Nobel medical management of primary bladder endometriosis with dienogest: a case report

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Summary

Background: Because of its low incidence, medical treatment of has not yet been well established although surgical excision is generally considered effective. We report the first case of primary bladder endometriosis successfully managed with a novel progestin dienogest. *Case:* A 39-year-old woman, nulligravida, presented with lower urinary tract symptoms, especially during menstruation. Cystoscopy, with subsequent cold cup biopsy, revealed a solitary submucosal mass (2 x 2 cm) in the bladder on the posterior wall; histopathology revealed the diagnosis of extraperitoneal endometriosis. MRI and laparoscopy confirmed no peritoneal endometriosis implants or adenomyosis. She was treated with oral 2 mg/day dienogest for six months. The measurable lesion exhibited a remarkable reduction in its size, accompanied with immediate relief of the lesion-related symptoms. At one year after medication cessation, she is well and symptom-free. *Conclusion:* Dienogest may be a novel conservative alternative for bladder endometriosis, in particular for women who wish to avoid surgical intervention.

Key words: Bladder endometriosis; Dienogest; Medical treatment; Extraperitoneal endometriosis; Adenomyosis.

Introduction

Although endometriosis is frequently encountered in women of reproductive age, urological endometriosis as the primary and sole form of presentation is very rare and the most common site of involvement is the urinary bladder, representing < 1% of all endometriosis cases [1, 2]. It may be aggressive in terms of ingrowth and fibrosis of the ureter, periureteral structures and bladder leading gradually to nephrologic complications. Therefore, timely diagnosis to prevent irreversible deterioration in renal function is essential. Its standard management has not yet been well established because of its relatively low incidence. Medical (conservative) therapy has proved effective in relieving symptoms, but the quick recurrence of irritative urinary symptoms after cessation of therapy indicates that surgery may be required. In the literature so far, partial cystectomy (or segmental bladder resection) has been considered as the treatment of choice [3-5].

Dienogest is a selective progestin that combines the pharmacologic properties of 19-norprogestins and progesterone derivatives, offering potent progestogenic effects without androgenic, mineral corticoid, or glucocorticoid activity [6-8]. Previous trials demonstrated that dienogest provides effective reduction in endometriosis-associated pelvic pain and laparoscopic measures of pathology [9-12]. In this paper, we report our successful experience with medical management of bladder endometriosis using dienogest.

Case Report

A 39-year-old woman, gravida 0, presented with pelvic discomfort, urinary urgency and frequency related to the menstrual cycle. Pelvic ultrasound showed an irregular 2 cm in size mass in the region of the bladder trigone. Hematuria was absent and CA 125 was 53.2 U/ml. Magnetic resonance imaging (MRI) showed a single nodule (2 x 2 cm) protruding in the backside of the bladder (Figure1a). The rectovaginal septum was not involved, and the uterus and bilateral ovaries were normal. To eliminate bladder malignancy, an examination under general anesthesia was scheduled. At cystoscopy, the protruding lesion was seen in the top of the bladder covered with normal bladder epithelium and well away from the ureters. At laparoscopy, there were no peritoneal endometriosis implants, and the ovaries were normal. Cystoscopic biopsy examination showed areas of active endometriosis within the submucosa and smooth muscle bundles of the bladder wall.

The patient was submitted to the therapy with dienogest (2 mg/day, Mochida Pharmaceutical, Japan) for six months in our clinic. She observed significant relief from the symptoms related with bladder endometriosis after two weeks of administration of this drug and on MRI the nodule shrunk to only one fifth of its pretreatment volume after six months (Figure 1b). Throughout one year after medication cessation, she had complete resolution of her bladder symptoms and cyclic discomfort.

Discussion

In the literature, two distinct forms of bladder endometriosis appear to exist: one is found in women without any medical history of uterine surgery (primary), and the other develops after cesarean section (iatrogenic or secondary) [3, 13]. In this paper, we report a case of primary bladder endometriosis in which the measurable bladder lesion exhibited a reduction in its size, accompanied with immediate relief of related symptoms.

Several investigators have suggested that extraperitoneal endometriosis derives from endoperitoneal disease [14, 15]. In their opinion, peritoneal lesions are able to penetrate under the peritoneum and develop into deeply infiltrating endometriosis. If this were the case, we would have found peritoneal endometriosis in our patient. Donnez *et al.* [3] analyzed data of the anatomic and pathologic characteristics from a series of 17 cases of

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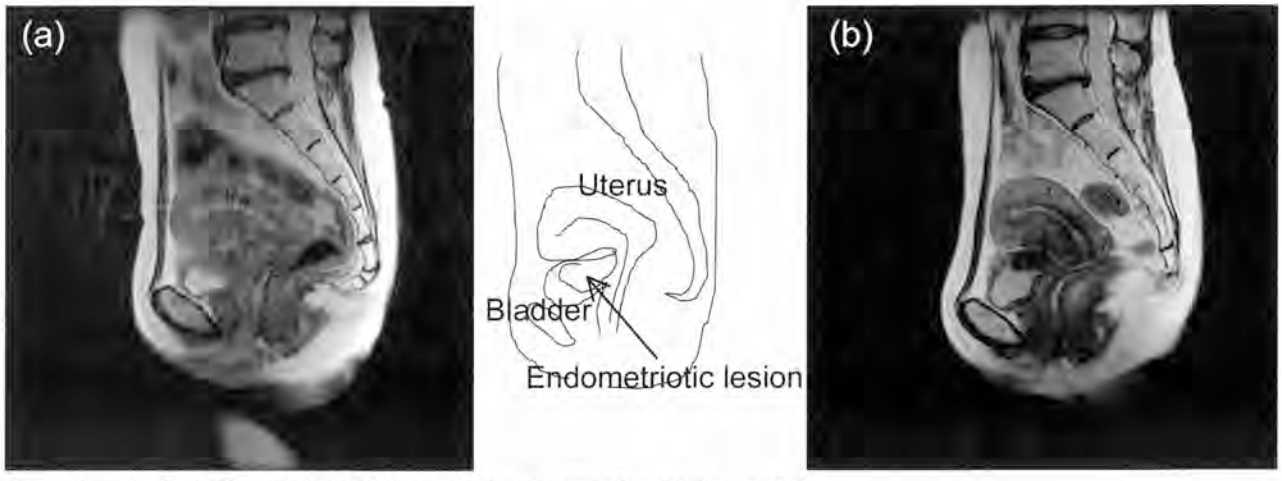

Figure 1. — Sagittal T2-weighted MR images before (a) and after (b) dienogest therapy.

bladder endometriosis. So-called primary bladder endometriosis must be considered as a retroperitoneal adenomyotic nodule, which is the consequence of metaplasia of müllerian rests [3]. Adenomyosis refers to a disorder in which endometrial glands and stroma are present within the uterine myometrium. The ectopic endometrial tissue appears to induce hypertrophy and hyperplasia of the surrounding myometrium, which results in a diffusely enlarged uterus. Medical treatment of adenomyosis with progestogen has been shown to provide symptomatic relief up to some years and may offer an alternative to surgery, when compared to endometriosis [16]. Taken our experience on bladder endometriosis, consideration of "bladder endometriosis as bladder adenomyosis" may suggest that dienagest can be a novel conservative alternative for bladder endometriosis.

To the best of our knowledge, this is the first report describing primary bladder endometriosis successfully managed with a progestine dienogest. The follow-up period of our study might be too short to consider the recurrence rate of bladder endometriosis after discontinuation of treatment. However, the efficacy and safety of long-term usage of dienogest have been demonstrated in previous controlled studies in a large number of patients with endometriosis [9-12]. More recently, Harada *et al.* [17] described four cases with rectosigmoidal and one with bladder endometriosis treated with 2 mg/day dienogest for 10-11 months. Dienogest may be a novel conservative alternative for primary bladder endometriosis, in particular for women who wish to avoid surgical intervention.

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