

Successful treatment of advanced endometriosis with extremely high CA 125 and moderately elevated CA 15-3 levels

M.T. Canda¹, M.D.; N. Demir¹, M.D.; O. Sezer¹, M.D.; L. Doganay², M.D.

¹Department of Obstetrics and Gynecology, and ²Department of Pathology, Kent Hospital, Izmir (Turkey)

Summary

We present the case of a patient with advanced endometriosis who presented with chronic pelvic pain, bilateral unruptured ovarian endometrioma, massive peritoneal implants and extremely elevated CA 125, and also elevated CA 15-3 levels. Laparoscopy revealed bilateral unruptured ovarian endometrioma and diffuse peritoneal endometriotic implants. Increased association of elevated levels of CA 125 and CA 15-3 is not so common in advanced endometriosis. The case was successfully treated with laparoscopy and combined low-dose oral contraceptive with one year of follow-up. To the best of our knowledge among the reported cases this is the highest CA 15-3 level ever reported with an extremely elevated CA 125 level.

Key words: Endometriosis, CA 125, CA 15-3, Laparoscopy.

Introduction

Endometriosis is a benign condition that usually presents with chronic pelvic pain and infertility. CA 125 is a tumor marker which is particularly used for monitoring of epithelial ovarian cancers, but which is also elevated in advanced endometriosis cases. CA 15-3 is another tumor marker mostly related with breast cancer. Extremely elevated levels of CA 125 are well documented in endometriosis, however, elevated levels of CA 125 and CA 15-3 with unruptured ovarian endometrioma out of the menstrual phase are not well documented.

Case Report

A 29-year-old woman, gravida 1, para 1, was admitted to our clinic with persistent pelvic pain. She had a history of dysmenorrhea for several years. She had regular periods and her last menstrual cycle was seven days earlier. Transvaginal ultrasound (US) revealed bilateral ovarian endometrioma (right 5 x 4 cm and left 4 x 3 cm in size). CA 125 level was 2345 U/ml (upper reference limit < 35 U/ml) and CA 15-3 level was 100.8 U/ml (upper reference limit < 29 U/ml). CA 19-9 was 0.6 U/ml (upper reference limit < 37). To rule out malignancy, magnetic resonance imaging (MRI) and breast US were performed. Pelvic MRI also revealed bilateral ovarian endometriomas whereas breast US was normal.

Laparoscopy showed that both ovaries with endometrioma cysts were located in the Douglas pouch. All pelvic peritoneal surfaces were found to be covered with diffuse endometriotic implants. Peritoneal washings were collected, laparoscopic excision of endometriotic cysts while preserving both ovaries was performed, and peritoneal biopsies were taken. Histopathological diagnosis was bilateral ovarian endometrioma and endometriotic foci. CA 125 and CA 15-3 were returned to reference ranges dramatically two weeks after laparoscopy. Con-

tinuous low-dose combined oral contraceptive was used for further endometriosis suppression for six months. After one year of follow-up the patient did not express any symptoms of pelvic pain and transvaginal US demonstrated normal ovaries with normal anatomical locations.

Discussion

Endometriosis is known as an extrauterine location of endometrial glands and stroma due to different mechanisms like retrograde menstruation and implantation [1], coelomic metaplasia [2] or vascular transport [3]. Regardless of any mechanism, ectopic localization of endometrial tissue might result in pelvic organ damage which is usually presented with pelvic pain and infertility.

CA 125 is a tumor antigen that is expressed from coelomic epithelium and its derivatives such as endometrial cells. CA 125 is particularly used as a tumor marker for epithelial ovarian cancers, as well as advanced carcinomas of the endometrium and endocervix. CA 125 can be elevated during pregnancy, menstruation, adenomyosis, leiomyomas, and pelvic inflammatory disease. Elevated levels of CA 125 were also reported in advanced endometriosis. Extremely high levels of CA 125 were reported both due to acute rupture of endometrioma and unruptured endometrioma cases (9300 U/ml and 7900 U/ml, respectively) [4, 5].

CA 15-3 is a tumor antigen particularly used to monitor breast cancer. CA 15-3 is a glycosylated transmembrane molecule which is produced by glandular epithelial cells and also present in endometrial glands. CA 15-3 levels were found to be the same throughout the ovarian cycle [6]. Elevated levels of CA 15-3 in endometriosis had been reported before [7, 8], but the levels were around normal values and we could not detect any CA 15-3 level as high as we have reported.

Revised manuscript accepted for publication March 20, 2008

CA 19-9 is another tumor antigen that can be elevated in endometriosis. Elevated levels of CA 125, CA 19-9 and CA 15-3 together, CA 125 and CA 19-9 together, CA 19-9 and CA 15-3 alone were also reported in endometriosis (9). One other study demonstrated high levels of CA 125, CA 19-9 and CA 15-3 in the peritoneal fluids of endometriosis cases (10). In all these cases serum levels of CA 15-3 did not pass the upper reference limit; only in the peritoneal fluid study were the values higher.

In the present case the question is; in the state of unruptured ovarian endometrioma the elevated levels of CA 125 and CA 15-3 out of the menstrual phase should result from endometrioma cysts, endometriotic foci or both? The answer should be ovarian endometrioma because in a two-week period both tumor markers returned to normal levels that it was not possible to destroy all the diffuse endometriotic foci during laparoscopy or within the low dose combined oral contraceptive that had been started after the operation. The reason why CA 19-9 levels did not change was unclear. Further in vivo and in vitro studies are needed to understand the exact association between tumor markers and endometriosis.

We have reported a case of advanced endometriosis with extremely high CA 125 and moderately elevated CA 15-3 levels. After ruling out malignancy, instead of high levels of tumor antigens by MRI or during the laparoscopy, taking peritoneal washings, laparoscopic excision of endometriomas and collecting peritoneal biopsies would be the choice of surgery. In cases of advanced endometriosis with massive peritoneal implants suppression therapy with low-dose combined oral contraceptive in a continuous fashion up to 6-12 months should be the choice of medical management [7]. To the best of our knowledge we have reported the highest CA 15-3 level with an extremely high CA 125 level in advanced endometriosis out of the menstrual period.

References

- [1] Liu D.T., Hitchcock A.: "Endometriosis: its association with retrograde menstruation, dysmenorrhea, and tubal pathology". *Br. J. Obstet. Gynaecol.*, 1986, 93, 859.
- [2] El-Mahgoub S., Yaseen S.: "A positive proof for the theory of coelomic metaplasia". *Am. J. Obstet. Gynecol.*, 1980, 137, 137.
- [3] Ueki M.: "Histologic study of endometriosis and examination of lymphatic drainage in and from the uterus". *Am. J. Obstet. Gynecol.*, 1991, 165, 201.
- [4] Johansson J., Santala M., Kauppila A.: "Explosive rise of serum CA 125 following the rupture of ovarian endometrioma". *Hum. Reprod.*, 1998, 13, 3503.
- [5] Kahraman K., Ozguven I., Gungor M., Atabekoglu C.S.: "Extremely elevated serum CA-125 level as a result of unruptured unilateral endometrioma: the highest value reported". *Fertil. Steril.*, 2007, 968, 15.
- [6] Bon G.G., Kenemans P., Dekker J.J., Hompes P.G., Verstraeten R.A., van Kamp G.J. *et al.*: "Fluctuations in CA 125 and CA 15-3 serum concentrations during spontaneous ovulatory cycles". *Hum. Reprod.*, 1999, 14, 566.
- [7] Abrao M.S., Podgaec S., Pinotti J.A., de Oliveira R.M.: "Tumor markers in endometriosis". *Int. J. Gynaecol. Obstet.*, 1999, 66, 19.
- [8] Matalliotakis I.M., Neonaki M.A., Panidis D.K., Goumenou A.G., Koumantakis E.E.: "Three-year of follow-up of [AC 125, CA 19-9, CA 15-3, SIL-2R, IL-6, IL-1a, TNF-a, sCD8 and sCD4] levels in a women with severe endometriosis". *Eur. J. Obstet. Gynecol. Reprod. Biol.*, 2000, 93, 127.
- [9] Panidis D., Vlasias G., Matalliotakis J., Skiadopoulou S., Kalogeropoulos A.: "Serum levels of oncofetal antigens CA-125, CA 19-9 and CA 15-3 in patients with endometriosis". *J. Endocrinol. Invest.*, 1988, 11, 801.
- [10] Matalliotakis I.M., Goumenou A.G., Mulayim N., Karkavitsas N., Koumantakis E.E.: "High concentrations of the CA-125, CA 19-9 and CA 15-3 in the peritoneal fluid between patients with and without endometriosis". *Arch. Gynecol. Obstet.*, 2005, 271, 40.

Address reprint requests to:
M.T. CANDA, M.D.
103 Sok. Melekoglu Apt.
No: 1/3 Goztepe,
35290 Izmir (Turkey)
e-mail: candatunc@yahoo.com