India's First Successful Surrogate Birth after Percutaneous Oocyte Retrieval following Modified Radical Hysterectomy and Right Ovarian Transposition to the Anterior Abdominal Wall

Priya Selvaraj, Kamala Selvaraj, Chitrathara Gangadharan¹, Vijaya Annigeri, Kalaichelvi Srinivasan, Mahalakshmi Sivakumar

above the pelvic brim.

G G Hospital, Fertility and Women's Speciality Centre, Chennai, Tamil Nadu, 'Department of Surgical and Gynaec Oncology, Lakeshore Hospital, Nettoor, Kochi, Kerala, India A 31-year-old woman, who is a known case of polycystic ovary syndrome, underwent modified radical hysterectomy and right ovarian transposition to the anterior abdominal wall for endometrioid adenocarcinoma Grade II. She then visited our facility for *in vitro* fertilization (IVF) and surrogacy in the year 2016. Three cycles of IVF were performed using gonadotropin-releasing hormone (GnRH) antagonist in the first two attempts and GnRH agonist in the third attempt, with percutaneous technique of oocyte retrieval from the transpositioned right ovary. In the third attempt in July 2017, we were able to retrieve five oocytes and subsequently froze three embryos and one blastocyst. The surrogate underwent sequential transfer in June 2018 which resulted in a positive clinical singleton pregnancy. The outcome of IVF following percutaneous oocyte retrieval led to a successful pregnancy and subsequent delivery by emergency

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cesarean by a healthy female baby on February 16, 2019. This is the first reported case of ovarian hyperstimulation and percutaneous aspiration of oocytes from a transpositioned right ovary (subcutaneous plane) in our country. Global literature survey revealed publications only of transabdominal retrieval of ovaries moved

Introduction

Ovarian transposition seems to be the most logical step in young women of reproductive age group who may need to undergo radiation following a diagnosis of cancer cervix or endometrium. In this context, ovarian transposition to a location on the lateral pelvic peritoneal wall, just above the pelvic brim after securing the vascular pedicle, seems to be the most feasible, although there may not be a complete protection from scatter radiation. However, this technique is commonly practiced.

We present an interesting case report of a successful pregnancy arising from oocyte retrieval, performed percutaneously from an ovary placed in the subcutaneous plane of the anterior abdominal wall, above the rectus sheath.



CASE REPORT

Mrs. N, a then 28-year-old woman, and a known case of polycystic ovary syndrome (PCOS), first came to our hospital for consultation with respect to fertility treatment and surrogacy on August 28, 2016. She had been previously diagnosed with endometrioid adenocarcinoma Grade I–II and had consulted with an oncosurgeon at a multispecialty hospital in another state. She subsequently underwent modified radical hysterectomy with left

Address for correspondence: Dr. Priya Selvaraj, G G Hospital, Fertility and Women's Speciality Centre, Chennai, Tamil Nadu, India. E-mail: drpriya@gghospital.in

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salpingo-oophorectomy and complete pelvic clearance in addition to a right ovary transposition to the anterior abdominal wall (subcutaneous plane) on July 21, 2014.

Her subsequent histopathological report revealed a less-than-half involvement of the myometrium with absence of any local or distal spread, ascites or positive pelvic or para-aortic lymphadenopathy. She was estrogen receptor and progesterone receptor positive and human epidermal receptor-2 Neu negative. Hence, the oncology team decided to defer radiation and opted to follow her up every few months. A computed tomography scan done a year later (July 13, 2015) revealed a normal study with a functioning right ovary with preserved vascularization and presence of multiple hypodense follicles on its surface. No other abnormal findings were noted.

At our hospital, we performed a comprehensive master health checkup, inclusive of a sonomammogram, vault smear, and ultrasound, which were found to be normal. The ultrasound revealed an ovarian size of 3.6 cm × 3.4 cm located on the right side of the abdomen, within the subcutaneous plane. The antral follicle count was eight. Her hormone values were consistent with PCOS, namely follicle-stimulating hormone (FSH) 9.52 mIU/ml, luteinizing hormone 12.43 mIU/ml, serum prolactin 8.55 mIU/ml, and anti-Mullerian hormone 4.6 ng/ml. The treatment plan was drawn, whereby she would consume a month of oral contraceptive pills and then undergo hormone evaluation on an assumed day

2/3rd of the cycle. This would be followed by stimulation for a short protocol using a combination of recombinant FSH and human menopausal gonadotropin along with an antagonist.

After adequate counseling and informed consent from the couple, three cycles were attempted (the last one with agonist), with a gap of few months between each hyperstimulation, the summary of which is provided in Table 1. In the first attempt, a pregnancy was achieved in a surrogate after the retrieval of one oocyte, which was fertilized and transferred on day 3, but, unfortunately, ended in a missed miscarriage. The second attempt yielded six oocytes, of which only three were mature oocytes and were injected; only one fertilized and cleaved, and a day-3 transfer in a surrogate yielded a negative result.

We initiated her 3rd cycle using a short protocol with gonadotropin-releasing hormone agonist (injection Gonapeptyl, Ferring Pharmaceuticals Pvt Ltd., Thane, India) and recombinant FSH (Recagon, Organon [India] Private Limited, Thane, India) along with gonadotropins (*in vitro* fertilization-M, LG Life Sciences India Pvt Ltd., Haryana, India). When the maximum follicular size reached 1.8 cm × 1.8 cm, a human chorionic gonadotropin (hCG) trigger was given (injection Ovitrelle 250 µg, Merck Specialities Private Limited, Mumbai, India). Owing to the heterotopic site of location, oocyte retrieval was meticulously planned. We decided to use the

Table 1: COH Protocols							
Cycle	Short	USG	Hormone levels	Oocytes	IVF Technique	Embryo transfer	Result
	protocol	(day 2/3)	(day 2/3)	retrieved	(ICSI)	to surrogate	
1 st	REC. FSH	6-8 SF	FSH-10.7 mIU/ml	1 OOCYTE	1+HS	1 (6-8) CELLS	POSITIVE
	(225 IU)	NO	LH - 8 mIU/ml	M - II	1 FERTILIZED	CLEAVING	Serum βhcg (mIU/ml)
	+	CYST	SP - 11.6 mIU/ml			G (II)	1 st →69.7
	HMG + XGRAST		E2-43.6 pg/ml				$2^{\text{nd}} \rightarrow 170.6$
			P - 0.13 IU/mL				3 rd →360.1
							Missed Miscarriage
							POC for Aneuploidy screening (NGS)
							NORMAL KT
2^{nd}	REC. FSH	8 SF	FSH- 10.18 mIU/ml	6 OOCYTES	6+HS	1 (4-5 CELLS)	NEGATIVE
		NO CYST	LH - 6.10 mIU/ml	3(M- I)	1 FERTILIZED	CLEAVING	
			SP - 9.82 mIU/ml	3(M- II)		G (I - II)	
			E2-28.87 pg/ml				
			P - 0.30 IU/mL				
$3^{\rm rd}$	REC. FSH (300 IU)	6- SF	FSH- 8.54 mIU/ml	5 OOCYTES	5+HS	2 (8cells) I-II,	POSITIVE
		NO	LH - 4.32 mIU/ml	2(M- I)	5 FERTILIZED	1 (6-8cells) I-II	1 st - 205.1 mIU/ml
	+	CYST	SP - 9.65 mIU/ml	3(M- II)		2 (4cells)	2 nd - 564.4 mIU/ml
	IVF-M		E2-17.01 pg/ml			cleaving (for BT)	
			P - 0.41 IU/mL				

conventional transvaginal ovum pickup needle. 16G (35 cm) double-lumen catheter (Cook Ireland Ltd., Limerick, Ireland). The oocyte retrieval was performed with ultrasonography (USG) guidance [Figure 1]. Under strict aseptic precautions and guidance of an abdominal ultrasound probe (GE Healthcare Voluson Logiq P6, India), the aspiration needle was introduced percutaneously into the subcutaneous plane to reach the outermost follicles mapped by USG. The right hand held the transducer, while the left hand maneuvered the ovum pick up needle [Figures 2-4]. Five oocytes were retrieved from the right ovary; all of them were injected with the husband's sperm which then fertilized. Two (8 cells, grade I-II) and one (6-8 cells, grade I-II) embryos were frozen on day-3 of development in separate high security vitrification (HSV) cryo-straws. Two (4 cells, grade I-II) cleaving, generated from the M-I oocytes, were left for blastocyst. One cavitating blastocyst was then frozen on day 5 [Figures 5-7].

A suitable surrogate was identified and prepared for frozen embryo transfer with hormone replacement therapy. She was initiated with estradiol valerate 2 mg in incremental doses up to 8 mg/day from day 3 of the cycle. Micronized

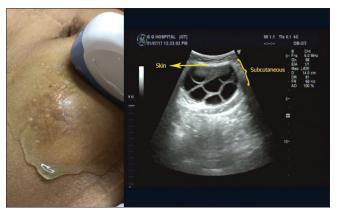


Figure 1: Transabdominal follicular study

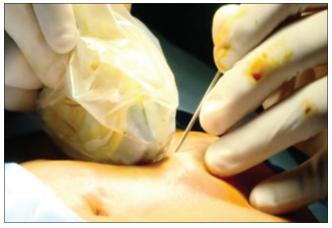


Figure 3: Percutaneous oocyte retrieval

progesterone was started from day 16 (1200 mg/day in three divided doses). A sequential transfer was performed on the surrogate with two embryos (one [six cells] and one [6-8 cells], G II) which were warmed and transferred on day 19 of her cycle, and one cavitating blastocyst was warmed and transferred on day 21 of the cycle. On the 28th day, her serum beta hCG value was 205.1 mIU/ ml and the same doubled on the 30th day as 564.4 mIU/ ml. Her transvaginal scan was done on the 38th day which showed a single intrauterine gestational sac. Fetal heart pulsations were observed on the 45th day. Her first-trimester screening (double marker with nuchal translucency) performed at 13 weeks of pregnancy, was normal. The antenatal period progressed uneventfully, and she delivered a healthy baby girl weighing 2.62 kg, on February 16, 2019. A general follow-up after a month showed normal development for age.

DISCUSSION

Giacalone *et al.*^[1] reported the first-ever case of pregnancy in a surrogate mother after stimulation of a transposed ovary following chemotherapy and pelvic irradiation. Following this, a series of pregnancies have



Figure 2: Percutaneous oocyte retrieval



Figure 4: Ovum pickup needle entering the follicle

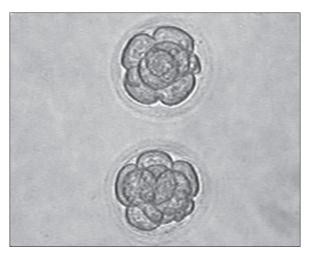


Figure 5: 2 embryos (8 cells, grade I-II)



Figure 7: 1 cavitating BT

been achieved by Azem *et al.*^[2] in 2003, Zinger *et al.* in 2004, and Steigrad *et al.*^[4] in 2005, making gestational surrogacy an important consideration in cancer patients who have undergone hysterectomy, as well as the technique of transabdominal oocyte retrieval.

Studies have shown that at a distance of about 3 cm from the pelvic inlet, the radiation received will be only 1%–10% of the total dose. Therefore, transposed ovaries possibly receive only 0.45–4.5 Gy of a total of 45 Gy, whereas retained ovaries could receive 20–32 Gy.^[5]

In our case, right ovarian transposition was done, placing the ovary in the right subcutaneous plane. Chitrathara *et al.*^[6] described a simple technique of positioning the ovary in the anterior abdominal wall [Figure 8]. In this technique, the ovary can be monitored easily and can be removed as an outpatient procedure whenever required. Similar to preparing for ovarian transposition outside the pelvis, the ovary with the pedicle is freed up to or beyond the pelvic brim. Pedicle length should be enough so as to bring



Figure 6: 1 embryo (6-8 cells, grade I-II)

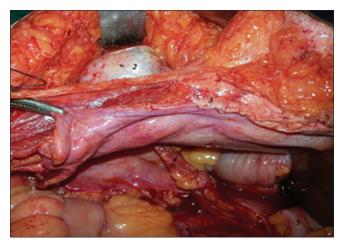


Figure 8: Ovary positioned in the anterior abdominal wall

it out without tension. The pedicle is brought out lateral to the cecum on the right side and lateral to the sigmoid-descending colon on the left side. Care is taken to ensure that the pedicle is not twisted. To facilitate easy bringing out and positioning of the ovary in the anterior abdominal wall, the fallopian tube is not removed earlier.

As suggested in the study by Giacalone *et al.*,^[1] this choice of location may entail complaints of pain following ovarian enlargement, which the patient did suffer from. Transposing ovaries to paracolic gutter seemed to be more common and had fewer complaints. However, in defense, our retrieval seemed far easier to perform as it was a percutaneous approach. However, as predictable with any transposition surgery, the ovarian response and quality of oocytes remain unpredictable.^[7] We did not encounter any cyst formation or infection but only ovarian enlargement.

Our case had undergone open surgery and had the ovarian and infundibular pelvic vascular pedicle

dissected and mobilized to elevate the right ovary with preserved blood supply to the subcutaneous plane. This too did not create any postprocedural issues. It remains, however, to be seen which method would work better — ovarian transposition to the lateral pelvic wall above the brim or to the subcutaneous plane.

Conclusion

This is the first-ever reported case of ovarian hyperstimulation and percutaneous aspiration of oocytes from a transpositioned right ovary in India. Global literature survey has shown published case reports of transabdominal aspiration for retrieval but none using percutaneous technique resulting in a successful pregnancy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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