



## Recurrent Endometriotic Cyst with High Ca-125 Level Mimicking Malignancy

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**Abstract:** Gynecologists who treat endometriosis, a chronic, disabling disease, face difficulties diagnosing and treating the condition. Endometriotic cyst, with internal septations and opacities sonologically, mimics malignancy. Increased levels of CA 125 Are used as a tumor marker in epithelial ovarian malignancies. It is also an important prognostic indicator and follow-up tool in managing ovarian malignancies. A moderate increase in CA125 levels is observed in physiological conditions like ovulation and benign conditions like endometriosis and PID. We present here a case of extremely elevated serum CA 125 level in a patient who presented with recurrent ovarian endometriosis. Mrs. X, 46 years old, presented with a complex ovarian cyst with CA 125 level- 1021 iu/ml. With a history of laparotomy for endometriotic cysts in the past. Intraoperatively bilateral complex ovarian cysts were identified, which were densely adherent to the lateral pelvic wall and rectum posteriorly. The ovarian cysts were excised with a hysterectomy. The Patient developed dribbling of urine on the third postoperative day. CT urogram revealed a right ureterovaginal fistula. Laparotomy done. Uretero ureteral anastomosis done by a urologist. The Postoperative patient remained dry. Histopathological evaluation revealed benign endometriosis. Extensive and aggressive surgeries are usually done for ovarian malignancies to provide optimal reduction. However, in our patient, risk assessment for malignancy based on radiological factors and tumor markers was highly suggestive of malignancy. Yet, the histopathology turned out to be benign endometriosis. Therefore, to avoid invasive investigations and surgeries associated with high morbidity, emphasis must be made on the possibility of raised CA 125 levels in benign conditions such as endometriosis.

**Keywords:** CA 125, endometriosis, recurrent endometriosis, ovarian endometrioma, peri-menopausal high CA 125.

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Received On 31 October, 2022

Revised On 20 April, 2023

Accepted On 3 May, 2023

Published On 1 November, 2023

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**Funding** This research did not receive any specific grant from any funding agencies in the public, commercial or not for profit sectors.

**Citation** Dr. Vidhya Selvam and Dr. C. Minu Priya , Recurrent Endometriotic Cyst with High Ca-125 Level Mimicking Malignancy.(2023).Int. J. Life Sci. Pharma Res.13(6), L153-L157 <http://dx.doi.org/10.22376/ijlpr.2023.13.6.L153-L157>

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Int J Life Sci Pharma Res., Volume13., No 6 (November) 2023, pp L153-L157



## I. INTRODUCTION

The cancer antigen CA 125 is a glycoprotein produced from coelomic epithelium. In contrast to typical mucin, CA 125 has little carbohydrate content and is primarily composed of nitrogen-linked oligosaccharides. Cells synthesize CA 125, secrete into the lumen when it reaches the luminal cell side. As long as junctional complexes between cells or basal membranes are intact, products from these cells cannot cross into the bloodstream. Here, we report a case of this unusually severe form of endometriosis in a patient initially diagnosed with advanced ovarian cancer before surgery. She presented with an increase in abdominal girth and was found to have bilateral ovarian cysts, massive hemorrhagic ascites, and an elevated CA-125 level. There may be excessive antigen shedding into cyst fluid in benign tumors, e.g., ovarian cysts, despite normal levels of circulating antigens. A topographically depolarized cell with an absent apical border expresses antigen circumferentially following malignant transformation. Antigens can re-enter the bloodstream through invasive tumor cells disrupting tissue architecture. This results in the detection of CA 125 antigen in serum. CA125 antigens are defined by antibodies OC 125, which identify conformational epitopes formed by saccharides and protein backbones. In addition to this epitope, another one has also been identified on the same molecule. A serous papillary cystadenocarcinoma patient's ascitic fluid was used to inoculate BALB/c mice with OC 125 McAb. A high molecular weight glycoprotein complex contains antigenic determinants named CA 125, which are recognized by the OC125 antibody. Only now has a consensus reached regarding this antigen's carbohydrate composition. On both non-mucinous and mucinous ovarian carcinomas, as well as endometrial and endocervical adenocarcinomas, CA 125 antigenic determinants have been found. Breast, pancreatic, colon, and lung cancer are other tumor types that express CA 125 to varying degrees. The CA 125 protein is commonly expressed in benign tumors such as endometriosis and ovarian tumors, mucinous and nonmucinous. Several types of epithelial invaginations and proliferations of the ovaries express CA 125 in normal ovaries. CA 125 expression is, therefore, neither specific for ovarian cancer nor all cancerous tissues. Human epithelial cells secrete CA 125, and the antigen may be shed from the cell surface, possibly due to active shedding. CA 125 is expressed by normal tissues such as the endometrium, peritoneum, pericardium, and ovarian epithelial carcinomas<sup>1</sup>. It is most commonly used as a cancer biomarker clinically in epithelial ovarian carcinoma diagnosis, disease progression, and treatment<sup>1</sup>. Levels of CA 125 are also used in differentiating lesions from the pelvis into benign or malignant and managing these conditions preoperatively, as higher CA 125 levels frequently relate to a higher probability of malignancy. Benign conditions such as uterine fibroids, endometriosis, PID (Pelvic inflammatory disease), menstruation, and early pregnancy can have elevated CA 125<sup>2,3</sup>. The positive predictive value (PPV) of CA 125 for ovarian cancer is high among postmenopausal women, accounting for 96%<sup>4</sup>; however, it is associated with a lower specificity among premenopausal women wherein benign lesions predominate in this age group, which mimics elevated CA 125 levels. Hence benign conditions such as endometriosis

must be considered a differential diagnosis in cases of high CA 125. Very rarely, profoundly raised CA 125 were reported in the absence of malignancy. Here we report a case of perimenopausal women who presented with recurrent endometriosis with markedly elevated CA 125. Endometriosis with enormous ascites causes abdominal distension and other symptoms that mimic cancer<sup>19</sup>. Endometriosis is the presence of endometrial tissue outside the uterine cavity, generally involving the peritoneum, ovaries, and rectovaginal septum. However, it may also occur at remote sites with unusual manifestations. Rare examples include pulmonary endometriosis and endometriosis associated with ascites<sup>19</sup>. In addition, endometriosis associated with massive ascites causing abdominal distension and other symptoms simulating a malignancy has been described in the literature<sup>20</sup>.

## 2. CASE PRESENTATION

The 46-year parous woman presented with complaints of abdominal pain for one week and heavy menstrual bleeding for 6 months.

### 2.1. Past History

The Patient came with a history of laparotomy for bilateral endometriotic cysts done in 2016. Intraoperative findings of past surgery were an 8 x 6 cm left ovarian cyst removed. The right side 20 x 16 cm ovarian cyst was aspirated, and deroofting was done as the cyst wall was adherent with bowels. Since then, the Patient has been on observation and medical management. No history of diabetes, hypertension, Tuberculosis, Bronchial asthma, Heart disease, or Thyroid disease. No history of blood transfusion, Drug allergies.

### 2.2. Marital History

Married for 12 years - Non Consanguineous marriage.

### 2.3. Obstetric History

She had one live child delivered by cesarean section. Sterilization was not done for the patient.

## 3. OBSERVATION

On examination, she had normal vital signs, and on abdominal examination, her abdomen was soft. On per-vaginal examination, the cervix was pushed towards the left side, high up, and the uterus was retroverted, measuring around 6-8-week size. In addition, a Cystic mass was felt in the right fornix.

## 4. INVESTIGATIONS

Transabdominal ultrasonography demonstrated a right adnexal complex cyst measuring 6.0x4.8 cm. CT pelvis showed a right ovary-complex cyst measuring 6 x 5 cm with solid components and a left ovary- cyst measuring 5x5.5 cm, as seen in Fig 1. Serum 125 level was 1021 U/ml. The RMI score was above 250.



**Fig 1: CT Image showing bilateral endometriotic cysts.**

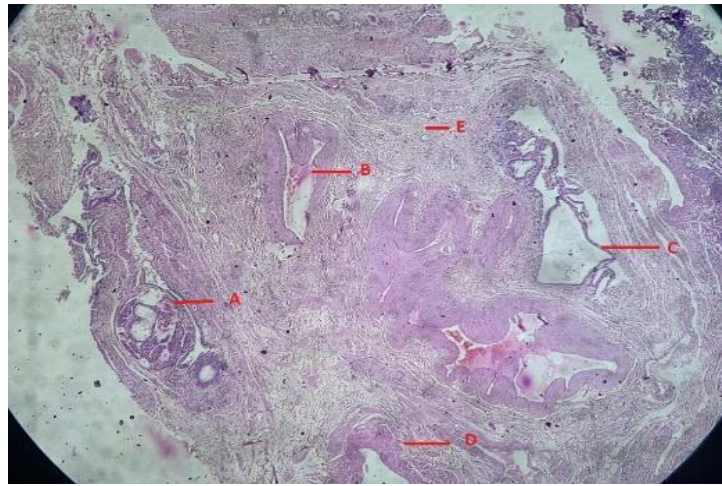
### **INTERVENTION DONE, AND THE INTRAOPERATIVE FINDINGS**

Oncosurgeon opinion was obtained. Considering the chance of malignant transformation of endometrioma/ de novo malignancy, the Patient was planned for staging laparotomy. Intraoperatively, the uterus was 6-8-week size and irregularly enlarged. As seen in Fig 2, a Right-sided ovarian cyst (size - 6x6 cm) adheres to the uterus's posterior wall and right lateral pelvic wall and bowels. In addition, a left-side ovarian cyst of size 5x4 cm adherent to the lateral pelvic wall and posterior wall of the uterus was also noted and proceeded with a Total abdominal hysterectomy.



**Fig 2: Endometriotic cyst can be seen adherent posteriorly and to the lateral pelvic wall.**

Since the suspicion of malignancy was high, we planned to completely remove the cyst without leaving the residual tissue. The cysts were dissected off the pelvic wall and bowel loops. A bilateral scalping-oophorectomy was done. Postoperatively, the patient developed a watery discharge. CT urogram showed Ureteric obstruction with uterovaginal fistula. Urologist's opinion was sought. Right ureteric reconstruction was done with a ureteric stent. The postoperative period was uneventful. The HPE of the cysts revealed endometrioma on both sides (Fig 3). The slide shows endometrial glands with hemosiderin loaded macrophages, a characteristic feature of endometriosis. No malignant transformation was evident in the tissues studied. The stent was removed after 6 weeks, and the patient remained dry.



**Fig 3: Histopathological image of endometrioma**

- A. Hemosiderin-loaded macrophages,  
 B. Congested Blood Vessel.  
 C. Endometrial Gland with cyst and secretions  
 D. Cyst wall  
 E. Stroma

## 5. DISCUSSION

CA 125 was first identified in 1981 as an ovarian cancer antigen. It was later developed as a biomarker for ovarian epithelial carcinomas when serum levels  $> 35$  U/ml<sup>4</sup>. The positive predictive value of CA 125 ( $> 95$  IU/ml) for ovarian cancer is high among postmenopausal women (96%) [4,5]. Serum CA 125 levels are associated with high sensitivity (69-97%) and specificity (81-93%)<sup>6</sup>. While most commonly used clinically for diagnosing ovarian carcinomas, serum CA 125 levels can also be elevated in other malignancies and various physiological and benign conditions, including endometriosis<sup>2,3</sup>. Hence CA 125 is associated with a poorer specificity among pre-menopausal women<sup>7</sup>. Therefore, a routine CA 125 level is not recommended in all women with a simple ovarian cyst<sup>8,9</sup>. Patients with endometriosis do not often have CA 125 levels  $> 100$  U/ml, but endometriosis is the most common benign condition with elevated CA 125 levels<sup>10-12</sup>. Two meta-analyses that studied the use of CA 125 as a biomarker for endometriosis concluded limited utility as a diagnostic marker for endometriosis given its low sensitivity (20-50%)<sup>13,14</sup>. International guidelines for endometriosis do not recommend measuring serum CA 125 level as part of the routine diagnostic workup in such cases<sup>15</sup>. However, elevated CA 125 levels in endometriosis can be used to measure the severity and progression of the disease<sup>16,17</sup>. Elevated serum CA 125 levels are commonly related to ovarian endometriomas, as in our case, and endometriosis of higher severity (stage III, IV)<sup>18</sup>. Also, following the management of medical and surgical cases, there is a reduction in CA 125 levels<sup>19</sup>. Extremely elevated CA 125 levels have been reported in ruptured [20-24] and unruptured endometriomas<sup>24-26</sup>. The highest CA 125 level reported in the literature with proven endometriosis is 9537 U/ml, following the rupture of an endometrioma acutely. Here we report a case of elevated serum CA 125 level of 1021 U/ml in women with recurrent ovarian endometriosis. It poses significant clinical importance because elevated CA 125 levels in the context of pelvic mass can raise suspicion of malignant tumors, leading to unnecessary invasive procedures<sup>27</sup>. Educating the Patient regarding the significance of an elevated tumor marker in the absence of a malignant tumor and management is important. Various theories are postulated for

raised CA 125 levels in endometriosis. The fluid within an endometriotic cyst or endometrioma is said to be rich in CA 125 (more than 10000 U/ml)<sup>28</sup>. Following the leakage of this endometriotic fluid from an endometrioma, it covers the peritoneal surfaces. It is later absorbed into the peripheral circulation, causing peritoneal inflammation and an elevated CA 125 level<sup>29-31</sup>. Generally, there is an increase in peritoneal fluid in mild endometriosis, and higher levels of CA 125 in peritoneal fluid compared to corresponding serum levels could contribute to elevated serum CA 125 measurements<sup>32</sup>. When compared to serum levels, the causes of raised CA 125 levels in cyst fluid can be due to the thick endometriotic cyst wall preventing these large CA 125 molecules from diffusing out of the cyst and reaching systemic circulation<sup>33</sup>. Another cause can be the higher surface area of endometrial tissue in endometriotic cysts, deep infiltrating endometriosis nodules, and adhesions. Concurrent menstruation has also raised CA 125 levels threefold among women with endometriosis<sup>34</sup>. When malignancy is suspected, all attempts will be taken to make optimal reduction leaving less than 1cm of the malignant tissue, which will need extensive dissections in case of adhesions with vital structures.

## 6. CONCLUSION

While there have been several reports of elevated serum CA 125 levels in both ruptured and unruptured endometriomas, the present case reports a rare finding of an elevated serum CA 125 level in the context of recurrent endometriomas. It highlights the rare possibility of having elevated CA 125 in benign endometriosis, which would avoid aggressive surgeries and increase the postoperative morbidity of the patient. The CA 125 is a helpful preoperative test for determining if a pelvic tumor is benign or malignant. Clinical criteria are less reliable than a blood CA 125 value alone in this function, and when ultrasonography and clinical data are added, a prediction accuracy of -90% may be reached. The rising CA 125 is the tumor marker widely associated with malignancy. Although the CA-125 test can be a good indicator of cancer, it has limitations. Nevertheless, preoperative serum CA-125 is an important predictor for patients with endometriosis. It should be considered when surgical management is suspected,

especially if the stage of disease, lesion size, and adhesion score are undertaken.

## 7. AUTHORS CONTRIBUTIONS STATEMENT

Dr. C. Minu Priya - conceptualization and designing of study, curation of data and preparation of draft, analysing data and

designing the draft. Dr. Vidhya Selvam- providing valuable data and contributed towards final draft

## 8. CONFLICT OF INTEREST

Conflict of interest declared none.

## 9. REFERENCES

- Nisenblat V, Bossuyt PM, Shaikh R, Farquhar C, Jordan V, Scheffers CS et al. Blood biomarkers for the non-invasive diagnosis of endometriosis. *Cochrane Database Syst Rev.* 2016;2016(5): CD012179. doi: 10.1002/14651858.CD012179, PMID 27132058.
- Bast RC Jr., Badgwell D, Lu Z, Marquez R, Rosen D, Liu J et al. New tumor markers: CA125 and beyond. *Int J Gynecol Cancer.* 2005;15; Suppl 3, no. 6:274-81. doi: 10.1111/j.1525-1438.2005.00441.x, PMID 16343244.
- Barbieri RL, Niloff JM, Bast RC Jr., Scaetzl E, Kistner RW, Knapp RC. We have elevated serum concentrations of CA-125 in patients with advanced endometriosis. *Fertil Steril.* 1986;45(5):630-4. doi: 10.1016/s0015-0282(16)49333-7, PMID 3457709.
- Boyer CM, Knapp RC, Bast RC Jr. Biology and immunology. In: Berek JS, Hacker NF, editors. *Practical gynecologic oncology.* 2nd ed. Baltimore: Williams & Wilkins; 1994. p. 89-90.
- Bast RC Jr., Feeney M, Lazarus H, Nadler LM, Colvin RB, Knapp RC. Reactivity of a monoclonal antibody with human ovarian carcinoma. *J Clin Invest.* 1981;68(5):1331-7. doi: 10.1172/jci110380, PMID 7028788.
- Myers ER, Bastian LA, Havrilesky LJ, Kulasingam SL, Terplan MS, Cline KE, et al. Management of adnexal mass. *Evid Rep Technol Assess (Full Rep).* 2006;130(130):1-145. PMID 17854238.
- Timmerman D, Testa AC, Bourne T, Ferrazzi E, Ameye L, Konstantinovic ML et al. Logistic regression model to distinguish between the benign and malignant adnexal mass before surgery: a multicenter study by the international ovarian tumor analysis group. *J Clin Oncol.* 2005;23(34):8794-801. doi: 10.1200/JCO.2005.01.7632, PMID 16314639.
- Rustin GJ, Bast RC, Kelloff GJ, Barrett JC, Carter SK, Nisen PD, et al. Use of CA-125 in clinical trial evaluation of new therapeutic drugs for ovarian cancer. *Clin Cancer Res.* 2004;10(11):3919-26. doi: 10.1158/1078-0432.CCR-03-0787, PMID 15173101.
- RCOG. Management of suspected ovarian masses in premenopausal women (Green-Top Guideline No. 62); 2011.
- Yilmazer M, Sonmezer M, Gungor M, Fenkci V, Cevrioglu S. Unusually elevated serum carbohydrate antigen 125 (CA125) and CA19-9 levels as a result of unruptured bilateral endometrioma. *Aust N Z J Obstet Gynaecol.* 2003;43(4):329-30. doi: 10.1046/j.0004-8666.2003.00088.x, PMID 14714723.
- Shiau CS, Chang MY, Chiang CH, Hsieh CC, Hsieh TT. Ovarian endometrioma is associated with very high serum CA-125 levels. *Chang Gung Med J.* 2003;26(9):695-9. PMID 14651169.
- Kahraman K, Ozguven I, Gungor M, Atabekoglu CS. The highest value reported is an extremely elevated serum CA-125 level due to unruptured unilateral endometrioma. *Fertil Steril.* 2007;88(4):968.e15-7. doi: 10.1016/j.fertnstert.2006.12.076, PMID 17544420.
- Mol BW, Bayram N, Lijmer JG, Wiegerinck MA, Bongers MY, van der Veen F et al. The performance of CA-125 measurement in the detection of endometriosis: a meta-analysis. *Fertil Steril.* 1998;70(6):1101-8. doi: 10.1016/s0015-0282(98)00355-0, PMID 9848302.
- Cheng YM, Wang ST, Chou CY. Serum CA-125 in preoperative patients at high risk for endometriosis. *Obstet Gynecol.* 2002;99(3):375-80. doi: 10.1016/s0029-7844(01)01731-8, PMID 11864662.
- Gynecologists TACoOa, "Practice bulletin no. 114: management of endometriosis," *Obstetrics and Gynecology*, 2010;116(1):223-36.
- Hornstein MD, Harlow BL, Thomas PP, Check JH. Use of a new CA 125 assay in the diagnosis of endometriosis. *Hum Reprod.* 1995;10(4):932-4. doi: 10.1093/oxford journals. humrep.a136064, PMID 7650145.
- Pittaway DE, Fayeze JA. Serum CA-125 antigen levels increase during menses. *Am J Obstet Gynecol.* 1987;156(1):75-6. doi: 10.1016/0002-9378(87)90207-9, PMID 3467595.
- Jacobs I, Bast RC Jr. The CA 125 tumor-associated antigen: a review of the literature. *Hum Reprod.* 1989;4(1):1-12. doi: 10.1093/oxford journals. humrep.a136832, PMID 2651469, P. 4.
- Jubanyik KJ, Comite F. Extrapelvic endometriosis. *Obstet Gynecol Clin North Am.* 1997;24(2):411-40. doi: 10.1016/s0889-8545(05)70311-9, PMID 9163774.
- London S, Parmley T. Endometriosis and ascites. *South Med J.* 1993;86(10):1173-5. doi: 10.1097/00007611-199310000-00022, PMID 8211342.