

# A Severe Case of Recurrent External Endometriosis in An Ovariectomized Young Woman

Mykhailo VM<sup>1\*</sup>, Marina YE<sup>2</sup>, Ioannis PK<sup>3</sup>, Antonio M<sup>4</sup>, Andrea T<sup>5</sup> and Ospan AM<sup>6</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, Dnipropetrovsk Medical Academy of Health Ministry of Ukraine, Dnepropetrovsk, Ukraine

<sup>2</sup>Department of Obstetrics, Gynecology and Reproductive Medicine, Peoples' Friendship University of Russia, Moscow, Russia

<sup>3</sup>Xatzikosta General Hospital, Ioannina, Ioannina, Greece Laboratory of Pilot projects, Greece

<sup>4</sup>Department of Obstetrics and Gynecology, Santa Maria Hospital, Bari, Italy

<sup>5</sup>Department of Obstetrics and Gynecology, Division of Experimental Endoscopic Surgery, Imaging, Minimally Invasive Therapy and Technology, Vito Fazzi Hospital, Piazza Muratore, Lecce, Italy

<sup>6</sup>The International Translational Medicine and Biomodeling Research, Department of Applied Mathematics, Moscow Institute of Physics and Technology (State University), Dolgoprudny, Moscow, Russi

## Abstract

This is a case of a 35-year-old ovariectomized woman with recurrent external endometriosis. During 15 years she has undergone 3 laparotomies, excisions of 159 recurrent abdominal wall endometriotic lesions and 12 vulvar, bilateral labia majora and pubis endometriotic lesions. Letrozole (7.5 mg/daily) treatment provided some relief of acute pain.

**Keywords:** Recurrent external endometriosis; Repeated surgical procedures; Ovariectomized young woman; Aromatase inhibitor; Letrozole treatment

## Introduction

Endometriosis is the growth of layers of tissues outside the uterus which is normally present inside the uterus. Mostly it occurs on the ovaries, fallopian tubes, and tissue around the uterus and ovaries. This is a case of a 35-year-old ovariectomized woman with recurrent external endometriosis. This is the first case of extremely aggressive external endometriosis occurring in a reproductive-age.

## Case Report

This is the case of a 35-year-old G1P1 with severe, recurrent endometriosis. 17 years ago she had initial abdominal surgery in which a right oophorectomy was performed due to a ruptured right ovarian cyst. Since then, she has undergone three abdominal surgeries for bilateral endometriomas and adenomyosis with a total hysterectomy, bilateral salpingo-oophorectomy and adhesiolysis. Between 2002 and 2007 her weight soared from 60 to 95 kg. In 2012 a rate of serum antimüllerian hormone (AMH) was 0.3 ng/ml, whereas fluctuated substantially higher serum estradiol levels above the laboratory referent value (55 pg/ml) were monitored between 2007 and 2012. Values of the gonadotropic hormones were higher or in the above border of referent values: LH (52-73 mIU/ml) and FSH (70-127 mIU/ml). Levels of progesterone, prolactin and other hormones, including thyroid hormones were within referent values.

Finally, in 2007, she was ovariectomized. Hormonal profile monitoring presented high levels of serum estradiol, and due to relapses with severe pain we added letrozole orally 2.5 mg/daily to her regimen of danazole 800 mg daily. As this provided some relief of acute pain which was associated with the onset of relapses, in 2012 by patient's own decision the dose was titrated up to 7.5 mg/day, which proved relatively beneficial in terms of symptoms and substantially decreased estradiol concentrations (Figure 1). However, this treatment was associated with side effects such as increased body mass, headaches, pain in the extremities, dizziness, insomnia, memory impairment.

An attempt to decrease letrozole dose (5 mg/day) was accompanied by a severe external endometriosis relapse both on the anterior abdominal wall and the labia majora. This called for an increased letrozole dose (7.5 mg) and surgical treatment.

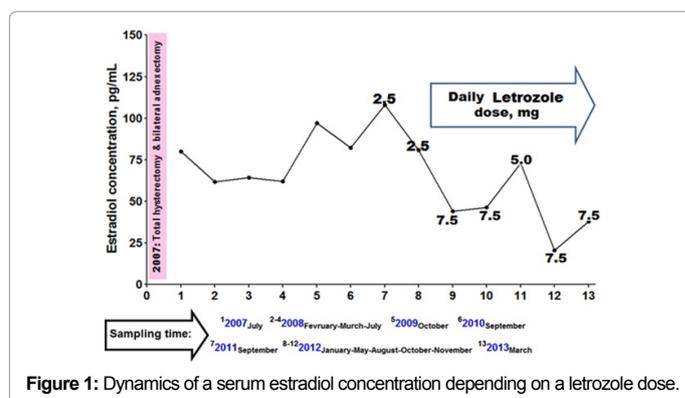


Figure 1: Dynamics of a serum estradiol concentration depending on a letrozole dose.

Most striking, however, are the 159 surgical procedures for recurrent abdominal wall endometriotic lesions and twelve surgeries for recurrent vulvar and bilateral labia majora and pubis (mons) endometriotic lesions (Figures 2-4). She had failed treatment with GnRH-agonists, testosterone derivatives, danazol, dienogest, norethisterone, NSAIDs and antibiotics. Therefore, she was subjected to recurrent multiple procedures in order to remove endometrial lesions.

We observed wound dehiscence with secondary healing or non-healing wound formation in cases of suturing. In some cases purulent lesion discharge from the wound was noted which was successfully healed after excision and removal of endometriotic lesions and wound debridement with severe disfigurement (Figure 5). Endometriotic tissue was confirmed only in 16 of 159 samples from abdominal wall lesions, whereas in most cases histological examination was not performed or severe purulent inflammation was registered.

**\*Corresponding author:** Mykhailo VM, Department of Obstetrics and Gynecology, Dnipropetrovsk Medical Academy of Health Ministry of Ukraine, Dnepropetrovsk, Ukraine, Tel: +380 56 713 5257; E-mail: [medvedev.mv@gmail.com](mailto:medvedev.mv@gmail.com)

Received May 15, 2017; Accepted August 18, 2017; Published August 24, 2017

**Citation:** Mykhailo VM, Marina YE, Ioannis PK, Antonio M, Andrea T, et al. (2017) A Severe Case of Recurrent External Endometriosis in An Ovariectomized Young Woman. J Clin Case Rep 7: 1007. doi: [10.4172/2165-7920.10001007](https://doi.org/10.4172/2165-7920.10001007)

**Copyright:** © 2017 Mykhailo VM, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.



Figure 2: A typical manifestation of vulvar endometriotic lesions relapses.



Figure 3: A surgical treatment of vulvar endometriotic lesions.



Figure 4: Prolonged wound healing after surgical treatment of vulvar endometriotic lesions.



Figure 5: A disfigurement anterior abdomen.

## Discussion

To our knowledge the first case of extremely aggressive external endometriosis occurring in a reproductive-age, ovariectomized woman was presented. She experienced 175 repeat surgical procedures and pain relief was achieved only by a daily triple dose of letrozole.

Briefly, our patient initially (1998) experienced LT for right

cystectomy due to a ruptured right ovarian cyst, then (1999) LS for resection of the left ovary and adhesiolysis because of left ovarian endometrioma and pelvic adhesions. A year later (2000) LT was performed to excise a previous scar. She had adhesiolysis with left adnexectomy and right tubectomy because of bilateral purulent salpingitis, endometriosis of the left ovary and pelvic viscera adhesions.

During the next LT (2007) she experienced adhesiolysis, total hysterectomy and right ovariectomy due to adenomyosis, an endometriotic right cyst and severe adhesions described as a frozen pelvis. Thus, in her thirties, our patient was ovariectomised. This was followed by 159 surgical procedures for recurrent abdominal wall endometriotic lesions and 12 surgeries for recurrent vulvar and bilateral labia majora and pubis (mons) endometriotic lesions in the ensuing 6 years.

Relapses were accompanied by severe localized pain. Rapid relief of symptoms was possible by the concurrent surgical removal of disparate endometriotic lesions.

All traditional conservative treatment options failed and due to persistent high concentrations of serum estradiol levels, letrozole was prescribed. Only high doses of this medication were successful in preventing relapses with decreased serum estradiol concentrations.

Several factors may be a cause of external endometriosis in individuals with severe external endometriosis relapses, such as the shift of a major source of circulating estradiol from the ovary to the adipose tissue [1] and the aromatization of androstendione by human adipose tissue stromal cells [2,3]. Therefore aromatase inhibitors were applied to treat patients with endometriosis. This in a case report of external endometriosis relapses after initial ovarian endometriosis in ovariectomized woman [4] and a series of four cases in premenopausal patients [5]. There are several studies that have shown the benefit of aromatase inhibitors in this kind of severe refractory endometriosis [4-6], although the role of aromatase in the development of endometriosis and its subsequent beneficial impact is under debate [7,8].

In our patient substantially decreased serum concentration of AMH, accompanied with increased serum estradiol and gonadotropins (FSH and LH) levels are features of postmenopausal hormonal profile. A decreased serum estradiol concentration after letrozole treatment is associated with interruption of extraovarian pathway of estradiol production.

In 2004, a similar case was published [4]. A young ovariectomized woman who presented with severe, recurrent endometriosis and an analogous letrozole treatment was initiated. Both her pelvic pain and dyspareunia significantly decreased after a three-month letrozole treatment. Decreased serum estradiol levels were observed and remained low until the end of treatment. Then, a beneficial impact of letrozole in the reduction of pain and urinary symptoms was shown in two patients with bladder endometriosis [6-8].

Letrozole has also been shown to impact refractory endometriosis-related chronic pelvic pain, as presented in four premenopausal patients [5]. Aromatase inhibitors have been examined in post-menopausal women as well [9].

Recently, in a phase-two, open-label, nonrandomized proof-of-concept study [10], a combination of letrozole and norethindrone acetate markedly reduced laparoscopically-visible and histologically-confirmed endometriosis in ten reproductive-age patients and significantly improved pain relief in nine out of ten women with endometriosis and chronic pelvic pain who had previously not responded to currently available treatment.

In all of these cases, aromatase inhibitors were found to be beneficial in recommended therapeutic doses. In our patient, pain relief and decreased estradiol concentrations were seen only after high doses of letrozole treatment, likely due to the strong de-activation of the androgen-to-estrogen conversion pathway [3,11]. However, when the recommended daily dose of letrozole was tripled up to 7.5 mg per day, there were undesirable side effects [12].

## Conclusion

This case of extremely aggressive external endometriosis occurring in a reproductive-age, ovariectomized woman represents a novel observation of hitherto unknown relevance. She obtained pain relief only from high doses of letrozole treatment, but produced undesirable side effects affecting her general health. We are fully aware of the undesirable side effects of this medication and it is not to be recommend as a treatment of choice for recurrent endometriosis.

More research needs to be done regarding this type of recurrent external endometriosis and the appropriate treatment options for this condition.

## Acknowledgements

We sincerely thank Prof. Camran Nezhat, Dr. Jillian Main and Ms. Veronique Berkein for their helpful discussion and advice during the preparation of this work.

We acknowledge the Moscow Institute of Physics and Technology (State University), The Department of Applied Mathematics, The International Translational Medicine and Biomodeling Research team for support OAM throughout the period of manuscript preparation.

## Conflict of Interest

We declare that we have no conflicts of interest and the patient has consented for publication of this case report and accompanying images.

## References

1. Simpson ER, Ackerman GE, Smith ME, Mendelson CR (1981) Estrogen formation in stromal cells of adipose tissue of women: Induction by glucocorticosteroids. *Proc Natl Acad Sci* 78: 5690-5694.
2. Ackerman GE, Smith ME, Mendelson CR, MacDonald PC, Simpson ER (1981) Aromatization of androstenedione by human adipose tissue stromal cells in monolayer culture. *J Clin Endocrinol Metab* 53: 412-417.
3. Stocco C (2012) Tissue physiology and pathology of aromatase. *Steroids* 77: 27-35.
4. Razzi S, Fava A, Sartini A, De Simone S, Cobellis L, et al. (2004) Treatment of severe recurrent endometriosis with an aromatase inhibitor in a young ovariectomised woman. *BJOG* 111:182-184.
5. Verma A, Konje JC (2009) Successful treatment of refractory endometriosis-related chronic pelvic pain with aromatase inhibitors in premenopausal patients. *Eur J Obstet Gynecol Reprod Biol* 143: 112-115.
6. Ferrero S, Biscaldi E, Venturini PL, Remorgida V (2011) Aromatase inhibitors in the treatment of bladder endometriosis. *Gynecol Endocrinol* 27: 337-340.
7. Colette S, Donnez J (2011) Are aromatase inhibitors effective in endometriosis treatment? *Expert Opin Investig Drugs* 20: 917-931.
8. Pavone ME, Bulun SE (2012) Aromatase inhibitors for the treatment of endometriosis. *Fertil Steril* 98: 1370-1379.
9. Polyzos NP, Fatemi HM, Zavos A, Grimbizis G, Kyrou D, et al. (2011) Aromatase inhibitors in post-menopausal endometriosis. *Reprod Biol Endocrinol* 9: 90.
10. Ailawadi RK, Jobanputra S, Kataria M, Gurates B, Bulun SE (2004) Treatment of endometriosis and chronic pelvic pain with letrozole and norethindrone acetate: a pilot study. *Fertil Steril* 81: 290-296.
11. Meinhardt U, Mullis PE (2002) The aromatase cytochrome P-450 and its clinical impact. *Horm Res* 57:145-152.
12. Lønning PE, Eikesdal HP (2013) Aromatase inhibition 2013: Clinical state of the art and questions that remain to be solved. *Endocr Relat Cancer* 20: 183-201.