

Ovarian cancer in a woman previously diagnosed with endometriosis and an extremely high serum CA-125 level

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Summary

Purpose: Follow-up of a woman with a serum CA-125 level > 1000 U/mL where laparoscopy only found endometriosis.

Methods: Case report - re-evaluation several years later.

Results: Extensive clear-cell carcinoma of ovary with metastases leading to death.

Conclusion: This case suggests that bilateral oophorectomy should be performed in women not desiring any more children if the serum CA-125 level is very high even if only endometriosis is found initially.

Key words: CA-125; Clear cell carcinoma; Ovary; Endometriosis.

Introduction

Elevations in serum CA-125 levels have been associated with epithelial ovarian cancer [2-4]. However, an elevation of this glycoprotein has been found in benign conditions of the pelvis [5-11].

One of the benign conditions associated with elevated CA-125 levels is endometriosis [6, 7, 10-16]. Some cases have been reported with serum CA-125 levels over 1,000 U/mL in women without ovarian cancer but with a diagnosis of endometriosis [1, 16-21]. The highest level to date recorded was 9,300 IU/mL in a woman with a ruptured endometriotic cyst [20], and the highest recorded level without cyst rupture was 6,114 IU/mL [21].

The question arises as to whether women with very high CA-125 levels and endometriosis have any greater risk of developing subsequent ovarian carcinoma. When high CA-125 levels are present in women no longer considering pregnancy, the demonstration of endometriosis involving the ovaries would normally result in oophorectomy as performed by Nagara *et al.* [22]. The first case report of a woman presenting with a serum CA-125 level >1,000 IU/mL was reported by Check *et al.* [1]. However for this patient who had a CA-125 level as high as 1,385 IU/mL, oophorectomy was refused by the 46-year-old woman and she insisted on laparoscopy only with laser fulguration of endometriosis for pelvic pain [1]. Unfortunately, this woman, who was the first one described with these extremely high levels, subsequently developed ovarian carcinoma as described herein.

Case Report

A 46-year-old nulligravida with amenorrhea presented with severe recurrent pelvic pain in 1989. She demonstrated a 24x23x22 mm cyst with low level internal echoes on the right ovary. CA-125 was 149 IU/mL. Her levels were watched for five

consecutive months and the levels rose to 231, 274, 267, 400, and 1,385 IU/mL, respectively, as previously described [1].

Based on the very high CA-125 levels, the presumptive diagnosis was possible ovarian cancer and referral to a gynecologic oncologist with probable exploratory laparotomy was recommended [1]. However the patient, who was a nun and a medical technologist, refused laparotomy stating that she had almost died from an arrhythmia related to her lupus cardiomyopathy when having previous surgery.

She found a reproductive endocrinologist who was willing to perform a laparoscopy with Yag laser fulguration of endometriosis [1]. The ovarian biopsy revealed ovarian stroma with hemosiderin-laden macrophages, consistent with, but not diagnostic of, endometriosis [1], since endometrial glands and stromas were not identified. Postoperatively the CA-125 level was 122 IU/mL and five months later it was 150 IU/mL and there was a recurrence of a right ovarian cyst [1]. Four years following surgery her CA-125 dropped to 64 IU/mL.

The woman stopped coming for evaluation of the CA-125 level or pelvic sonography until May of 1999 (5 years from her CA-125 level of 64 IU/mL in 1994) complaining of marked fatigue. An abdominal mass was easily palpated. Abdominal ultrasound (she could not withstand the vaginal probe) showed a 177x101x129 mm mass with complex echoes with an irregularly shaped dense area and fluid seen inside of the mass. Fluid was found in the left lower quadrant measuring 53x67x60 mm. Hydronephrosis of the right kidney was found.

A CT scan of the abdomen and pelvis showed a large pelvic mass measuring 14.4x10.7x12.0 cm with cystic and solid components noted. The mass had septations and two foci of calcifications. The mass was anterior to the uterus and midline. Also severe right hydronephrosis and dilatation of the left ureter secondary to this large mass was also noted.

Laparotomy was performed and the large tumor was excised and identified as a clear cell carcinoma. The woman died one year later.

Discussion

One of the problems with using the CA-125 assay to diagnose ovarian cancer is that some ovarian cancers do not demonstrate high CA-125 levels until they become

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very advanced and some benign lesions, e.g. endometriosis, may present with extremely high serum CA-125 levels. One study found that if the serum CA-125 level was >1,000 IU/mL, 89% had gynecologic cancer, 7% non-gynecologic cancers and 3% benign conditions [18]. One could certainly question that had bilateral oophorectomy been performed when the CA-125 was so high ten years earlier, might early cancer have been detected in the patient described and could advanced metastatic disease have been averted? Unfortunately, the patient refused bilateral oophorectomy [1]. Frequent co-occurrence of endometriosis in the same ovary has been found [23, 24]. However, it is possible that histopathological evaluation of both ovaries might have found nothing more than endometriosis.

There have been several publications suggesting that the presence of endometriosis is associated with a greater chance of developing carcinoma of the ovary [25-31]. The first case of suspected malignant transformation in endometriosis was published in 1925 [32]. According to 15 published reports to date the incidence of ovarian endometriosis in ovarian cancer is closely related to histologic type, 3.3% - serous type, 3.0% - mucinous type, 39.2% - clear cell type, and 21.2% - endometrioid type [24, 29, 33-45].

The number of reported cases of endometriosis and very high CA-125 levels are small [1, 22] and at least one of them has already presented with advanced carcinoma of the ovary several years later. It is possible that some clinicians might use the aforementioned case report as an example of how benign endometriosis can present with very high CA-125 levels and thus use this case as a precedent for merely ablating endometriotic implants if they are present [1]. The 10-year follow-up of this case, as reported herein, strongly suggests that bilateral oophorectomy be performed if the woman has finished child bearing. For those who still desire another child this case could suggest unilateral oophorectomy on the side of endometriosis (if bilateral disease is not present) with subsequent removal of the contralateral ovary after delivery. For those patients not adhering to these suggestions then close monitoring every six months with pelvic sonography should be performed.

Now that the first case reported with serum CA-125 levels >1,000 IU/mL has subsequently developed ovarian cancer, it is imperative to aggressively follow all subsequent cases with such high levels with serial ultrasound and perhaps consider prophylactic oophorectomy if no further children are desired.

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