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Severe endometriosis treated with long-term GnRHa : case report

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Abstract

Gonadotrophin-releasing hormone agonist (GnRHa) therapy for endometriosis is rarely used for long periods of time because it leads to decreased bone density and menopausal syndrome. Here, we describe a patient with severe endometriosis who underwent a colostomy and hysterectomy at a young age and has been on GnRHa therapy for 13 years since the surgery.

The patient is a 37-year-old G0P0 woman who underwent a colostomy for ileus of the sigmoid colon and rectal endometriosis at the age of 21 years. At the age of 22 years, she underwent total abdominal hysterectomy, chocolate cystectomy, and partial rectectomy. After the surgery, her ovarian endometrioma recurred and ureteral endometriosis developed. She was then started on GnRHa therapy and has been on continuous therapy for 13 years up to the present. Side effects as such as decreased bone mineral density and menopausal syndrome have not been observed. Although GnRHa therapy is generally not used chronically because of its side effects, it has been possible to use it in this patient over a long period of time by ongoing monitoring for the development of deleterious side effects and adjusting the dose as needed.

Key words : endometriosis, ovarian cyst, gonadotropin-releasing hormone

Introduction

Endometriosis is characterized by the presence of endometrium-like lesions outside the uterine cavity. This condition is an estrogen-dependent disease that occurs in 10% of women of reproductive age and regresses after the menopause or ovariectomy. The main symptoms are pelvic pain, including dysmenorrhea, chronic pelvic pain and deep dyspareunia and infertility.

In gynecological practice, gonadotropin-releasing hormone agonist (GnRHa) therapy is often used for endometriosis. Continuous administration of GnRHa leads to downregulation of the expression of GnRH receptors and the consequent suppression of luteinizing hormone and follicle-stimulating hormone secretion. The result is a state of low estrogen, so that GnRHa therapy is called pseudo-menopausal therapy. The efficacy of GnRHa therapy against the pain of endometriosis and ovarian endometrioma has been reported,[1] but because long-term GnRHa therapy may lead to decreased bone mineral density and menopausal syndrome, it is not used for chronic therapy.[2,3] There have been recent reports on therapies to reduce the adverse side effects of GnRHa while maintaining its therapeutic efficacy, such as "add-back" therapy, which administers small doses of estrogen-progestin, and "draw-back therapy", which administers GnRHa at longer intervals.[4,5] To the best of our knowledge, although there are reports of the long-term use of GnRHa using these methods, there is no published report on the use of GnRHa therapy for 10 years or longer without using these methods.

In this report, we describe a patient with severe endometriosis who needed a colostomy and

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hysterectomy in early adulthood, and who has been receiving GnRHa therapy for 13 years for ureteral endometriosis, ovarian endometrioma, and repeated exacerbations of endometriosis after her surgery.

Case

The patient is a 37-year-old G0P0 woman, 150 cm tall, weighing 50 kg (body mass index 22.2 g/m^2) with a history of acute lymphatic leukemia at the age of 5 years that was cured with chemotherapy, and no history of endocrine disease or significant family history.

At the age of 21 years, she underwent a colostomy for ileus of the sigmoid colon in the Department of Surgery of another hospital. A biopsy was diagnosed as rectal endometriosis and she underwent a laparotomy, which became exploratory because of findings of severe adhesions. Postoperatively, the patient continued to have severe menstrual pain and developed an ovarian endometrioma.

At the age of 22 years, she was diagnosed in the Gynecology/Obstetrics Department of another hospital with refractory endometriosis and underwent abdominal hysterectomy, chocolate cystectomy, partial rectectomy, and rectal end-to-end anastomosis. Three months later, a 6 cm right ovarian endometrioma recurred, and her CA125 level increased to 280 U/ml. The patient also developed bilateral hydronephrosis, which was diagnosed as ureteral endometriosis. A left percutaneous nephrostomy was performed, and a double-J catheter was placed in the right ureter.

At the age of 23 years, the patient was begun on nafarelin acetate at 400 μg/day. The CA125 level decreased to 50 U/ml and the ovarian endometrioma remained stable. When nafarelin acetate administration was stopped 6 months later, the CA125 increased to over 1,000 U/ml and the endometrioma enlarged to 10 cm. Nafarelin acetate was restarted at 200 μg/day. Since then, she has been free of pelvic pain and the ovarian endometrioma has decreased to 3 cm. Annual bone density measurements have not shown decreases in bone mineral content. The patient's left ureterocutaneous fistula was closed after her left hydroneprhosis improved.

The patient was first seen by us at the age of 30 years. Ultrasonography revealed a 3 cm endometrioma of the right ovary. Her CA125 was 21 U/ml, and estradiol was 18 pg/ml. A double-J catheter remained in the right ureter. The bone mineral content measured at the distal radius was 0.743 g and bone mineral density was 0.672 g/cm2, which is 100% of the young adult mean value (YAM). She was continued on nafarelin acetate at 200 μg/day.

The patient is now is 37 years old and has been on nafarelin acetate for 13 consecutive years since it was first prescribed at another hospital. Her CA125 is stable, ranging from 10 to 50 U/ml. Her right ovarian endometrioma is unchanged at 3 cm, and she has a double-J catheter in the right ureter. Annual bone density measurements are normal. At present she is not receiving prophylaxis for osteoporosis such as active vitamin D and bisphosphonates. The patient has a normal social life free of menopausal syndrome. Her most recent laboratory values include CA125, 14 U/ml ; estradiol, 20 pg/ml ; bone mineral content, 0.75 g ; and bone mineral density, 0.67 g/cm^2 (100% YAM) (Table 1).

Table 1 Results of annual blood and bone density tests.

Age (Years)	21	22		23		24
CA125 (U/ml)	46	280		50		1000 ↑
Treatment	Colostomy	Hysterectomy		Nafarelin acetate 400 μg/day		

Age (Years)	24	30	31	32	35	36	37
CA125 (U/ml)		52	21	31	20	12	14
Estradiol (pg/ml)		18	22	24	20	24	20
Bone mineral density (g/cm^2)		0.672	0.673	0.672	0.673	0.672	0.673
Treatment	Nafarelin acetate 400 μg/day						

Discussion

Endometriosis is a common disorder that is often encountered in daily practice. Rarely, in severe cases, it occurs outside the pelvic cavity and causes ureteral endometriosis and intestinal endometriosis. Some of these cases require ureterectomy or enterectomy.[6,7] Our patient underwent a primary colostomy because of intestinal endometriosis in the sigmoid colon and rectum that had developed in her youth. Despite her nulliparity, a hysterectomy was performed because of severe dysmenorrhea. She subsequently developed ureteral endometriosis, and underwent cutaneous nephrostomy with insertion of a double-J catheter. Such severe exacerbation of difficult-to-treat endometriosis is very rare.

After the recurrence of ovarian endometrioma concurrent with ureteral endometriosis, GnRHa therapy with 400 μg naferelin acetate nasal solution daily, was begun. Because of potential adverse effects, including decreased bone mineral density, hyperlipidemia, and menopausal syndrome, GnRHa therapy is generally not used for longer than 6 months. Bone density in the lumbar spine has been reported to be reduced by 6. 14% after a 6-month administration of nafarelin acetate at 400 μg/day.[3] When GnRHa therapy was stopped after 6 months, our patient's endometriosis worsened. In contrast to the "add-back" and "draw-back" GnRHa therapies to reduce side effects,[4,5,8] our patient then received continuous administration of nafarelin acetate at 200 μg/day, and was then followed carefully with regard to clinical symptoms, bone density, CA125 and estradiol blood levels. Neither menopausal syndrome nor bone mineral loss have been observed, her endometrioma and CA125 values have remained stable, and her hydronephrosis has improved. We believe that the adverse effects were reduced because she received 200 μg/day of nafarelin acetate, which is 50% of the normal dose. However, bone mineral density measured at the radius may be less effective for evaluation than densitometry of the lumbar spine.

CA 125 is a glycoprotein cell surface antigen that is commonly used as a tumor marker to assist in the diagnosis, prognosis, and evaluation of treatment of tumors including ovarian cancer. The CA 125 value may also be useful as a prognostic indicator for treated endometriosis because highly specific cyclic elevations in CA 125 are found in patients with moderate to severe endometriosis.[9] Thus, in the case presented here, a stable CA 125 level indicates that endometrial proliferation remains adequately suppressed with the current dose of nafarelin acetate.

In conclusion, our patient has received continuous GnRHa therapy for 13 years, which to the best of our knowledge, is the longest administration of GnRHa. We believe that GnRHa therapy can be administered on a chronic basis if patients are followed for the occurrence of potential side effects such as bone mineral loss.

The Patient was informed that data concerning the case would be submitted for publication, and they provided their consent.

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