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ORIGINAL ARTICLE

Reproductive outcome re-evaluation for women with primary ovarian insufficiency using office microlaparoscopy

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Abstract *Objective & Aim:* The objective of this study was to analyze the usefulness of office microlaparoscopy in the re-assessment of ovarian morphological picture, relevant clinical types and future fertility prognosis of primary ovarian insufficiency (POI). *Methods:* Forty-five patients with POI diagnosed in a private fertility care center between October 2009 and December 2014, who gave informed consent and underwent office microlaparoscopy were studied. Pelvic ultrasound had failed to visualize and morphologically assess both ovaries in the women included. The cases were divided into four groups based on the microlaparoscopic ovarian morphology: Group N (near to normal), Group G (Gyrus shaped), Group A (atrophied), and Group S (streak shaped). These groups were analyzed with respect to patient background, blood hormone levels, the level of antinuclear antibodies measured, and their individual fertility prognosis. *Result:* No significant differences in patient background and serum hormone levels were observed between groups. There was complete absence of both ovaries in 5 patients included. Groups N and G had shown some improvement, such as regular spontaneous menstruation, and forthcoming pregnancy, which happened once in Group N. Many other internal genital anomalies could be diagnosed during the same office procedure. *Conclusion:* Office microlaparoscopy under augmented local anesthesia is a useful procedure in the definite demarcation, and the differentiation between the types of POI, regarding their menstrual regularity and future fertility prognosis.

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1. Introduction

Some authors prefer the use of the term premature ovarian dysfunction, in an attempt to reflect the reversible nature of this condition, and avoiding the idea of failure. More recently, some authors have preferred the term primary ovarian

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insufficiency, as this is thought to be more accurate and informative for patients. It is a personal view that ''insufficiency'' is a vague term that is helpful for, and widely supported by patients, as some women clearly have a complete cessation to menstruation, which does not quite match the concept of ''insufficient follicles'', given that no term is accurate (1–4).

A definitive diagnosis of POI is difficult to make, and the criteria for defining POI are not always standard. Most clinicians would make the diagnosis based on amenorrhea for 3–6 months, and the demonstration of follicle stimulating hormone (FSH) concentrations above 40 mIU/ml on at least two occasions was taken several months apart, and low estrogen levels. FSH needs to be measured on several different occasions to exclude intermittent ovarian activity as a cause of elevated gonadotropins. Oestradiol levels are typically low, with levels of 50 pg/ml or less (5–8).

Several non-invasive methods, such as transvaginal ultrasonography and autoantibody measurement, have been advocated but no consensus has been established on their usefulness (9–13). Unfortunately, both ovaries could not be visualized using pelvic ultrasound in most cases with POI. The objective of this method was to evaluate the effectiveness of office microlaparoscopic under augmented local anesthesia, First: to re-assess the morphology of both ovaries in POI, after failure of pelvic ultrasound examination to demarcate and assess the measures of both ovaries and Second: to try to correlate this ovarian morphology with other POI markers for the future prognosis of ovarian hormonal functions and fecundability.

2. Materials and methods

Forty-five cases of POI diagnosed at a private clinic had been recruited during the 5-year period from October 2009 to March 2014, and underwent microlaparoscopy. All the patients gave informed consent and the study was approved by the Regional Institutional Ethical Review Board.

Primary ovarian insufficiency (POI) was diagnosed when all the following four criteria were fulfilled: (i) subjects under 40 years of age; (ii) second degree amenorrhea (low estrogen and progesterone); (iii) serum FSH level of 40 mIU/mL or higher, and serum estradiol (E2) level less than 30 pg/mL; and (iv) 46, XX karyotype. (v) Both ovaries could not be visualized and measured using pelvic ultrasound.

The age and body mass index (BMI) at presentation, as well as the age of menarche and amenorrhea period based on the medical history, were reviewed. The amenorrhea period was calculated after excluding the period of primary amenorrhea. Serum hormones were measured at presentation or during the period without treatment. Serum LH and FSH were measured by commercial immunoradiometric assay kits (Spack-S LH & FSH; Daiichi Radio-isotope Laboratories, China). E2 was measured using a solid-phase radioimmunoassay (RIA) assay (DPC Estradiol Kit; Diagnostic Products Corporation, China). Antinuclear antibody rates were measured by the fluorescent antibody method, with 40 units or higher as positive.

The ovaries had been examined whether each ovary could be definitely visualized, and its measures could be accurately evaluated, using transvaginal ultrasonography (Sonoview EX, if: 6 MHz, Toshiba, Japan). For each subject, the examination was conducted at least for two times, and no ovaries could be visualized and morphologically assessed in all patients included.

2.1. Microlaparoscopic surgical procedure

Microlaparoscopy was performed in all patients who gave full informed consent to undergo the procedure. Microlaparoscopy was conducted as a day surgery with 24 h admission, using the following surgical procedure. The microlaparoscopic system consists of a light source, a high speed pneumoperitoneum device, and a 1CCD video camera. The diameter of the scope was 2.2 mm, and the grasping forceps, scissors, needle probes, biopsy forceps and irrigator–aspirator were also 2.2 mm in diameter (all equipment made by Olympus, Tokyo, Japan).

The instruments could be used by specially designed trocar (access needle; Ethicon, Cincinnati, OH, USA), 12-cm long and 2.5 mm in diameter metal sleeve that fits over the veress needle. Pre-medication consisting of 0.5 mg of atropine sulfate and 1 mg/kg of midazolam was given intramuscularly. One mg/kg of fentanyl followed by 1.5 mg/kg of ketamine was intravenously administered through a drip infusion line. The patient was placed in a lithotomy position. An access needle (Ethicon, Tokyo, Japan) was inserted through a small incision created in the subumbilical region using the closed method, after been locally infiltrated with Xylocaine local anesthesia.

Pneumoperitoneum was induced with carbon dioxide gas. Other access needles were then inserted into both sides of the hypogastric region under microlaparoscopy. Four ml/port of 0.25% bupibacaine was locally injected at the trocar insertion sites in advance. All the scopes and forceps used were from the microlaparoscopy set of 2.2 mm in outer diameter (Olympus, Tokyo, Japan), while the ovarian ligament was held with holding forceps to fix it.

The ovaries were observed under the microlaparoscope. During microlaparoscopy procedure, the size of the ovary was measured using Maryland forceps. When the forceps are extended, the distance between the two arms is 1.4 cm and this distance was used to measure the length, width and depth of the ovary. Ovaries were classified into four morphological groups (Figs. 1 and 2): (i) normal appearance (Group N); (ii) Gyrus type (Group G); (iii) Atrophic type (Group A); and (iv) streak type (Group S). The degree of normality was considered to be in descending order from Group N to Group S.

Other internal genital anomalies had been diagnosed. Moreover tubal patency had been tested using the dye test in all the cases operated on, even with the clear microlaparoscopic absence of both tubes. Assessment of the uterus, regarding its morphological parameters, and any associated anomalies available. Pain mapping and patient acceptance for the office procedure had been assessed during the office microlaparoscopic procedure. Moreover, an extra analgesia needed intraoperatively and postoperatively had been recorded. The time of the patient postoperative discharge had been also recorded, in addition to the final patient opinion about the procedure.