

CASE REPORT

Focal Seizures as an Unusual Presentation of Neonatal Lupus Erythematosus

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SUMMARY Neonatal lupus erythematosus is an uncommon passive autoimmune disease in which there is a transplacental passage of anti-Ro/SSA and/or anti-La/SSB maternal autoantibodies. Common clinical manifestations include cardiac disease, notably congenital heart block, cutaneous lupus lesions, hematologic disorders, and hepatobiliary disease. During the past decade, however, it has become clear that central nervous disease may also be a manifestation of neonatal lupus. We report a male neonate with the disease who had focal seizures in addition to cutaneous lupus, anemia, and thrombocytopenia. Brain ultrasound revealed normal ventricular size without a midline shift or intracranial or intraventricular hemorrhage. A brain CT showed generalized low density involving the periventricular and deep white matter. A sleep EEG revealed rare spikes axial to the right parietal lobe. The neonate had a high titer of antinuclear antibodies (1:640) with a speckled pattern, anti-Ro/SSA and anti-La/SSB antibodies, but no anti-dsDNA antibodies. He was given anti-convulsant drugs with dramatic improvement of his symptoms. One month later, a sleep EEG was normal, and he had no further seizures.

Neonatal lupus erythematosus (NLE) is a passive autoimmune disease in which maternal autoantibodies are transferred across the placenta. These antibodies can be detected in affected infants for the first few months of life. The major clinical manifestations of NLE are cutaneous lesions, congenital heart block, hematologic disorders (anemia, thrombocytopenia, leukopenia), and hepatobiliary disease (hepatitis, hepatosplenomegaly, cholestasis). However, there are a few reports of central nervous system (CNS) involvement in NLE.^{1,2} We report a 20-day-old male neonate who had focal seizures associated with NLE.

CASE REPORT

A male child was born at 38 weeks of gestation to a gravida 1 para 1 mother by normal delivery. There was no pre-labor rupture of membranes, and

the baby cried immediately at birth. Neonatal screening tests for hypothyroidism, glucose-6-phosphatase-dehydrogenase, galactosemia, homocystinuria, and phenylketonuria were all negative. His mother had a history of systemic lupus erythematosus (SLE).

The patient had been diagnosed at 4 days of age with neonatal lupus erythematosus. Initial laboratory results were hemoglobin 15.8 g/dl, a white blood cell count of 11,680/mm³, platelets 34,000/mm³, a high titer of antinuclear antibodies (1:640) with a speckled pattern, positive anti-Ro/SSA and anti-La/SSB antibodies. Cutaneous lupus lesions were also noted. However, his mother noted a focal seizure of the left upper extremity, lasting about 10 seconds, when he

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was 20 days old. He had trismus and mild lip cyanosis along with a tonic posturing of the arm. Seizures with a similar pattern recurred over the next 4 days, so the infant was brought to the hospital. He had no fever, vomiting, unusual odor, or a family history of epilepsy, and he had not been given any drugs. His mother described his general level of activity as fair.

On admission, he was alert, his temperature was 37.4°C, pulse 140/minute and respiratory rate 26/minute. He weighed 3,904 g, was 51 cm long, and had a head circumference of 36 cm. His conjunctivae were pale. There were multiple annular skin lesions in the periorbital area and on the trunk and extremities. They had an erythematous, scaly border with a depressed, ecchymotic central area (Fig. 1). The anterior fontanel was not bulging.

Biochemistry data including sugar, potassium, sodium, and calcium were within the normal range. However, he had hemoglobin of 7.8 g/dl and a platelet count of 29,000/mm³. The white blood cell count of 6,740/mm³ was normal. Liver function was direct bilirubin 2.0 mg/dl, total bilirubin 4.4 mg/dl, aspartate aminotransferase 82 U/l, alanine aminotransferase 35 U/l. Brain ultrasonography revealed normal ventricular size without a midline shift or intracranial or intraventricular hemorrhage. A brain CT showed generalized low density of the periventricular and deep white matter (Fig. 2). A sleep EEG revealed rare spikes axial to the right parietal area. There was still a high titer of antinuclear antibodies (1:640) with a speckled pattern, anti-Ro/SSA antibodies and anti-La/SSB antibodies were positive, and anti-dsDNA antibodies were negative. The diagnosis of NLE with focal seizures was made.

Phenobarbital was prescribed initially but did not control the frequent focal seizures. Diphenylhydantoin was then given, which successfully stabilized the patient. He was discharged 8 days later on phenobarbital. One month later, a sleep EEG was normal, and the anti-convulsant was discontinued. He remained totally seizure free thereafter.

DISCUSSION

The incidence of NLE is about 1 in 20,000 live births, and has been reported in a number of different ethnic groups.³ Overall, 13% of mothers with SLE have babies who develop NLE.⁴ Among mothers



Fig. 1 Annular erythematous skin rash with fine scale on the face.

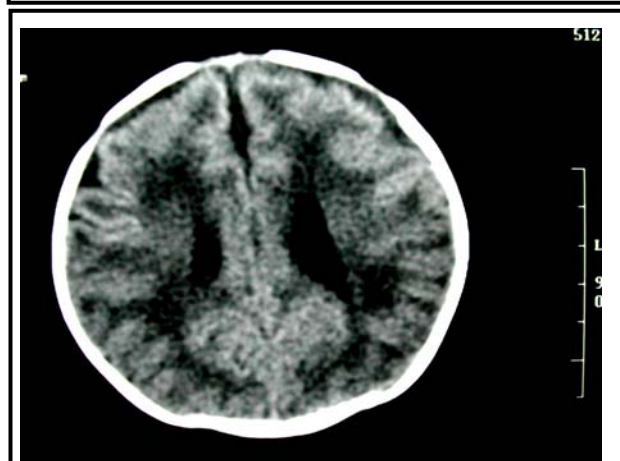


Fig. 2 Transverse axial CT scan of the brain shows symmetrically reduced density of the periventricular and deep white matter bilaterally.

of babies with NLE, 40% to 60% are asymptomatic, while the remaining women have clear evidence of SLE, Sjogren's syndrome, or undifferentiated connective tissue disease.⁵

The earliest report of apparent CNS involvement in NLE was a myelopathy with an abnormal gait noted by Kaye and Butler in 1987.⁶ Although there have been more cases since, it is still reported to occur in less than 1.4% of patients with NLE.⁷ In 1996, CNS vasculopathy in NLE was first described by Cabanas.⁸ In 1999, Cabral *et al.*¹ reported a patient with a typical NLE rash who had intractable seizures at 2.5 years of age. A brain MRI showed abnormal peritrigonal white matter, a nonspecific change representing previous white matter injury.

The underlying pathology of neuroimaging abnormalities in NLE is unclear. The major antibodies in NLE target Ro/SSA and La/SSB antigens. Ro/SSA consists of a 52 kDa and 60 kDa polypeptide while SSB/La consists of one 47-to-50 kDa polypeptide. These Ro and La antigens are widely distributed in the skin, fetal cardiac conducting system, myocardium, liver and other internal organs, including the brain. Anti-Ro/SSA antibodies are known to play an important role in skin damage.⁹ Sjogren's syndrome, another disorder characterized by circulating anti-Ro/SSA antibodies, is also recognized to have CNS involvement.¹⁰ It has therefore been suggested that neurologic lesions in NLE are related to the presence of anti-Ro/SSA antibodies of maternal origin that damage the fetal or neonatal brain.¹¹ An autoantibody-mediated inflammatory reaction involving the cerebral vessels is a possible mechanism.² It has also been proposed that hydrocephalus relates to the large number of SS-A/Ro antigens in brain tissue.¹² Although thrombocytopenia is commonly present in NLE, neurological deficits in these children have not been reported in association with intracerebral hemorrhage.¹³

The most commonly reported CNS manifestation of NLE is seizures. However, other severe neurologic manifestations, including non-obstructive hydrocephalus, abnormal gait, spastic paraparesis, and a disturbed level of consciousness have been reported.¹²⁻¹⁴ The typical skin lesions of NLE, including a characteristic predilection for the upper and lower eyelids, are usually transient. However, the disease occasionally causes residual lesions, including telangiectasia, skin atrophy and hypopigmentation.⁹ If cutaneous disease can result in long-term sequelae, it is possible that there may also be late or persistent manifestations of CNS involvement.^{2,13} One boy with NLE and residual skin atrophy has been reported to have developed a severe seizure disorder at 2 years of age.² A 17-year-old with a history of NLE as an infant had the onset of a CNS vasculopathy resembling moyamoya disease.¹⁴

The diagnosis of NLE requires detection of maternal antibodies to Ro/SSA and/or La/SSB in the infant in association with either a characteristic skin rash or heart block, with or without hematologic or hepatic involvement. While CNS involvement is rare, it would be worthwhile doing a brain echo in

babies diagnosed with NLE. Sonography may reveal hyperechoic white matter accompanied by a subependymal cyst or a subdural effusion; or it may be normal.² Reduced attenuation on a CT scan indicates increased water content and is commonly due to inflammatory edema. Prendiville *et al.*² reported markedly reduced attenuation of the cerebral white matter as a neuroimaging abnormality of NLE.

Our patient clearly had NLE, based on the typical skin and hematologic findings in the presence of anti-Ro/SSA and anti-La/SSB antibodies. As there was no other obvious cause for his seizures and he had typical low density white matter on brain CT, we believe it is reasonable to attribute his transient seizure disorder to NLE. The potential for CNS abnormalities to cause symptomatic neurologic disease in NLE is uncertain. It is believed that CNS involvement is usually a transient phenomenon that resolves as maternal antibodies disappear from the infant's circulation, a contention further supported by the clearing of brain imaging abnormalities, as was found by Prendiville in one infant. The child had diffuse attenuation of the white matter in a brain CT at 5 weeks of age but a normal scan at 13 months.²

There is no standard treatment for CNS involvement in NLE. It is appropriate to control seizures with anti-convulsants. In cases where a subdural effusion or hydrocephalus is noted, a ventricular-peritoneal shunt or medication such as acetazolamide have been used.¹²

In summary, focal seizures may be the clinical feature of NLE involving the CNS, and like other manifestations of NLE, they are probably transient. However, such neonates should be followed closely.

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