Anesthetic management of patient with Sjogren's syndrome who underwent cesarean section
-a case report-

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Sjogren's syndrome is one of the most common autoimmune disorders and has a female predominance. Maternal circulating autoantibodies such as anti-Ro/SSA and anti-La/SSB antibodies can cause congenital heart block of fetus, and in severe case, emergency pacemaker implantation may be needed for neonate. Therefore, it is very important to understand maternal and fetal condition and pay attention to the status of the neonate during delivery. In this paper, we present a case of patient with Sjogren's syndrome who underwent cesarean section under spinal anesthesia.

Key Words: Anesthesia, Congenital heart block, Pregnancy, Sjogren's syndrome.

Pregnancy and fetal outcomes can be affected by maternal autoimmune disorders owing to the presence of circulating maternal autoantibodies [1-4]. Sjogren's syndrome is one of the most common autoimmune disease with a 0.1%–4.8% prevalence [1,2]. It is predominant in women and is usually diagnosed in the fourth or fifth decade of life, but can occur in all age groups [1,2]. Offsprings of Sjogren's syndrome mothers are at increased risk of developing congenital heart block (CHB), and such neonates may require close monitoring of cardiac function and eventual pacemaker implantation [2,3,5]. Therefore, it is important to understand the pregnancy outcome of Sjogren's syndrome mothers and pay attention to the status of the baby during delivery. In this paper, we present a case of a pregnant woman with Sjogren's syndrome who underwent a cesarean section.

Case Report

A 40-year-old woman (weight, 70 kg; height, 165 cm) was scheduled for a repeat cesarean section at 38 + 1 weeks of gestation. She was a second gravida, and had been diagnosed with systemic lupus erythematosus (SLE) due to an erythematous rash on her nose and chins during the prior pregnancy. At that time, she had undergone a cesarean delivery under epidural anesthesia, and there had been a rash on the skin of neonate for several months after birth. After delivery, no residual symptoms were noted and no medication was administered. During the second pregnancy, she complained of similar rash on her nose along with mild itching and dry skin in the first trimester. An autoimmune disease such as SLE was suspected, and laboratory tests were performed to identify autoantibodies (Table 1). The results revealed that anti-Ro/SSA and anti-La/SSB antibodies were positive; hence, the patient was diagnosed with Sjogren's syndrome rather than SLE. Because of the risk of CHB, fetal echocardiograms were routinely checked from 15 weeks of ges-

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Table 1. Results of Laboratory Tests

	Results	Reference ranges
C3 (mg/dl)	108.0	90–180
C4 (mg/dl)	19.0	10–40
Anti-phospholipid antibodies IgG (U/ml)	1.0	< 10
Anti-phospholipid antibodies IgM (U/ml)	0.7	< 10
Anti-nuclear antibodies	1 : 1280	< 1 : 40x
Anti-ds DNA antibodies IgG (IU/ml)	< 1.0	≤ 4.0
Anti-Smith antibodies	Negative	
Anti-Ro/SSA antibodies (AU)	1.22*	< 1.0
Anti-La/SSB antibodies (AU)	7.99*	< 1.0
Anti-beta2-glycoprotein I antibodies IgG	Normal	
Anti-beta2-glycoprotein I antibodies IgM	Normal	

*Anti-Ro/SSA and anti-La/SSB antibodies were positive.

tation, and fetal heart rate was approximately 150 beats/min at each examination. The skin rash on the patient improved spontaneously after the second trimester, and there were no other symptoms such as dry eyes, dry mouth, or arthralgia. To prevent cardiac complications of fetus, the patient received hydroxychloroquine from 25 weeks of gestation until delivery.

An elective cesarean section was scheduled at 38 + 1 weeks of gestation. Preoperative laboratory tests, electrocardiogram (ECG), and chest X-ray were normal. After arriving in the operating room, noninvasive blood pressure, ECG, and pulse oximetry monitoring commenced. Her initial blood pressure was 118/71 mmHg, heart rate was 77 beats/min, respiratory rate was 16 breaths/min, and oxygen saturation was 100%. Oxygen at 5 L/min was supplied via a facial mask.

After placing the patient in the right lateral decubitus position, the median approach was performed with the 25 G Whitacre spinal needle at the L3-4 intervertebral space. After the stylet was removed and cerebrospinal fluid was confirmed to be draining well, 9 mg of 0.5% hyperbaric bupivacaine with 20 μg of fentanyl was injected. Then, she was positioned supine with a left lateral tilt of 15°, and the height of the block checked by a pin-prick test was T4.

Nine minutes after the skin incision, a female neonate (weight, 2.8 kg) was delivered and her Apgar score was 8 at 1 minute and 9 at 5 minutes. Two minutes after the delivery, the placenta was removed and intravenous infusion of 20 International Units (IU) of oxytocin mixed with 800 ml of 0.9% saline was started. The initial neonatal heart rate was 160 beats/min, and the neonate was transferred to the neonatal intensive care unit (NICU) immediately for continuous monitoring of ECG. The patient's vital signs were stable during the operation, and the estimated blood loss was about 500 ml. During the NICU stay, the neonate's ECG findings showed no abnormality, and the heart rate was approximately 140–170 beats/min. The patient and her neonate were

discharged on the fifth postoperative day without any complication.

Discussion

Systemic autoimmune diseases, also called connective tissue diseases, include SLE, rheumatoid arthritis, systemic sclerosis, and Sjogren's syndrome [6]. The pathogenetic mechanism underlying these disorders is an inappropriate and excessive immunologic reaction by the patient's autoantibodies [6]. Because many patients suffering from autoimmune disorders are predominantly women [1], the impact of these disorders and their management on pregnancy and fetal outcomes should be considered.

In pregnant woman with systemic autoimmune disease, circulating maternal autoantibodies can be transferred through the placental barrier, and can affect the cardiovascular system, skin, and liver of the fetus [3,6]. These manifestations are together called neonatal lupus syndrome [3]. Congenital heart block (CHB) is the most important clinical feature of neonatal lupus syndrome, and can be associated with neonatal lupus rash, thrombocytopenia, elevated liver enzymes or cholestasis [3].

The main autoantibodies associated with CHB are anti-Ro/SSA and anti-La/SSB antibodies [1,3,4]. The occurrence rate of CHB is 2% in women with anti-Ro/SSA antibodies and 3% in women with anti-La/SSB antibodies [1]. The recurrence rate of CHB in a subsequent pregnancy is about 16%–18% [1], and the occurrence rate after a previous child born with cutaneous neonatal lupus is about 13%–18% [7].

Transplacental transfer of maternal autoantibodies is thought to occur at approximately 12 weeks of gestation [3]. Antibodies can bind specific cellular components of the conduction system of the fetal heart, and may cause myocarditis, hemorrhage, or necrosis of the fetal conduction system [3,8]. These autoantibodies also have an arrhythmogenic effect [3].

CHB occurs between 16–24 weeks of gestation in fetus with structurally normal heart, and is usually complete and irreversible [3]; however, incomplete block, sinus bradycardia, or QTc prolongation have also been reported [3,9]. CHB is suspected when auscultation of fetal heart sounds reveals a slow heart rate. Therefore, routine fetal echocardiograms and obstetric sonograms are recommended in pregnant woman with anti-Ro/SSA or anti-La/SSB antibodies from 16 weeks of gestation [3,4,10]. In our case, fetal heart rate was checked regularly from 15 weeks of gestation and there was no episode of fetal bradycardia during pregnancy.

If fetal heart block is diagnosed, maternal drug therapy may be initiated to reduce the autoimmune responses and fetal cardiac inflammatory injuries [10]. Although steroid therapy is thought to be effective in reducing the immune responses of maternal autoantibodies, established complete heart block does

not respond to steroids and there is risk of development of maternal side effects such as oligohydramnios and hypertension [10]. Therefore, prophylactic maternal steroid treatment is not recommended, and steroids are administered only if the block is incomplete or is of recent onset, or if signs of fetal distress are accompanied with a complete heart block [3].

Recently, there has been suggested that the activation of a Toll-like receptor is involved in the pathogenesis of CHB [11]. Therefore, hydroxychloroquine, which inhibits endosomal acidification required for optimal Toll-like receptor signaling, is suggested as a preventive medication for fetal cardiac injury in patients with autoimmune disorders [11,12]. Izmirly et al. [12] reported that exposure to hydroxychloroquine during pregnancy might decrease the risk of development of CHB in neonates born to mothers with anti-Ro/SSA or anti-La/SSB antibodies. Izmirly et al. [11] also reported that maternal use of hydroxychloroquine might reduce the risk of recurrence of cardiac complications of neonatal lupus in neonates born to mothers with anti-Ro-SSA antibodies. In our case, anti-Ro/SSA and anti-La/SSB antibodies were all positive; therefore, the patient received hydroxychloroquine during pregnancy to prevent fetal cardiac complications.

Mortality associated with complete CHB is reported to be 16%–30% [3,4,13]. Waltuck and Buyon [4] reported that the total mortality rate associated with CHB was 19%, of which 27% died in utero and 45% died within the first three months after delivery. Eronen et al. [13] reported a total mortality rate of 15%, of which 73% occurred during the first 12 months after delivery. Poor outcome was associated with low fetal and neonatal heart rates (less than 55 beats/min), fetal hydrops, low birth weight, male sex, or problems related to prematurity or neonatal lupus [13].

Because fetal status by fetal heart rate cannot be monitored during labor and there is an increased risk of fetal growth retardation in Sjogren's syndrome pregnancies, there is a high likelihood of delivery by cesarean section [2]. To determine the type of anesthesia for cesarean section, several factors including anesthetic, obstetric, or fetal risk factors, the preference of the patient, and the judgement of the anesthesiologist should be considered [14]. Although general anesthesia may be the most rapid and appropriate method in some emergencies such as profound fetal distress, ruptured uterus, severe hemorrhage, and severe placental abruption, regional anesthesia is preferred to general anesthesia for most cesarean sections [14,15]. General anesthesia increases maternal complications such as failure of endotracheal intubation or pulmonary aspiration of gastric contents [15]. In addition, general anesthesia is associated with an increased risk of intubation and low Apgar scores in the neonate, and the risk increases when general anesthesia is used for a repeat cesarean section [15]. In our case, the patient had a history of a prior cesarean section, and the results of preoperative laboratory tests including coagulation profiles were normal, and there were no signs to suggest severe fetal distress. Therefore, we decided to perform spinal anesthesia.

After delivery, though many neonates are asymptomatic with adequate heart rates and do not require treatment, more than 50% of affected children require pacemaker implantation in the newborn period [13]. ECG monitoring of the neonate in the initial 5–10 days is necessary to observe ventricular rate and occurrence of ventricular arrhythmia [3]. Beta adrenergic agonists can be administered to increase heart rate temporarily, and pacemaker implantation is indicated for neonates with complete heart block with a heart rate less than 55 beats/min [3].

In conclusion, maternal circulating autoantibodies including anti-Ro/SSA and anti-La/SSB may induce CHB in neonates born to women with Sjogren's syndrome, and in severe cases, emergency surgery for pacemaker implantation may be indicated. Therefore, the anesthesiologists should have a clear understanding of the condition of the Sjogren's syndrome mother and the fetus, and after delivery, close monitoring of neonatal heart function is essential.

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