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Successful Controlled Ovarian Stimulation and Livebirth in a Patient with MoyaMoya Disease: A Case Report

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Abstract

The cerebrovascular disorder, MoyaMoya disease (MMD), increases the risk of ischemic stroke due to stenosis of the cerebral vasculature. Progressive occlusion leads to the development of weak collateral vessels, which can cause hemorrhagic stroke. Controlled ovarian stimulation for procreation by assisted reproductive technologies induces supraphysiologic serum estrogen levels up to 100 times or greater above baseline values and has been shown to increase the risk of venous thrombosis, making assisted reproduction a unique challenge in patients with MMD. This case report describes a controlled ovarian stimulation and subsequent livebirth in a patient with MMD as well as Factor V Leiden, a thrombophilia that predisposes patients to venous thrombosis.

Keywords

MoyaMoya Disease (MMD), Ovarian Stimulation, *In Vitro* Fertilization, Assisted Reproductive Technologies, Thrombosis

1. Introduction

MoyaMoya disease (MMD), meaning "puff of smoke" in Japanese, is a rare cerebrovascular disease with a high prevalence in Asia and a growing incidence in the United States of about 0.57 cases per 100,000, with women affected three times more than men [1] [2]. MMD is marked by stenosis of the internal carotid artery and its branches, which supply the cerebral hemispheres. Disease onset in childhood is associated with more rapid and greater progression of occlusive lesions compared to adult-onset disease [3]. This progressive occlusion of the cerebrovas-

culature leads to the formation of fragile collateral blood vessels. These collateral vessels have a characteristic "puff of smoke" appearance on brain imaging, which inspired the name. Consequently, patients with MMD are at high risk of ischemic stroke due to their stenotic vessels and hemorrhagic stroke due to their fragile collateral vessels. Therefore, care must be taken with interventions that may further elevate thromboembolic or cerebrovascular risk, including controlled ovarian stimulation for assisted reproductive technology (ART), such as *in vitro* fertilization.

Venous thromboembolism risk in healthy reproductive-age women is approximately 1 - 5 per 10,000 [4]. This risk is elevated in the presence of heritable thrombophilias, such as Factor V Leiden, rendering Factor V resistant to degradation by activated protein C, leading to a hypercoagulable state [4]. During pregnancy, venous thrombosis risk increases by about 4 - 6 fold [4]. Compared to spontaneous pregnancy, controlled ovarian stimulation induces supraphysiologic serum concentrations of estrogen and poses an even greater risk of thrombosis, up to 10-fold above baseline. It has been shown that factors favoring coagulation are upregulated during controlled ovarian stimulation, including von Willebrand factor, factors VIII, V, and fibrinogen, and antithrombotic factors are downregulated, including antithrombin and Proteins C and S [5] [6]. While the cause of this procoagulant state is multifactorial, elevated estrogen levels are thought to play a large role in its development. Thus, fertility treatment should be approached with caution in patients predisposed to severe complications of venous thromboembolism, such as MMD patients.

With rising infertility rates in the United States and patients delaying childbearing into the third and fourth decades of life, patients with these types of rare conditions must have representation in the literature to guide fertility treatment for clinicians [7]. Here, we describe the successful controlled ovarian stimulation and ART in a patient with MoyaMoya disease and homozygous Factor V Leiden.

2. Case Description

A 34-year-old patient, G2P0121, with MoyaMoya disease, was seen in our clinic for fertility treatment. She was diagnosed with MMD in childhood after suffering a middle cerebral artery stroke at the age of four. At that time, she had undergone a bilateral superficial temporal artery to middle cerebral artery bypass (STA-MCA), a standard revascularization procedure in MMD. At age 17, she had another revascularization procedure, an encephalo-myo-synangiosis, after an episode of left-hand weakness and sporadic transient ischemic attacks, and had been taking 325 mg aspirin per day for stroke prophylaxis. She also has intermittent migraine headaches with aura. She did not have a history of hemorrhagic stroke. She presented to our clinic after trying to conceive for three years. She had one living daughter, conceived naturally with a different partner, and had a spontaneous second-trimester twin pregnancy loss one year before seeing us. Additionally, she had genetic testing-confirmed homozygous Factor V Leiden with no known

history of venous thrombosis.

Her infertility work-up included a male factor diagnosis indicated by 5% sperm motility (normal ≥ 40%); all other sperm parameters were normal. Table 1 details the results of her serum hormone levels. Her AMH was adequate for her age. Her TSH, free T_4, and prolactin levels were all within normal limits, and she experienced regular menstrual cycles, occurring every 24 days and lasting approximately 6 days. Hysterosalpingogram revealed a normal uterine cavity without polyps, fibroids, or evidence of adhesions, and the uterine tubes were patent bilaterally.

Table 1. Infertility laboratory workup.

Test	Laboratory Test Results		
	Result	Reference Range	Interpretation
AMH	3.3 ng/mL	1.0 - 4.0 ng/mL	Normal ovarian reserve
TSH	0.44 mIU/mL	0.27 - 4.2 mIU/mL	Normal
Free T_4	1.10 ng/dL	0.93 - 1.7 mIU/mL	Normal
Prolactin	11.88 ng/mL	4.8 - 23.3 ng/mL	Normal

Note: The reference range for AMH is age-based. The reference range for prolactin is based on a non-pregnant, non-lactating female.

She underwent three unsuccessful intrauterine insemination cycles with clomiphene citrate before opting for conception by *in vitro* fertilization (IVF) procedure. A multidisciplinary team, including reproductive endocrinology, neurology, hematology, and maternal fetal medicine, was involved in counseling the patient on the risks of controlled ovarian stimulation given her high risk of venous thrombosis secondary to Factor V Leiden and stroke secondary to MMD. With full knowledge of the risks and informed consent, she decided to pursue IVF. For stroke prophylaxis during stimulation, her neurologist and hematologist agreed that she should continue aspirin 325 mg daily for stroke prophylaxis during stimulation, while anticoagulation was avoided due to her high risk of hemorrhagic stroke. Given that oral contraceptive pills are contraindicated because of her stroke risk and migraines with aura, a short stimulation protocol was used, outlined in Figure 1(A). Follicle-stimulating hormone (FSH, Follistim®) and a gonadotropin-releasing hormone agonist (Lupron®) were started on day 3 of her cycle. Serum estradiol was measured on days 3, 8, 10, 11, and 12, and ovarian follicle growth was monitored with transvaginal ultrasound on days 9, 10, 11, and 12, as shown in Figure 1(B). On day 12, greater than two 18 mm follicles were noted, and so ovulation was triggered on day 12 with human chorionic gonadotropin alpha (Ovidrel®). Fifteen mature oocytes were collected 34 hours post-trigger under transvaginal ultrasound guidance. Conscious sedation was used during oocyte retrieval to allow for strict blood pressure control and maintenance of normocapnia, which are critical for patients at high risk for ischemia. Cabergoline was administered as a prophylaxis for ovarian hyperstimulation syndrome.

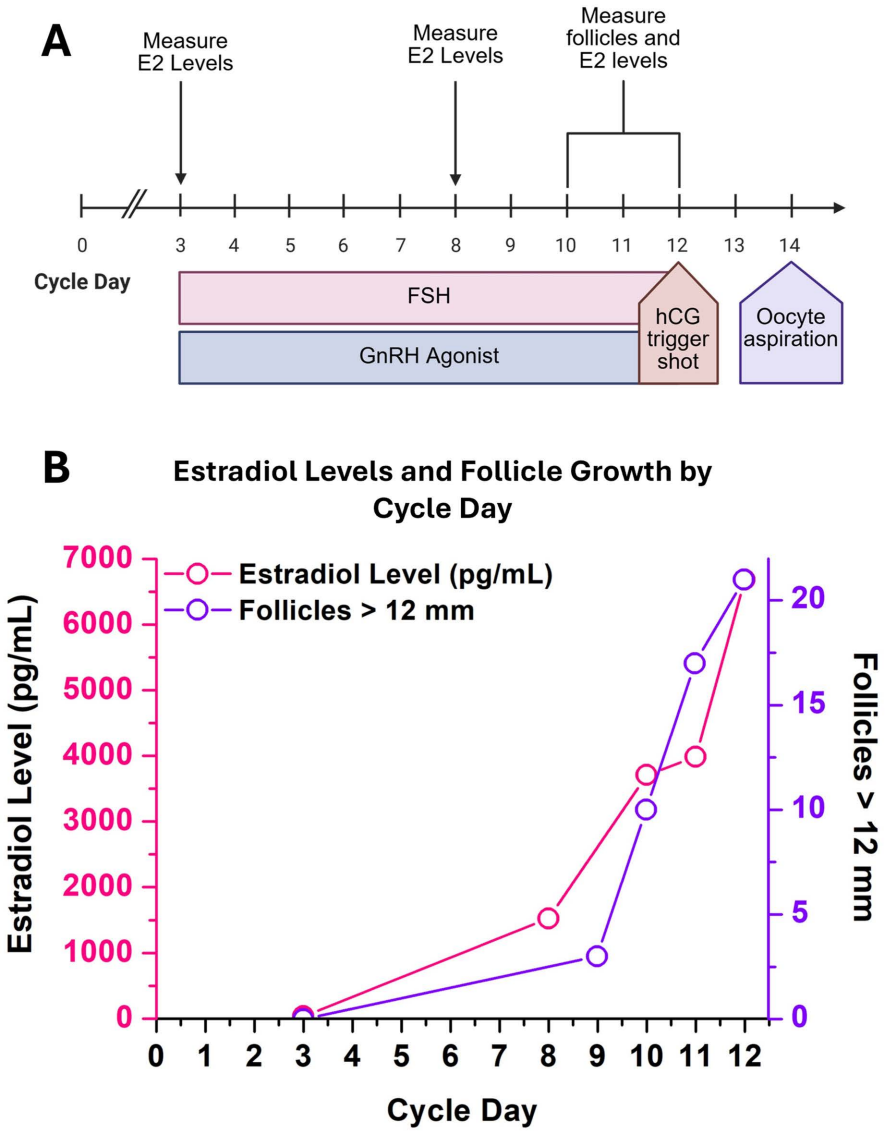

Figure 1. (A) Controlled ovarian stimulation protocol used. (B) Serum estradiol levels in pg/mL and the bilateral sum of ovarian follicles greater than 12 mm by cycle day during controlled ovarian stimulation.

Her controlled ovarian stimulation was routine and uncomplicated after receiving a total of 1600 IU of Follistim®. She remained free of new neurologic deficits and venous thrombosis and did not develop symptoms of hyperstimulation. Of the 15 oocytes retrieved, 14 were injected with intracytoplasmic sperm injection, and 9 were successfully fertilized. The resulting zygotes underwent extended embryo culture in Global medium (Life Global group) supplemented with 10% serum substitute supplement (Irvine Scientific) at 37˚C under a reduced O_2 environment (5% O_2 + 6% CO_2 + balance nitrogen). Five embryos that developed to blastocysts by day 6 in culture were biopsied for preimplantation genetic testing for aneuploidy, and all were confirmed as euploid. Biopsied embryos were cryopreserved using the blastocyst fast freeze kit (Life Global Group) following the

manufacturer's suggested protocol. She subsequently underwent frozen embryo transfer (FET) in the following cycle to reduce the risk of ovarian hyperstimulation, permit blastocyst-stage preimplantation genetic testing, and avoid pregnancy during the hyperestrogenic stimulation period, thereby mitigating thrombotic risk in this high-risk patient.

For FET, a single cryopreserved and euploid embryo was thawed by using blastocyst fast freeze thaw kit (Life Global Group) following the manufacturer's suggested protocol. For endometrial preparation, a baseline transvaginal ultrasound performed on day 1 of the patient's menstrual cycle showed 3 - 4 pre-antral follicles bilaterally, no ovarian cysts, and an endometrial thickness of less than 5 mm. Estrace 2 mg was started on cycle days 1 - 5, then increased to 4 mg for 3 days, and then increased to 6 mg daily. Although transdermal estrogen has been associated with lower thrombotic risk in the postmenopausal population, oral estradiol was chosen in this case due to its superior titratability and ability to mimic physiologic estrogen escalation during endometrial preparation, which was prioritized to ensure adequate endometrial development for FET. Daily monitoring of endometrial thickness with transvaginal ultrasound began on cycle day 10. Once the endometrial thickness reached 8 mm, progesterone in oil was started, beginning with 100 mg and then 15 mg daily until FET. FET took place 5 days after initiating progesterone. Serum β-hCG level was measured to determine pregnancy status 10 days after FET.

Patient successfully conceived and delivered a healthy male infant via cesarean section after 32 weeks and 4 days of gestation. Thromboprophylaxis with aspirin 325 mg was continued, informed by successful use in her prior pregnancy and recommendations from neurology and hematology. Again, anticoagulation was avoided due to her risk of hemorrhagic stroke. At 32 weeks' gestation, the patient developed preeclampsia with severe features refractory to antihypertensive therapy and magnesium sulfate, prompting indicated preterm cesarean delivery. Antenatal steroids were administered at 31 weeks for fetal lung development.

3. Discussion

This case demonstrates successful and complication-free controlled ovarian stimulation in a patient with both MoyaMoya Disease and Factor V Leiden, two conditions that independently increase the risk of ischemic stroke. Further, it demonstrates the feasibility of safely managing ovarian stimulation in the presence of dual high-risk conditions through collaboration with a multidisciplinary team. We want to highlight the importance of thorough counseling and shared decision-making with high-risk patients. Similarly, patients with MMD should be counseled on the risks of pregnancy; generally, patients do well during pregnancy, especially those with a history of revascularization, which appears protective [8]. Patients should be followed closely during pregnancy for the development of pregnancy-induced hypertension, which increases their risk for hemorrhagic stroke [9].

Another option for this patient population is the addition of an aromatase inhibitor, as has been utilized in patients with breast cancer, to reduce estrogen levels throughout stimulation [10]. It has been hypothesized that reducing estrogen levels with an aromatase inhibitor may lower thrombosis risk; however, no studies have directly compared thrombotic risk between standard stimulation and aromatase-inhibitor protocols. Although an aromatase inhibitor-based protocol was considered to limit estrogen exposure during stimulation, it was not selected due to its lower and less reliable follicle yield. Given the goal of maximizing oocyte number to improve the likelihood of obtaining a euploid embryo in the setting of advanced maternal age, a conventional gonadotropin-based protocol was favored following multidisciplinary risk-benefit assessment.

To our knowledge, this is the first reported description of the management of controlled ovarian stimulation in a patient with MMD, and we hope this case will help guide future management for MMD patients seeking fertility treatment to reach their pregnancy goals.

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Authors' Contributions

B.Y.S. was the clinician who cared for the patient, contributed to the conception of the report, and reviewed the manuscript. K.S.F. contributed to the report's conception, drafted the manuscript, and created the figures. N.C. and H.M. contributed to the content of the report and assisted in writing and reviewing the manuscript. K.A. performed all IVF laboratory procedures involved. S.P. and L.P. comprised the patient's andrology team and assisted in manuscript review.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Zhang, H., Zheng, L. and Feng, L. (2019) Epidemiology, Diagnosis and Treatment of Moyamoya Disease (Review). *Experimental and Therapeutic Medicine*, **17**, 1977-1984. https://doi.org/10.3892/etm.2019.7198

[2] Starke, R.M., Crowley, R.W., Maltenfort, M., Jabbour, P.M., Gonzalez, L.F., Tjoumakaris, S.I., *et al.* (2012) Moyamoya Disorder in the United States. *Neurosurgery*, **71**, 93-99. https://doi.org/10.1227/neu.0b013e318253ab8e

[3] Kuroda, S., Ishikawa, T., Houkin, K., Nanba, R., Hokari, M. and Iwasaki, Y. (2005) Incidence and Clinical Features of Disease Progression in Adult Moyamoya Disease. *Stroke*, **36**, 2148-2153. https://doi.org/10.1161/01.str.0000182256.32489.99

[4] Eichinger, S., Evers, J.L.H., Glasier, A., La Vecchia, C., Martinelli, I., Skouby, S., *et al.* (2013) Venous Thromboembolism in Women: A Specific Reproductive Health Risk. *Human Reproduction Update*, **19**, 471-482. https://doi.org/10.1093/humupd/dmt028

[5] Chan, W.S. and Dixon, M.E. (2008) The "ART" of Thromboembolism: A Review of Assisted Reproductive Technology and Thromboembolic Complications. *Thrombosis Research*, **121**, 713-726. https://doi.org/10.1016/j.thromres.2007.05.023

[6] Westerlund, E., Henriksson, P., Wallén, H., Hovatta, O., Wallberg, K.R. and Antovic, A. (2012) Detection of a Procoagulable State during Controlled Ovarian Hyperstimulation for *in Vitro* Fertilization with Global Assays of Haemostasis. *Thrombosis Research*, **130**, 649-653. https://doi.org/10.1016/j.thromres.2011.11.024

[7] Driscoll, A.K. and Hamilton, B.E. (2025) Effects of Age-Specific Fertility Trends on Overall Fertility Trends: United States, 1990-2023. *National Vital Statistics Reports*, **6**, Article 1.

[8] Lai, P.M.R., Beazer, M., Frerichs, K.U., Patel, N.J., Aziz-Sultan, M.A. and Du, R. (2024) Association between Moyamoya Revascularization Surgery and Neurologic Events during Pregnancy: Systematic Review. *Neurosurgery*, **96**, 948-957. https://doi.org/10.1227/neu.0000000000003184

[9] Yajima, H., Miyawaki, S., Sayama, S., Kumasawa, K., Ikemura, M., Imai, H., *et al.* (2023) Hypertensive Disorders of Pregnancy in Moyamoya Disease: A Single Institution Experience. *Journal of Stroke and Cerebrovascular Diseases*, **32**, Article 107377. https://doi.org/10.1016/j.jstrokecerebrovasdis.2023.107377

[10] Oktay, K., Hourvitz, A., Sahin, G., Oktem, O., Safro, B., Cil, A., *et al.* (2006) Letrozole Reduces Estrogen and Gonadotropin Exposure in Women with Breast Cancer Undergoing Ovarian Stimulation before Chemotherapy. *The Journal of Clinical Endocrinology & Metabolism*, **91**, 3885-3890. https://doi.org/10.1210/jc.2006-0962