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Case Report

Clinical management and successful pregnancy outcomes in women with empty Sella syndrome undergoing assisted reproductive technology: a case-based approach

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ABSTRACT

Empty Sella syndrome (ESS) is a radiological condition characterized by a partially or completely flattened pituitary gland within the sella turcica, which may impact reproductive function. This case report presents two women with ESS undergoing *in vitro* fertilization (IVF). Despite having ESS, patient A had a normal ovarian reserve and conceived after frozen embryo transfer (FET) and regulated ovarian stimulation. Patient B needed an oocyte donation program in order to achieve pregnancy because of their significantly reduced ovarian reserve (AMH=0.01 ng/ml). The fact that both patients were able to conceive shows how important it is to use customized assisted reproductive technology (ART) plans depending on ovarian function. ESS presents a heterogeneous impact on fertility, necessitating tailored treatment plans, including optimized ovarian stimulation, embryo transfer protocols, and donor oocyte utilization. A multidisciplinary approach involving reproductive endocrinologists and fertility specialists is crucial in managing ESS-related infertility to maximize pregnancy success.

Keywords: Empty Sella syndrome, Infertility, Ovarian stimulation, Assisted reproductive technology

INTRODUCTION

Empty Sella syndrome (ESS) is a radiological condition that consists of herniation of the subarachnoid space into the Sella turcica with consequent flattening or partial disappearance of the pituitary gland. ESS can be classified as primary ESS, which occurs as a consequence of a congenital diaphragm sellae defect that leads to compression of the pituitary gland by cerebrospinal fluid, and secondary ESS, occurs as a consequence of such factors as pituitary surgery, infarction, radiation, or trauma. Although ESS is normally considered an incidental brain imaging study finding, clinical importance is described with the onset of hormonal imbalance, which could be of importance regarding fertility.[1]

Women with ESS can have a wide range of hormonal profiles, ranging from normal endocrine function to partial pituitary hormone deficiencies. The most commonly affected hormones are gonadotropins like follicle-stimulating hormone (FSH) and luteinizing hormone (LH), growth hormone (GH), and prolactin, all of which are crucial for reproductive function.[2] ESS can in some cases be associated with hypogonadotropic hypogonadism, leading to anovulation, menstrual irregularities, or infertility. However, a subset of patients with ESS can have normal ovarian function and be responsive to controlled ovarian stimulation.[3]

ART has transformed the treatment of infertility in women with endocrine disorders such as ESS. Ovarian stimulation protocol is extremely crucial since excessive gonadotropin stimulation can result in inadequate follicular response or ovarian hyperstimulation syndrome (OHSS) in patients with deranged hypothalamic-pituitary axis. In cases of severely diminished ovarian reserve, oocyte donation is usually the most feasible option for successful conception.[4,5] Current case report describes 2 distinct

clinical presentations of women with ESS undergoing IVF treatment. Patient A, despite her ESS diagnosis, had normal ovarian function and succeeded in conception after controlled ovarian stimulation and FET. Patient B, on the other hand, had very poor ovarian reserve and hence an oocyte donation program was needed for successful conception. These cases highlight varied reproductive outcomes in ESS patients and need for individualized ART protocols to achieve optimal fertility outcomes.

CASE REPORT

Patient A, 30 years old, with five years of primary infertility presented for IVF treatment. She was diagnosed with ESS, a clinical condition where the pituitary gland inside the Sella turcica is partially or completely flattened. She did not present with any major hormonal imbalances that may interfere with ovarian stimulation. Although she had irregular menstrual cycles, neither polycystic ovary syndrome (PCOS) nor hirsutism was present. The patient also did not have any past history of thyroid failure, adrenal insufficiency, or other endocrine diseases.

The 30-year-old husband had normal semen parameters, with sperm concentration 65 million/ml, progressive motility 40, and morphology of 20% of sperm classified as normal. His body mass index (BMI) was 25.3, and serological examination was negative for infectious diseases. The couple did not have any known genetic disorders or major medical comorbidities. The patient's baseline serum prolactin level was 2.96 ng/ml (normal: 4.8-23.3 ng/ml), and FSH and LH levels were both within normal limits (FSH: 3.5-12.5 mIU/ml; LH: 2.4-12.6 mIU/ml in the follicular phase). Gonadotropin-releasing hormone (GnRH) therapy was used as part of the controlled ovarian stimulation protocol. The antagonist protocol was chosen to prevent premature luteinization and daily recombinant FSH (rFSH) was initiated. During the stimulation, recombinant FSH was administered at an initial dose of 300 IU on day 1, which was gradually reduced to 150 IU on day 11 based on follicular response and serum estradiol levels. A total of 12 metaphase II (MII) oocytes were retrieved, along with 4 oocytes at metaphase I (MI) and 2 at the germinal vesicle (GV) stage. The retrieved oocytes were subjected to intracytoplasmic sperm injection (ICSI) due to a mild male factor infertility concern related to borderline sperm morphology. Seven oocytes were successfully fertilized, and embryo culture was carried out to the blastocyst stage.

A FET cycle was planned due to concerns about potential OHSS and to optimize endometrial receptivity. The patient was endometrial prepared using estrogen and progesterone support. On transfer day, the endometrial thickness was 9.8 mm, and transfer was smooth under ultrasound guidance. Two embryos were chosen and transferred. Serum beta-human chorionic gonadotropin (β-hCG) levels at 12 days post-transfer was 8437 mIU/ml, indicating successful implantation. Ultrasound follow-up at six weeks gestation showed a single intrauterine pregnancy with fetal heartbeat. The pregnancy was uneventful, and the patient delivered a healthy neonate at full term by spontaneous vaginal delivery. Postpartum course was uneventful, and no maternal or neonatal complications were seen.

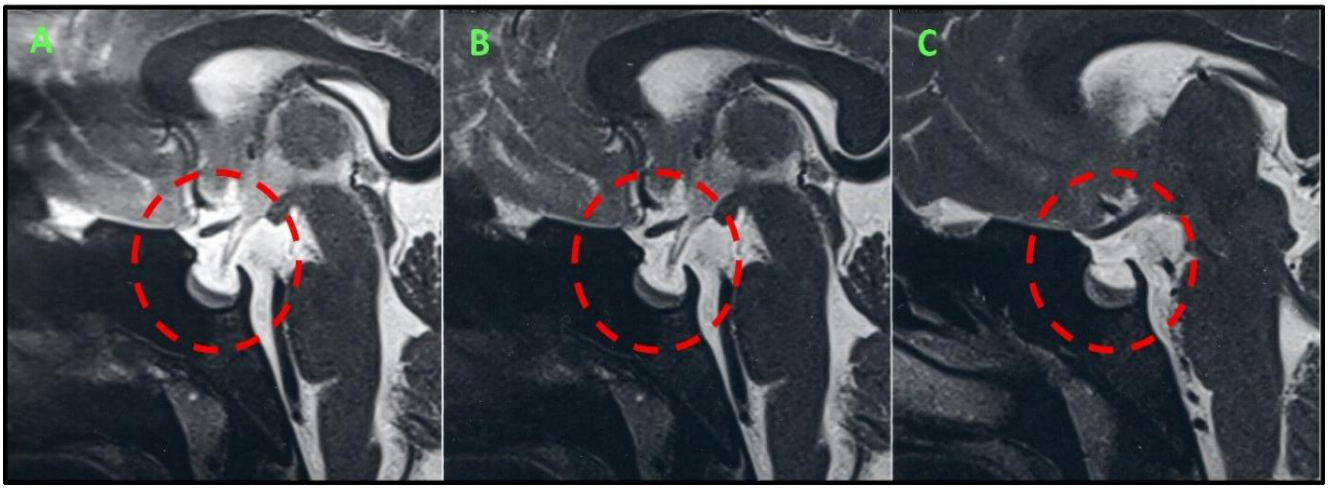

Figure 1 (A-C): MRI image of Sella.

A 28-year-old patient B presented with menstrual irregularity and was diagnosed with ESS thereafter. Her BMI was recorded as 32.4 at the time of evaluation, and she was classified as obese. Initial investigations, including serological tests, were negative and therefore ruled out any possible infectious etiology. The serum prolactin level was recorded at 7.56 ng/ml, which was within normal limits, and indicated the lack of any serious dysfunction of the pituitary gland in relation to lactotroph cells. However, her ovarian reserve was low, as her anti-Mullerian hormone (AMH) was recorded at a mere 0.01 ng/ml, and natural ovarian stimulation and self-oocyte collection were found to be impossible. With these observations, the use of an oocyte donor program was found to be the most appropriate means of ensuring conception.

The male partner, aged 32 years, also tested negative for serological markers and then underwent a semen analysis. The semen analysis showed a semen volume of 2 ml, sperm concentration of 65 million/ml, progressive motility of 40%, non-progressive motility of 20%, and a morphology rate of 4% that was graded as normal. These semen parameters were within the acceptable range, making him a suitable candidate for traditional sperm selection techniques. However, to increase the chances of fertilization, ICSI was applied to the donor oocytes. Following fertilization, seven embryos were successfully formed on day 3. By day 5, a total of seven blastocysts had developed, with all embryos graded as high-quality (Grade A), indicating good viability for implantation. To ensure optimal uterine receptivity, the patient underwent hormone replacement therapy (HRT) for endometrial preparation. The endometrial thickness (ET) measured 7.8 mm on the day of the planned FET, which was considered an adequate measurement for successful implantation.

A FET was performed, during which two high-quality blastocysts were carefully transferred into the uterine cavity. The procedure was smooth and uneventful, with no complications or difficulties during the transfer process. Post-transfer monitoring was conducted, and β-hCG levels were assessed on day 12, revealing a high value of 1202 mIU/ml, confirming a positive pregnancy outcome. Currently, the pregnancy is progressing well with regular monitoring to ensure maternal and fetal well-being.

DISCUSSION

ESS is a rare anatomical condition in which the Sella turcica is partially or completely filled with cerebrospinal fluid, leading to a flattened or atrophic pituitary gland. While some patients with ESS exhibit significant endocrine dysfunction, others, like the cases presented here, may have relatively preserved pituitary function.[6] The impact of ESS on reproductive health remains a subject of interest, as pituitary hormones play a critical role in ovarian stimulation, folliculogenesis, and endometrial receptivity.

The two cases in this report highlight different reproductive strategies for managing infertility in ESS patients. In patient A, ovarian stimulation was feasible, despite irregular menstrual cycles. The controlled ovarian stimulation protocol involved a GnRH antagonist approach with recombinant FSH, which resulted in a satisfactory ovarian response with 12 MII oocytes retrieved. The patient's normal baseline gonadotropin levels may have contributed to a successful response to ovarian stimulation. The decision to perform ICSI was based on the husband's borderline sperm morphology, ensuring optimal fertilization rates. The subsequent blastocyst culture and selection of high-quality embryos contributed to a successful FET cycle and implantation.

Conversely, patient B presented with severely diminished ovarian reserve, as indicated by an AMH level of 0.01 ng/ml and an undetectable antral follicle count. Given the extremely low ovarian reserve, ovarian stimulation was not a viable option, necessitating the use of an oocyte donor.[7] Oocyte donation has been a well-established approach for women with primary ovarian insufficiency or extremely poor ovarian reserve, allowing them to achieve successful pregnancies with ART. The use of donor oocytes in this case, coupled with ICSI for optimal sperm selection, led to the formation of multiple high-quality blastocysts, providing a favourable prognosis for implantation and pregnancy.

In both cases, endometrial preparation was achieved through HRT, ensuring an optimal environment for embryo implantation. In patient A, an endometrial thickness of 9.8 mm was achieved, which is well within the recommended range for successful implantation. Similarly, patient B reached an endometrial thickness of 7.8 mm, which, although slightly lower, was still adequate for embryo transfer.[8] Both patients achieved successful pregnancies following embryo transfer, as confirmed by significantly elevated serum β-hCG levels. In patient A, the β-hCG level of 8437 mIU/ml (normal >50 mIU/ml at 12 days post-FET) strongly suggested a robust implantation, and subsequent ultrasonography confirmed a single intrauterine pregnancy with a normal fetal heartbeat. This pregnancy progressed without complications, culminating in a healthy term delivery. This case underscores the potential for spontaneous conception in ESS patients with preserved ovarian function, despite the presence of anatomical abnormalities in the pituitary gland.

In contrast, patient B achieved a pregnancy via oocyte donation, with a β-hCG level of 1202 mIU/ml, indicative of a successful implantation. Although her pregnancy is ongoing, regular monitoring is essential to assess fetal development and maternal well-being. Given her BMI of 32.4, she is at an elevated risk for gestational complications such as gestational diabetes mellitus (GDM) and hypertensive disorders of pregnancy.[9] These two cases highlight distinct approaches to managing infertility in patients with ESS. The successful pregnancy in patient A demonstrates that some ESS patients with preserved ovarian function can undergo conventional ovarian stimulation and achieve pregnancy through IVF. However, the case of patient B illustrates the challenges associated with severely diminished ovarian reserve, necessitating oocyte donation as the most viable reproductive option.

The presence of ESS should prompt a thorough endocrinological evaluation, particularly assessing gonadotropin levels, AMH, and antral follicle count to determine the most appropriate ART strategy. The selection of either ovarian stimulation or oocyte donation should be based on individualized patient factors, including hormonal profiles, ovarian reserve markers, and personal reproductive goals. Future research should focus on long-term reproductive outcomes in ESS patients undergoing ART, including the impact of various

stimulation protocols, endometrial receptivity optimization strategies, and maternal-fetal health during pregnancy. Additionally, given the association between ESS and obesity in patient B, further investigations into the metabolic implications of ESS in reproductive-age women may provide valuable insights for improving fertility management in this population.[10]

CONCLUSION

Both individuals' successful pregnancies and deliveries shows that, with the right care, ESS need not be a barrier to successful reproduction. Individualized ART regimens and regulated ovarian stimulation can result in successful pregnancies for women with healthy ovaries. Oocyte donation is still a practical and efficient option when ovarian reserve is reduced. Crucially, each patient's endocrine profile and ovarian response must be taken into consideration when selecting the stimulation regimen, luteal phase support, and embryo transfer approach. In order to maximize fertility results for women with ESS, these instances highlight the need for a multidisciplinary strategy comprising endocrinologists, reproductive experts, and embryologists. Also, in order to enhance ART success rates, further study is necessary to examine long-term reproductive patterns in ESS patients.

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