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Case Report

Case report of successful live birth in an infertile couple with male idiopathic hypogonadotropic hypogonadism/azoospermia and atypical polypoid adenomyoma of the uterus

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Summary

The authors report a unique case of a successful live birth in an infertile couple both with male factor (idiopathic hypogonadotropic hypogonadism, IHH/azoospermia) and female factor [atypical polypoid adenomyoma (APA) of the uterus]. According to the history of ejaculation disorder and low values of serum follicle stimulating hormone, luteinizing hormone, and testosterone concentration, an infertile man was diagnosed with IHH. Gonadotropin therapy failed to produce ejaculated spermatozoa, but microdissection testicular sperm extraction was successful for retrieval and cryopreservation of motile testicular spermatozoa. Meanwhile, in the course of infertility workup for his female partner, fluid hysteroscopy detected multiple endometrial polypoid lesions in her uterine cavity. Hysteroscopic resection and histopathologic examinations revealed that the lesions were APA. Repeated hysteroscopic and histopathologic examinations did not find any evidence of the recurrence. She underwent controlled ovarian stimulation, oocyte pickup, and intracytoplasmic sperm injection using thawed testicular spermatozoa. She had a pregnancy in the first frozen-thawed blastocyst transfer cycle and gave birth to a healthy baby.

Key words: Azoospermia; Idiopathic hypogonadotropic hypogonadism; Atypical polypoid adenomyoma; Infertility.

Introduction

Male idiopathic hypogonadotropic hypogonadism (IHH) is recognized as inability to synthesize, secrete, or respond to gonadotropin-releasing hormone, resulting in low male sex steroids and low/normal gonadotropin levels, and oligoasthenozoospermia [1]. Meanwhile, atypical polypoid adenomyoma (APA) is a rare benign mixed epithelial and mesenchymal tumor of the uterus that potentially transforms into endometrial adenocarcinoma and is occasionally identified during the course of the infertility workup [2, 3].

Here, the authors report a unique case of an infertile couple with male IHH/azoospermia along with APA of the uterus. Gonadotropin therapy failed to produce ejaculated spermatozoa, but microdissection testicular sperm extraction (micro TESE) was successful for retrieval and cryopreservation of motile testicular spermatozoa in the male partner. Meanwhile, in the course of infertility workup for his female partner, hysteroscopy detected multiple endometrial polypoid lesions in her uterine cavity. Hysteroscopic resection and histopathologic examinations revealed that the lesions were APA. As repeated hysteroscopic and histopathologic examinations did not find any evidence of the recurrence, she underwent controlled ovarian stimulation (COS), oocyte pickup, and intracytoplasmic sperm injection (ICSI) using thawed testicular spermatozoa. She had a pregnancy in the first frozen-thawed blastocyst transfer cycle and gave birth to a healthy baby.

Case Report

A couple was referred to our clinic for infertility due to ejaculation disorder of 40-year-old male partner for two years. He had a past history of urinary tract stone and his physical examination was unremarkable. The blood examination demonstrated the low values of follicle-stimulating hormone (FSH, 0.1 mIU/mL), luteinizing hormone (LH, 0.2 mIU/mL), and testosterone (26.9 ng/dL). He was diagnosed with IHH. Following one-month administration of recombinant FSH and human chorionic gonadotropin agents, he began to produce semen samples. Repeated semen analyses, however, failed to detect any spermatozoa in his ejaculates during the course of 10-month hormone therapy. He underwent micro TESE, which was successful for retrieval and cryopreservation of motile testicular spermatozoa.

His 32-year-old nulligravid female partner presented without any health problems. In the course of infertility workup, fluid hysteroscopy detected multiple endometrial polypoid lesions in her uterine cavity. Hysteroscopic resection was performed to remove the intrauterine polypoid lesions. According to the proliferation of irregularly-shaped endometrial glands, the formation of squamous morule within the glands, and a prominent cellular, smooth muscle stroma, the histopathologic diagnosis was APA. We performed the second-look hysteroscopic and histopathologic examinations in one month following the surgery and the third-look examinations in three months and did not find any evidence of the recurrence. Due to the strong demand of the couple for early resumption of infertility treatment, they proceeded to oocyte pick-up cycle under a written informed consent. As the female partner had a normal ovarian reserve with serum anti-Mullerian hormone concentration 3.10 ng/mL and antral follicle count 12, COS was started from day 3 of the cycle using a gonadotropin-releasing hormone agonist short pro-

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tocol to prevent premature LH surge. Fifteen oocytes were picked up on day 13 by ultrasound-guided transvaginal follicular aspiration without a sign of ovarian hyperstimulation syndrome. ICSI was performed using thawed testicular spermatozoa. Four blastocysts were obtained in embryo culture and cryopreserved in liquid nitrogen. She had a pregnancy in the first frozen-thawed embryo transfer cycle without any obstetrical complications. Any particular maternal complications were not seen in the course of the pregnancy. She gave birth to a 2,900 g healthy boy at 37 weeks of gestation by elective caesarean section due to breech presentation.

Discussion

To our best knowledge, no studies reported infertile couples with APA along with male IHH. In this report, the authors provide a case where IHH was identified in an infertile man with ejaculation disorder and APA was incidentally found in his female partner during the course of infertility workup following motile spermatozoa retrieval by micro TESE. Successful pregnancy was achieved in assisted reproductive technology using thawed testicular spermatozoa.

Approximate 30 cases with successful live birth are literally identified in women with a history of APA [4-10]. Previous studies utilized uterus-conserving surgery such as endometrial curettage or hysteroscopic resection for women desiring babies, along with hormonal treatment with high-dose medroxyprogesterone acetate (200-600 mg/day) [4, 5]. The reported persistence and/or recurrence rate of APA following hysteroscopic resection (10.0%) is lower than that following endometrial curettage (23.8%-44.8%) [6-10]. The authors did not find any evidence of the recurrence in the second- and third-look hysteroscopic/histopathologic examinations.

Due to the strong demand of the couple for early resumption of infertility treatment, they proceeded to assisted reproductive technology under written informed consent. As the female partner had a normal ovarian reserve, gonadotropin-releasing hormone agonist short protocol was adopted to prevent premature LH surge in the COS/oocyte pick-up cycle, which resulted in successful retrieval of 15 oocytes without ovarian hyperstimulation syndrome and four blastocysts in ICSI treatment and subsequent embryo culture. She conceived in the first frozen-thawed embryo transfer cycle without any obstetrical complications and gave birth to a healthy baby.

In this report, we provided a rare case of an infertile couple with both male (IHH/azoospermia) and female (APA of the uterus) factors. Gonadotropin therapy failed to obtain spermatozoa in ejaculates during 10-month hormone therapy, but micro TESE was successful to retrieve motile testicular spermatozoa. Meanwhile, APA was incidentally found in the histopathological examinations following hysteroscopic resection of endometrial polypoid lesions. A successful live birth was achieved in COS, oocyte pickup, ICSI and frozen-thawed blastocyst transfer using thawed testicular spermatozoa.

Ethics Approval and Consent to Participate

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Reproduction Clinic Osaka (approval number: 2020-001).

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Conflict of Interest

The authors declare no conflict of interest.

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References

[1] Sykiotis G.P., Hoang X.H., Avbelj M., Hayes F.J., Thambundit A., Dwyer A., *et al*.: "Congenital idiopathic hypogonadotropic hypogonadism: evidence of defects in the hypothalamus, pituitary, and testes". *J. Clin. Endocrinol. Metab*., 2010, *95*, 3019-3027.

[2] Němejcová K., Kenny S.L., Laco J., Škapa P., Staněk L., Zikán M., *et al*.: "Atypical polypoid adenomyoma of the uterus: an immunohistochemical and molecular study of 21 cases". *Am. J. Surg. Pathol.*, 2015, *39*, 1148-1155.

[3] Mikos T., Tsolakidis D., Grimbizis G.F.: "Clinical presentation and management of atypical polypoid adenomyomas: systematic review of the literature". *Eur. J. Obstet. Gyncol. Reprod. Biol.*, 2019, *236*, 14-21.

[4] Rizzuto I., Nicholson R., Dickinson K., Juang H.J., MacNab W., Rufford B.: "A case of incidental endometrial adenocarcinoma diagnosed in early pregnancy and managed conservatively". *Gynecol. Oncol. Rep.*, 2019, *28*, 101-103.

[5] Nomura H., Sugiyama Y., Tanigawa T., Matoda M., Kanao H., Kondo E., *et al*.: "Long-term outcomes of fertility-sparing treatment of atypical polypoid adenomyoma with medroxyprogesterone acetate". *Arch. Gynecol. Obstet.*, 2016, *293*, 177-181.

[6] Di Spiezio Sardo A., Mazzon I., Gargano V., Di Carlo C., Guida M., Mignogna C., *et al*.: "Hysteroscopic treatment of atypical polypoid adenomyoma diagnosed incidentally in a young infertile woman". *Fertil. Steril.*, 2008, *89*, 456.e9-e12.

[7] Wong A.Y., Chan K.S., Lau W.L., Tang L.C.: "Pregnancy outcome of a patient with a typical polypoid adenomyoma". *Fertil. Steril.*, 2007, *88*, 1438.e7-e9.

[8] Yahata T., Nonaka T., Watanabe A., Sekine M., Tanaka K.: "Complete hysteroscopic resection of a large atypical polypoid adenomyoma, followed by a successful pregnancy". *Fertil. Steril.*, 2011, *95*, 2435.e9-e11.

[9] Guida M., Greco E., Di Spiezio Sardo A., Di Carlo C., Lavitola G., Tarsitano F., *et al*.: "Successful pregnancy after four-step hysteroscopic technique for the treatment of atypical polypoid adenomyoma". *Fertil. Steril.*, 2008, *89*, 1283-1284.

[10] Chen Q., Lu W., Lu B.: "Pregnant outcomes of atypical polypoid adenomyoma treated with progestin therapy". *J. Obstet. Gynaecol. Res.*, 2018, *44*, 323-330.

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