

Case Report

# A Successful Live Birth with *In Vitro* Fertilization from a Woman with a Huge Uterus Due to Recurrent Multiple Uterine Fibroids after Abdominal Myomectomies

Chun Yang<sup>#</sup>, Chunyan Chen<sup>#</sup>, Jing Cai, Yanhui Li and Ying Gao<sup>\*</sup>

Department of Obstetrics and Gynecology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, 430022, China

<sup>#</sup>Authors contributed equally to this work

## Abstract

We report a successful live birth with *in vitro* fertilization (IVF) from a woman with an extremely huge uterus. A 30-year-old woman with an uterus of approximately 13×10×12 cm<sup>3</sup> due to recurrent multiple fibroids after two myomectomies presented to our hospital with a desire to become pregnant. She has undergone one cycle of fresh embryo transfer and two cycles of frozen-thawed embryo transfer following Gonadotropin-releasing hormone (GnRH) agonists treatment. The IVF procedures for the woman resulted in a pregnancy that led to a live birth of a healthy male baby weighing 3400 g delivered at 39 weeks. Thus, we concluded that for women with huge uterus and multiple fibroids, or otherwise unexplained infertility, assisted reproduction might lead to pregnancy and live birth, even if previous myomectomy and GnRH agonists treatment didn't exhibit beneficial effects on fibroids.

**Keywords:** Multiple uterine fibroids; *In vitro* fertilization; Myomectomy; Huge uterus; Live birth

## Introduction

Uterine fibroids, or leiomyomas, are the most common benign tumor of the uterus, occurring in up to 77% of women. Estimated to be present in 27% of infertile women, they may be a sole factor responsible for only 2-3% of infertility cases [1-3]. Uterine fibroids may interfere with sperm migration and ovum transport by (1) anatomic distortion of the cervix or the tubes, (2) enlarging or deforming the uterine cavity, (3) interfering with ovum capture, and (4) impairing the uterine contractility [4]. In addition, the presence of fibroids can cause implantation failure by (1) physically changing the shape of endometrium, (2) preventing discharge of intrauterine blood, (3) reducing blood supply to endometrium, and (4) altering the normal endometrial environment by local inflammation and bleeding [5-7].

The recurrence rates of uterine fibroids in patients undergoing primary myomectomy are between 15-45% within a 5-10 year period [8,9]. Particularly, patients with multiple uterine fibroids and those in the third decade of life showed an increased risk of symptomatic recurrence after surgery [10]. After myomectomy the pregnancy rate was about 20-50% in patients with otherwise unknown cause of infertility. However, more than 50% of patients remain infertile 5 years after primary myomectomy [8,11-13]. The postmyomectomy pregnancy rate was negatively associated with the number and size of the removed myoma [11].

Small-to-moderate uterine fibroids, regardless of their location, are likely not to impact outcomes of IVF [14]. However, submucosal and intramural fibroids causing distortion of the endometrial cavity have been associated with decreased pregnancy rate as well as increased risk of miscarriage following IVF [15,16].

Here, we describe a successful pregnancy and live birth following IVF treatment in a woman with huge uterus harboring recurrent multiple fibroids who had twice undergone abdominal multiple myomectomy.

## Case Report

A 30-year-old woman with a 6-year history of primary infertility was referred to our department in May 2012. In 2008, the patient

underwent the first abdominal hysteromyomectomy, in which more than ten fibroids were removed. However, multiple uterine fibroids were diagnosed again by ultrasound after 3 years. Despite a treatment with GnRH agonists (GnRHa) 3.75 mg for 6 months, the uterine fibroids continued to grow. In March 2012, the patient received her second hysteromyomectomy, in which again more than ten fibroids were removed. Two months after the second myomectomy, she presented to our unit with a desire to become pregnant. Her body weight was 62kg and height was 167 cm. The menstrual cycle was 28 days. The sizes of ovaries were 41×18 mm<sup>2</sup> (right) and 24×17 mm<sup>2</sup> (left). Hysterosalpingography indicated that the fallopian tubes appeared dilated, tortuous and folded. The routine semen analysis of the patient's husband was normal.

Based on her history and results of relevant examinations, the patient was considered to be a candidate for ovulation induction. Before beginning with the ovulation induction, to shrink the myomata, the patient received ultralong postoperative therapy with subcutaneous injection of GnRHa 3.75 mg for 5 months (Table 1). Twenty-eight days after the last administration of GnRHa, she had serum E2 of 10.00 pg/ml and luteinizing hormone (LH) of 0.24 IU/L. In addition, transvaginal ultrasound revealed an enlarged uterus (89×88×82 mm<sup>3</sup>) with ten intramural uterine fibroids of 12~37 mm in maximum diameters. Four days later, the patient started to be treated with recombinant FSH (100 IU daily, subcutaneous) and hMG (150 IU daily, intramuscular). On stimulation day 11, she had serum E2 of 9371.31 pg/ml, LH of 1.11 IU/L, and endometrium thickness of 12 mm. Dominated follicles reached 18 mm in diameter. Intramuscular injection of HCG 10,000

**\*Corresponding author:** Ying Gao, Department of Obstetrics and Gynecology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, 430022, China, Tel: +86 27 85351593; Fax: +86 27 85351593; E-mail: 1211746863@qq.com

**Received** April 04, 2016; **Accepted** April 19, 2016; **Published** April 26, 2016

**Citation:** Yang C, Chen C, Cai J, Li Y, Gao Y (2016) A Successful Live Birth with *In Vitro* Fertilization from a Woman with a Huge Uterus Due to Recurrent Multiple Uterine Fibroids after Abdominal Myomectomies. JFIV Reprod Med Genet 4: 180. doi:10.4172/2375-4508.1000180

**Copyright:** © 2016 Yang C, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Date	Treatment	E <sub>2</sub> (pg/ml)	LH (IU/L)	Progesterone (ng/ml)	Size of uterus (mm <sup>3</sup> )
06/22/2012	GnRHa for 5 months				829350
12/07/2012		10	0.24		642224
12/11/2012	rFSH+hMG	705.76	0.29		680400
12/21/2012	HCG	9371.31	0.59		794880
12/28/2012	ET				856520
2/24/2013	GnRHa for 3 months				966508
6/16/2013	Oral estradiol valerate				720900
7/1/2013	Progesterone	1849	0.45	0.24	1019700
7/7/2013	ET				
11/3/2013	GnRHa for 3 months				1524000
2/23/2014	Oral estradiol valerate				1284660
3/8/2014	Progesterone	246	12.79	0.09	1553060
3/13/2014	ET				

Table 1: Summary of parameters.

IU was administrated followed by oocyte retrieval 36 hours thereafter. A total of 20 oocytes were retrieved, and eighteen of them were found to be metaphase II. Fifteen embryos were available on day 3. Due to enlarged ovaries, all of the embryos were cultured to day 5. and six blastocysts of 4BB and one of 4CB were available according to Gardner grading; the sizes of the ovaries were 84×63 mm<sup>2</sup> (right) and 63×58 mm<sup>2</sup> (left); the endometrium thickness was 14 mm; the uterine size was 98×95×92 mm<sup>3</sup>. Transfer with two blastocysts of 4BB was performed without difficulty. The other five blastocysts were vitrified. The patient's serum β-HCG was 22.27 IU/L twelve days after the embryo transfer (ET). But unfortunately, it became negative six days later.

In February 2013, the patient demanded to receive frozen-thawed-ET. Nevertheless, transvaginal ultrasound showed a further enlarged uterus (106×97×94 mm<sup>3</sup>) with more than twenty intramural uterine fibroids with maximum diameters of 16-39 mm. To decrease the uterus size, the patient received GnRHa treatment for 3 months. Twenty eight days after the last administration of GnRHa, when the uterus size was 89×90×90 mm<sup>3</sup>, the patient began to receive oral estradiol valerate (4 mg daily). Eighteen days later, the endometrium thickness was 9 mm and the uterus size was 103×100×99 mm<sup>3</sup>. Progesterone 40 mg/d, 60 mg/d, 80 mg/d, 80 mg/d, 80 mg/d, and 80 mg/d were intramuscular injected in the next 6 days, respectively. Then two frozen-thawed blastocysts of 4BB were transferred. Twelve days after the ET, serum β-HCG was 110.86 IU/L and rose to 397.25 IU/L four days later. Intrauterine single fetal heart beat was confirmed by ultrasound observation 30 days after the ET. Unfortunately, the patient underwent a miscarriage of 8 gestational week.

In November 2013, the patient demanded to receive the second cycle of frozen-thawed-ET. However, the uterus was even larger (127×96×125 mm<sup>3</sup>). Then the patient was given GnRHa treatment for three months again. Transvaginal ultrasound revealed more than twenty intramural uterine fibroids with maximum diameters of 22-41 mm and uterus size of 117×90×122 mm<sup>3</sup>. Thereafter, the patient received oral estradiol valerate 4 mg per day for 16 days. Sixteen days later, the patient's uterus size was 134 ×95×122 mm<sup>3</sup> and endometrium thickness was 10 mm. Her serum progesterone was 0.09 ng/ml, and E<sub>2</sub> was 246.00 pg/ml. Then progesterone was administered in doses of 40 mg/d, 60 mg/d, 80 mg/d, 80 mg/d, 80 mg/d, 80 mg/d in the following six days followed by ET with two 4BB blastocysts. The β-HCG was

121.45 IU/L 12 days after the ET and rose to 553.37 IU/L four days later. Fetal heart beat was confirmed by ultrasound observation 40 days after the ET. The uterus size was 167×148×180 mm<sup>3</sup>. The patient successfully delivered a healthy male infant weighing 3400 g at 39 weeks of gestation via cesarean section. APGAR score was evaluated at 8. No neonatal problems have been reported. Hysterectomy was performed due to postpartum hemorrhage.

## Discussion

This is a case report of successful pregnancy and live birth with extremely huge uterus and recurrent multiple intramural fibroids, following two abdominal myomectomies and IVF treatment, although the recurrent multiple fibroids continued to grow up during IVF despite the GnRHa treatment prior to each IVF cycle.

Indeed, submucosal fibroids can adversely affect implantation and pregnancy rates in assisted reproduction cycles [17,18]. Intramural fibroid of 5 cm or less in diameter halves the chances of an ongoing pregnancy after assisted reproduction [15]. In addition, intramural or submucosal fibroids increase the rate of spontaneous abortion in IVF cycles [19]. Sunkara et al. [20] performed a meta-analysis to clarify the effect of fibroids on pregnancy outcomes after IVF, in which 19 studies involving 6087 cycles were analyzed. They found the presence of intramural fibroids without uterine cavity involvement was associated with a significant reduction in live birth rate and clinical pregnancy rate. Another meta-analysis investigating the influence of fibroids location on IVF outcomes reported that submucosal fibroid strongly interfered with the pregnancy rate after IVF, while intramural ones exhibited only modest negative effects [21]. A recent study suggested that non-cavity-distorting fibroids did not affect IVF/ICSI outcomes, whereas intramural fibroids greater than 2.85 cm in size significantly impaired the delivery rate of patients undergoing IVF [22]. In our patient, an enlarged uterine cavity and multiple uterine intramural fibroids should be responsible for her chemical pregnancy and miscarriage, which may be explained by altered uterine vascular perfusion, myometrial contractility, endometrial receptivity, embryo migration or myometrial/endometrial gene expression.

Thus, it appears to be generally accepted that submucosal, and possibly intramural and subserosal fibroids decrease implantation rates and that their removal might solve the problem [17,23]. Approximately

50% of the women with infertility and myoma become pregnant after myomectomy. However, it is still not easy to solve the current dilemma of management of intramural myoma: myomectomy or IVF? Many previous studies have suggested that myomectomy can improve pregnancy rate and reduce abortion rate [16,24]. Moreover, the impact of previous myomectomy on IVF outcome was also investigated. Narayan et al. and Surrey et al. both described IVF outcomes of patients after myomectomy for submucosal fibroids were not different compared with patients without fibroids [25,26]. However, considering the effects of myomectomy for recurred fibroids on fertility in particular, there is few literature available. A prospective cohort study of reproductive outcome after a second myomectomy for recurring myomas suggested 9 of 58 (15.5%) women became pregnant after the second surgery and only 5 (56%) had live births [27]. It is not recommended to perform myomectomy with more than seven large fibroids because the surgeon can miss the smaller fibroids after the uterus has been incised and repaired in too many places. In light of the poor fertility results of our patient, who had underwent twice abdominal myomectomies, another myomectomy is not advisable to perform. On the other hand, assisted reproduction should be a valid alternative form of treatment.

A recent study suggested that women with very long (>9.0 cm) uterine lengths are less likely to experience live birth [28]. Extremes of uterine length may signify anatomical variations that contribute a decreased likelihood of implantation. GnRH agonists cause myoma shrinkage by inducing hypoestrogenemia. In our patient, GnRHa was used before ET to facilitate implantation by reducing the fibroids and uterine sizes. However, the GnRHa treatment increases the likelihood of a recurrence of fibroid [29]. Fortunately, our patient had conceived successfully with a huge uterus which size was 134 mm × 95 mm × 122 mm.

In conclusion, our case suggests that for women with huge uterus and multiple fibroids, or otherwise unexplained infertility, assisted reproduction might lead to pregnancy and live birth, even if previous myomectomy and GnRH agonists treatment didn't exhibit beneficial effects on fibroids.

## References

1. Lethaby A, Vollenhoven B (2011) Fibroids (uterine myomatosis, leiomyomas). *BMJ Clin Evid* 2011.
2. Practice Committee of the American Society for Reproductive Medicine (2006) Myomas and reproductive function. *Fertil Steril* 86: S194-199.
3. Bajekal N, Li TC (2000) Fibroids, infertility and pregnancy wastage. *Hum Reprod Update* 6: 614-620.
4. Practice Committee of American Society for Reproductive Medicine in collaboration with Society of Reproductive Surgeons (2008) Myomas and reproductive function. *Fertil Steril* 90: S125-130.
5. Practice Committee of the American Society for Reproductive Medicine (2004) Myomas and reproductive function. *Fertil Steril* 82 Suppl 1: S111-116.
6. Donnez J, Jadoul P (2002) What are the implications of myomas on fertility? A need for a debate? *Hum Reprod* 17: 1424-1430.
7. Sylvestre C, Child TJ, Tulandi T, Tan SL (2003) A prospective study to evaluate the efficacy of two- and three-dimensional sonohysterography in women with intrauterine lesions. *Fertil Steril* 79: 1222-1225.
8. BROWN AB, CHAMBERLAIN R, TE LINDE RW (1956) Myomectomy. *Am J Obstet Gynecol* 71: 759-763.
9. Candiani GB, Fedele L, Parazzini F, Villa L (1991) Risk of recurrence after myomectomy. *Br J Obstet Gynaecol* 98: 385-389.
10. Radosa MP, Owsianowski Z, Mothes A, Weisheit A, Vorwergk J, et al. (2014) Long-term risk of fibroid recurrence after laparoscopic myomectomy. *Eur J Obstet Gynecol Reprod Biol* 180: 35-39.
11. Babaknia A, Rock JA, Jones HW Jr (1978) Pregnancy success following abdominal myomectomy for infertility. *Fertil Steril* 30: 644-647.
12. Dubuisson JB, Chapron C, Chavet X, Gregorakis SS (1996) Fertility after laparoscopic myomectomy of large intramural myomas: preliminary results. *Hum Reprod* 11: 518-522.
13. Sudik R, Hüsck K, Steller J, Daume E (1996) Fertility and pregnancy outcome after myomectomy in sterility patients. *Eur J Obstet Gynecol Reprod Biol* 65: 209-214.
14. Vimercati A, Scioscia M, Lorusso F, Laera AF, Lamanna G, et al. (2007) Do uterine fibroids affect IVF outcomes? *Reprod Biomed Online* 15: 686-691.
15. Hart R, Khalaf Y, Yeong CT, Seed P, Taylor A, et al. (2001) A prospective controlled study of the effect of intramural uterine fibroids on the outcome of assisted conception. *Hum Reprod* 16: 2411-2417.
16. Li TC, Mortimer R, Cooke ID (1999) Myomectomy: a retrospective study to examine reproductive performance before and after surgery. *Hum Reprod* 14: 1735-1740.
17. Farhi J, Ashkenazi J, Feldberg D, Dicker D, Orvieto R, et al. (1995) Effect of uterine leiomyomata on the results of in-vitro fertilization treatment. *Hum Reprod* 10: 2576-2578.
18. Eldar-Geva T, Meagher S, Healy DL, MacLachlan V, Breheny S, et al. (1998) Effect of intramural, subserosal, and submucosal uterine fibroids on the outcome of assisted reproductive technology treatment. *Fertil Steril* 70: 687-691.
19. Gianaroli L, Gordts S, D'Angelo A, Magli MC, Brosens I, et al. (2005) Effect of inner myometrium fibroid on reproductive outcome after IVF. *Reprod Biomed Online* 10: 473-477.
20. Sunkara SK, Khairy M, El-Toukhy T, Khalaf Y, Coomarasamy A (2010) The effect of intramural fibroids without uterine cavity involvement on the outcome of IVF treatment: a systematic review and meta-analysis. *Hum Reprod* 25: 418-429.
21. Somigliana E, Vercellini P, Daguati R, Pasin R, De Giorgi O, et al. (2007) Fibroids and female reproduction: a critical analysis of the evidence. *Hum Reprod Update* 13: 465-476.
22. Yan L, Ding L, Li C, Wang Y, Tang R, et al. (2014) Effect of fibroids not distorting the endometrial cavity on the outcome of in vitro fertilization treatment: a retrospective cohort study. *Fertil Steril* 101: 716-721.
23. Stovall DW, Parrish SB, Van Voorhis BJ, Hahn SJ, Sparks AE, et al. (1998) Uterine leiomyomas reduce the efficacy of assisted reproduction cycles: results of a matched follow-up study. *Hum Reprod* 13: 192-197.
24. Marchionni M, Fambrini M, Zambelli V, Scarselli G, Susini T (2004) Reproductive performance before and after abdominal myomectomy: a retrospective analysis. *Fertil Steril* 82: 154-159, quiz 265.
25. Surrey ES, Minjarez DA, Stevens JM, Schoolcraft WB (2005) Effect of myomectomy on the outcome of assisted reproductive technologies. *Fertil Steril* 83: 1473-1479.
26. Narayan R, Rajat, Goswamy K (1994) Treatment of submucous fibroids, and outcome of assisted conception. *J Am Assoc Gynecol Laparosc* 1: 307-311.
27. Frederick J, Hardie M, Reid M, Fletcher H, Wynter S, et al. (2002) Operative morbidity and reproductive outcome in secondary myomectomy: a prospective cohort study. *Hum Reprod* 17: 2967-2971.
28. Hawkins LK, Correia KF, Srouji SS, Hornstein MD, Missmer SA (2013) Uterine length and fertility outcomes: a cohort study in the IVF population. *Hum Reprod* 28: 3000-3006.
29. Farquhar C, Brown PM, Furness S (2002) Cost effectiveness of pre-operative gonadotrophin releasing analogues for women with uterine fibroids undergoing hysterectomy or myomectomy. *BJOG* 109: 1273-1280.