Successful Natural Pregnancy Using Whole Systems Traditional Chinese Medicine in a Complex Anovulatory Patient After Multiple Unsuccessful *In Vitro* Fertilization Treatments: A Case Report

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ABSTRACT

Background: Women who have anovulatory infertility due to polycystic ovary syndrome (PCOS) rely primarily on medical fertility treatment to conceive. If this treatment fails, the odds of success of conceiving naturally are extremely small, limited by the lack of ovulation and its unpredictability. Whole systems Traditional Chinese Medicine (WS-TCM), which includes acupuncture, Chinese herbs, nutrition and supplements, and lifestyle recommendations, has traditionally been used to prepare the body for pregnancy and to induce ovulation in PCOS patients with anovulatory infertility.

Case: This case describes the treatment of a complex anovulatory PCOS patient using a WS-TCM approach to induce ovulation and produce a natural uncomplicated pregnancy after multiple rounds of *in vitro* fertilization with and without preimplantation genetic screening and also with and without acupuncture were unsuccessful.

Results: After 9 unsuccessful frozen embryo transfers, 3 of which with genetically tested euploid embryos, this previously anovulatory patient was able to ovulate, conceive, and carry a healthy pregnancy to term.

Conclusions: This case suggests that in challenging cases of infertility in the setting of PCOS, the multifaceted approach of WS-TCM may provide an alternative means to induce ovulation and increase the odds of conceiving.

Keywords: anovulatory infertility, whole systems Traditional Chinese Medicine (WS-TCM), acupuncture, Chinese herbs, polycystic ovary syndrome (PCOS)

INTRODUCTION

PRESENTLY, THERE IS ONLY ONE STUDY that looks at whole systems Traditional Chinese Medicine (WS-TCM) and infertility, and in this study WS-TCM is considered as an adjuvant treatment to *in vitro* fertilization (IVF).¹ To the authors' knowledge, there are no studies on use of WS-TCM as a stand-alone treatment for infertility in the peer-reviewed English language literature. Most published research focuses

only on acupuncture, leaving out Chinese herbs, nutrition, and lifestyle guidance.^{2,3} However, these elements are important tools of TCM and widely utilized in acupuncture and TCM practices. To the authors' knowledge there are also no case reports describing using WS-TCM as a stand-alone treatment to achieve a healthy pregnancy specifically after multiple IVF failures.

This case describes the use of WS-TCM in a patient who was anovulatory without intervention. After a total of 9

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embryo transfers, she discontinued medical fertility treatment. After a 4-month program of WS-TCM, she had a successful pregnancy leading to a live birth.

PATIENT INFORMATION

The patient is a Caucasian woman trying to conceive her second child. She had a body mass index of $\sim 19 \text{ kg/m}^2$. In her adulthood, the patient was anovulatory without intervention. From menarche at age 12 until 18 years old she reports having very infrequent menses, $\sim 1\text{--}2$ per year. It is not known whether these were ovulatory cycles. She had a vaginal septum that was repaired at 18 years old. She began taking oral contraceptive pills (OCPs) at 18 years to “regulate her cycle” and discontinued it at 29 years old when she wanted to get pregnant. Three months later she had not ovulated and was diagnosed with polycystic ovary syndrome (PCOS). She did 4 rounds of clomiphene citrate (Clomid), followed by 4 rounds of intrauterine insemination (IUI) with gonadotropins, all of which were unsuccessful. She developed ovarian torsion in the third round of IUI, so it was discontinued, and surgery was performed to untwist and save the ovary.

At 30 years old, she began acupuncture the month before her first IVF cycle. Her follicle-stimulating hormone at that time was 4.1 mIU/mL. She was put on a multivitamin (Designs for Health Twice Daily Multi) that at that time contained 800 μg of folic acid. She had acupuncture 1–2 times per week through her IVF cycle and continuing until week 10 of her pregnancy. At week 18 of her pregnancy, she developed ovarian torsion a second time on the same side and had a laparotomy and unilateral oophorectomy to remove the affected ovary. Endometriosis was noted during the surgery. At 33 weeks, the patient noticed a decrease in fetal movement. The baby was found to be in distress and was delivered by emergency cesarean section producing a live birth. The baby was in neonatal intensive care for 4 weeks. After the birth of her first child, she pumped breast milk and breast fed for 3 months. After a year she had not had a menses, and then began OCPs for 2 years for contraceptive purposes.

At age 33 years she began to attempt to conceive her second child, as summarized in Table 1. She attempted 2 frozen embryo transfers (FETs) using untested embryos from her first IVF retrieval several years earlier, both of which failed. She had acupuncture weekly around the following 2 FETs. When those 2 FETs were unsuccessful, she then discontinued acupuncture for 8 months. During this

TABLE 1. TIMELINE OF EVENTS BEFORE WHOLE SYSTEMS TRADITIONAL CHINESE MEDICINE

Date	Medical intervention	Embryo transfer	WS-TCM interventions	Outcome
September 2010	IVF retrieval No. 1	No. 1 frozen, untested		Miscarriage
February 2011		No. 2 frozen, untested		Negative
April 2011		No. 3 frozen, untested	Acupuncture	Negative
June 2011		No. 4 frozen, untested	Acupuncture	Biochemical
August 2011	IVF retrieval No. 2	No. 5 fresh, untested		Negative
September 2011	IVF retrieval No. 3	No. 6 fresh, untested		Negative
October 2011	IVF retrieval No. 4			
January 2012		No. 7 frozen, euploid embryo		Miscarriage, dilation and curettage normal products of conception
	Blood tests show proteins C and S deficiency. MTHFR, PAI. Added Folgard baby aspirin and Lovenox			
April–June 2012			Acupuncture and Chinese herbs, methylated folate	2 ovulatory cycles in 3 months. Both negative
July 2012	Baby aspirin, Lovenox	No. 8 frozen, euploid embryo	Acupuncture, methylated folate	Negative
October 2012	Baby aspirin, Lovenox	No. 9 frozen, euploid embryo	Acupuncture, methylated folate	Negative

IVF, *in vitro* fertilization; WS-TCM, whole systems Traditional Chinese Medicine.

time, she did another 3 IVF retrievals as described below. The embryos from the last IVF retrieval (No. 4) were tested with preimplantation genetic screening (PGS) and yielded 3 normal embryos. Her anti-Müllerian hormone (AMH) was elevated at 5.1 ng/mL. Thyroid stimulating hormone was within normal limits. Her husband's semen analysis showed poor morphology but good count.

Her first FET with a PGS normal embryo achieved a pregnancy, but she later miscarried. The products of conception later showed a euploid fetus. A thrombophilia panel showed protein C deficiency, borderline protein S deficiency, and homozygous mutations for the MTHFR gene (A1298C) and PAI-1. She was given enoxaparin sodium (Lovenox) and baby aspirin and high-dose folic acid, vitamin B₆, and vitamin B₁₂ (Folgard) during the subsequent embryo transfers. Shortly after this miscarriage she took a break from medical fertility treatment, resumed acupuncture, and began taking Chinese herbs for PCOS and anxiety. She had 2 ovulatory cycles in 3 months, confirmed by progesterone test, but no pregnancy. This was the first time in her life she had confirmed ovulatory menstrual cycles without pharmaceutical intervention.

She then discontinued the herbs and resumed medical fertility treatment and did the remaining 2 FETs with weekly acupuncture with the remaining 2 tested embryos, both of which were unsuccessful. Other noteworthy findings in her history are that she described herself as anxious, had been borderline anemic, experienced vertigo, and also had a history of yeast infections and tinea versicolor in her history and a flare after her last miscarriage. She had occasional constipation. Her tongue was pale with a red tip. Her pulse was thin and wiry.

CLINICAL FINDINGS

At age 35 years she decided to discontinue assisted reproductive therapies and all the associated medications and begin a full program of WS-TCM as described in Table 2. She began a low glycemic diet and continued with regular weekly acu-

puncture. She resumed using Chinese herbs and switched from Folgard to a multivitamin that at that time contained 400 µg of a combination of folic acid and methylated folate (Designs for Health Twice Daily Multi) plus an additional 800 µg of methylated folate (Metagenics Folapro). From this point forward she had 2 ovulatory cycles tracked by basal body temperature charting, which both showed a clear temperature shift and then menses ~14 days later. She reported that her energy and overall sense of well-being improved, and her anxiety diminished during this period of time. In the third cycle, a pregnancy was confirmed, upon which she discontinued herbs and began enoxaparin sodium (Lovenox) and baby aspirin. She also used progesterone throughout the pregnancy because of her history of preterm delivery. She had an uncomplicated pregnancy and a scheduled cesarean section (due to her prior cesarean section) at 39 weeks.

DIAGNOSTIC ASSESSMENT

This was a complex patient. From a medical standpoint, she had multiple medical diagnoses (PCOS, anovulation, amenorrhea, endometriosis, Protein C & S deficiency, MTHFR and PAI-1 mutations, and 1 remaining ovary). From a Chinese medical standpoint, she had multiple Chinese Medicine patterns of imbalance. As a reproductive-age woman with no natural menses, she was considered Liver blood deficient. Since she did not produce a luteal or Yang phase of the menstrual cycle, she was considered Kidney Yang deficient. As she had 1 remaining ovary, there was some element of Kidney Jing Deficiency, but since her AMH was relatively high implying that the remaining ovary had a good ovarian reserve, this was not a main focus. She suffered from anxiety and she had been borderline anemic at times, which implies she tended toward general blood deficiency and specifically Heart blood deficiency. The fluid filled aspect of the PCOS cysts are considered to be phlegm or dampness due to Spleen Qi Deficiency. In addition, she

TABLE 2. TIMELINE OF EVENTS FOLLOWING WHOLE SYSTEMS TRADITIONAL CHINESE MEDICINE

<i>Date</i>	<i>Medical intervention</i>	<i>WS-TCM interventions</i>	<i>Outcome</i>
January 2013	Discontinued medical fertility treatment		
January –April 2013		Acupuncture, Chinese herbs, low glycemic diet, methylated folate, baby aspirin	3 ovulatory cycles in 4 months: 2 negative 1 positive Pregnancy confirmed
April 2013 April–December 2013	During pregnancy: Lovenox and progesterone	Continued acupuncture until week 8 of pregnancy. Discontinued herbs, continued low glycemic diet, methylated folate, baby aspirin	
December 2013	Scheduled cesarean section		Live birth at 39 weeks

had a tendency to develop yeast infections and also tinea versicolor. This suggests she may have had trouble metabolizing sugars and simple carbohydrates, further reinforcing her diagnosis of Spleen Qi Deficiency and possibly contributing to her PCOS. The cysts of PCOS are also considered to have a blood stasis component because of the formation of abnormal tissue. In her case, she had multiple clotting issues including protein C deficiency, borderline protein S deficiency, and homozygous mutations for the MTHFR gene (A1298C) and PAI-1, as well as endometriosis, which all contribute to her blood stasis diagnosis. Her last miscarriage showed a genetically normal fetus, so that rules out genetic issues for at least that attempt and implies the presence of other implantation or uterine issues.

THERAPEUTIC INTERVENTION

The WS-TCM approach was to address each of her diagnoses and patterns of imbalance through a multifaceted program as summarized in Table 3.

First, she was anovulatory due to PCOS, so ovulation was a necessary first step. Acupuncture alone may not be sufficient to improve ovulation and live birth in PCOS patients.⁴

When she began the Chinese herbs, she had 2 ovulatory cycles in 3 months but did not achieve a pregnancy.

Second, since PCOS is associated with insulin resistance, she was put on a low glycemic diet to reduce her body's insulin demands. This is a strategy similar to using metformin to help patients with PCOS conceive and reduce the chance of miscarriage.⁵

Third, the herbs she took had several other strategies in addition to helping her to ovulate:

- They contained herbs that nourish blood and calm the spirit that are traditionally used for anxiety.⁶
- They also contained herbs that strongly invigorate blood and break blood stasis that may have addressed her clotting issues before she began taking Lovenox.⁶
- They also contained herbs that strengthened her body's ability to digest food and absorb its nutrition, called Qi tonics.⁶ These may have helped with her energy.

Fourth, she was put on methylated folate to address her homozygous MTHFR A1298C mutation based on the idea that it may help with embryo viability.⁷

Fifth, on the mental and emotional level, she was no longer operating under the mental stress of preparing for another IVF cycle or embryo transfer, which may have contributed to calming her anxiety.

TABLE 3. WHOLE SYSTEMS TRADITIONAL CHINESE MEDICINE INTERVENTIONS

<i>Traditional Chinese Medicine or (medical) diagnosis</i>	<i>Acupuncture</i>	<i>Herbs (g)</i>	<i>Nutrition</i>
Anovulatory (PCOS)	Chong Mai SP 4 PC 6 Zi Gong Xue	Zao Jiao Ci 9 Chuan Bei Mu 9	Low glycemic diet
Liver blood deficiency	LR 3	Shu Di Huang 4 Dang Gui 12 Bai Shao 9	
Heart blood deficiency/Calm the Spirit (anxiety)	BL 14 15 H 7 KI 1 Ear Shen Men	Suan Zao Ren 9 Long Yan Rou 2 Zhi Gan Cao 3 Yuan Zhi 6 Hu Po 5	
Blood stasis (thrombophilias)	SP 8	San Leng 2 E Zhu 3	
Spleen Qi deficiency	ST 36 CV 4 6 12 BL 20	Shan Yao 12 Huang Jing 5 Ren Shen 9 Huang Qi 12 Bai Zhu 9 Fu Ling 9	Low glycemic diet
Kidney Yang deficiency	KI 3 KI 7 GV 20 BL 23	Yin Yang Huo 9 Tu Si Zi 9	Vitamin D ₃ 2,000 IU/day
Kidney Yin deficiency	LU 7 KI 6 SP 6 BL 23		
Qi stagnation (Homozygous MTHFR A1298C mutation)	GB 20 21 34 41	Mu Xiang 6	Methylated folate Green leafy vegetables

IU, international units; PCOS, polycystic ovary syndrome.

Sixth, she no longer had the physiologic stress of going on and off medications and hormones.

And last, she continued acupuncture that likely eased her anxiety and calmed her nervous system as she considered it to be a time for her to relax and unwind.

ACUPUNCTURE

The treatment principles used were to tonify Spleen Qi, blood, Kidney Yin and Yang, move blood, and calm the spirit. The most important combination was SP 4 and PC 6 to open the Chong Mai and to tonify and move blood in the reproductive system. The points chosen are traditional acupuncture points related to her TCM diagnosis.⁸ In general, points on the front of the body were used in the follicular and ovulatory phases, and back shu points were used in the luteal phase.

CHINESE HERBS

The Chinese herbs focused on treating her PCOS since that was what was likely preventing her from ovulating, and was her biggest obstacle to pregnancy. The formula listed is the formula she was taking at the time she got pregnant. It is based on a formula used for PCOS and modified with the addition of herbs that Calm the Spirit to address her anxiety.⁹ This formula contains herbs that nourish blood, Yang, and Qi, invigorate blood, and resolve phlegm. San Leng and E Zhu are among the strongest herbs in the *Materia Medica* for treating blood stasis.⁶ Herbs in this category have blood thinning properties that may be helpful for her thrombophilias. It also contains Zao Jiao Ci and Chuan Bei Mu that are commonly used in PCOS formulas to clear the cysts of PCOS that are considered to contain phlegm.^{8,9}

The initial formula used contained higher dosages of Shu Di Huang (12 g), Huang Jing (12 g), Yin Yang Huo (12 g), Chuan Bei Mu (12 g), and Long Yan Rou (6 g). The formula was modified over time in several ways. Shu Di Huang and Huang Jing were reduced to make it more digestible because she was getting a lot of gas. Once she started ovulating, the dosages of Yin Yang Huo and Chuan Bei Mu were lowered. And once her anxiety improved, the dosage of Long Yan Rou was reduced. The formulas were prepared by Kamwo in New York City, United States, as a granule formula at 5:1 concentration. The formulas were written as hereunder and adjusted by Kamwo to be 100 g total per bottle. At the time she conceived, she was taking a relatively low dosage of 2 g, 2× per day.

NUTRITION

For the PCOS/Spleen Qi deficiency, she was advised to eliminate most simple sugars and simple carbohydrates, limit fruit to 1 serving per day, to fill half of her plate with

nonstarchy colorful vegetables, especially green leafy vegetables, and only have small amounts of starchy complex carbohydrates, such as 1/4–1/3 cup brown rice per day.

SUPPLEMENTS

For the MTHFR mutation, she was switched from Foliard (high-dose folic acid, vitamin B₆, vitamin B₁₂) to a multivitamin that is high in B vitamins (Designs for Health Twice Daily Multi), which at that time contained 400 µg of a combination of folinic acid and methylated folate plus 800 µg additional methylated folate (Metagenics FolaPro). During pregnancy vitamin D₃ 2,000 international units (IU) per day was added to support her Yang energy.

LIFESTYLE GUIDANCE

In her case, lifestyle was not a major issue. She got a reasonable amount of exercise and sleep. When attempting her second pregnancy, she was an attending in a hospital, so there was some work stress, but overall, she reports being less stressed than when she was trying to get pregnant with her first child when she was a medical resident.

FOLLOW-UP AND OUTCOMES

During the time when she began the WS-TCM, she reported feeling more relaxed, energetic, and well. She had a healthy uncomplicated second pregnancy and live birth by scheduled cesarean section at 39 weeks.

DISCUSSION

This case is a description of a typical multifaceted approach of WS-TCM to induce ovulation and pregnancy in complex patients with multiple diagnoses and multiple IVF failures. There are limitations to this case report. This case occurred 6 years ago. In current practice, some clinics would perform a CD-138 endometrial biopsy to test for endometritis after multiple FETs, especially those with euploid embryos, had failed.^{10,11} If positive, she and possibly her partner would have been put on antibiotics before another FET. Also, next-generation sequencing that identifies mosaic embryos would have been used instead of the older (Array CGH) version of PGS.¹² It is possible that the PGS embryos had tested as euploid but were actually mosaic, but that was impossible to know at the time. Or she might have been tested for endometrial BCL6, and if positive, put on 2 months of leuprolide acetate (Lupron) or had laparoscopic surgery for her endometriosis.¹³ Some clinics might also use endometrial receptivity testing to evaluate possible mistimed window of implantation.

It is impossible to confirm that WS-TCM was what helped her to ovulate and conceive. It may have been coincidence and good luck.

CONCLUSION

This case suggests that that in the setting of multiple IVF failure in anovulatory PCOS patients, the multifaceted approach of WS-TCM may be a treatment option to consider, particularly before advising patients to move on to using egg donation or adoption. WS-TCM may provide an alternative means to induce ovulation and increase the odds of conceiving. More research is needed.

PATIENT PERSPECTIVE

“After multiple rounds of IVF cycles that didn’t work, I decided I was done with that. Basically, that’s when we started the herbs and acupuncture. That’s when I started getting my period regularly and naturally. Soon after that I got pregnant with my second child. The nutrition part felt more familiar to me because I had done a low glycemic diet during my first pregnancy. The herbs tasted disgusting initially but then I got used to them. Besides regulating my hormones, it felt like they improved my energy. I felt more well, and this felt like a big component. I looked at acupuncture as a restful, peaceful time for myself. It helped my anxiety and stress which probably also helped my whole system. I felt a lot more energetic and rested overall.

Why didn’t I do the acupuncture and herbs sooner? Would life have been different if I had done it earlier? The second pregnancy went so much more smoothly than the first because I got pregnant naturally. And I felt so much better during it.”

INFORMED CONSENT

Verbal and written.

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AUTHOR DISCLOSURE STATEMENT

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