Extra-ordinary High CA-125 and CA19-9 Serum Levels in an Ovarian Endometrioma: Case Report

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Abstract

Endometriosis is an estrogen dependent disease. Levels of Cancer antigen-125 are significantly higher in women with moderate to severe endometriosis. However, patients with unruptured endometriosis rarely have serum CA-125 levels more than 1000 U/mL. This case report presents a diffuse, unruptured ovarian endometrioma in a 29- year-old woman, leading to an extraordinary high serum CA-125 and CA19-9 levels; usually typical of advanced ovarian carcinoma. Our experience emphasizes on benign gynecologic conditions such as endometrioma, which should be taken into account as a possible differential diagnosis in women with exaggerated elevation of the serum CA-125 level.

Keywords: Endometriosis, Tumor markers, Ovarian cyst, Endometrioma, CA-125, CA19-9

Introduction

Endometriosis is an estrogen dependent disease. It varies in appearance from a few minimal lesions on otherwise intact pelvic organs to massive ovarian endometriotic cysts that distort tubo ovarian anatomy with extensive adhesions (1). Endometrioma is a solitary, non neoplastic mass containing endometrial tissue and blood (2). Levels of Cancer antigen-125 (CA-125), a marker found on derivatives of the coelomic epithelium and common to most non mucinous epithelial ovarian carcinomas, have been found to be significantly higher in women with moderate or severe endometriosis(1). A value higher than 35 U/mL had a positive predictive value of 0.58 and a negative predictive value of 0.96 in establishing the presence of endometriosis (2).

Increased concentrations of CA-125 have been related specifically to the presence of endometriotic cysts and deep endometriosis (2). It has been hypothesized that endometriotic lesions contain a greater amount of CA125 than normal endometrium and that the associated inflammation could lead to an increased shedding of CA125 (1).

More recent studies reported that the value of CA125 in diagnosis of endometriosis is limited but higher for moderate to severe disease, especially if serum CA125 concentrations are measured during the mid-follicular phase (1). Many studies have demonstrated elevated serum CA-125 levels in patients with endometriosis (3-10). Rupture of a large ovarian endometrioma can lead to a high serum

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concentration of CA 125, a condition which, in addition to the detected pelvic mass, may mimic a malignant process (6, 9, 11).

However, patients with unruptured endometriosis rarely have serum CA-125 levels more than 1000 U/mL. (5)

Case Report

A 29-year-old unmarried woman was referred to gynecology clinic of Shariati Hospital for abdominal pain. Her chief complaint was constant lower abdominal pain from few months ago. She reported regular menstrual cycle with a decreasing interval in the last 5 months. A mild degree of dysmenorrhea was also noted beginning from menarch which was worsened in the last year. She had a past surgical history of appendectomy and rhinoplasty 11 and 9 years ago, respectively.

Seeking medical consultation, she underwent frequent ultrasound exams, all of them detecting large cystic masses with regular surface and several septa and internal echogen areas in her left and right ovaries. She was virgin, pelvic examination was not performed; abdominal and rectal examinations revealed no mass, tenderness or abnormalities. Serum CA-125 level was 2000 U/ml (reference range<35 U/ml). Measurement of serum CA-125 level was repeated after one week and again it was more than 1000 U/ml. Serum CA-125 levels was measured by using appropriate chemiluminescent immunoassay kits (ROCHE company, ELECSYS2010 device).

Serum alpha fetoprotein (α-FP), carcinoembryonic antigen (CEA) and Cancer antigen 19-9(CA19-9) levels were also 1.3, 0.8 and >1000 U/ml, respectively.

Malignant ovarian tumors were considered as the possible differential diagnosis. After achieving written consent of the patient and under general anesthesia, laparatomy was conducted through a midline incision. A unilateral ovarian endometrioid cyst measuring 6×5 centimeters was detected on the left ovary. A 3×3 centimeter endometrioma was found in the right ovary. Several diffuse but small endometriotic foci (black puckered lesions) were detected on the omentum. According to Revised American Society for Reproductive Medicine, the diagnosis was stage IV which considered severe disease (1).

Chocolate-like content of the larger cyst was aspirated and bilateral cystectomy was performed. Endometriotic implants on both ovaries and omental surface were cauterized. There were abundant adhesions around ovaries and fallopian tubes, although some strong adhesions were found on posterior cul de sac.

Peritoneal washing for cytological examination was reported to be benign and definitive histopathological diagnosis revealed endometrioma (figures 1 and 2). The patient was recommended to receive subsequent ovarian suppression using combined oral contraceptive pills.

Figure 1: Extra-ordinary elevated tumor markers in an ovarian endometrioma

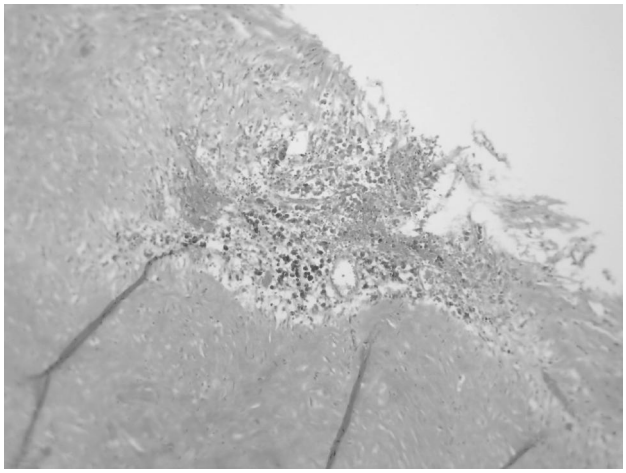
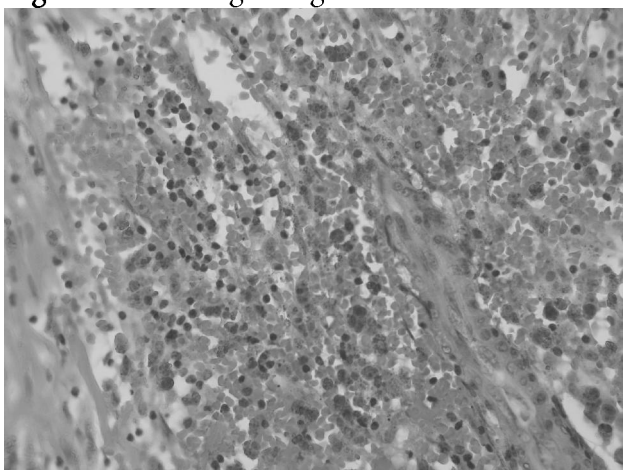


Figure 2: Pathologic diagnosis of endometrioma



Discussion

In this paper we presented a case of young woman with bilateral un-ruptured ovarian endometrioma associated with an extra ordinary high serum CA-125 and CA19-9 levels, usually typical of advanced ovarian carcinoma.

The reference value for CA-125 is 35 U/mL based on the pioneering work by Bast (12) who reported that only 1 % of apparently healthy women and 6.3% of women with benign disease had values above that level. Levels of CA- 125 > 65 U/mL correlate highly with ovarian malignancy and distinguish malignant from benign disease with a specificity of 88 to 92% and a sensitivity of 75% to 83%(13,14). Plasma CA-125 > 194 U/mL is considered a positive criterion for differentiating malignant pelvic masses from benign pelvic masses (15).

CA-125 a high-molecular-weight glycoprotein expressed on the cell surface of some derivatives of embryonic coelomic epithelium, is often elevated in cases of mild-severe endometriosis, as well as other conditions, including acute pelvic inflammatory disease, adenomyosis, uterine leiomyoma, menstruation, pregnancy, epithelial ovarian cancer, pancreatitis, and chronic liver disease(2). The most common benign gynecologic conditions associated with elevated serum CA-125 concentrations in patients appear to be caused by ovarian endometriomas and deeply infiltrating endometriosis, especially in the more severe forms (revised American Fertility Society classification, classes III and IV). In one study, 79% of patients with endometriomas had CA-125 levels > 35 U/ml (15).

The human endometrium produces and secretes CA-125. The CA-125 concentration, thus, in the cystic fluid of an ovarian endometrioma may be high, even more than 1000000 U/ml (16). However, the serum CA-125 concentration is low compared to that in endometriotic cyst fluid (11). The thick wall of the endometriotic cyst prevents the large CA-125 glycoprotein molecules from reaching the peripheral circulation (16). However, Patients with endometriosis rarely have a CA125 concentration more than 100 IU/ml (11).

The mechanisms by which endometriosis may elevate serum CA125 and CA19-9 concentration are only partly understood, and may be due to many reasons. Some of the CA125 molecules from the ruptured ovarian tumor may be transferred through the peritoneum, thereby increasing serum CA125 concentration (6). There is evidence that peritoneal mesothelial cells are even more potent than ovarian cancer cells in producing CA-125 (17). Some of the CA-125 molecules leaking from the endometriotic cyst may be transferred through the peritoneum and the associated inflammatory reaction of the mesothelial cells of the peritoneum probably contribute to the presence of very high level of serum CA-125 (8). In addition, superficial endomertiotic implants of the ovarian endometriomas mainly secret towards the peritoneal cavity from where CA-125 is slowly resorbed through the peritoneum (18).

Serum CA 125 level of 6144 U/ml and 9300 U/ml were reported in patients with endometriomas, which was associated with peritoneal irritation due to the acute rupture of the cyst (3, 11). Adhesions in the peritoneum, omentum, ovary, fallopian tube, and colon, and cul-de-sac, size of the cyst, an enlarged surface area of endometrial tissue and stage of the endometriosis have been reported as the cause of elevated serum CA-125 levels in patients with endometriosis (11, 19). Thus, in our case, an enlarged surface area of endometrial tissue, advanced stage of the endometriosis, diffuse endometrial foci on the omentum ,and adhesions in the peritoneum may be the cause of extra-ordinary elevation of CA125 level.

High CA-125 values of unruptured endometriomas with histologically confirmed endomertiosis has been reported so far (3,5,6,8,10). In accordance with these cases our present case demonstrated that abnormally high levels of plasma CA-125 may be encountered in un-ruptured endometriomas. However, some serum CA-125 levels reported previously were higher than ours (3,5,6,8). The highest value reported in unruptured endometrioma is 9537 U/mL (6). Serum CA-125 levels of 3890 U/mL (3), >6000 U/mL(8),1741 U/mL(10) and7900 U/mL(5) were also reported.

This case is the highest value reported for CA19-9 with histologically confirmed endomertioma. Our present case demonstrated that abnormally high levels of plasma CA19-9 may also be encountered in unruptured endometrioma. There are other reports of elevated CA19-9 concentrations of 289 U/mL (3) and 170.9 U/mL (10) in endometriomas, too.

Serum CA19-9 concentrations are elevated in patients with gastrointestinal system malignancies, or malignant and benign ovarian tumors (20, 21). Some of the CA19-9 molecules may be transferred through the peritoneum, thereby increasing serum CA19-9 concentration (6). However, there is no sufficient

information about the use of this marker in endometrioma.

In conclusion, elevated levels of serum CA-125 and CA19-9 are detected in advanced stages and diffuse even unruptured endometriomas. Thus, endometrioma should be taken into account as a possible differential diagnosis in women with an adnexal mass with exaggerated elevation of the serum CA-125 level.

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