Case Reports

Complete remission of OC-resistant catamenial shoulder joint pain and inguinal pain associated with extraperitoneal endometriosis following personalized GnRH agonist therapy

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Summary

Background: Patients with severe extraperitoneal endometriosis require rapid remission and cannot wait for the effects of oral contraceptive hormones (OCs) to appear. *Case:* We successfully achieved personalized gonadotropin-releasing hormone agonist (GnRHa) therapy for a patient with catamenial right shoulder joint pain and right inguinal pain associated with extraperitoneal endometriosis, which was completely unable to be suppressed by OCs. A total of 15 subcutaneous GnRHa depot injections over a period of 19 months was performed according to the serum estradiol and LH levels, in order to maintain long-term amenorrhea without any estrogen-deprivation effects. No recurrence of the catamenial symptoms has been observed for more than 35 months after the final GnRHa depot injection. *Conclusion:* Personalized GnRHa therapy should become the first-choice therapy for OC-resistant inoperable extraperitoneal endometriosis.

Key words: Endometriosis; GnRH agonist; Leuprolide acetate; Oral contraceptive; Shoulder joint pain.

Introduction

Anti-endometriosis therapy must be determined for each individual patient according to the severity of their signs and symptoms, desire to become pregnant, and localization and size of the endometriotic lesions. There are still no standard therapeutic protocols for extraperitoneal endometriosis, despite the fact that surgical and medicinal therapies for intraperitoneal endometriosis are almost established. Extraperitoneal endometriosis often results in severe and lethal symptoms [1]. Recently, oral contraceptives (OCs) have been commonly applied to patients with extraperitoneal endometriosis. However, OCs are not applicable for severe and emergency cases of endometriosis that require rapid therapeutic effects, since their effects may occur several months after the initiation of the therapy. Gonadotropin-releasing hormone agonist (GnRHa) therapy can certainly induce complete remission within a short time. However, if GnRHa depots are injected every month over a prolonged period of time, the patients develop severe menopausal malaises due to estrogen deprivation and require estrogen supplementation [2, 3]. Here, we describe a very rare case of catamenial shoulder joint pain and inguinal pain complicated with inguinal endometriosis that was successfully and completely treated by personalized GnRHa therapy without any estrogen-deprivation effects, rather than by OC therapy.

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Case Report

The patient visited the gynecology outpatient clinic of our university hospital complaining of a right inguinal mass with increasing catamenial right inguinal pain every month for the previous six months. She was a 47-year-old multiparous woman with dysmenorrhea and hypermenorrhea due to pelvic endometriosis and adenomyosis. She had a past history of two cycles of 6-month GnRHa depot therapy for abdominal endometriosis when she was 40 and 42 years of age, respectively. She was initially treated with three cycles of OCs, but the catamenial inguinal pain remained unrelieved. Histopathological examination of a surgically resected inguinal nodule confirmed that the right inguinal pain was due to inguinal endometriosis (Figure 1). After the surgical resection, the patient received a further three cycles of OCs. Although her dysmenorrhea and hypermenorrhea were completely suppressed by the OC therapy, the right inguinal pain remained. Moreover, right shoulder joint pain appeared and increased with every menstruation, despite the OC treatment (Figure 2). Since OCs did not show any suppression of the catamenial shoulder joint pain or inguinal pain, personalized GnRHa therapy was carried out. After initial administration of two 3.75-mg leuprolide acetate depots to the patient with a 4-week interval in order to avoid flare-up phenomena, 1.8-mg GnRHa depots (leuprolide acetate or goserelin acetate) were injected subcutaneously at five to seven week intervals. The inter-injection intervals were modulated to achieve stable endocrine conditions with 15-50 pg/ml serum estradiol and 0-5 IU/l serum LH, in order to maintain stable long-term amenorrhea without any estrogen-deprivation effects. Three months after the final depot injection (15th injection), regular menstruation reappeared, but no catamenial shoulder pain, inguinal pain or dysmenorrhea have been observed for over 35 months (Figure 2). From 11.3 pg/ml serum estradiol and 84.33 IU/l serum FSH levels, a diagnosis of spontaneous menopause was made ten months after the last GnRHa injection.

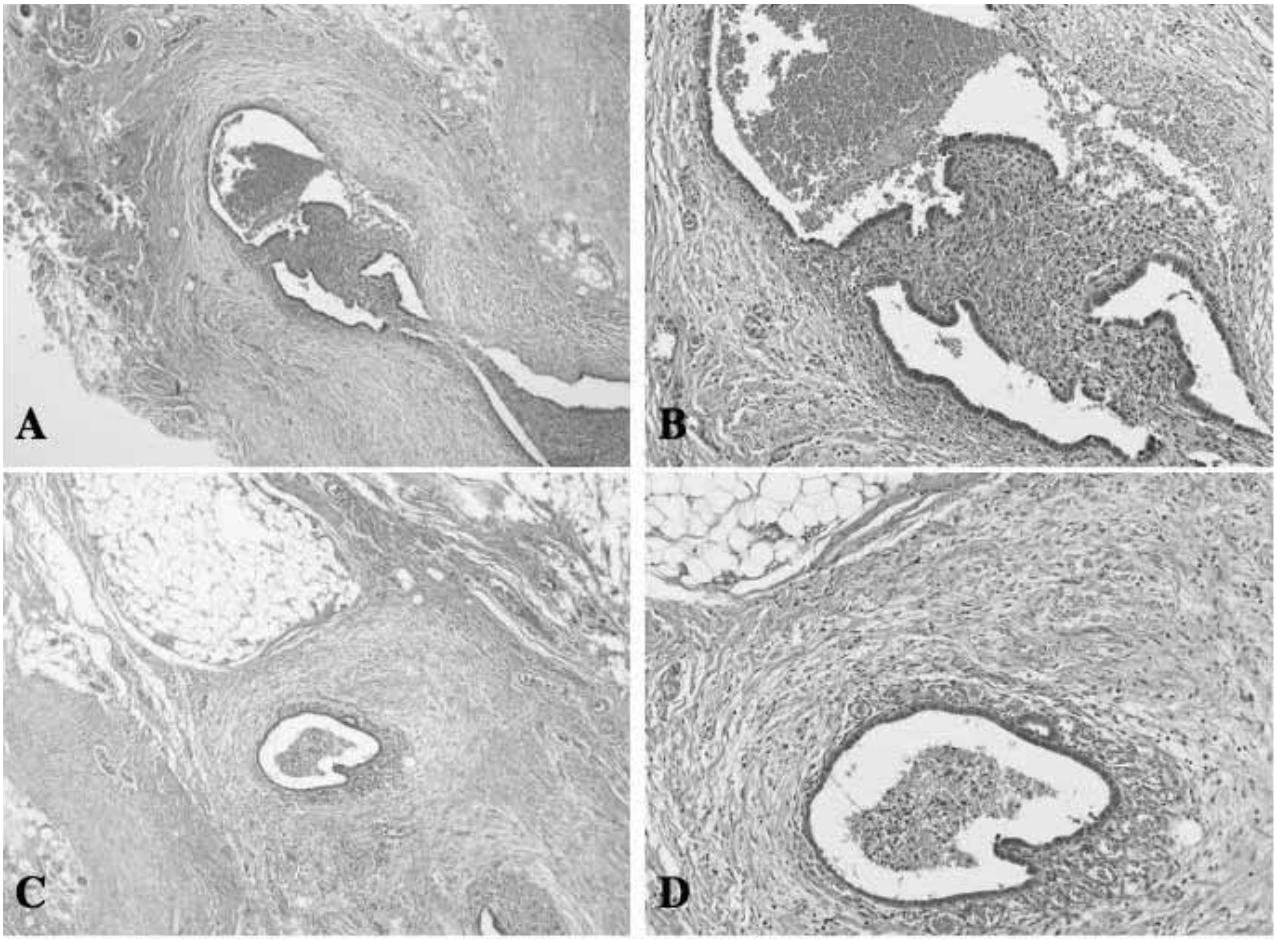

Figure 1. — Histological findings of the resected inguinal lesions.
Inguinal nodule containing typical endometriotic lesions in the subcutaneous tissue. Endometrium-like epithelium on stromal cells with hemorrhage is present in the inguinal subcutaneous tissue (A, B). Endometriotic lesions invading the subcutaneous adipose tissue (C, D). B and D show magnified views (x100) of A and C (x60), respectively.

Discussion

The present case may represent the first report of possible endometriosis in a shoulder joint. Although the catamenial shoulder joint pain could not be examined histopathologically since no superficial tumorous lesions were detected around the joint, this shoulder joint pain was considered to be one symptom associated with endometriosis for the following reasons: the inguinal lesion was histopathologically proven to be extraperitoneal endometriosis as shown in Figure 1; the shoulder joint pain appeared simultaneously with inguinal pain due to endometriosis only during menstruation; the shoulder joint pain was only observed in the menstrual period; during the amenorrhea period induced by the GnRHa therapy, the patient had neither inguinal pain nor shoulder joint pain. Although several previous papers have reported that catamenial shoulder tip pain associated with endometriotic pneumothorax can be cured after treatment of diaphragmatic endometriosis [4-6], endometriotic pneumothorax was excluded in the present case because the patient had never complained of chest pain or dyspnea and a chest X-ray examination did not show any signs of pneumothorax.

Although solitary intraperitoneal endometriotic lesions may be radically cured by surgery, medicinal therapy, rather than surgical therapy, is theoretically the first choice for radical therapy of endometriosis, since most endometriotic patients have multiple lesions. For patients with severe extraperitoneal endometriosis who cannot be cured radically by surgery, the best medicinal therapy must be a long-acting, safe and curative treatment that can reduce the endometriotic lesions for a prolonged period of time. Therefore, OCs are currently the first-choice drugs for remission-maintenance therapy after remission-induction, since they are very safe medicines with few adverse effects [7]. However, for patients with severe inoperable endometriosis, such as our present case, OC therapy is too slow-acting for the required rapid induction of complete remission. In fact, several cycles of OC therapy induced complete remission of the dysmenorrhea in the present case, but had no effects on her catamenial

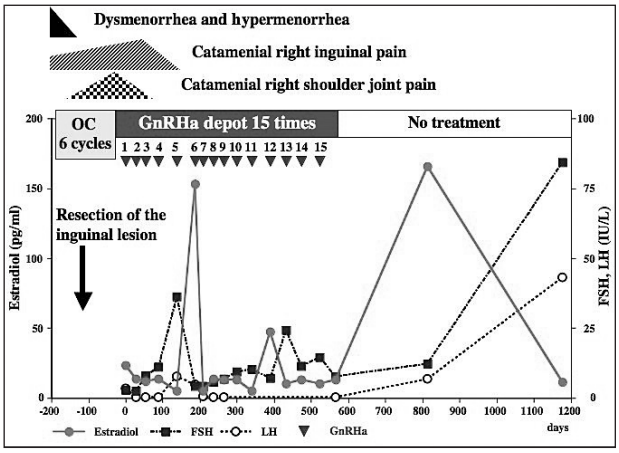

Figure 2. — Personalized GnRHa therapy and catamenial symptoms.
Closed triangles: GnRHa depot injections; closed circles: serum estradiol levels; closed squares: serum FSH levels; open circles: serum LH levels. During the OC therapy, the catamenial lower abdominal pain and hypermenorrhea were completely suppressed. However, the catamenial shoulder joint pain and inguinal pain were only suppressed by the GnRHa therapy.

right shoulder joint pain or right inguinal pain. Therefore, in order to avoid any adverse effects associated with long-term GnRHa therapy, we performed personalized GnRHa therapy that was regulated according to the serum LH and estradiol levels of the patient. Personalized GnRHa therapy is considered to be a safe and long-acting therapy that can efficiently and completely inhibit menstruation, and radically cure endometriotic lesions. At the present time, there has been no recurrence of the catamenial shoulder joint pain or inguinal pain for 35 months since the cessation of the personalized GnRHa therapy, indicating that the patient's extrauterine endometriotic lesions may have been almost radically suppressed by GnRHa therapy. The results for the present case suggest that personalized GnRHa therapy should become the first-choice therapy for OC-resistant inoperable extraperitoneal endometriosis.

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