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CASE REPORT

Seizures associated with Lupus during pregnancy

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Key Clinical Message

A sudden flare of previously stable SLE may give rise to CNS lupus. During pregnancy, seizures associated with CNS lupus can cause hypoxic-ischemic encephalopathy (HIE) in the infant.

Keywords

CNS lupus, HIE, pregnancy, SLE.

Introduction

Systemic lupus erythematosus (SLE) occurs most often in females of reproductive age. Therefore, many reports have dealt with pregnancies complicated by SLE but central nervous system (CNS) lupus in pregnant women has only rarely been described [1–3]. Convulsion is a clinical manifestation of CNS lupus, yet there are as yet no reports focusing on the effects of CNS lupus-induced seizures on infants and such effects thus remain unknown. We describe maternal seizures associated with CNS lupus which caused hypoxic-ischemic encephalopathy (HIE) in the infant.

Case Presentation

The patient was a 34-year-old primigravida Japanese woman. At age 23, she had presented with symptoms of arthritis, fever, and facial malar rash. She was diagnosed with SLE, and biopsy proven WHO class IV lupus nephrosis concurrently; however, no accompanying antiphospholipid syndrome was noted. At the age of 30 years, she was weaned off her medications, as her disease state had stabilized, and was no longer advised against becoming pregnant. She was jointly managed by an obstetrician and a rheumatologist. Immunological tests performed prior to pregnancy indicated that the level of double-stranded DNA (dsDNA) antibodies was 121 IU/mL (reference value, 0–12 IU/mL), whereas the level of anti-La/SSB antibodies was 93.8 U/mL (reference value, 0–10 U/m+); however, the patient did not have any signs of SLE flare even though no medication was administered. All complete blood count, renal function test, and uric acid measurement results at 28 gestational weeks were within their normal ranges. There was no decrease in serum complement level, and anticardiolipin antibodies were negative. Thereafter, a physical examination, complete blood count, and urinalysis were performed every 2 weeks. Her pregnancy course was uneventful, with no findings suggestive of increased SLE activity, until 35 gestational weeks. However, she experienced repeated generalized tonic-clonic seizures at 35 gestational weeks and was rushed to our hospital. The seizures developed after 4 days of persistent headache, right-sided neck pain, and general malaise; follow-up observation/checkups were being conducted without any medication for these symptoms.

On arrival, she had disturbance of consciousness, her blood pressure was 170/90 mmHg, and a qualitative urine protein test was strongly positive. Arterial blood gas

analysis showed a pH of 6.790 and a base deficit of 23.8 mmol/L, indicating metabolic acidosis. Blood tests disclosed hemoconcentration with uric acid elevation to 6.8 mg/dL, raising suspicion of eclamptic seizures due to preeclampsia. However, a computed tomography (CT) scan of the head demonstrated an extensive low-density area in the left cerebral hemisphere, strongly suggesting cerebral infarction.

Meanwhile, the fetal heart rate showed bradycardia in the range of 70 beats per minute. Due to nonreassuring fetal status, the patient underwent an immediate cesarean section, delivering a female infant weighing 1852 g, with Apgar scores of 6 and 8 at 1 and 5 min, respectively. Umbilical cord arterial blood gas analysis showed an arterial blood pH of 6.832 and a base deficit of 23.8 mmol/L. Neonatal seizures, beginning the day of birth, necessitated ongoing administration of an antiepileptic medication. Furthermore, a T1-weighted magnetic resonance imaging (MRI) scan of the head performed on day 15 after birth showed high-intensity areas in the basal ganglia, thalamus, and corticocerebral motor area, findings not inconsistent with HIE (Fig. 1). However, the child has shown normal growth without neurological or other sequelae for 3 years, to date.

The mother was managed in the intensive care unit with antihypertensive and anticonvulsant medications. T2-weighted MRI scans of the head obtained the day after delivery demonstrated multiple high-intensity areas in the left frontal and parietal lobes, which led to the diagnosis of cerebral infarction and cerebral edema (Fig. 2). Cerebrospinal fluid examination (CSF) revealed an abnormally high interleukin-6 (IL-6) level of 465 pg/mL (reference value: <4 pg/mL), and electroencephalography indicated an abnormal pattern of diffuse slow wave activity, both of which indicated findings consistent with CNS lupus. Furthermore, blood examinations showed low complement levels and a high ds-DNA antibody titer, and she was also noted to be positive for anticardiolipin antibodies, indicative of concurrent antiphospholipid syndrome. She received methylprednisolone pulse therapy (500 mg daily for 3 days) and then consecutively received cyclophosphamide pulse therapy (500 mg/body). She was discharged on the 16th postpartum day. However, sequelae of left hemiparesis have remained.

Discussion

This case highlights two important clinical issues: a sudden flare of previously stable SLE may give rise to CNS lupus, and during pregnancy, seizures associated with CNS lupus can cause HIE in the infant.

First, SLE, even when stable, may give rise to CNS lupus as a result of a sudden flare of the underlying SLE. CNS lupus appears to represent an especially severe manifestation of SLE and may involve far greater maternal and fetal risks than previously recognized [2]. The seizure risk in SLE is increased in patients with higher disease activity at baseline, prior neuropsychiatric SLE disease, or who are positive for anticardiolipin and anti-Smith antibodies [3]. However, an increase in SLE activity can occur in a significant number of patients, even with well-controlled disease [4]. The present patient had already been weaned

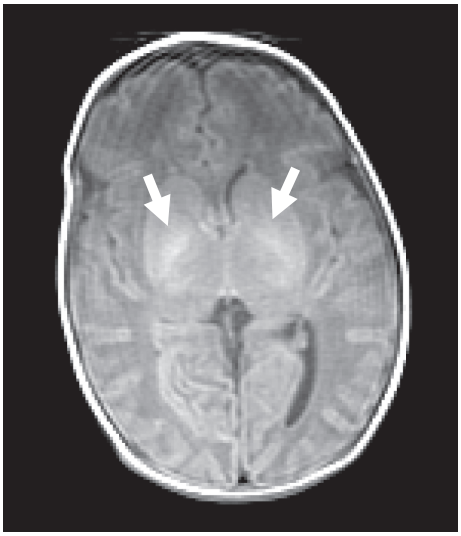

Figure 1. High-intensity areas, suggestive of a hypoxic-low perfusion state, can be seen in the basal ganglia and thalamus.

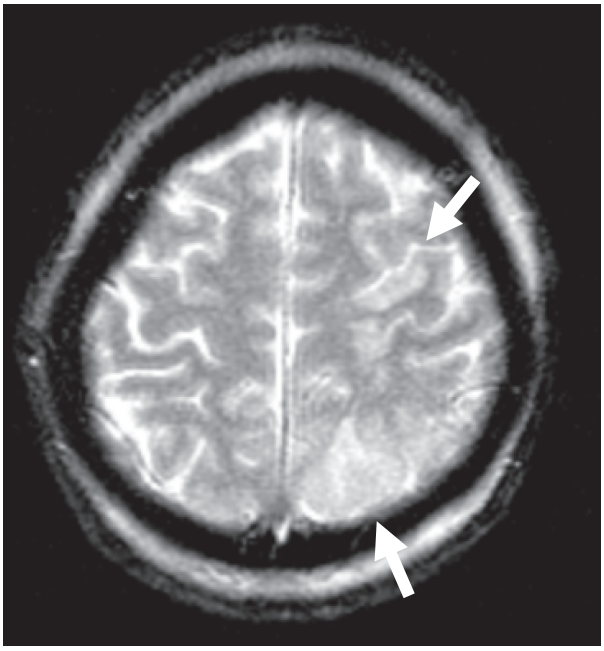

Figure 2. Multiple, ill-defined high-intensity areas are noted in the left frontal and parietal lobes along with swelling of the gyri.

off medications and her SLE activity had been stable throughout pregnancy. However, 4 days before the onset of convulsive, she experienced headache, pain in the right neck, and general malaise, suggestive of prodromal CNS lupus. Had appropriate treatment been given at that time, seizures associated with CNS lupus might have been prevented.

Second, seizures due to CNS lupus can cause HIE in the infant. Although the most frequent cause of seizures in pregnancy is eclampsia [5], CNS lupus should also be considered in the differential diagnosis of convulsions. Seizures associated with CNS lupus and eclamptic seizures can both be of the tonic-clonic, as well as other, types. Eclamptic seizures, nevertheless, are almost always self-limiting and seldom last longer than 3–4 min (usual duration, 60–75 sec). Maternal hypoxemia evoked by eclamptic seizures leads to such fetal heart rate changes as bradycardia, transient late decelerations, and decreased beat-to-beat variability, but these changes usually resolve spontaneously within 3–10 min after termination of the convulsions and correction of maternal hypoxemia. Thus, a hastened delivery by cesarean section is reportedly not warranted [6]. Meanwhile, seizures associated with SLE are, however, associated with diverse symptoms. In a survey of 75 patients suffering seizures associated with SLE reported by Duarte et al. [1], 58 (77%) had tonic-clonic seizures, 9 (12%) complex partial seizures (PS), 5 (7%) simple partial motor seizures, and 3 (4%) secondary tonic-clonic seizures, whereas 17 patients (24%) had more than three seizures during the first episode but only 3 (4%) presented with status epilepticus. Clearly, status epilepticus is not uncommon. Our extensive search of the literature employing PubMed identified no reports documenting a case of maternal seizures associated with CNS lupus that resulted in HIE in the infant. However, there is a likelihood that, in cases suffering seizures associated with SLE, hypoxia and hypercarbia due to maternal convulsions may cause HIE in the infant as in the case documented herein.

In conclusion, women with SLE have the potential risk of developing CNS lupus, even when their SLE is stable, and seizures associated with CNS lupus may cause HIE in the infant. Therefore, women with SLE need to be strictly monitored by a rheumatologist and an obstetrician working cooperatively. Moreover, care providers need to inform patients that they should visit a medical institution immediately if any symptoms appear, since SLE has diverse clinical manifestations.

Conflict of Interest

The authors declare that they have no conflicts of interest to declare.

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