Bartholin's gland cyst with markedly elevated CA19-9 level: A case report

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Abstract. This case report describes a 43-year-old woman who presented with a symptomatic left Bartholin's gland cyst accompanied by a markedly elevated serum CA19-9 levels (>1,000 U/ml). Despite initial concerns for malignancy, comprehensive evaluation, including contrast-enhanced CT and serial biomarker monitoring, revealed rapid CA19-9 normalization (83% reduction within 24 h post-marsupialization), reaching the normal range by day 59 post-drainage, suggesting an inflammatory etiology. This case underscores two key clinical insights: CA19-9 elevations exceeding 1,000 U/ml may occur in benign mucinous cysts and short-interval biomarker reassessment aids in differential diagnosis. These findings expand the current understanding of tumor marker dynamics in benign gynecological pathology.

Introduction

Carbohydrate antigen 19-9 (CA19-9) is a highly glycosylated mucin-type tumor biomarker identified by the monoclonal antibody 1116-NS-19-9. It serves as a key diagnostic and prognostic monitoring tool primarily for pancreaticobiliary and gastrointestinal malignancies (1). Its physiological basis stems from Lewis blood group antigen-related glycan structures expressed in normal epithelia of the pancreatobiliary ducts, gastrointestinal tract, endometrium and fallopian tubes. However, CA19-9 has well-documented limited specificity. Elevated levels are increasingly recognized in various benign conditions because of mechanisms such as inflammation-induced disruption of epithelial barriers facilitating antigen leakage into the circulation or excessive production by metaplastic or hyperplastic mucinous epithelia (1-3). Common benign conditions include acute cholangitis, liver cirrhosis, pelvic inflammatory disease and notably, gynecological cysts such as ovarian endometriomas and uterine adenomyotic cysts (1-3).

Bartholin's gland cysts are among the most common benign vulvar lesions, typically resulting from ductal obstruction leading to mucus retention and account for ~2% of vulvar masses in women (4). To the best of our knowledge, no prior studies have reported an association between Bartholin's gland cysts and markedly elevated CA19-9.

Notably, similarly high CA19-9 levels (>1,000 U/ml) in benign gynecological conditions are rare. Documented cases are rare and predominantly involve uterine adenomyotic/endometriotic cysts, such as, Zheng *et al* (5) reported a case with CA19-9 >1,000 U/ml (alongside elevated CA125); Imaoka *et al* (6) reported levels of 846 U/m in cystic adenomyosis. Ovarian endometriomas: While mild elevations (<200 U/ml) occur in ~30% of endometriosis cases, values exceeding 1,000 U/ml are reported in <2% of cases and are often associated with cyst rupture (2,7). Other benign entities: Moderate elevations have been noted in conditions such as hydrosalpinx and cervical mucinous cysts (3,8), but levels persistently >1,000 U/ml remain rare and necessitate thorough investigation to exclude occult malignancy.

The present case report presents the first documented case of a Bartholin's gland cyst accompanied by a notably elevated CA19-9 level (>1,000 U/ml). This striking finding challenges the conventional clinical tenet that 'CA19-9 >1,000 U/ml is pathognomonic for malignancy'. This finding underscores the need to reevaluate the interpretation of tumor markers within the context of benign mucin-producing cysts and highlights the risk of misdiagnosis, leading to unnecessary anxiety or aggressive interventions.

Through detailed analysis of diagnostic pathway of this case, therapeutic intervention (marsupialization) and rapid biomarker dynamics, the present case report aims to provide evidence-based insights that can be used to improve differential diagnostic strategies. The aim is to equip clinicians with the ability to distinguish such benign yet biomarker-alarm presentations from true malignancies, thereby preventing unnecessary interventions.

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Case report

Admission. A 43-year-old woman was admitted to the Department of Gynecology of the Second Affiliated Hospital of Tianjin University of Traditional Chinese Medicine (Tianjin, China) in January 2025, with a chief complaint of a palpable mass in the vulva for 4 days accompanied by pain for 1 day.

Medical history. This patient had a regular menstrual history with a cycle of 28-30 days and moderate flow, without dysmenorrhea. The last menstrual period of the patient was 19 days before admission. The patient had undergone laparoscopic ovarian cystectomy and cesarean section in 2003, both of which yielded benign pathology results. There was no history of chronic diseases such as diabetes, hypertension or coronary heart disease, as well as infectious diseases such as hepatitis, tuberculosis, typhoid fever or malaria. There was also no other surgical history, trauma or blood transfusion, and the patient had received routine vaccinations.

Physical examination. On admission, the vital signs of the patient were stable, with a temperature of 36.5˚C, a pulse rate of 90 beats per min, a respiratory rate of 18 breaths per min and a blood pressure of 130/85 mmHg. Cardiopulmonary examination revealed no notable abnormalities. Abdominal examination revealed a soft abdomen without hepatosplenomegaly or lower limb edema. Gynecological examination revealed a 4-cm cystic mass in the left Bartholin's gland with tenderness and fluctuation, a patent vagina, a smooth cervix, a normal-sized anteverted uterus and no notable abnormalities in the adnexa.

Laboratory and imaging. Most of the laboratory tests, including the tests for coagulation profile (six items), complete blood count, hepatitis B surface antigen/antibody, hepatitis C antibody, syphilis antibody, and HIV antibody were within normal limits. However, laboratory tests revealed elevated levels of CA19-9 (>1,000 U/ml; normal range, 0-27 U/ml), which were measured via an electrochemiluminescence immunoassay on a Roche Cobas e 801 analyzer (Roche Diagnostics). Pelvic ultrasound revealed multiple uterine fibroids (the largest measuring 3.9x4.4x3.6 cm) and pelvic effusion. Abdominal and pelvic CT scans revealed a full uterus with an irregular shape and a cyst in the upper pole of the left kidney.

Diagnosis and treatment. Patient was diagnosed with a Bartholin's gland cyst. The clinical presentation was typical for a Bartholin's gland cyst. An abdominal examination revealed a soft abdomen without hepatosplenomegaly or lower limb edema. Gynecological examination revealed a 4-cm cystic mass in the left Bartholin's gland with tenderness and fluctuation, a patent vagina, a smooth cervix, a normal-sized anteverted uterus and no notable abnormalities in the adnexa. The attending physician proceeded with surgical drainage under local anesthesia on the day of admission. The procedure involved making a longitudinal incision over the cyst, with transparent fluid drainage and placement of Vaseline gauze for drainage. Postoperatively, the patient was managed with routine gynecological care, including daily wound dressing changes. The medication used included one subcutaneous injection of 0.1 g lidocaine and one intravenous infusion of 500 ml 0.5% glucose.

Follow-up. Changes in CA19-9 levels are shown in Fig. 1. The postoperative course of the patient was uneventful, with no signs of infection or complications. The elevated CA19-9 levels prompted further evaluation via an abdominal and pelvic CT scan, which revealed reduced enhancement in the tail of the pancreas. Gastrointestinal endoscopy revealed mild gastritis. CA19-9 results were obtained postoperatively, which led to retrospective monitoring of tumor markers (including tests for α-fetoprotein, carcinoembryonic antigen, CA125, squamous cell carcinoma antigen, human epididymis protein 4 and human chorionic gonadotropin) and imaging studies (pelvic ultrasound, and abdominal and pelvic CT). While monitoring the patient for 2 months, no new diseases were observed, and other possible diseases that could cause elevated CA19-9 levels were successfully ruled out. It was ultimately confirmed that the increase in this indicator was only related to the Bartholin's cyst.

Discussion

As a key tumor marker, CA19-9 is secreted by various epithelial cells under normal physiological conditions and is mainly distributed in tissues such as the biliary tract, pancreatic duct epithelium, endometrium, fallopian tubes, endocervix and bronchial gland epithelium (9). CA19-9 is a substance similar to monosialylated Lewis blood group antigen and its synthesis involves the catalytic action of glycosyltransferases (such as β3GALT5 and FUT3). In malignant tumor cells, the increase in glycosyltransferase activity leads to the overproduction of CA19-9. In patients with digestive system forms of cancer, the level of CA19-9 is markedly elevated, with the incidence of elevated CA19-9 levels in patients with malignant tumors being markedly increased compared with that in patients with benign lesions and healthy individuals. The most common type of cancer is pancreatic cancer (62.04%), followed by liver cancer (44.25%), gastric cancer (26.40%) and colorectal cancer (26.32%) (10). Luo *et al* (11) revealed that the level of CA19-9 in patients with pancreatic cancer is considerably increased compared with that in healthy individuals or patients with benign pancreatic diseases (such as pancreatitis), with a diagnostic sensitivity of ~70%, and it is positively associated with pathological stage: the later the stage, the higher the levels of CA19-9.

The liver, as the main organ for clearing CA19-9, carries out a key role in its metabolism. In hepatobiliary diseases, biliary obstruction (due to stones or tumor compression) can lead to impaired excretion of CA19-9, whereas secondary biliary tract inflammation or infection can stimulate the overproduction of CA19-9 by biliary epithelial cells (12).

The level of CA19-9 in patients with cholangiocarcinoma is markedly increased compared with that in patients with benign biliary diseases. In the diagnosis of colorectal cancer with liver metastasis, the diagnostic sensitivity of CA19-9 is 72.3% (13,14). Zhang *et al* (15) confirmed that a CA19-9 level >309 μg/l is a specific threshold for diagnosing malignant biliary obstruction (89%), whereas a CA19-9 level >1,000 U/ml indicates a poor prognosis for patients with

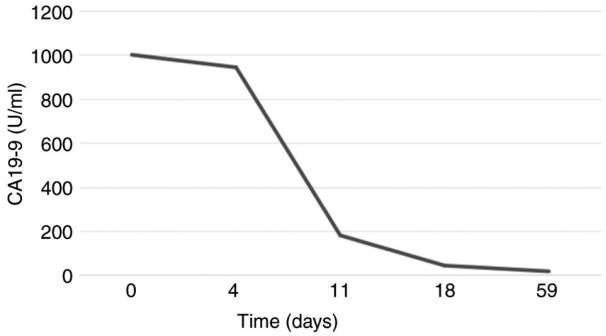

Figure 1. Changes in the serum CA19-9 level. CA19-9, carbohydrate antigen 19-9.

liver metastasis (with a median survival of only 8 months). In gastric cancer, CA19-9 levels are highly consistent with tumor cell proliferation activity and are markedly elevated in advanced-stage patients. It is often necessary to combine CA19-9 with other markers, such as CEA, CA72-4 and CA125, to enhance diagnostic efficacy (16,17). There are also reports revealing that CA19-9 is elevated to varying degrees in ovarian malignant tumors, especially in the middle and late stages of ovarian cancer, where its level can rise notably (18).

However, elevated CA19-9 is not a specific manifestation of malignant tumors. Among the healthy population undergoing physical examinations, 97.9% of individuals with elevated CA19-9 levels have non-malignant causes of increased CA19-9 levels (19). The main mechanisms involve inflammation-induced epithelial hyperplasia (such as increased ductal secretion caused by chronic pancreatitis) and oversecretion by cystic lesions. For example, Zurli *et al* (20) reported a case of a large atypical hepatic cyst in which the CA19-9 level of a patient reached 638 U/ml. Subsequent detection of CA72.4 in the cystic fluid confirmed that the lesion was benign (21). Moreover, although a CA19-9 level >1,000 U/ml usually raises concerns regarding malignant tumors, certain benign gynecological conditions can also demonstrate detectable expression of this marker (22-24).

The present case also adds new evidence to the elevation in benign mucinous cysts: Zheng *et al* (5) reported that CA19-9 levels in a uterine adenomyotic cyst were >1,000 U/ml, which returned to normal 6 weeks after resection; Imaoka *et al* (6) reported a level of 846 U/ml in cystic adenomyosis, attributing it to mucinous exudation; Takemori and Sugimura (7) and Rokhgireh *et al* (2) reported that although 30% of endometriosis cases showed mild elevation of CA19-9 (<200 U/ml), values exceeding 1,000 U/ml occurred in <2% of cases, usually accompanied by cyst rupture; other benign diseases, such as hydrosalpinx and cervical mucinous cysts, may show moderate elevation of CA19-9 (3,8), but levels exceeding 1,000 U/ml are still considered abnormal.

The patient in this case was a 43-year-old woman who presented with a palpable vulvar mass. After examination, the patient was ultimately diagnosed with a Bartholin's gland cyst. The attending physician carried out surgery for the Bartholin's gland cyst following the examination. The patient received routine postoperative care and did not develop any infections or other complications. However, the CA19-9 level of the patient exceeded the normal range (peak >1,000 U/ml). A series of tests were then conducted and malignancy was ruled out. Unexpectedly, the present case report confirmed that the elevation of the CA19-9 levels of the patient was likely associated with the Bartholin's cyst. This case is the first to show that a Bartholin gland cyst may cause a considerable increase in the serum CA19-9 concentration, which may be associated with the following factors: First, active secretion by the mucinous epithelium can occur. It has been confirmed that numerous patients with benign cysts (such as hepatic, renal and ovarian cysts) have a certain probability of experiencing elevated CA19-9 levels (21). We reasonably suspect that Bartholin's cysts may also fall into this category. Moreover, research by Yan *et al* (21) revealed that the serum CA19-9 positivity rate in patients with benign mucinous cystic diseases was 19.8%, which also supports the conclusion in the present case that the elevation of CA19-9 is likely due to the Bartholin's cyst. Second, multiple studies have demonstrated that key inflammatory factors in this disease, such as IL-6 and tumor necrosis factor-α (TNF-α), are associated with tumor markers (25-27). These factors may be the main cause of the sharp increase in the CA19-9 levels of the patient in the present case report. The fact that the CA19-9 level in this case decreased rapidly within 7 days (postoperative days 4-11) further indirectly demonstrates that the elevation was driven by inflammation. Third, regarding the physical characteristics of the cyst, Yan *et al* (21) revealed that in patients with benign cystic lesions, the CA19-9 level is positively associated with the cyst diameter (21,28).

For patients with elevated CA19-9 levels, a rational differential diagnosis pathway is key. On the basis of this case and the literature (5,6,29), the present case report proposes a strategy that includes dynamic monitoring, imaging and the combined use of multiple tumor markers for diagnosis. First, it is necessary to rule out false positives caused by detection interference (such as heterophilic antibodies or hemolysis) (30). The dynamic changes in CA19-9 can also be valuable for differentiating benign and malignant diseases and for monitoring therapeutic effects. CA19-9 should be retested at short intervals: If the level is >1,000 U/ml, retesting within 24-48 h is recommended. A rapid decline (a decrease of >50% within 24 h) strongly supports a benign lesion. In the case of tumor recurrence, CA19-9 may rise again and this may occur before imaging diagnosis. Therefore, it can also be used to monitor tumor recurrence (31). It is also recommended to combine the detection of tumor markers to improve the accuracy and effectiveness of disease identification (18,32). Second, for patients with confirmed elevated CA19-9 and no abnormal liver or kidney function, imaging should be carried out on the basis of symptoms: Pelvic MRI to rule out deep adenomyotic cysts (7) and if CA19-9 levels continue to rise, CT or PET-CT should be carried out to rule out pancreaticobiliary malignancy (33). In addition, cyst fluid analysis is also important. In future cases, CA19-9 in the drainage fluid should be quantified (a concentration much higher compared with that in serum suggests local secretion) and combined with markers such as CA72-4 and CEA to confirm local production.

However, the present study also has certain limitations. First, the tracking of inflammatory factors such as IL-6 and TNF-α could be increased to assess their potential impact on tumor

markers. In addition, the present case report has a single-case design and lacks analysis of cyst fluid biomarkers. Future studies should include immunohistochemical analysis of CA19-9 in the cyst epithelium (5), tracking the relationship between inflammatory cytokines (such as IL-6 and CRP) and CA19-9, and establishing a multicenter registry for rare CA19-9 elevations.

This case highlights the importance of a comprehensive approach for managing patients with elevated tumor marker levels and benign gynecological conditions. This underscores the need for clinicians to consider benign conditions when interpreting elevated tumor marker levels, potentially reducing unnecessary anxiety or aggressive interventions.

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Availability of data and materials

The data generated in the present study are included in the figures and/or tables of this article.

Authors' contributions

All authors contributed to the data collection and discussed the final version of the paper. WZ and TZ made substantial contributions to the conception or design of the work, acquisition, analysis and interpretation of the work, drafting the work or critically revising it for important intellectual content. All authors have read and approved the final manuscript. WZ and TZ confirm the authenticity of all the raw data. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics approval and consent to participate

The research complied with all the relevant national regulations, institutional policies and was in accordance with the tenets of the Helsinki Declaration, ethics approval was waived by the medical ethics review board of the Second Affiliated Hospital of Tianjin University of Traditional Chinese Medicine (waiver no. EfE2024/003/01). Informed consent for participation and publication was obtained from the patient prior to the start of the study.

Patient consent for publication

Written informed consent for publication was obtained from the patient.

Competing interests

The authors declare that they have no competing interests.

Use of artificial intelligence tools

During the preparation of this work, artificial intelligence tools (https://china.aje.com/cn/rubriq) were used to improve the readability and language of the manuscript, and subsequently, the authors revised and edited the content produced by the artificial intelligence tools as necessary, taking full responsibility for the ultimate content of the present manuscript.

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