An IVF pregnancy in a woman with mullerian anomaly and poor ovarian reserve: A success story

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ABSTRACT

Pregnancy in a congenitally anomalous uterus is difficult and can be often missed on routine investigation such as transabdominal ultrasonography. Here we discuss a fascinating case of an accidentally diagnosed with unicornuate uterus having a communicating rudimentary horn with a live pregnancy in a 34-year-old sub fertile primigravida with IVF conception who was a known case of hypothyroidism. This rare diagnosis of Mullerian anomaly was made intraoperatively while the patient was undergoing caesarean section. Though there is massive advancement in the fields of imaging modalities and diagnostic ultrasonography, antenatal diagnosis has still remained elusive.

Keywords: Mullerian anomaly, subfertility, poor ovarian reserve, unicornuate uterus, IVF conception

1. INTRODUCTION

Congenital uterine anomalies demonstrate a large variety of abnormalities of uterine anatomy which results from absorption, fusion and elongation defects of the bilateral Mullerian ducts. It occurs during the period embryogenesis generally between 6-20 weeks of gestational age (Engmann et al., 2004). According to ESHRE–ESGE (The European Society of Human Reproduction and Embryology–European Society for Gynecological Endoscopy). There are 2 recognized varieties of unicornuate uterus: 1) Hemi-uterus having a functional rudimentary contralateral cavity, which could be either communicating or non-communicating type, as a resultant of a partial Mullerian duct development (class IVA). 2) Hemi-uterus of isolated type resultant of a unilateral-agenesis of Mullerian duct (class IVB) (Grimbizis et al., 2016). Development of ovary is generally not affected, though ovary on the compromised side could have been displaced at a higher level in the abdominal cavity or even could have been absent in some rare instances which could ultimately lead to infertility (Reichman et al., 2009). Infertility is a challenge in itself both for the patient and the doctor. Patients presenting with an inadequate response to ovarian induction pose a laborious challenge in the
world of IVF. Only with those few eggs that can be collected, the success rates of this procedure are comparatively lower and several other management techniques are often required to finally achieve the target of pregnancy. In the past few years, ovulation stimulation has significantly contributed to the outrageous success of (ART) assisted reproduction techniques, as well as embryo transfer (ET) and in vitro fertilization (IVF). The ultimate aim of all these fertility techniques is to deliver a single, normal and healthy child (Zafeiriou et al., 2000). Although there is enormous advancements in the field of diagnostic ultrasonography and other imaging techniques, the antenatal diagnosis is still found to remain elusive and that laparotomy surgery is considered a definitive diagnosis (Kaveh et al., 2018).

2. CASE DESCRIPTION

We report a case of Mullerian Duct Anomaly which was diagnosed intraoperatively while performing a planned caesarean section on a pregnant woman presenting with history of subfertility and hypothyroidism. A 34 year old Nulligravida came to the IVF lab at rural set up in Maharashtra with a history of 12 years of infertility. Patient was willing for Intrauterine Uterine Insemination IUI for which she has been evaluated. A detailed history revealed regular cycles with scanty flow. All laboratory tests and hormone profile were done. Her anti-Mullerian Hormone AMH levels were 0.8ng/ml. Figure 1 shows a Trans Vaginal Ultrasonography which was suggestive of poor ovarian reserve. She was then posted for chromo-pertubation which reported normal fallopian tubes with bilateral spillage. All the male factors have been investigated and were found to be normal. She then had to undergo IUI 4 times consecutively, which were unsuccessful. Considering her borderline AMH levels of 0.8ng/ml and increasing age in view of idiopathic infertility she was then advised IVF-ICSI. It was successfully carried out with antagonist cycle and agonist trigger. In first stimulation two M2 oocytes were retained and in the second stimulation two more M2 oocytes were retained. From these oocytes a two-day four morula were freezed out and frozen Embryo transfer was done. Beta HCG revealed values was 1500 on day 14th indicating pregnancy which was then confirmed on ultrasonography. After the IVF conception she experienced continuous stretching pain in the perineum from 13th week onwards so prophylactic cervical encerclage was done. After this her antenatal journey was smooth and at around 38 weeks an elective caesarean section was planned. She delivered a healthy male child of 2.4 kgs with APGAR score of 8/10 and 9/10 at 1 minute and 5 minutes after birth respectively.

When the baby was delivered, intraoperatively the uterus was found to be horizontally elongated. Figure 2 demonstrates anunicornuateuterus with communicating type of rudimentary horn. The placenta was retained for approximately 5 Mins so manual removal was tried and then it was realized that the placenta was deeply situated in the tubular canal of the uterus, so we had to insert our hand approximately 12-15cm in a tubular manner and found it to be adhered to the left cornu of the uterus. It was then removed meticulously without causing any damage to the uterus and surrounding viscera. After the placenta was removed the uterine cavity was thoroughly examined and at that time it was appreciated that the patient had been suffering from A1 type (according to AFS classification) of Mullerian anomaly. Post operatively there were no further complications. Both mother and child were healthy and have been advised regular follow up.

Figure 1 Trans Vaginal Ultrasonography showing poor ovarian reserve
Figure 2 Unicormuate Uterus with communicating type of Rudimentary Horn

3. DISCUSSION

Infertility in itself a challenge both for the patient as well as the doctor. It is mandatory to have knowledge on whether or not the patient has regular menstrual cycle to assess her ovulation status. There are various investigations available for diagnosis of ovulation like Biphasic Basal body temperature pattern, Serum progesterone level is to be estimated on day 21 of menstrual cycle, values less than 3ng/ml signify anovulatory cycle, monitoring of urinary LH, serial TVS, ruptured follicle presents with free fluid in pouch of Douglas. Adequate ovulation stimulation protocols that are followed in IVF-ET, which when combined with appropriate pituitary desensitization protocols, result in required preovulatory estrogen levels, which play apivotal in permitting the clinician to retrieve the best possible oocytes regarding both in quality and number. This will indeed result in high rates of maturity, fertilization, cleavage, transferability and successful pregnancy rates.

The use of gonadotropin for ovarian induction plays a vital role in the management of infertility (Lunenfeld, 2004). Various kinds of ovarian stimulation regimes are now available but an ideal ovarian stimulation regime of IVF should be that of a lower cancellation rate, with minimal drug expenses, low side effects and risks should require minimal monitoring for practical convenience and should result in maximum cumulative live birth rate pre oocyte retrieval procedure. There are three components for a typical ovarian stimulation regime for IVF-(a) First is exogenous gonadotropins to stimulate multifollicular growth, (b)Second GNRH analogues to prevent spontaneous ovulation before the retrieval of oocyte and (c) Third is LH activity in form of HCG to induce oocyte maturation(Hozyen and Saadeldin, 2022). There are various protocols for ovulation stimulation like: Down regulation by GNRH Agonist: This is considered a long protocol, where GNRH agonists are found to flare-up gonadotropin
stimulation protocol, GNRH antagonist-gonadotropin stimulation protocol, Double stimulation, and Controlled ovarian stimulation.

A study was carried out to assess double cycle of ovarian induction followed by double egg collection during the same cycle of menstruation that are yet to provide a true advance for estimated poor responders seeking IVF treatment. A study of randomized trial carried out in the country of Spain has brought to light that this double stimulation protocol popularly known as "Duo stim" is more efficient than conventional inductions in two different cycles and profoundly decreases the time period to conceive among a group of patients who rarely have any time on their side. Since the initial days of IVF management, whether in a stimulated or natural cycle, management has largely involved only one attempt in one cycle. Induction has been carried out using fertility hormones such as gonadotropins which aim to produce multiple eggs that aid both collection and fertilization.

Unlike traditional IVF protocols where patients undergo a single round of ovarian stimulation with fertility drugs and egg retrieval in one menstrual cycle, in the Duo stim protocol patients undergo two rounds of ovarian induction and double egg retrievals in the same menstrual cycle. Dual stimulation strategy has been so far applicable mainly to those group of patients whose AMH (ovarian reserve tests) demonstrated a poor response to ovarian stimulation. Patients with Mullerian anomalies, especially those with unicornuate uterus are found to suffer from several gynecological symptoms such as cyclical chronic pelvic pain and dysmenorrhea and require elaborate care (Liu et al., 2017).

4. CONCLUSION
Patients with unicornuate uterus have profound risk of gynecological problems which either present early at menarche or may present later on in life. Those who are presenting with such symptoms should always be screened thoroughly. Nevertheless, ultrasonographic diagnosis could be missed, particularly in inexperienced hands. It can however be prevented by utmost vigilance and knowledge especially in diagnosing cases of Mullerian duct anomalies.

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Author Contribution
Dr. Manisha Andelaand has collected information and prepared the manuscript which has been thoroughly reviewed by Dr. Deepti Shrivastava and Dr. Kamlesh Chaudhary. Dr. Arti Mishra has helped in further modification of the manuscript.

Informed Consent
Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

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Conflict of interest
The authors declare that there is no conflict of interests.

Data and materials availability
All data sets collected during this study are available upon reasonable request from the corresponding author.

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