

Extreme elevation of serum CA-125 in two women with severe endometriosis: case report

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Abstract

Two women with elevated preoperative serum CA-125 levels were found to have extensive endometriosis - one, the highest level related to endometriosis ever reported in the English literature. Endometriosis was found to be etiologic as seen by the prompt reduction in serum CA-125 levels following surgical treatment limited to endometriosis. Thus, a very high CA-125 level does not necessarily forebode ovarian malignancy.

Introduction

Serum CA-125 levels have been found to be elevated in association with benign and malignant pelvic masses¹. It has been reported that a threshold level of 65 IU/ml of the antigen has 78% sensitivity and 83% specificity in effectively distinguishing malignant from benign disease¹. With respect to endometriosis, substantially higher levels than this threshold for CA-125 have been reported². The highest previously reported value in the English literature with surgically confirmed endometriosis is 1200 IU/ml². We report two cases of abnormally elevated preoperative serum CA-125 levels, with case 2 measuring the highest reported value attributable to endometriosis in the literature to date.

Case reports

Case 1

A 33-year-old nulligravida was first seen in our office for primary infertility and severe dysmenorrhea. Physical examination was suspicious for endometriosis. Initial ultrasound on day 11 of a 30-day cycle revealed large cystic ovaries, with the left containing a 46 mm cyst (average diameter) and the right, a 25 mm cyst. Serum CA-125 at this time was 14 IU/ml.

Stage 3 endometriosis was confirmed laparoscopically. Although preoperative serum CA-125 (obtained on day 9 of cycle) had risen to 435 IU/ml, these results were not made known until 5 days postsurgery. Eight months later the patient underwent laparotomy. The uterus was normal in size, shape and contour. The right ovary was enlarged, containing two endometrial cysts measuring approximately 45 mm and 30 mm in diameter, the right Fallopian tube was adhered to the right ovarian fossa and covered by the right ovary; the left oviduct was normal, except for the presence of two superficial implants on the ampullary serosa of the tube. The left ovary was normal. The peritoneum covering the bladder was covered with superficial endometriotic implants measuring a total of 25 x 15 mm². There were also superficial implants seen on the posterior leaf of the broad ligament above the left uterosacral ligaments and over the left uterosacral ligaments totaling 15 x 10 mm². The ovarian cysts were excised and laser vaporization of endometriotic implants was carried out. Stage 4 endometriosis, without signs of malignancy, was the surgical diagnosis. The pathology report confirmed surgical findings. Postsurgical serum CA-125 was 24 IU/ml.

Case 2

A 46-year-old nulligravida, with amenorrhea, initially presented with severe recurrent pelvic pain. The patient reported three occurrences of ruptured ovarian cysts during the previous year, the last resulting in peritonitis. Our initial ultrasound revealed a cyst in the right ovary averaging 24 mm, and a left ovarian cyst of 32 mm located adjacent to the uterus. The initial CA-125 was 149 IU/ml.

Surgical diagnosis was deferred, due to the patient's hesitance to undergo surgery after transient asystolic complications with a prior surgery. Therefore, serial CA-125 levels were followed for 5 months consecutively. Monthly values were: 231 IU/ml, 274 IU/ml, 267 IU/ml, 400 IU/ml and 1385 IU/ml.

In response to the level of 1385 IU/ml, laparoscopic surgery was scheduled. The patient refused laparotomy and removal of any pelvic organs. Dilatation and curettage, laparoscopic lysis of adhesions, Yag laser fulguration of endometriosis and attainment of pelvic washings were performed. Findings included a 7-8-week myomatous uterus, atrophic left ovary and cystic right ovary adhered to the posterior cul de sac, exuding endometrial tissue. No other deep endometriotic implants were noted. There was no evidence of malignancy. Pelvic washings were negative for malignant cells. Ovarian biopsy revealed ovarian stroma with hemosiderin-laden macrophages, consistent with endometriosis. Postsurgical serum CA-125 measured 122 IU/ml, rising to 150 IU/ml 5 months later. Repeat ultrasound demonstrated recurrence of right ovarian cysts, but so far no further increases in CA-125 levels.

The CA-125 assay was measured by solid-phase radioimmunoassay (Centocor, Malvern, PA). The result of levels over 500 IU/ml was obtained by diluting the serum sample ten-fold, according to the manufacturer's instructions, therefore bringing it within the linear range of the assay. Studies by the manufacturer have

shown the intra- and inter-laboratory coefficient of variation to be less than 10% up to 1500 IU/ml.

Discussion

Although elevation in serum CA-125 levels may be present in both benign and malignant pelvic disorders, some critical cut-off level may exist, such that a woman with a level higher than this threshold would be more likely to have malignant disease. Soper and colleagues found that seven of the 13 patients with endometriomas had elevated CA-125 levels; the highest level, however, was less than 100 IU/ml¹. A case of stage III endometriosis was reported by Malkasian with a CA-125 level of 726 IU/ml³. The two cases described by Nagara and colleagues², which demonstrated very high serum CA-125 levels in women with endometriosis and adenomyosis, left some question as to whether endometriosis *per se* may cause such levels, or is the presence of adenomyosis a co-requisite for this complication. Although the levels dropped precipitously following surgery, both patients had bilateral oophorectomies and hysterectomies. Our two cases also showed marked decreases in extremely high CA-125 levels postoperatively. However, in both cases, only the endometriosis was surgically treated. This further supports the concept that endometriosis without uterine involvement may cause extreme elevations of serum CA-125.

The variable levels of CA-125 seen in both patients do not represent a variation in assay, but instead implied rapidly rising levels which were only to drop after therapy.

We believe that case 2, with a preoperative serum CA-125 of 1385 IU/ml, represents the highest level ever reported in relation to endometriosis, and possibly the highest non-pregnant value reported secondary to benign disease. Pittaway and Favez demonstrated that the CA-125 level may increase significantly during menses in patients with endometriosis⁴; however, none of the sera samples from patients 1 and 2 were obtained during the menses. Levels over 1000 IU/ml have been reported in pregnant women during the early first trimester who subsequently had spontaneous abortions, even after establishing fetal viability sonographically⁵.

The highest serum CA-125 level found in a series of 87 patients with laparoscopically confirmed endometriosis was 361 IU/ml⁶. They also found more elevated levels in a higher frequency with more advanced stage III and stage IV (AFS) compared to stage I and II⁶. They also found a statistical reduction following danazol therapy or surgery⁶.

These cases demonstrate that very high CA-125 levels do not necessarily indicate ovarian malignancy, and also that even very rapidly rising levels are still consistent with benign disease, e.g. endometriosis.

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