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Case Report

Dual diagnostic complexity in ART: pituitary microadenoma and heterotopic pregnancy - a case-based insight

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ABSTRACT

Pituitary microadenomas are benign adenohypophyseal tumors most commonly related to hormonal dysregulation, possibly affecting fertility and reproductive function. This case report presents a 24-year-old female with a pre-existing preclinical diagnosis of pituitary microadenoma presenting to assisted reproductive treatment for subfertility. In spite of regular menstrual cycles and lack of any of the features of hyperprolactinemia at treatment, her clinical history warranted meticulous hormonal assessment and customized stimulation protocol. After controlled ovarian stimulation, ICSI, and frozen embryo transfer of two blastocysts, she got pregnant. To her astonishment, she was diagnosed with a heterotopic pregnancy, as evidenced by the presence of intrauterine and tubal gestation. This case points towards the intricate interplay between pituitary pathology and ART outcome. It emphasizes the need for individualized fertility management in patients with pituitary disease, who could have atypical or unpredictable responses to stimulation and implantation. The successful diagnosis and management of this uncommon dual-gestation event emphasize the caution required in the evaluation and multidisciplinary management in ART cycles with underlying endocrine pathology.

Keywords: Pituitary microadenomas, Controlled ovarian stimulation, ICSI, Frozen embryo transfer

INTRODUCTION

Pituitary microadenomas are benign anterior pituitary adenomas (<10 mm) that can potentially affect endocrine and reproductive function. While typically asymptomatic, they can secrete hormones like prolactin or growth hormone or impinge on the pituitary stalk, causing GnRH pulsatility changes and resulting secondary impacts on the HPO axis.[1,2] Even non-functional microadenomas can subtly impair fertility by modifying folliculogenesis, oocyte maturation, or endometrial receptivity.

Prolactinomas are the most common functional microadenoma subtype and are defined by their correlation with menstrual disturbances and anovulatory cycles, which are largely due to suppression of GnRH and the consequent reduction in luteinizing hormone (LH) and follicle-stimulating hormone (FSH). However, even with serum prolactin levels kept within normal and regular menstrual cycles, fertility problems can still exist, hence the need for a workup for possible subclinical pituitary dysfunction.[3] Among patients with pituitary microadenomas, in the context of assisted reproductive technology (ART), there is a particular challenge. Although they can be managed by standard stimulation regimens, unanticipated endocrine consequences and rare complications can arise. One such complication, heterotopic pregnancy, simultaneous intrauterine and ectopic pregnancy, is very rare in spontaneous pregnancies (1 in 30,000) but more frequent in ART (up to 1 in 100 pregnancies), especially following multiple embryo transfer.[4] This case report presents a rare and instructive case of a 24-year-old woman with a pituitary microadenoma diagnosed who had regular ovulatory cycles and then underwent controlled ovarian stimulation, intracytoplasmic sperm injection (ICSI), and frozen embryo transfer (FET) to give rise to a heterotopic pregnancy. This case has emphasized individualized treatment plans and watchful observation in ART cycles with the presence of underlying pituitary pathology.

CASE REPORT

This study was conducted in the department of obstetrics A 24-year-old woman with known pituitary microadenoma attended the fertility clinic with primary infertility of 3 years' duration. She had normal menstrual cycles and no headache, visual disturbances, or galactorrhoea. Transvaginal ultrasonography and clinical examination were normal, but marginally raised serum prolactin (18.66 ng/ml; within normal range but on the higher side) was detected on serum hormonal evaluation. The patient was neurologically asymptomatic and was not a candidate for dopamine agonist therapy; therefore, ART intervention was started without pre-treatment of the adenoma.

The patient's anti-müllerian hormone (AMH) level was 4.85 ng/ml, with an antral follicle count (AFC) of 7, showing sufficient ovarian reserve. A GnRH antagonist-controlled ovarian stimulation protocol was used. Recombinant FSH and HMG were administered from day 2 to day 7 of the cycle, and doses were titrated according to the response of the follicles. A total of 9 oocytes were retrieved, 8 of which reached metaphase II (MII). ICSI was conducted in six oocytes, and two high-quality blastocysts were cryopreserved for future embryo transfer (Grades A and B).

Following an adequate endometrial preparation cycle on hormone replacement therapy (HRT), a FET of the two blastocysts was undertaken. The thickness of the endometrium was 0.85 cm in a trilaminar pattern, favourably, and a preceding mock transfer had confirmed uncomplicated passage. Serum β-hCG on day 14 following transfer was 1406 mIU/ml, in keeping with early pregnancy. Transvaginal sonogram at 5 weeks of gestation revealed an intrauterine gestational sac with cardiac activity (P1), and a second gestational sac in the left adnexa (P2), with high suspicion of heterotopic pregnancy. Left tubal ectopic pregnancy was confirmed by laparoscopy, which was managed surgically with left salpingectomy while conserving the intrauterine pregnancy. The patient remained neurologically stable, with no signs of pituitary apoplexy, visual field deficit, or deterioration of endocrinopathy, during the stimulation and early gestational period. The intrauterine pregnancy progressed uneventfully. Long-term follow-up of the pituitary adenoma after delivery was advised.

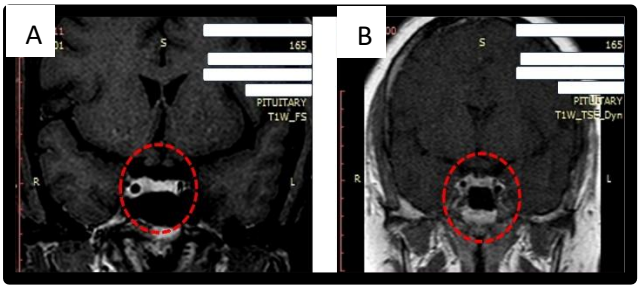

Figure 1 (A and B): MRI of pituitary microadenoma.

DISCUSSION

Pituitary microadenomas are common incidental discoveries in women of reproductive age presenting for fertility evaluation. The majority of microadenomas are asymptomatic and non-functional, but they can modestly disrupt the HPO axis by mechanical interference with hypothalamic dopamine transport or GnRH pulsatility, influencing reproductive outcomes with otherwise normal cycles and ovulatory parameters.[2,5]

In our instance, the patient had a pituitary microadenoma diagnosed on structural imaging (Figure 1), with regular menstrual cycles and mild hyperprolactinemia only, suggesting the presence of an insignificantly active or non-functioning lesion. While curative treatment with dopamine agonists is the treatment of choice for macroprolactinomas or symptomatic microadenomas, asymptomatic cases with mild hyperprolactinemia are typically managed conservatively.[1] Our patient was managed conservatively in this way, with controlled ovarian stimulation without pharmacologic suppression of pituitary function. Despite having a microadenoma, the patient's good ovarian response is clinically concerning. Nine oocytes were obtained, with a satisfactory MII rate of 88.9%, together with acceptable rates of fertilization and blastocyst formation, indicating that the HPO axis function was largely preserved. This emphasizes that not every microadenoma influences ovarian response to stimulation, confirming earlier findings that fertility treatment can be safely and effectively provided in such patients with appropriate monitoring.[3]

The heterotopic pregnancy phenomenon, though rare, underscores the importance of embryo transfer procedures and ongoing follow-up after transfer in ART. Transfer of two blastocysts not only enhances cumulative pregnancy rates but also enhances the risk of multiple implantation events, including ectopic gestation. Heterotopic pregnancies are seen in 1–3% of ART pregnancies and may pose diagnostic challenges because of overlap of symptoms and false impressions of an intrauterine pregnancy.[4] Early detection by early ultrasonography and surgery, as performed in this case, was critical in preserving the viable intrauterine pregnancy.

From an endocrinological perspective, the current case emphasizes the necessity of follow-up of pituitary adenomas during pregnancy. Conceptually feasible, pregnancy-associated pituitary hyperplasia can be dangerous for tumor growth or apoplexy, especially in macroadenomas, but microadenomas are usually well-controlled in pregnancy.[2] There were no signs of pituitary enlargement or apoplexy in the current case, reiterating that pregnancy can be safely maintained with monitoring. This case is particularly reminiscent of the fact that women with incidental pituitary microadenomas and normal reproductive endocrinology can successfully undergo ART, though at increased risk for heterotopic pregnancy complications. The simultaneous pathology in this patient

subclinical pituitary insufficiency and ectopic implantation, requires individualized protocols of treatment, complete hormonal assessment, guarded embryo transfer protocols, and multidisciplinary management.

CONCLUSION

This case demonstrates that asymptomatic women with pituitary microadenomas can undergo controlled ovarian stimulation and ART with successful outcomes, utilizing proper monitoring. The integrity of the hypothalamic-pituitary-ovarian axis, despite the adenoma, ensured effective oocyte retrieval, fertilization, and embryo development. However, the fact that heterotopic pregnancy occurred in this case underscores the need for strict embryo transfer protocols and rigorous early pregnancy monitoring. Clinicians need to adopt a multi-disciplinary approach that balances fertility requirements against endocrinological monitoring to achieve optimal outcomes for patients with intracranial lesions who are opting for ART.

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