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Original Article

Medical Treatment of Ureteral Obstruction Associated With Ovarian Remnants and/or Endometriosis: Report of Three Cases and Review of the Literature

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ABSTRACT **Study Objective:** Experience with low-dose intermittent danazol or prolonged gonadotropin-releasing hormone agonist (GnRH-a) with and without add-back therapy in endometriosis-associated ureteral obstruction.

Design: Retrospective case series (Canadian Task Force classification II-2).

Setting: University-affiliated teaching hospital.

Patients: Three women with endometriosis-associated ureteral obstruction.

Intervention: The regimen of GnRH-a alone or with add-back included (1) leuprolide acetate 3.75 mg intramuscularly monthly; (2) micronized 17α-estradiol 1 mg/day by mouth; (3) pulsed norethinedrone 0.35 mg/day by mouth, 2 days on and/or 2 days off; and (4) letrozole 2.5 mg by mouth for the first 5 days of the first GnRH-a injection. Danazol, 100 mg/day by mouth, was prescribed as a regimen of 3 months on, 3 months off, for 4 years.

Measurements and Main Results: The first case was a 50-year-old woman, gravida 3, para 3, body mass index (BMI) 27 kg/m^2, with multiple surgeries, including hysterectomy and bilateral salpingo-oophorectomy (HBSO), and history of a stroke. She presented with right-sided pain and hydro-uretero-nephrosis. Magnetic resonance imaging identified a right adnexal cyst (4.5 × 3.4 × 2.4 cm). She was treated with leuprolide acetate monthly injections and a ureteric stent. The cyst, pain, and hydro-uretero-nephrosis resolved after 12 months. The second case was a 45-year-old woman, G_2P_2, BMI 28 kg/m^2 with multiple surgeries, including HBSO. She presented with left-sided pelvic pain. Ultrasound identified a left adnexal cyst and hydronephrosis. After 3 months of leuprolide acetate and add-back therapy, the cyst, pain, and hydronephrosis resolved. The third case was a 46-year-old woman, G_2P_2, BMI 25 kg/m^2, who presented with left flank and pelvic pain. Magnetic resonance imaging indicated moderate left hydronephrosis and left adnexal pelvic side-wall involvement with possible endometriosis. Due to many previous surgeries, this patient was a high-risk surgical candidate, and therefore, she was offered medical therapy. After a normal serum liver and lipid profile, she was started on danazol, 100 mg/day for 3 months. After 3 months of therapy, there was complete resolution of the patient's hydronephrosis and pain. She was then advised to continue with a 3-month on, 3-month off regimen. She discontinued the danazol and remained asymptomatic with no recurrence of hydronephrosis at 3 years.

Conclusions: Low-dose intermittent danazol or GnRH-a alone or with add-back, may be effective long-term therapies in endometriosis-associated ureteral obstruction when surgery is contraindicated, refused, or difficult to perform. Journal of Minimally Invasive Gynecology (2015) 22, 462–468 © 2015 AAGL. All rights reserved.

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Endometriosis is a systemic disease commonly diagnosed in women of childbearing age with an estimated prevalence of 10% to 20%. It affects multiple body organs and systems, and is associated with chronic pelvic pain, reproductive issues, and sometimes with organ obstruction [1].

Women with moderate to severe endometriosis frequently undergo a variety of medical or conservative surgical therapies depending on their age, needs, and wishes, as well as the experience and/or bias of the therapist. However, when all of these therapies fail, many patients undergo definitive treatment in the form of hysterectomy and bilateral salpingo-oophorectomy (HBSO). Frequently in such cases, hysterectomy, by any route and/or method may be quite difficult and challenging due to extensive adhesive disease and scar formation between the uterus, tubes, and ovaries and the adjacent pelvic organs and structures, including the bowel, bladder, and especially, the ureters. Under such circumstances, remnants of ovarian tissue and/or endometriosis implants may be left in situ, attached to ureters or the bowel inadvertently or even deliberately when dissection is deemed to be difficult or dangerous.

There is ample evidence that residual ovarian tissue can remain viable and functional despite previous transection of its blood supply and removal of the ovaries, because remnants of the ovarian cortex can become neovascularized by the adjacent peritoneum or viscera. Patients with ovarian remnants usually present with signs and symptoms, which are referred to as ovarian remnant syndrome (ORS), up to 3 years after oophorectomy. These patients typically present with pelvic pain, which may or may not be associated with an apparent mass during pelvic examination or diagnostic imaging. In a large cohort study of 186 women surgically managed for ORS, the most common preoperative complaints were constant, chronic pelvic pain (84%), dyspareunia (26%), cyclic pelvic pain (9%), dysuria (7%), and pain with defecation (6%) [2]. On occasion, ovarian remnants may also cause extrinsic ureteric obstruction and hydro-uretero-nephrosis, giving rise to flank and/or back pain [3–5].

Although several authors have reported case series on surgical excision of ovarian remnants through laparoscopy or laparotomy [2,6–8], surgical removal may be contraindicated, risky, or difficult to undertake. Under such circumstances, alternative treatments, including medical suppression [2,9] or radiotherapy [10,11], have been used with varying degrees of success.

Ureteral endometriosis is typically unilateral (it more commonly occurs on the left side) [12], usually involves the lower one-third of the ureteric tract (due to its proximity to the uterosacral ligaments) [13], and is most frequently associated with endometriosis elsewhere in the pelvis [14]. It is thought that the main mechanism that leads to ureteral endometriosis is extension through contiguity from pelvic endometriosis [15–17]. In a group of women with pelvic endometriosis, routine urinary ultrasonography identified associated uterohydronephrosis in 23.3% of women, 56.5% of whom were asymptomatic [18].

Specific symptoms include cyclical hematuria [19], bilateral and/or unilateral ureteric obstruction that may be cyclical, hypertension, and anuria in the presence of a solitary kidney [16,20–25]. Urinary frequency, urgency, and back pain have also been reported [26]. The condition can at times be asymptomatic, leading to silent obstructive uropathy and renal failure, which is a significant concern [27].

Treating endometriosis and ureteric endometriosis can be a challenge because surgery to alleviate endometriosis-associated pain has yet to be shown to be effective and to have durable long-term outcomes. In adolescents, there are no published data on the outcomes of surgical therapy for endometriosis-associated pain [28]. In adult women, reports on pain recurrence following laparoscopic therapy for endometriosis are high, ranging from 30% to 74%, with a median time of 20 months [29–34].

Surgical treatment for ureteric endometriosis can be even more challenging and is not without risk. One study reported on performing various ureteric laparoscopic surgeries on 56 patients with preoperative or intraoperative moderate-to-severe ureteric dilatation. The authors reported a major complication in 13 (23%) patients [1]. In contrast, medical therapies can be very effective in alleviating pain, but their use is sometimes limited due to patient intolerability and adverse systemic effects.

In the present study, we report our experience in 3 women with endometriosis who presented with chronic pelvic pain and moderate to severe hydro-uretero-nephrosis. Two women had HBSO and presented with ORS, and 1 had ureteral endometriosis. All signs and symptoms, including the obstructive uropathy, resolved completely after medical treatment and remained asymptomatic 4 to 5 years later.