

Pregnancy in Premature Ovarian Failure after Therapy Using Chinese Herbal Medicine

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We present ovulation that occurred after the administration of traditional Chinese herbal medicine for 3 months in a woman with premature ovarian failure (POF) and secondary amenorrhea for 8 years. Traditional Chinese medicine concentrated herbal extracts of cooked rehmannia, Chinese yam, wolfberry fruit, dogwood fruit, cyathula root, dodder seed, antler glue, tortoise-plastron glue, epimedium and morinda root were prescribed, which were a modification of the herbal formula *Zuo-gui-wan*. When the patient discontinued the Chinese herbal medicine treatment and tried therapy with clomiphene citrate, neither ovulation nor conception occurred. Eight months after beginning clomiphene citrate therapy, the concentrations of follicle stimulating hormone and luteinizing hormone were still in the postmenopausal range. The modified formula of *Zuo-gui-wan* was prescribed again and the patient conceived 1 month after taking *Zuo-gui-wan*. Thus, we suggested that Chinese herbal medicine restored ovarian function effectively and promptly, and offers another option for treating infertility in patients with POF. (*Chang Gung Med J* 2003;26:449-52)

Key words: premature ovarian failure, traditional Chinese medicine, ovulation, pregnancy.

The incidence of premature ovarian failure (POF) in women with secondary amenorrhea is about 10%.⁽¹⁾ Although numerous causes have been reported, most cases of POF are classified as idiopathic.⁽²⁾ The estimated pregnancy rate following diagnosis is about 5-10% using various methods of intervention.⁽³⁾ In addition to oocyte donation, other therapeutic approaches to improve the fertility of POF patients are still under investigation. Estrogen progesterone cyclic replacement therapy is usually recommended when the diagnosis of POF is confirmed. According to the theory of traditional Chinese medicine (TCM), the pathogenesis of disorders of menstruation and reproduction are related to "Kidney deficiency", so a modified formula of *Zuo-gui-wan*, which is used to reinforce Kidney function, is usually prescribed for patients with POF.

CASE REPORT

A 26-year-old single woman was seen at the Chinese medicine clinic in August 2000. She had had secondary amenorrhea of 8 years. Her menarche was at the age of 12 years and she had oligomenorrhea with irregular 6 to 12-month menstrual cycles subsequently. After the age of 18 years, she had complete amenorrhea, but did not receive any treatment except for occasional hormone injections for withdrawal bleeding at private clinics. Previous pelvic sonographic examination revealed no abnormal findings. Hormone evaluation showed that the follicle stimulating hormone (FSH) concentration was 50.4 mIU/ml, the luteinizing hormone (LH) concentration was 11.5 mIU/ml, and the estradiol concentration was 13.8 pg/ml in April 2000.

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There was no history of systemic disease. Her family history was also negative of endocrine, autoimmune and genetic diseases. Results of physical examination were normal. Laboratory examination results revealed that the concentrations of both FSH and LH were high (80.0 mIU/ml and 19.6 mIU/ml, respectively), and estradiol was low (25.8 pg/ml). The concentrations of prolactin, thyroid stimulating hormone and testosterone were within normal limits. Chromosomal study was suggested, but the patient refused. A modified TCM formula of *Zuo-gui-wan* in the form of concentrated herbal extracts (package dosage 15 g, containing 5 g of cooked rehmannia, 2.5 g of Chinese yam, 2.5 g of wolfberry fruit, 2.5 g of dogwood fruit, 2 g of cyathula root, 2.5 g of dodder seed, 2.5 g of antler glue, 2.5 g of tortoise-plastron glue, 3 g of epimedium and 3 g of morinda root, in powder, daily) was prescribed for 3 months, and menstrual bleeding occurred on December 8, 2000. Evidence of ovulation using biphasic basal body temperature was also noted. The patient was married in January 2001 and discontinued Chinese herbal medicine therapy thereafter. She consulted another gynecologist with complaints of amenorrhea and infertility, but ovulation and pregnancy did not occur after ovulation induction using clomiphene citrate. She returned to our clinic in August 2001, and her serum FSH and LH levels were still in the postmenopausal range (43 mIU/ml and 11 mIU/ml, respectively). She again received the modified formula of *Zuo-gui-wan* in the form of concentrated herbal extracts, and conceived 1 month after beginning *Zuo-gui-wan*. A healthy female baby weighing 3450 g was delivered by Cesarean section.

DISCUSSION

POF is characterized by hypergonadotropic hypogonadism before the age of 40 years.⁽⁴⁾ It is estimated that about 1% of women may experience POF.⁽⁵⁾ The serial measurements of serum FSH concentration in this report were all > 40 mIU/ml, which met the criterion for POF.^(2,3) Although POF patients may ignore their menstrual abnormalities, they usually have to face the problem of infertility. Estrogen replacement therapy has the advantages of improving the hypogonadism side effects of POF, and sometimes is able to achieve

pregnancy.⁽³⁾ However, some studies suggested that estrogen replacement therapy does not improve the rates of ovulation and pregnancy.^(3,6) Previous reports of successful pregnancies have dealt with drug interventions with hormone replacement therapy,⁽⁶⁾ gonadotropin-releasing hormone agonist,⁽⁷⁾ human menopausal gonadotropin⁽⁸⁾ and corticosteroids,⁽⁹⁾ but it is not possible to compare the effectiveness of the drugs due to the different study protocols.⁽³⁾

TCM therapy has been used for a long time, but many of its clinically successful reports are doubted because of the limited number of scientific studies. Although the exact mechanism of the action of Chinese herbal medicine remains to be proven, we suggest that it is an effective alternative therapy for POF. The functions of "kidney" in TCM include not only the function of the kidney as known in Western medicine, but also the functions of the reproductive and endocrine systems. The kidney stores reproductive essence derived from the parents and controls growth, menstruation, conception and aging in women. According to the principles of TCM therapy, Kidney deficiency syndrome is the pattern of patients with POF, and Chinese herbal medicine formulas with kidney reinforcing effects should be used. Because the kidney reinforcing effects of *Zuo-gui-wan* were mainly for supplementing Yin, epimedium and morinda root, which have the effects of supplementing Yang, were added to enhance the effects of *Zuo-gui-wan*.

Many etiological factors have been identified in patients with POF, including some genetic disorders of X chromosome and autosomal disorders.⁽¹⁰⁾ The therapeutic outcome of patients with POF after TCM treatment should be related to the existence of ovarian follicles such as resistant ovary syndrome.⁽¹¹⁾ The rate of ovulation is lower in patients with POF who have had amenorrhea for a long time.⁽³⁾ Our patient had amenorrhea of 8 years. Chinese herbal medicine led to ovulation after only 3 months of treatment. Although she did not respond to clomiphene therapy, she conceived when she received Chinese herbal medicine again for only 1 month. *Zuo-gui-wan* has been thought to be a good Chinese herbal formula for many gynecologic disorders because of its efficacy and safety for 400 years. We found it usefulness in treating our patient with POF. Further investigation of more patients is needed to evaluate the efficacy of Chinese herbal medicine in restoring ovarian

function and improving the pregnancy rate of patients with POF.

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中藥治療早發性卵巢衰竭成功懷孕

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本病人患有早發性卵巢衰竭，已無月經8年，在接受中藥方劑左歸丸加味治療3個月後，即見排卵性月經。婚後停用中藥約8個月，曾以clomiphene治療，但未見排卵或懷孕，且血清濾泡刺激素和黃體刺激素之濃度仍為更年期範圍，故再服左歸丸加味，治療1個月即告懷孕。由此病例，我們發現中藥能使早發性卵巢衰竭患者排卵，且提供另一種能藉由自己的卵子生育的治療方法。(長庚醫誌 2003;26:449-52)

關鍵字：早發性卵巢衰竭，中藥，排卵，懷孕。

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