—Case Reports—

Reversible Posterior Leukoencephalopathy Syndrome due to Eclampsia in a Woman with a Twin Pregnancy Produced with Donated Oocytes

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Abstract

A 35-year-old primigravida with severe ovarian dysfunction underwent in vitro fertilization with oocytes donated by her sister. A twin pregnancy ensued, and she received prenatal care at our hospital. She underwent a cesarean section at 35 weeks' gestation because of pregnancy-induced hypertension (PIH) and breech presentation at the onset of labor. Eclampsia with a generalized seizure occurred 5 hours after the cesarean section, while the patient was receiving medical treatment for disseminated intravascular coagulation secondary to an atonic uterus. Reversible posterior leukoencephalopathy syndrome (RPLS) was diagnosed with magnetic resonance imaging the following day. With control of the hypertension and seizures, the condition of the patient was stabilized, and the RPLS resolved several days later. Eclampsia and RPLS associated with pregnancy can be life-threatening and are typically closely related to PIH. Thus, this case illustrates that the risk of PIH is increased in pregnancies produced with donated oocytes.
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Key words: reversible posterior leukoencephalopathy syndrome (RPLS), pregnancy induced hypertension (PIH), eclampsia

Introduction

Approximately 20% of pregnancies produced with donated oocytes are complicated by pregnancy-induced hypertension (PIH)[1]. Because PIH can be threaten the lives of the mother and the fetus, vigilance is required when caring for women with a pregnancy produced with donated oocytes. In Japan, obstetricians have limited experience in the management of such pregnancies, because the guidelines of the Japan Society of Obstetrics and Gynecology prohibit the use of oocytes donated by a nonanonymous third party in assisted reproductive technology. In most cases of pregnancy following oocyte donation in Japan, the donation was performed abroad. We present a case of reversible posterior leukoencephalopathy syndrome (RPLS) due to eclampsia in a women with ovarian dysfunction who conceived with oocytes donated by her sister.

Case Report

A 35-year-old primigravida underwent in vitro fertilization (IVF) using oocytes donated by her sister. The oocytes had been donated because of

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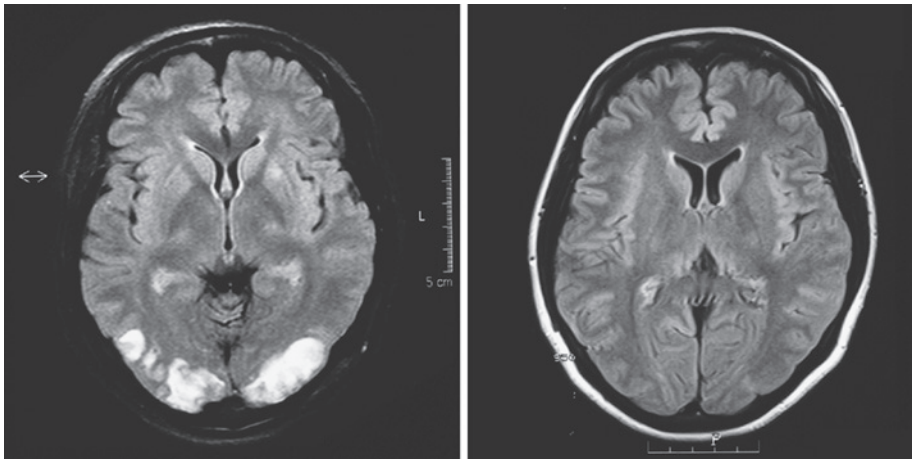

Fig. 1 Left: MRI 2 hours after the seizure. Bilateral areas of increased signal intensity are apparent in the parieto-occipital lobes. Right: MRI 11 days after cesarean section. The increased signal intensity is no longer present.

ovarian failure following two surgical procedures for bilateral benign ovarian tumors at ages 13 and 18 years. A twin pregnancy ensued, and the patient received prenatal care at our hospital. Her first visit to our hospital was at 13 weeks' gestation, and the pregnancy progressed uneventfully until 30 weeks' gestation, when she was admitted to our hospital because of proteinuria (107 mg/dL). On admission, the blood pressure was normal (124/78 mm Hg). After admission, the urinary protein level increased to 2.13 g/day, and the blood pressure gradually increased.

At 35 weeks' 5 days' gestation, spontaneous labor began. Blood pressure was 150/90 mm Hg. Because the first twin was in breech presentation, cesarean section was performed. Both neonates were of appropriate size for gestational age. The first neonate was a 2,118-g girl and the second was a 2,490-g boy. The Apgar scores for both neonates were 8 and 9 at 1 and 5 minutes, respectively. At cesarean section, both ovaries appeared small and streaklike. The estimated blood loss during surgery was 1,900 g. Postoperatively, the mother was treated with blood transfusion, fresh frozen plasma, and uterotonins. The hemorrhage had been caused by disseminated intravascular coagulation due to an atonic uterus. During the 20 hours following delivery, the total blood loss was 5,555 g.

Five hours after cesarean section, the blood pressure of the patient increased to 176/110 mm Hg. She was treated with a hydralazine infusion. Approximately 20 hours after cesarean section, a generalized tonic seizure occurred, and the patient lost consciousness. The blood pressure was 171/115 mm Hg. Nicardipine and $MgSO_4$ were infused to inhibit seizures and lower the blood pressure. An emergency computed tomography scan of the brain indicated no cerebral hemorrhage. An hour later, the patient's level of consciousness improved; however, she complained of a slight visual deficiency. Magnetic resonance imaging (MRI) 2 hours after the seizure demonstrated bilateral areas of increased signal intensity in the parieto-occipital lobes (**Fig. 1**). Magnetic resonance angiography revealed narrowing of the posterior cerebral artery. The level of consciousness improved and the visual disturbance resolved over the 3 days after the seizure, and the blood pressure had normalized by the 10^{th} postpartum day. The MRI abnormalities were no longer present 11 days after cesarean section. The patient remained hospitalized until 22 days postpartum because of a pulmonary effusion due to hypoproteinemia.

Discussion

According to a recent meta-analysis, PIH was present in 22.6% of 2,308 women who had conceived

with donated oocytes. The odds ratios for PIH in these women compared with women who had conceived with IVF using their own oocytes and women who had conceived without assisted reproductive technology were 2.56 (95% confidence interval, 1.91–3.47) and 6.60 (95% confidence interval, 4.55–9.57), respectively[1]. A case of maternal death has recently been reported[2].

The risk of PIH increases in the setting of artificial insemination with donor sperm and embryo donation, as well as in cases of oocyte donation. The increased risk of PIH may be due to altered or inadequate immunoprotection from exposure to the fetoplacental unit in oocyte recipients, secondary to the short duration of exposure to nonmaternal antigens[3]. Disrupted immune adaptation is assumed to be the central cause for the development of PIH[4]. The search for the cause of this disrupted immune adaptation has focused on the interaction of HLA-C antigen with maternal natural killer cells[5,6]. Cytokines produced by natural killer cells influence the trophoblast-mediated modulation of uterine spiral arteries[7–9]. Disrupted trophoblast invasion and reduced endovascular transformation of the spiral arteries will result in PIH via placental ischemia[10].

Advanced age, IVF, and twin pregnancy, as seen in the present case, have been identified as predisposing factors for PIH. However, a recent study has found that these factors do not have independent effects on the development of PIH in women who have conceived with donated oocytes; only the use of donated oocytes was found to have an independent effect[1]. Furthermore, the early onset of ovarian failure, as seen in the present case, is associated with maternal antibodies against the zona pellucida and against granulosa cells, leading to interference with the invasion of trophoblasts on the endometrial border, thus resulting in poor trophoblast invasion in PIH[11].

RPLS is characterized by transient neurological disturbances, including seizures, visual disturbances, headache, and altered consciousness, with radiological changes of the bilateral white and grey matter predominantly affecting the posterior cerebral hemispheres[12]. These changes disappear over time in most cases; however, irreversible damage might occur without appropriate treatment. The most common causes of RPLS are acute hypertensive disorder and immunosuppressive therapy. MRI is the most appropriate diagnostic tool. Brain lesions are considered to be due to brain edema, which causes acute hypertension in pregnant women[13]. Vasoconstriction has also occasionally been seen on angiography[14].

Eclampsia and PIH are representative predisposing factors for RPLS in pregnancy. Fujiwara et al.[15] and Mackinney et al.[14] have reported that the cause of RPLS (n=76) was eclampsia in 5.5% of patients. Management should be directed toward the control of blood pressure and seizures. RPLS due to eclampsia in singleton pregnancies produced with donated oocytes has been reported in 2 cases[2,16]. Whether a twin pregnancy exacerbates hypertension resulting in eclampsia and whether disseminated intravascular coagulation or atonic bleeding due to twin pregnancy plays a role in the pathophysiology of eclampsia in oocyte recipients remains unclear. However, to ensure the safety of oocyte recipients during pregnancy, it is necessary to recognize that the risk of hypertension is increased. When such hypertension occurs, prompt, aggressive therapy is indicated.

A PubMed literature search using the key words “oocyte donation,” “eclampsia,” and “RPLS” yielded no case reports on pregnant Japanese women with eclampsia who conceived with oocytes donated in Japan. In Japan, no laws currently govern oocyte donation for IVF, and the guidelines of the Japanese Society of Obstetrics and Gynecology prohibit the use of oocytes donated by a nonanonymous third party for IVF. However, information about Japanese women who have become pregnant with donated oocytes is easily obtained from the Internet. Many such cases of IVF and oocyte donation have probably been performed abroad. However, a few cases like present, which occurred several years ago, may have been performed in Japan. No official or scientific information is currently available about how often oocyte donation is performed for Japanese women and whether the procedure is performed in Japan or overseas. In any case, when we care for pregnant women, regardless whether conception is

natural or artificial (even with oocyte donation), all efforts must be made to ensure maternal, fetal, and neonatal health. The risks incurred by women who become pregnant with donated oocytes need to be acknowledged.

In conclusion, we have reported on a Japanese woman with a twin pregnancy produced with donated oocytes and complicated by PIH, eclampsia, and RPLS. Pregnancies produced with donated oocytes should be regarded as being at a high risk for hypertensive complications.

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