

# Ovarian Endometrioma Associated With Extremely Elevated Serum CA-125 Levels: Utility of Imaging in a Diagnostic Dilemma

Aysun KARABULUT<sup>1</sup>, Nevzat KARABULUT<sup>2</sup>, A. Baki YAĞCI<sup>2</sup>

<sup>1</sup>Clinic of Obstetrics and Gynecology, Denizli State Hospital, Denizli, Turkey

<sup>2</sup>Department of Radiology, Pamukkale University Hospital, Denizli, Turkey

## Abstract

Elevated CA-125 levels in patients with endometrioma can create a diagnostic dilemma. We report the sonographic and magnetic resonance imaging findings in a case of ovarian endometrioma with a serum CA-125 level of 2229 IU/ml, and discuss the utility of imaging features in the assessment of potential malignancy.

**Keywords:** endometrioma, endometriosis, CA-125, ultrasonography, magnetic resonance imaging

## Özet

### Yüksek Serum CA-125 Düzeyinin Eşlik Ettiği Ovarian Endometrioma: Tanısal İkilemde Görüntüleme Yöntemlerinin Yararları

Endometriomalı hastalarda aşırı yüksek CA-125 düzeyleri tanısal zorluk çıkarabilir. Bu çalışmada serum CA-125 düzeyi 2229 IU/ml olan over endometriomalı bir olguda sonografik ve manyetik rezonans görüntüleme bulguları sunulmuş ve potansiyel malignitenin tayininde görüntüleme yöntemlerinin yararlılığı tartışılmıştır.

**Anahtar sözcükler:** endometriyoma, endometriozis, CA-125, ultrasonografi, manyetik rezonans görüntüleme

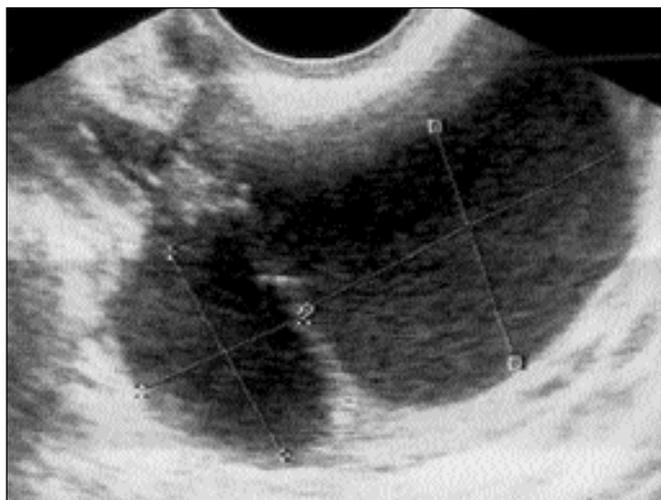
## Introduction

Serum CA-125, a tumor associated antigen, is elevated in epithelial ovarian carcinomas, and mildly elevated in some women with benign gynecologic disorders. Despite the low positive predictive value for malignancy, CA-125 levels greater than 300 IU/ml are usually associated with malignancy even in premenopausal patients. However, serum CA-125 levels greater than 1000 IU/ml has occasionally been reported in patients with ovarian endometriosis (1,2). Elevated CA-125 levels in patients with endometrioma can cause a diagnostic dilemma mimicking ovarian cancer. Moreover, endometrioma has occasionally been shown to be accompanied by malignant ovarian tumors (3,4). We report a rare case of ovarian endometrioma with extremely elevated serum CA-125 levels, and discuss the utility of imaging features in the assessment of potential malignancy.

## Case Report

A 26-year-old nulligravid woman without previous history of gynecologic disorder was seen for preconceptional counseling. Her menstrual cycle was regular (30/5/2), and she was on day 23 of her cycle. Physical and pelvic examinations were unremarkable. The complete blood count and blood biochemistry were within normal limits. Transvaginal ultrasonography examination showed a well-delineated 4x3 cm biloculated cystic mass within right ovary with low-level internal echoes (Figure 1). The serum CA-125 level was 2229 IU/ml (Enzyme immunoassay, upper reference limit, <35 IU/ml). CA 19-9 and CA 15-3 levels were normal. Transabdominal Doppler ultrasound revealed no abnormal vascularity. Magnetic resonance (MR) imaging of the pelvis showed the mass to be homogeneously hyperintense on T1-weighted images (Figure 2A), which shaded on T2-weighted sequences. The wall and the septum were hypointense on both T1- and T2-weighted images. The internal signal remained high on fat-saturated sequences (Figure 2B). There was no evidence for a mural nodule, solid component or enhancement after intravenous injection of gadolinium. Based on the imaging features, the lesion was considered to be an endometrial cyst without evidence of associated malignancy. Subsequ-

**Corresponding Author:** Dr. Aysun Karabulut  
Hastane Cad. Umut Apt. No: 5/3 20010 Denizli, Türkiye  
Phone : +90 (258) 262 32 52  
          +90 (532) 569 33 52  
Fax : +90 (258) 373 86 97  
E-mail : aysunkarabulut@yahoo.com



**Figure 1.** Transvaginal sonography shows biloculated cystic mass with low-level internal echoes.



**Figure 2.** T1-weighted MR images without (A) and with (B) fat-suppression reveals bilobed cystic mass in the right adnexa containing hyperintense fluid and surrounded by hypointense wall. Fat-suppression (B) increases lesion conspicuity and differentiates endometrioma from fat-containing ovarian masses.

ent CA-125 level on day of 3 of her next cycle was 738 IU/ml. At laparoscopy, a right ovarian endometrioma with brown fluid was detected. Adhesions were seen in the fimbrial end of the right ovarian tube. The uterine serosa and the left adnexa were normal. A right cystectomy was performed and adhesions were lysed along with neosalpingostomy. Histopathologic examination confirmed the diagnosis of endometrioma. On the 15th postoperative day, serum CA-125 level dropped to 79 IU/ml.

## Discussion

Endometriosis is a common gynecologic disorder that affects women of reproductive age, and characterized by endometriomas (chocolate cysts), peritoneal implants and adhesions. Endometriomas are complex lesions containing multiple hemorrhagic cysts that have blood products of different ages within them. Although the disease is recognized as benign, endometriosis is occasionally accompanied by malignant ovarian tumors, especially endometrioid and clear cell adenocarcinoma (3,4). CA-125, a high molecular weight glycoprotein, was reported to be elevated in moderate-to-severe endometriosis (5). CA-125 levels increase with the stages of endometriosis, omental adhesions and rupture of endometrioma. In a series of 685 women with endometriosis, Cheng et al. (5) reported that patients with preoperative CA-125 levels higher than 65 IU/ml were at high risk for advanced stages of endometriosis or severe pelvic adhesions or rupture. They reported a mean CA-125 level of 427.47 IU/ml in patients with ruptured endometrioma and that of 77.96 IU/ml in patients with unruptured cysts. Associated peritoneal inflammation is a strong contributor of elevated CA-125 levels. In our patient, there was no sign of rupture at laparoscopy, but the fimbrial adhesions might in part be the cause of the abnormally high tumor marker.

Extremely elevated serum CA-125 levels are occasionally associated with endometriosis (1,2). A serum CA-125 level of 3890 IU/ml was reported in a patient with endometriosis (1), and that of 6114 IU/ml and 9357 IU/ml in a patient with ruptured endometrioma (2). The size of the endometriomas associated with elevated CA-125 levels is generally large. In our case, the size of the lesion was 4x3 cm, smaller than the previously reported cases. The timing of blood sample for CA-125 is crucial, because elevated CA-125 levels greater than 1000 IU/ml have been reported during menstruation (6). Therefore, sampling should not be done during or immediately after menstruation when tumor marker determination is required. However, serum samples were obtained during menstruation in most of the case reports showing extremely high CA-125 levels (1,2). The CA-125 level was 2229 IU/ml during luteal phase in our patient and 738 IU/ml during menstruation. We cannot explain the reason of decline of the marker during menstruation.

Elevated CA-125 levels in patients with endometriosis can create diagnostic problems mimicking ovarian cancer. Furthermore, malignant transformation has been reported as a rare complication of endometriosis, with an incidence of 0.6-

1.0% (3,4). Imaging findings can aid to diagnose or exclude an associated ovarian cancer. Ultrasound is usually performed as an initial study in the evaluation of pelvic diseases during reproductive years. Endometriomas have been described as having a homogeneous low-level echogenicity within loculated cysts and they are better appreciated by transvaginal ultrasound over transabdominal ultrasound in part by the better definition of the degree of internal echogenicity. Although the absence of mural nodule or solid components is helpful in the exclusion of carcinoma, sonographic evaluation is limited in ruling out ovarian malignancy (7). It may also be difficult on sonography to detect echogenic endocystic vegetations. Conversely, blood clot or focal fibrosis caused by recurrent hemorrhage may show focal wall nodularity on sonography, which is difficult to differentiate from malignant findings (7). The value of Doppler ultrasound is limited and confusing because low resistance blood flow was reported in cases of endometrioma (1-3). MR imaging is superior to ultrasound in the characterization of adnexal masses with sensitivity and specificity of greater than 90% in the detection of endometriomas (8). Therefore, patients with indeterminate sonographic findings and in whom there is suspicion of endometriosis may benefit from MR imaging. The addition of fat-saturated T1-weighted imaging has improved diagnostic accuracy in the evaluation of both endometriomas and peritoneal implants by augmenting lesion conspicuity, and differentiating lipid-containing ovarian masses from those containing blood (8). Endometriomas are characteristically homogeneously hyperintense on T1-weighted images and heterogeneous high and central low signal intensity or shading on T2-weighted sequences. They are surrounded by a low signal intensity wall representing hemosiderin or fibrous capsule. The presence of blood degradation products such as methemoglobin and hemosiderin, protein and the viscosity of the cyst contribute to MR imaging signal. Chronicity of cyst contents is directly proportional to the iron concentration and viscosity with a corresponding decrease in the T2 relaxation times. Tanaka *et al.* (4) reported MR imaging features of ovarian carcinoma in 10 patients with endometriosis. The presence of low signal intensity mural nodule on T1-weighted images, the absence of low signal intensity on T2-weighted images and enhancement of nodule on postcontrast T1-

weighted images were shown in endometriomas associated with carcinoma. The sonographic features of the lesion in our case were consistent with endometrial cyst and Doppler investigation did not reveal abnormal vascularity. MR imaging confirmed the diagnosis of endometrioma without evidence of malignant transformation such as low signal intensity mural nodule enhancing on postcontrast T1-weighted images. The exclusion of associated malignancy by the complementary imaging findings in our case helped us undertake laparoscopic cystectomy protecting the ovary instead of an extensive surgery for ovarian carcinoma.

This case illustrates the diagnostic dilemma clinicians' encounter when a CA-125 level is abnormally high in the presence of pelvic mass. Imaging findings are helpful in the diagnosis of endometriomas and the assessment of malignancy in patients with an adnexal mass and extremely elevated tumor markers. In a daily practice, ultrasound is adequate for diagnosis and planning operative approaches in most cases. MR imaging can be used as problem-solving tool in patients with indeterminate clinical and sonographic findings due to its superiority in the characterization of adnexal masses.

## References

1. Atabekoglu CS, Sonmezer M, Aydinuraz B, Dunder I. Extremely elevated CA 125 level due to an unruptured large endometrioma. *Eur J Obstet Gynecol Reprod Biol* 2003;110:105-6.
2. Kurata H, Sasaki M, Kase H, Yamamoto Y, Aoki Y, Tanaka K. Elevated serum CA125 and CA19-9 due to the spontaneous rupture of ovarian endometrioma. *Eur J Obstet Gynecol Reprod Biol* 2002;105:75-6.
3. Heaps JM, Nieberg RK, Berek JS. Malignant neoplasms arising in endometriosis. *Obstet Gynecol* 1990;75:1023-8.
4. Tanaka YO, Yoshizako T, Nishida M, Yamaguchi M, Sugimura K, Itai Y. Ovarian carcinoma in patients with endometriosis: MR imaging findings. *AJR* 2000;175:1423-30.
5. Cheng YM, Wang ST, Chou CY. Serum CA-125 in preoperative patients at high risk for endometriosis. *Obstet Gynecol* 2002;99:375-80.
6. Imai A, Horibe S, Takagi A, Takagi H, Tamaya T. Drastic elevation of serum CA125, CA72-4 and CA19-9 levels during menses in a patient with probable endometriosis. *Eur J Obstet Gynecol Reprod Biol* 1998;78:79-81.
7. Patel MD, Feldstein VA, Chen DC, Lipson SD, Filly RA. Endometriomas: diagnostic performance of US. *Radiology*. 1999;210:739-45.
8. Gougoutas CA, Siegelman ES, Hunt J, Outwater EK. Pelvic endometriosis: various manifestations and MR imaging findings. *AJR* 2000;175:353-58.