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CASE REPORT

The lowest surviving birth weight infant delivered from a systemic lupus erythematosus mother with antiphospholipid syndrome

Running head: Infant from SLE mother

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ABSTRACT

We report the intact surviving case of a newborn with a birth weight of 412 g delivered from an active systemic lupus erythematosus (SLE) mother with antiphospholipid syndrome. A review of the literature revealed that our infant is the lowest surviving birth weight in newborns from SLE mothers to date.

Key words:

systemic lupus erythematosus, antiphospholipid syndrome, extremely low birth weight infant, intrauterine growth restriction, intact survival

Pregnancies with active systemic lupus erythematosus (SLE) with antiphospholipid syndrome (APS) have a very poor fetal/neonatal outcome. The reasons for this poor outcome include development of fetal death/distress, preterm delivery, and severe intrauterine growth restriction (IUGR) [1-7]. We present a case of the lowest intact surviving birth weight infant with severe IUGR delivered from an active SLE mother with APS, and review the literature about the lowest surviving birth weight infant delivered from a SLE mother to date.

CASE REPORT

A 28-year-old woman, gravid 1, para 0, artificial abortion 1, was transferred to our perinatal center at 25 0/7 weeks of pregnancy with an acute abdomen, complicating fever, oligohydramnios, and severe fetal growth restriction. Soon after admission, ultrasonography and computed tomography were performed on her abdomen, and gastrointestinal fiberoscopy was also performed. However, we were unable to diagnose her acute abdominal pain, fever, and fetal growth restriction before delivery. Intravenous treatment with ritodrine hydrochloride was started for tocolysis, and 12 mg betamethasone was injected twice intramuscularly to accelerate fetal lung maturity. At 26 0/7 weeks of pregnancy, the patient underwent emergency Caesarean section because her intractable abdominal pain could not be

relieved and there was evidence of worsening fetal distress. Upon delivery, an extensive area of old infarction was found in the placenta. Pathology of the placental specimen showed multiple microscopic and small infarcts involving the peripheral and central areas of the placenta as well as placental calcifications.

After delivery, the patient had a low titer of CH50, C3, C4, and was positive for anti-nuclear antibody, double-stranded and single-stranded DNA antibodies, anti-cardiolipin antibody, and anti-mitochondrial antibody in her serum. She was diagnosed with SLE with non-erosive arthritis, proteinuria, and pancytopenia. She was also diagnosed with APS because of results of the finding of placental infarcts and positive for anti-cardiolipin antibody in her serum on 2 different days 6 weeks apart. When the patient's SLE disease activity was evaluated using the SLE disease activity index (SLEDAI), her SLEDAI was 22 points, indicating an extremely active SLE; patients with a SLEDAI of ≥ 4 points are generally diagnosed as having an active SLE [1]. Oral prednisolone therapy with a dose of 40 mg/day was initiated from 9 days after delivery. The patient currently has well-controlled SLE by prednisolone therapy.

The female newborn was born at 26 0/7 weeks of gestation with a birth weight of 412 g (-4.3SD), height of 25.5 cm (-3.1SD), head circumference of 20.2 cm (-2.2SD), and chest

circumference of 16.4 cm (-2.4SD) without any surface anomalies. Her Apgar scores were 2 at 1 minute and 6 at 5 minutes after birth. She was intubated tracheally soon after birth, received an artificial pulmonary surfactant for severe respiratory distress syndrome, and then ventilated using conventional mandatory ventilation. Her initial arterial blood pressure was 28/17 mmHg. She continued to have a refractory low blood pressure that did not respond to treatment with a volume expander (albumin and fresh frozen plasma) and a high dose of catecholamine support, and was diagnosed with severe early-onset circulatory collapse. Therefore, at 15 hours after birth a single dose of intravenous hydrocortisone (1.5 mg/kg) was administered. After hydrocortisone therapy, circulatory collapse immediately diminished and urination appeared. Her ductus arteriosus spontaneously closed 2 days after birth. There were no complications, which are often observed in extremely low birth weight (ELBW) infants, such as intraventricular hemorrhage, sepsis, and necrotizing enterocolitis 7 days after birth.

Routine management for ELBW infants in our hospital was then carried out as follows: nutrition with breast milk, and respiratory management with high frequency oscillation ventilation, fluid intake with mild restriction, administration of diuretics, and inhaled corticosteroids for chronic lung disease. Severe cytopenias were prolonged until 21 days after birth (29 weeks of postconceptional age). The minimum leukocyte and platelet counts were

1,600/ μ l at 2 days after birth and 42,000/ μ l at 18 days after birth, respectively. The infant did not show symptoms of neonatal lupus erythematosus, such as atrio-ventricular block and cutaneous symptoms, and neonatal thrombosis resulting from transplacental passage of maternal antibodies. The double-stranded and single-stranded DNA antibodies in her serum disappeared at 20 days and 70 days after birth, respectively.

The infant was able to fully feed at the age of 26 days and her tracheal tube was extubated at the age of 67 days. Both of her eyes developed retinopathy of prematurity, which had a ridge with extraretinal fibrovascular proliferation in the vitreous overlying the retina. However, it was successfully controlled by retinal photocoagulation, resulting in a good visual prognosis. The infant was discharged at the age of 122 days (43 weeks of postconceptional age) with a weight of 2,146 g without any neurological symptoms and abnormal findings on brain magnetic resonance imaging and auditory brainstem response. At the age of 6 months (a corrected age of 3 months), she weighed 4,200 g, was able to fully smile, make visual contact, and had a steady head with normal physical and cognitive development.

DISCUSSION

SLE is a common autoimmune disease occurring at the reproductive age of women. A pregnant woman with SLE (SLE pregnancy) is an increasing risk for pregnancy-induced hypertension, preterm delivery, severe IUGR, and intrauterine fetal death. During the past several decades, obstetrical management for SLE pregnancies has considerably improved. The rate of fetal loss in SLE pregnancies has decreased from a mean value of 43% in 1960-1965 to 17% in 2000-2003 [2]. However, the rate of preterm delivery did not change from 1980 to 2000 (37.3% to 32.0%) [2]. Disease activity before and during pregnancy appears to be an important factor in SLE pregnancy outcomes. More frequent preterm deliveries and IUGR have been reported for women with active SLE during pregnancy compared with women with inactive SLE [3].

APS is also a systemic autoimmune disorder with antiphospholipid antibodies (i.e., lupus anticoagulant and anti-cardiolipin antibody). These antibodies can impair the physiologic development of a fetus during pregnancy not only by causing thrombosis of the placental vessels, but also by directly binding trophoblast cells and modifying their functions. Consequently, the presence of these antibodies in pregnant women is linked to an increased rate of pregnancy complications, such as preeclampsia, hemolysis, elevated liver enzymes, and low platelets syndrome, IUGR, uteroplacental insufficiency, fetal distress, and preterm

delivery. An active SLE pregnancy with APS is a major risk factor for a poor outcome, both for the mother and infant [4].

Our case is the active SLE pregnancy with APS and the highest SLEDAI ever reported, with the worst expected prognosis for pregnancy and the fetus. Soon after delivery, the mother in our case was treated as the active SLE. Her SLE was well-controlled by prednisolone therapy. The newborn had the severest small-for-gestational age ever reported, -4.3SD compared with the median birth weight in Japanese newborns at 26 weeks of gestation, and severe early-onset circulatory collapse, severe cytopenias, and chronic lung disease after birth as major complications. However, we were able to successfully manage her to achieve intact survival without any neurological complications due to our constant observation for a newborn patient and interventions for complications at the appropriate time.

In Japan, the mortality rates during admission for ELBW infants have been markedly improved since the year 2000 [8]. However, the mortality rate during admission for infants with < 500 g at birth was still 53.5% in 2005 [8], suggesting that the survival of these infants remains difficult, even if newborns were delivered from a non-SLE mother. There are several reports with regard to ELBW infants delivered from a SLE mother (Table 1) [5-7,9,10]. A literature review from 1986-2006 showed that the lowest surviving birth weight infant

delivered from a SLE mother was 470 g (-3.6SD) [5]. From 2007 onwards, there was a low birth weight infant of 980 g (+0.3SD) who survived with congenital heart block [9]. Whitelaw *et al.* have reviewed 47 SLE pregnancies and reported that the lowest surviving birth weight was 847 g [6]. Imbasciati *et al.* have reported 3 cases of ELBW infants (700, 700, and 670 g) from reviews of 113 pregnancies with lupus nephritis; however, they didn't all survive because of respiratory distress syndrome [10]. Cavallasca *et al.* have reported that the lowest surviving birth weight was 820 g among 72 cases delivered from SLE mothers [7].

To the best of our knowledge, our infant with a birth weight of 412 g, is the lowest surviving birth weight infant with the severest IUGR in newborns delivered from SLE mothers to date. Furthermore, she has survived without any neurological handicap at the age of 6 months (a corrected age of 3 months).

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Table 1. Recent reports about the lowest birth weight infants delivered from SLE mothers

Author, published year	Birth weight	Neonatal outcome
Spiegel J et al. 2007 [5]	470 g (-3.6SD)	Survival
Filippi L et al. 2007 [9]	980 g (+0.3SD)	Survival
Whitelaw DA et al. 2008 [6]	847 g (*)	Survival
Cavallasca JA et al. 2008 [7]	820 g (*)	Survival
Imbasciati E et al. 2009 [10]	670 g (*)	Death
Our case	412 g (-4.3SD)	Survival

(): SD values compared to median birth weight in Japanese newborns at the same gestation.

*: no data on gestational age at birth in the literature.