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BEYOND MALIGNANCY: CA-125'S UNUSUAL MIMICS – A CASE REPORT ON CA-125 ELEVATION IN ADENOMYOSIS

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Abstract

CA-125 is a widely recognized tumor marker, primarily associated with ovarian malignancies. However, its elevation is not exclusive to cancer and can be seen in benign conditions such as endometriosis, adenomyosis, and pelvic inflammatory disease. We present a case of a 47-year-old female with a three-month history of abdominal pain and heavy menstrual bleeding. Clinical examination revealed mild pallor, an anteverted uterus, and left forniceal fullness. Ultrasound findings showed a bulky uterus with multiple small fibroids and bilateral ovarian cysts. Laboratory investigations revealed an elevated CA-125 level (>1000 IU/mL), raising suspicion for malignancy. However, subsequent imaging with MRI and contrast-enhanced CT confirmed the presence of multiple heterogeneous myometrial lesions consistent with adenomyosis and non-enhancing simple bilateral adnexal cysts, likely paraovarian cysts. The patient underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy. Gross examination revealed an irregularly enlarged uterus with adenomyosis and simple serous paraovarian/paratubal cysts. Histopathological analysis confirmed adenomyosis and bilateral paratubal simple serous cysts. Cytology of peritoneal fluid was negative for malignancy. Postoperatively, the patient had an uneventful recovery, and repeat CA-125 levels decreased to 101 IU/mL. This case shows the importance of considering benign causes of CA-125 elevation to avoid misdiagnosis and unnecessary anxiety. Adenomyosis should be included in the differential diagnosis when evaluating elevated CA-125 levels, emphasizing the role of imaging and histopathology in establishing an accurate diagnosis.

INTRODUCTION

Cancer Antigen 125 (CA-125), also known as Mucin 16 (MUC16), is a high molecular weight glycoprotein that serves as a tumor marker, primarily associated with epithelial ovarian cancer. Since its identification in 1981 through the development of the OC125 monoclonal antibody targeting ovarian cancer cells, CA-125 has become integral in the clinical management of ovarian malignancies (1).

Beyond ovarian cancer, elevated CA-125 levels have been documented in various malignancies, including those of the endometrium, fallopian tubes, pancreas, breast, colon, lung, and stomach (1). This elevation is attributed to the expression of CA-125 on the surface of these cancer cells, leading to its release into the bloodstream. Consequently, CA-125 serves not only as a diagnostic marker but also plays a pivotal role in monitoring treatment response and detecting disease recurrence. For instance, a decline in CA-125 levels during therapy often indicates a favorable response, whereas stable or rising levels may suggest treatment resistance or disease progression (1).

Notably, CA-125 is not exclusively elevated in malignant conditions. Several benign disorders can also result in increased serum CA-125 levels, which poses challenges in differential diagnosis. These benign conditions include: Endometriosis, adenomyosis, uterine fibroids, pelvic inflammatory disease, menstruation, and pregnancy have all been associated with elevated CA-125 levels (2). Liver diseases such as cirrhosis, peritonitis, pancreatitis, and conditions causing serosal inflammation can also elevate CA-125 levels (3-5).

The presence of elevated CA-125 in these benign conditions is thought to result from irritation or inflammation of serous membranes, leading to increased production and release of CA-125 into the circulation (6).

Adenomyosis is a benign uterine condition characterized by the presence of endometrial glands and stroma within the myometrium. This ectopic endometrial tissue induces hypertrophy and hyperplasia of the surrounding myometrium, leading to a diffusely enlarged uterus. Common clinical manifestations include dysmenorrhea, menorrhagia, and chronic pelvic pain (2). The pathophysiological mechanisms underlying elevated CA-125 levels

in adenomyosis are not entirely elucidated. However, it is postulated that the disruption of the endometrial-myometrial interface and the invasion of endometrial tissue into the myometrium provoke a local inflammatory response. This inflammation may stimulate the production of CA-125 by mesothelial cells lining the peritoneum. Additionally, the increased vascularity and permeability associated with inflammation could facilitate the entry of CA-125 into the bloodstream, resulting in elevated serum levels (2,4).

The overlap in CA-125 elevation between malignant and benign conditions, such as adenomyosis, presents a diagnostic dilemma. Reliance solely on CA-125 levels for diagnosing ovarian cancer can lead to false-positive results, unnecessary anxiety, and potentially unwarranted invasive procedures (3,5). Therefore, it is imperative to interpret CA-125 levels within the broader clinical context, considering patient history, physical examination findings, and imaging studies. In cases where adenomyosis is suspected, imaging modalities like transvaginal ultrasound and magnetic resonance imaging (MRI) are valuable. MRI, in particular, offers superior soft-tissue contrast and can delineate the extent of adenomyosis, aiding in accurate diagnosis. Histopathological examination remains the definitive method for diagnosing adenomyosis, typically confirmed after hysterectomy (7).

This case report aims to highlight an atypical presentation of markedly elevated CA-125 levels in a patient with adenomyosis, emphasizing the necessity for comprehensive evaluation to distinguish between benign and malignant etiologies. By presenting this case, we seek to raise awareness among clinicians regarding the potential for significant CA-125 elevation in benign conditions like adenomyosis, thereby promoting more accurate diagnosis and appropriate management strategies.

CASE PRESENTATION

A 47-year-old female presented with complaints of abdominal pain during menstruation and heavy menstrual bleeding persisting for three months. She reported a history of menorrhagia, characterized by a 5/30-day cycle, requiring 6–8 pad changes per day without any passage of clots. The symptoms were progressively worsening, causing significant discomfort and affecting her quality of life. There was no history of weight loss, loss of appetite, or postmenopausal bleeding.

On general physical examination, the patient appeared mildly pale, suggesting possible anemia secondary to chronic heavy menstrual bleeding. On abdominal examination, the abdomen was soft with no palpable masses or tenderness. Per speculum examination revealed a healthy cervix and vagina with no visible abnormalities. Per vaginal examination showed that the cervix was pointing downward, the uterus was anteverted and normal in size, and left forniceal fullness was noted, raising suspicion of an underlying pathology affecting the left adnexa. The patient underwent ultrasound (USG) of the abdomen and pelvis, which revealed a bulky uterus measuring 8.7 × 8 × 7.8 cm, containing multiple small fibroids. The right ovary showed a 2.9 × 2.5 cm simple cyst, whereas the left ovary had a 5.4 × 4.7 × 4.5 cm simple cyst with evidence of peripheral vascularity, suggesting a possibility of a functional or paraovarian cyst.

Given the suspicion of an underlying gynecological disorder, serum CA-125 levels were measured and found to be markedly elevated (>1000 IU/mL). This high level raised concerns about the possibility of malignancy, prompting further imaging studies. A contrast-enhanced computed tomography (CECT) scan and magnetic resonance imaging (MRI) were performed for further evaluation. The imaging findings demonstrated multiple enhancing heterogeneous lesions within the myometrium, suggestive of adenomyosis versus intramural fibroids. In addition, simple cystic structures were identified in both adnexal regions, likely representing paraovarian cysts.

Given the significant symptom burden and imaging findings, surgical intervention was planned, and the patient underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH + BSO). Intraoperatively, the uterus was irregularly enlarged, corresponding to a 10–12 week-sized uterus with adenomyotic changes. The left adnexa contained a simple serous cyst measuring 8 × 8 cm, likely a paraovarian or paratubal cyst. Similarly, a 2.5 × 2.5 cm simple serous cyst was noted in the right adnexa. No evidence of peritoneal implants, adhesions, or other signs of malignancy was observed.

Histopathological examination of the excised uterus confirmed the presence of adenomyosis, characterized by the invasion of endometrial glands and stroma into the myometrium. The bilateral fallopian tubes contained paratubal simple serous cysts, which were benign. Cytological examination of the peritoneal fluid was negative for malignancy, further confirming that the elevated CA-125 levels were likely due to a benign etiology rather than an underlying gynecological malignancy. The patient had an uneventful postoperative recovery, with no immediate or delayed complications. Postoperatively, serum CA-125 levels were reassessed and had significantly decreased to 101 IU/mL, further supporting the diagnosis of a benign pathology rather than malignancy. The patient was discharged with appropriate postoperative care instructions and was advised regular follow-up.

The importance of considering benign conditions such as adenomyosis as potential causes of elevated CA-125 levels, which are often mistakenly associated with malignancy is seen here. A thorough clinical, radiological, and histopathological evaluation is crucial to ensure accurate diagnosis and avoid unnecessary anxiety or overtreatment in patients presenting with similar findings.

DISCUSSION

Cancer Antigen 125 (CA-125) is a glycoprotein commonly used as a tumor marker, particularly in the context of ovarian malignancies. However, elevated CA-125 levels are not exclusive to malignant conditions; they can also be observed in various benign disorders, including adenomyosis, endometriosis, pelvic inflammatory disease, and liver cirrhosis (8). This case report highlights a patient with significantly elevated CA-125 levels in the setting of adenomyosis, highlighting the necessity of considering benign etiologies in the differential diagnosis to prevent misdiagnosis and unnecessary interventions.

Adenomyosis is characterized by the presence of endometrial glands and stroma within the myometrium, leading to uterine enlargement and symptoms such as dysmenorrhea and menorrhagia. The exact mechanism by which adenomyosis leads to elevated CA-125 levels remains unclear. However, it is postulated that the invasion of endometrial tissue into the myometrium disrupts the endometrial-myometrial interface, provoking a local inflammatory response. This inflammation may stimulate the production of CA-125 by mesothelial cells lining the peritoneum (8). Additionally, the increased vascularity and permeability associated with inflammation could facilitate the entry of CA-125 into the bloodstream, resulting in elevated serum levels (8).

In this case, the patient's CA-125 level exceeded 1000 IU/mL, which is markedly elevated. While such high levels are often associated with malignancies, there are documented instances where benign conditions like adenomyosis present with CA-125 levels surpassing 1000 IU/mL (9). For example, a study reported that severe adenomyosis could lead to significantly elevated CA-125 levels, correlating with the extent of uterine enlargement (9). Another case highlighted a patient with severe adenomyosis and a CA-125 level over 1000 IU/mL, emphasizing that such elevations can occur in benign gynecologic conditions (10). The differential diagnosis for elevated CA-125 levels is broad, encompassing both malignant and benign conditions. Malignant causes include ovarian, endometrial, fallopian tube, pancreatic, breast, colon, lung, and stomach cancers. Benign conditions associated with elevated CA-125 levels include endometriosis, adenomyosis, uterine fibroids, pelvic inflammatory disease, menstruation, pregnancy, liver diseases such as cirrhosis, peritonitis, pancreatitis, and conditions causing serosal inflammation (9). This overlap necessitates a comprehensive evaluation to accurately interpret elevated CA-125 levels.

Imaging studies play a pivotal role in differentiating between these conditions. Transvaginal ultrasound and magnetic resonance imaging (MRI) are valuable tools in assessing uterine pathology. MRI, in particular, offers superior soft-tissue contrast and can delineate the extent of adenomyosis, aiding in accurate diagnosis (11). Histopathological examination remains the definitive method for diagnosing adenomyosis, typically confirmed after hysterectomy. In this case, imaging findings were consistent with adenomyosis, and histopathological analysis of the excised uterus confirmed the diagnosis. It is also noteworthy that CA-125 levels can be elevated in other benign conditions, such as pelvic inflammatory disease (PID). A study demonstrated that elevated CA-125 levels correlate with the severity of PID, with levels reaching as high as 656 U/mL in severe cases (12). This further complicates the interpretation of elevated CA-125 levels, as both benign and malignant conditions can present with significant elevations.

The importance of considering benign causes of elevated CA-125 levels, such as adenomyosis, to avoid misdiagnosis and unnecessary anxiety is addressed here. A comprehensive evaluation, including detailed clinical assessment, imaging studies, and histopathological confirmation, is essential for accurate diagnosis. Clinicians should be aware of the potential for significant CA-125 elevation in benign conditions and interpret these levels within the broader clinical context to guide appropriate management strategies.

CONCLUSION

This case highlights the importance of recognizing benign causes of markedly elevated CA-125 levels, particularly adenomyosis, to prevent misdiagnosis and unnecessary anxiety. While CA-125 is a well-established tumor marker for ovarian malignancies, its elevation is not exclusive to cancer and can be observed in several benign gynecological and systemic conditions. Adenomyosis, due to its inflammatory and infiltrative nature, can lead to significant CA-125 elevations, sometimes exceeding levels typically associated with malignancy. A comprehensive diagnostic approach, including clinical evaluation, imaging studies such as transvaginal ultrasound and MRI, and histopathological confirmation, is essential in distinguishing adenomyosis from malignancies. This case reinforces the need for caution when interpreting CA-125 results and emphasizes that its

elevation should always be assessed in the broader clinical and radiological context. By raising awareness of this diagnostic challenge, clinicians can avoid unnecessary surgical interventions and ensure appropriate management for patients with benign gynecological conditions.

REFERENCES

1. Bast RC Jr, Klug TL, St John E, et al. A radioimmunoassay using a monoclonal antibody to monitor the course of epithelial ovarian cancer. N Engl J Med. 1983;309(15):883-7.
2. Erdemoglu N, Saygili U, Soysal S, et al. Serum CA-125 levels in patients with adenomyosis. J Obstet Gynaecol Res. 2010;36(5):988-92.
3. Kammerer-Doak DN, Magrina JF, Nemiro JS, Lidner TK. Benign gynecologic conditions associated with a CA-125 level > 1,000 U/mL. A case report. J Reprod Med. 1996;41(3):179-82.
4. Masahashi T, Matsuzawa K, Ohsawa M, et al. Serum CA 125 levels in patients with endometriosis: changes in CA 125 levels during menstruation. Obstet Gynecol. 1988;72(3 Pt 1):328-31.
5. Ghaemmaghami F, Karimi Zarchi M, Hamedi B. High levels of CA125 (over 1,000 IU/ml) in patients with gynecologic disease and no malignant conditions: three cases and literature review. Arch Gynecol Obstet. 2007;276(5):559-61.
6. Koninckx PR, Meuleman C, Demeyere S, et al. CA125 in endometriosis. Hum Reprod Update. 1996;2(6):505-14.
7. Bischof P, Bianchi PG, Campana A. Molecular biology of normal and neoplastic ovarian cells. Hum Reprod Update. 1997;3(5):435-45.
8. Kiyoshi H, Yukihiro T, Yoshiyuki S, Kazuhiro T. Serum CA125 concentration in patients with benign endometrial cysts. Int J Gynaecol Obstet. 2013;123(1):37-41.
9. Patel MD, Feldstein VA, Chen DC, Lipson SD, Filly RA. Endometriomas: diagnostic performance of US. Radiology. 1999;210(3):739-45.
10. Li X, Liu L, Yan D, Guo SW. Predicting recurrence risk for endometrioma after conservative surgery: a novel CA125-based nomogram. Reprod Sci. 2020;27(12):2107-17.
11. Takeuchi M, Matsuzaki K, Harada M. Magnetic resonance imaging findings of adenomyosis: correlation with histopathological features and diagnostic pitfalls. World J Radiol. 2017;9(1):1-12.
12. Vasilev SA, Schlaerth JB, Campeau J, Morrow CP. Serum CA 125 levels in preoperative evaluation of pelvic masses. Obstet Gynecol. 1988;71(5):751-6.