

## Unusual rise in CA 125 levels in Endometriosis

**Abstract:** CA 125 is expressed in the surface of coelomic epithelium and help to distinguish benign from malignant ovarian lesion as higher levels have association with malignant ovarian masses. In this case report we see rise in CA125 levels in benign condition that is endometriosis.

Key words- CA125, endometriosis, malignancy

### Introduction:

Endometriosis is defined as the presence of endometrial glands and stroma located outside the uterus and is characterized by pain and sub fertility. It affects up to 75% of symptomatic women yet it is commonly under-diagnosed. The gold standard diagnostic test is histological diagnosis.<sup>1</sup> CA125 was first identified by Bast et al in 1981.<sup>2</sup> CA-125 is a high molecular weight glycoprotein expressed on the surface of the coelomic epithelium of the endocervix, endometrium, fallopian tube, pelvic peritoneum, placental tissues, pericardium and epithelial ovarian carcinomas.<sup>3</sup> CA125 plays an important role in differentiating benign and malignant abdominopelvic masses as higher CA 125 levels are associated with a higher probability of malignancy<sup>4</sup>. However, serum CA 125 levels can be elevated in other malignancies as well as various physiological and benign conditions such as endometriosis, uterine fibroids, pelvic inflammatory disease, early pregnancy, and normal menstruation.<sup>5</sup>

### Case presentation:

27 years old nulligravida presented to us in gynaecological outpatient department with complaints of acute pain abdomen for one day associated with nausea and vomiting. Pain relieved on taking analgesics. Menstrual cycles were regular but were associated with dysmenorrhea from last 6 months. Her past history was unremarkable. On examination vitals were stable and slightly tender lower abdomen. On per vaginal examination uterus was normal

size mobile retroverted with firm to cystic mass of 4x4cm felt over right fornix slightly tender. No nodularity felt in the pouch of Douglas.

Transvaginal sonography revealed normal looking uterus with right sided cystic homogenous mass of 4x4cm with low level of echo and left adnexa appears normal. Her computed tomography showed right sided adnexal mass with no solid areas, with no ascites and lymphadenopathy.

Tumour marker CA125 and CA19.9 were significantly raised with the level of 5109U/ml and 479 ng/ml. Other tumour markers like alpha fetoprotein (AFP) -3.16 ng/ml, beta Hcg- 0.69, inhibin B- 44.3, CEA 0.79 and LDH- 101, all were within normal limit. Upper GI and lower GI endoscopy done was normal. Her routine investigations were normal.

In view of raised CA125 level with adnexal mass, patient was planned for staging laparotomy. On laparotomy uterus was normal. There was dense adhesion between mass of 5x4cm with right side of uterus. Pouch of Douglas was obliterated. On adhesiolysis cyst ruptured and thick chocolate coloured fluid aspirated. In left ovary 1-2 small endometriotic spots were present. Small endometriotic spots were present over peritoneum. Right ovarian cyst enucleated and remaining normal appearing ovarian tissue reconstructed. Bilateral fallopian tube and fimbria were normal looking. Patient discharged on third post operative day. Final histopathology report confirmed the diagnosis of endometriosis. Subject given oral contraceptive after confirmation of diagnosis. CA-125 level returned to 32 U/ml after 3 weeks and 2 years post surgery she is fine with normal CA 125.

#### Discussion:

Young women with raised CA 125 levels and ovarian masses always poses diagnostic dilemma between benign and malignant masses. Education of the patient for the significance of raised tumor marker and further affecting the management is important. The relationship between elevated CA 125 levels and endometriosis has been well established in the literature, with levels reflecting both the severity and the progression of the disease<sup>6</sup>. Multiple theories have been put forward to explain high serum CA 125 levels in endometriosis such as enlarged surface area of endometriotic tissue<sup>7</sup>, inflammatory reaction to the endometriotic foci, blood and endometrial shedding to peritoneal cavity<sup>8</sup>. CA125 concentration in the cyst fluid of endometrioma is very high but thick walls of cyst prevent large glycoprotein molecule to reach into the peripheral

circulation.<sup>9</sup> Leakage of endometriotic fluid into the peritoneal cavity leads to peritoneal irritation and absorption into peripheral circulation leading to raised CA 125 levels.<sup>10</sup>

Gold standard for diagnosis of endometriosis is histopathology and visual inspection of abdominal cavity by laparotomy or laparoscopy. However invasive testing for large scale population is not possible. Thus non invasive test such as pelvic examination, transvaginal ultrasonography<sup>11</sup>, MRI pelvis and CA125 level are used for diagnosis. Endometriosis is the most common benign condition associated with raised CA125<sup>12</sup>. Raised CA125 >35 U/ml were found in 80% of women with epithelial ovarian cancer and only 1% healthy women. The positive predictive value of CA 125 (> 95 IU/ml) for ovarian cancer is high among postmenopausal women (96%)<sup>12</sup>. In endometriosis CA-125 levels are > 35 U/ml<sup>13</sup> but does not exceeds >100U/ml<sup>12</sup>. Extremely elevated CA 125 levels have been reported in the presence of both ruptured<sup>13, 14</sup> and unruptured endometriomas<sup>15</sup> and highest reported was 9537 U/ml following acute rupture of an endometrioma<sup>16</sup>. In the present case report CA 125 was 5109 U/ml with unilateral endometrioma with widespread peritoneal deposits although there was no rupture or leakage of endometriotic fluid. CA 125 levels were in reducing trends post surgery.

#### Conclusion:

CA 125 is the non invasive and most frequently used marker to diagnose ovarian masses. High CA 125 levels do not necessarily indicate ovarian malignancy. Reproductive age women presenting with adnexal mass with raised CA 125 levels endometriosis should be considered if finding suggestive of malignancy has been ruled out.

#### References

1. Hirsch M, Duffy JMN, Davis CJ, Nieves Plana M, Khan KS, on behalf of the International Collaboration to Harmonise Outcomes and Measures for Endometriosis. Diagnostic accuracy of cancer antigen 125 for endometriosis: a systematic review and meta-analysis. *BJOG* 2016;123:1761–1768.
2. Bast RCJ, Feeney M, Lazarus H. Reactivity of a monoclonal antibody with human ovarian carcinoma. *J Clin Invest* 1981;68:1331-37.

3. V. Nisenblat, P. M. Bossuyt, R. Shaikh, C. Farquhar, V. Jordan, C. S. Scheffers et al., "Blood biomarkers for the non-invasive diagnosis of endometriosis," *Cochrane Database of Systematic Reviews*, no. 5, 2016.
4. R. C. Bast Jr., D. Badgwell, Z. Lu et al., "New tumor markers: CA125 and beyond," *International Journal of Gynecological Cancer*, vol. 15, Suppl 3, no. 6, pp. 274–281, 2005.
5. R. L. Barbieri, J.M.Niloff, R. C. Bast Jr., E. Scaetzi, R.W.Kistner, and R. C. Knapp, "Elevated serum concentrations of CA-125 in patients with advanced endometriosis," *Fertility and Sterility*. vol. 45, pp. 630–634, 1986.
6. M. D. Hornstein, B. L. Harlow, P. P. Thomas, and J. H. Check, "Use of a new CA125 assay in the diagnosis of endometriosis," *Human Reproduction*, vol. 10, pp. 932–934, 1995.
7. J. Johansson, M. Santala, and A. Kauppila, "Explosive rise of serum CA 125 following the rupture of ovarian endometrioma," *Human Reproduction*, vol. 13, pp. 3503-3504, 1998.
8. Falconer H, Bambra CS, Chai D, Cornillie FJ, Hill JA, D'Hooghe TM. The effect of endometriosis, cycle stage, lymphocyte suppression and pregnancy on CA-125 levels in peritoneal fluid and serum in baboons. *Hum Reprod* 2005;20:3033–8.
9. Koninckx, P.R., Muyldermans, M., Moerman, P., Meuleman, C., Deprest, J., Cornillie, F., 1992. CA 125 concentrations in ovarian "chocolate" cyst fluid can differentiate an endometriotic cyst from a cystic corpus luteum. *Hum. Reprod.* 7, 1314–1317.
10. C. S. Shiau, M. Y. Chang, C. H. Chiang, C. C. Hsieh, and T.T. Hsieh, "Ovarian endometrioma associated with very high serum CA-125 levels," *Chang Gung Medical Journal*, vol. 26, no.9, pp. 695–699, 2003.
11. Guerriero S, Ajossa S, Mais V, Risalvato A, Lai MP and Melis GB (1988) The diagnosis of endometriomas using colour Doppler energy imaging. *Hum Reprod* 13,1691–1695
12. C. M. Boyer, R. C. Knapp, and R. C. Bast Jr., "Biology and immunology," in *Practical Gynecologic Oncology*, J. S. Berek and N. F. Hacker, Eds., pp. 89-90, Williams & Wilkins, Baltimore, MD, USA, 2nd edition, 1994.
13. M. Yilmazer, M. Sonmezer, M. Gungor, V. Fenkci, and S.Cevrioglu, "Unusually elevated serum carbohydrate antigen 125 (CA125) and CA19-9 levels as a result of

unruptured bilateral endometrioma,” Australian and New Zealand Journal of Obstetrics and Gynaecology, vol. 43, no. 4, pp. 329-330, 2003.

14. M. Yilmazer, M. Sonmezer, M. Gungor, V. Fenkci, and S.Cevrioglu, “Unusually elevated serumcarbohydrate antigen 125 (CA125) and CA19-9 levels as a result of unruptured bilateral endometrioma,” Australian and New Zealand Journal of Obstetrics and Gynaecology, vol. 43, no. 4, pp. 329-330, 2003.
15. A. K. Rani and D. Kapoor, “Ruptured ovarian endometrioma with an extremerise in serumCA125 level -Acase report:Ovarian endometrioma with very high CA-125 level,” Gynecologic Oncology Reports, vol. 2, no. 3, pp. 100-101, 2012.
16. H. Kurata, M. Sasaki, H. Kase, Y. Yamamoto, Y. Aoki, and K.Tanaka, “Elevated serum CA125 and CA19-9 due to the spontaneous rupture of ovarian endometrioma,” European Journal of Obstetrics, Gynecology, and Reproductive Biology, vol. 105, no. 1, pp. 75-76, 2002.