

Long-term personalized GnRH agonist therapy without estrogen supplementation for recurrent endometriotic catamenial pneumothorax - case report

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Summary

A patient with diaphragmatic endometriosis who showed immediate relapse following radical thoracoscopic surgery received personalized GnRH agonist (GnRHa) therapy. GnRHa depots were subcutaneously injected by modulating injection intervals according to serum estradiol and LH levels in order to maintain long-term amenorrhea without any adverse effects. A leuprolide acetate depot was injected 24 times for 34 months. Therefore, so far, 1.88 mg of leuprolide acetate depot have been injected every seven weeks to achieve a stable endocrine condition with 15-30 pg/ml serum estradiol, 3-10 IU/l serum LH, and 7-15 IU/l serum FSH.

Key words: Endometriosis; GnRH agonist; Leuprolide acetate; Endometriosis; Catamenial pneumothorax.

Introduction

Anti-endometriotic therapy must be determined for each patient according to severity of signs and symptoms, wish for pregnancy, and localization of endometriotic lesions. Although surgical and medicinal therapies for intraperitoneal endometriosis are almost established, there is still no standard therapeutic protocol for extraperitoneal endometriosis. Extraperitoneal endometriosis may result in severe and lethal symptoms. Severe catamenial pneumothorax complicated with diaphragmatic and pleural endometriosis is frequently involved in relapses after surgery or hormonal therapy [1]. Recently, oral contraceptives (OCs) have been commonly applied to patients with catamenial pneumothorax. However, OCs are not applicable to severe emergent cases that need rapid therapeutic effects for endometriosis, because effects of OCs may occur a few months after the beginning of therapy. While gonadotropin-releasing hormone agonist (GnRHa) therapy can certainly induce complete remission within a short time, any usual protocols with 6-month GnRHa therapy for endometriosis can result in relapse in almost all treated patients. However, if GnRHa depots are injected monthly for a prolonged time, patients will develop severe menopausal malaises due to estrogen deprivation, and will need estrogen supplementation [2, 3]. We show here a severe case of postoperative recurrent catamenial pneumothorax associated with diaphragmatic endometriosis that was completely treated with personalized GnRHa therapy for three years without any adverse effects.

Case Report

The patient presented to the gynecology department of our university hospital complaining of increasing catamenial pneumothorax every month for a duration of three years, and of post-surgical relapse of pneumothorax. She had two children, was 42 years old, 161-cm tall and weighed 51 kg. She also had a past history of two laparotomic surgeries for abdominal endometriosis when she was 27 and 28 years old. She complained of 10-day chest pains with dyspnea at every menstruation for the last three years. Two months before she underwent radical thoracoscopic surgery, and was histopathologically diagnosed with diaphragmatic endometriosis (Figure 1). However, immediately after the surgery, the right pneumothorax relapsed in the second postoperative menstruation. She visited our gynecology outpatient clinic to cure her catamenial pneumothorax radically.

When she first came to our gynecology clinic, pelvic examinations and a transvaginal ultrasound study did not show any abnormal findings in her pelvic cavity. No signs suggesting pelvic endometriosis or adenomyosis were detected. A chest X-ray study during menstruation showed recurrence of severe right pneumothorax immediately after surgery (Figure 2). In order to achieve complete remission as soon as possible, personalized GnRHa therapy was started at once. According to her endocrinological condition, 1.88 mg or 3.75 mg leuprolide acetate (LA) depots were injected subcutaneously every three to eight weeks to maintain 20-40 pg/ml serum estradiol. So far, the patient has been injected with LA depots 24 times for 34 months (Figure 3). The personalized LA therapy did not induce any menopausal malaise requiring estrogen replacement therapy. The patient has been without any pneumothorax for 34 months. At present, she is undergoing injections with 1.88 mg LA about every seven weeks to stably achieve 15-20 pg/ml serum estradiol, 3-10 IU/l serum LH, and 7-15 IU/l serum FSH. While we proposed that she change from LA therapy to OC therapy, the patient refused and wishes to continue personalized GnRHa therapy.

Discussion

Although solitary intraperitoneal endometriotic lesions might be radically cured by surgery, medicinal therapy

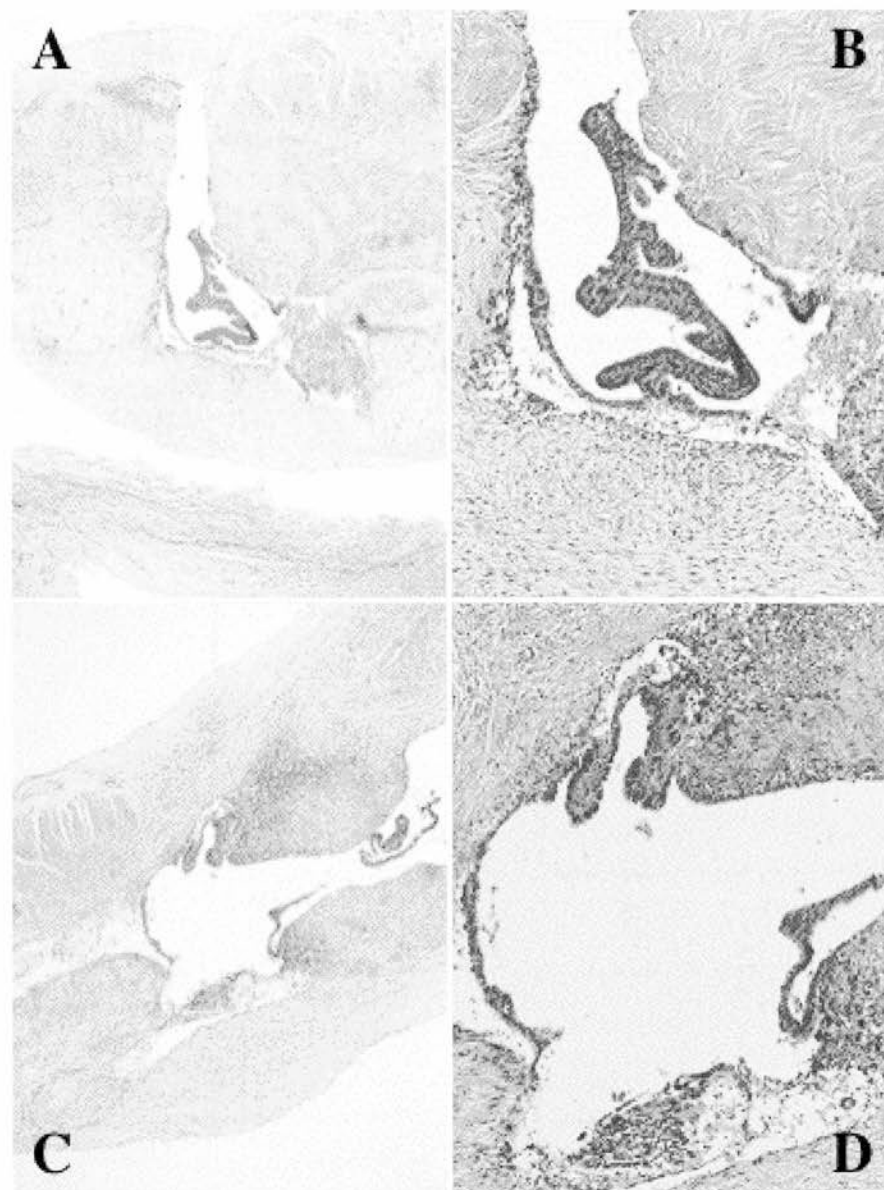


Figure 1. — Histopathological findings of diaphragmatic lesions. B and D show magnified views (x100) of A and C (x 60), respectively. Endometrium-like epithelium on stromal cells, and fresh intradiaphragmatic hemorrhage were found.

but not surgical therapy is theoretically the first choice for radical antiendometriotic therapy because most endometriotic patients have multiple lesions. Established anti-endometriotic medicines include OCs [4], danazol [5-7], GnRHa [8-13], and herbal medicines [14, 15]. For severe extraperitoneal endometriosis patients who cannot be cured radically by surgery, the best medicinal therapy must be a long-acting, safe, and curative treatment that can reduce endometriotic lesions for a prolonged time. Herbal medicines cannot be administered to such patients because effects of herbal medicines may have late onset [14, 15]. Although danazol therapy has been reported to have some effects on endometriotic pneumothorax [5-7], it is not applicable to such severe extrauterine endometriotic

patients because danazol is a slow-acting medicine with a high frequency of severe adverse effects. Today, OCs are the first choice drugs for remission-maintenance therapy after remission-induction, because OCs are very safe with few adverse effects [4]. However, for severe endometriotic patients such as our present case, OC therapy may be too slow-acting to rapidly induce complete remission.

We decided on treatment for the present case based on the following. The patient's extraperitoneal endometriotic lesions could not be radically cured by surgery because pneumothorax recurred immediately after surgery. Her pneumothorax could have had lethal complications at any time. Since the patient was 42 years old, she would have

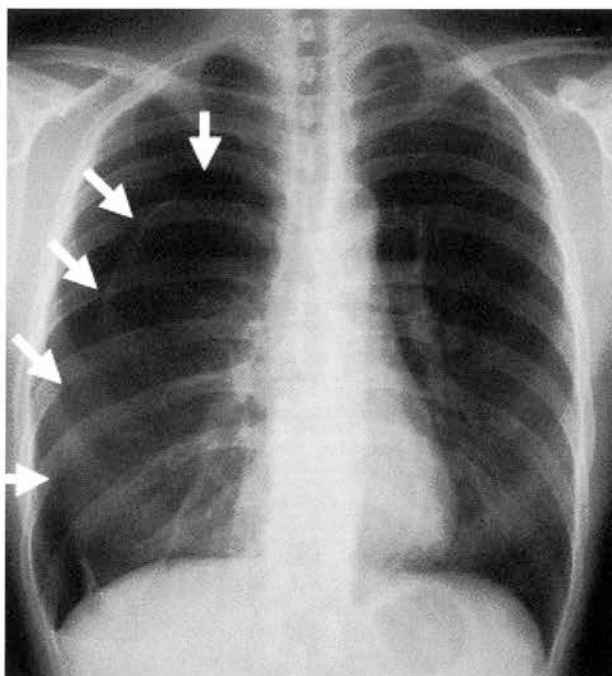


Figure 2. — Recurrent pneumothorax after thoracoscopic surgery. Arrows indicate margins of the right lung.

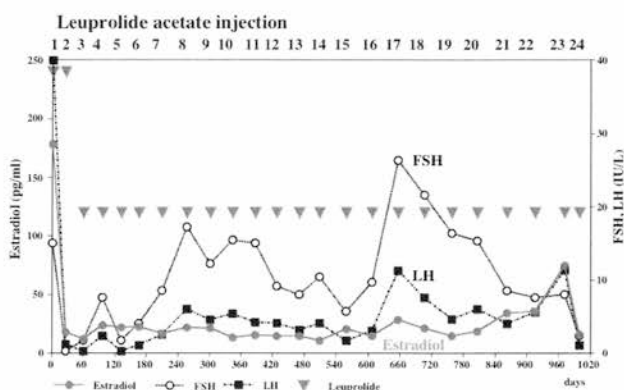


Figure 3. — Personalized GnRH therapy and endocrinological changes. The closed triangles indicate leuprolide acetate injections. The closed circles indicate serum estradiol levels. The closed squares indicate serum LH levels. The open circles represent serum FSH levels.

had to wait for about ten years until spontaneous menopause. Since pneumothorax had been appearing every month for the previous three years, she had to be treated with a precise and rapidly effective therapy. Her thyroid function was within normal limits, thus GnRHa therapy was considered to be the treatment of choice for endometriosis [16]. Since endometriotic pneumothorax often occurs after general therapies with OCs or GnRHa, long-term GnRHa therapy was performed in the present case. Although there are many reports on GnRHa therapy for catamenial pneumothorax, usual GnRHa therapies have been reported to require estrogen supplementation therapy or oriental medicines with herbal medicines to

rescue menopausal malaise [17]. Therefore, to avoid any adverse effects with long-term GnRHa therapy, we performed personalized GnRHa therapy that can be regulated according to serum LH and estradiol levels of each patient. Personalized GnRHa therapy is thought to be a safe and long-acting therapy to efficiently inhibit menstruation completely, and radically cure endometriotic lesions. As shown in the present case, personalized GnRHa therapy should become the first-choice therapy for severe extraperitoneal endometriosis.

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