregnancy loss (Branch and Khamashta 2003). These antibodies are lupus anticoagulant, anticardiolipin antibodies, and anti-β2 microglobulin anticores. The antibodies are produced against antigens of the inner or outer wall of cells and are independent risk factors for thrombosis and subsequent defective placentation, abortion, premature birth, early onset preeclampsia, intrauterine growth retardation, and placental abruption. Approximately 50% of pregnancies terminate early without treatment, but >75% reach full term with heparin or aspirin (Andreoli et al. 2012; Ernest et al. 2011; Branch and Khamashta 2003). CG can also be observed as an early symptom of APS.

The physiopathology of CG might be related to vascular lesions or autoimmune-mediated excitatory mechanisms (Paus et al. 2001). Ischemic brain lesions are frequently noted in patients with CG, but very few patients with CG have been examined via SPECT or PET for brain functions; decreased blood flow in the basal membrane and hypermetabolism in the striatum have also been reported (Tanne and Hassin-Baer 2001). A study that included 50 patients with CG reported that in most cases pregnancy or use of oral contraceptives were etiological. Among the patients, 33% were observed to have had cerebral infarctions based on CT or MRI (Tanne and Hassin-Baer 2001). The choreiform movements associated with APS may not only be due to an increase in dopaminergic sensitivity as a result of sex hormones, but may be due to degeneration of the integrity of the basal ganglia caused by antiphospholipid antibodies (Kim et al. 2009; Paus et al. 2001). Similarly, psychiatric symptoms may be a component of CG, but psychiatric disorders have been reported in lupus patients with central nervous system involvement and those with high levels of antiphospholipid antibodies; therefore, the immune-mediated effects of antiphospholipid antibodies may play a role in the pathogenesis of CG (Paus et al. 2001; Tanne and Hassin-Baer 2001).

Herein we reported the importance of APS as a frequent cause of CG. The patient's accompanying psychiatric symptoms during her first pregnancy resulted in the misdiagnosis of conversion disorder. Basal ganglial involvement and changes in dopaminergic sensitivity may cause depression and psychosis (Nicolas et al. 2012; Robert et al. 2012). On the other hand, as the mechanism is immune mediated spontaneous recovery in the presented patient's first pregnancy was not surprising and is in agreement with earlier reports (Najjar et al. 2011). The presented patient with CG and associated psychiatric symptoms gave birth to a full-term healthy baby following appropriate treatment.

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