What is your diagnosis?

A 55 year-old, post-menopausal woman presented to the gynecology outpatient department with a complaint of gradual, painless distension of the abdomen over the preceding three months. She also reported that for the last six months, her husband had complained of severe pain in the penile region after intercourse. The husband had undergone a complete genito-urinary examination, which was completely normal. There was no history of post-menopausal or post-coital bleeding. There was no history of shortness of breath, loss of appetite or weight, or bowel and bladder disturbances. The patient had become menopausal 15 years earlier, and she was not on any hormone replacement therapy. Her obstetric history revealed that she had two pregnancies, both of which were conceived spontaneously without any history of infertility treatment. Her last childbirth was 25 years earlier. She was hypertensive, treated with amlodipine 5 mg once daily for the previous two years. There was no history of any other chronic medical illness in the past.

The patient was conscious and coherent on examination, moderately built with stable vitals, and general and systemic examinations were unremarkable. Per-abdominal examination revealed a cystic, abdominopelvic mass of 22-24 weeks gravid uterus, occupying the hypogastrium, right and left iliac fossa, with restricted mobility. It had a smooth surface and regular borders. Fluid thrill was present, but there was no shifting dullness. Per speculum examination, the cervix was flushed with the vagina and taken up, and vaginal walls appeared atrophic and pale. On bimanual examination, the uterus was normal in size, and the same cystic mass of approximately 20x20x10 cm was palpated; it was not fixed to the uterus or pelvic side wall. These findings were reconfirmed on rectal examination. Rectal mucosa, recto-vaginal septum, and parametrium were healthy on P/V/R examination. Blood test results for tumor markers were CA-125 16 U/mL and CA-19-9 4.6 U/mL. Lactate dehydrogenase, carcinoembryonic antigen, alpha-fetoprotein and human chorionic gonadotropin were within normal limits.

A radiologist with more than 15 years of experience in gynecologic ultrasound (USG) performed a transabdominal USG scan. An irregular, lobulated, unilocular cystic lesion measuring 184x104 mm was found, arising from the left adnexa and extending into the lower abdomen. The lesion had thin walls with echogenic mobile contents. An incomplete, thin septation was present showing minimal vascularity (CS-2). There were no solid components. The inner margins appeared irregular, with focal wall thickening. There was no evidence of ascites or para-aortic lymphadenopathy. Neither ovary could be visualized. The uterus was unremarkable (Figure 1). All these features favored a lesion of intermediate risk (Ovarian-Adnexal Reporting Data System USG score 4). The patient was referred for cross-sectional imaging for better characterization and detection of additional findings. A contrast-enhanced computed tomography of the abdomen was performed. It revealed a large (220x180x120 mm) lobulated, cystic lesion with a thin septation, arising from the left adnexa and extending into the abdomen. The wall of the lesion showed focal areas of thickening with enhancement. Enhancement of the septation was present. Two enhancing papillary projections (13x10 mm) were noted in the posterior wall of the lesion. There was no ascites or para-aortic lymphadenopathy. The right ovary and uterus were normal but the left ovary was not separately identifiable. Features favored a left ovarian cystic mass lesion of intermediate concern (Figure 2). A pap smear was negative for malignant cells. USG of breast and upper and lower gastrointestinal endoscopies were unremarkable.

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Address for Correspondence: *Mishu Mangla*
e.mail: mishusingla83@gmail.com ORCID: orcid.org/0000-0003-0708-1037

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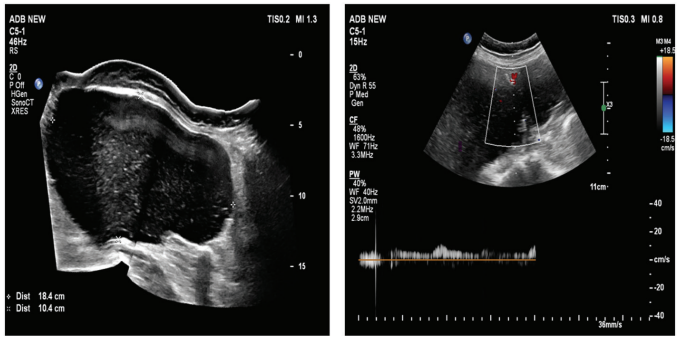

Figure 1. Greyscale ultrasound image of the pelvis showing an irregular, lobulated, unilocular cystic lesion measuring 184x104 mm, arising from the left adnexa extending into the lower abdomen. Note the presence of thin walls with echogenic mobile contents. An incomplete thin septation showing minimal vascularity (CS-2) was also present

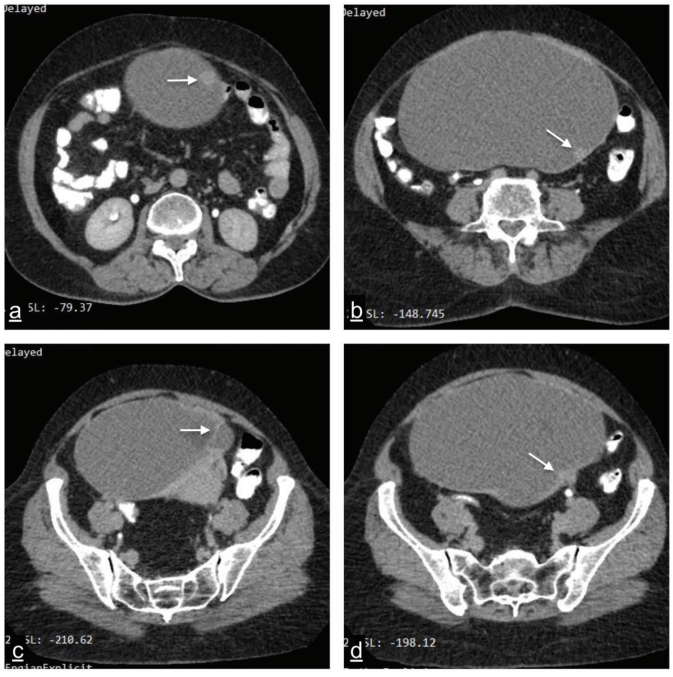

Figure 2. CECT images show a large (220x180x120 mm) lobulated cystic lesion with a thin septation in the left adnexa extending into the abdomen. The wall of the lesion showed focal areas of thickening with enhancement. Enhancement of the septation was present. Two enhancing papillary projections (13x10 mm) were noted in the posterior wall of the lesion

CECT: Contrast-enhanced computed tomography

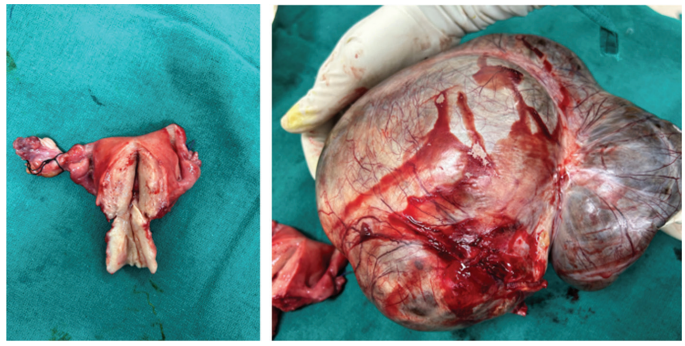

Figure 3. Intraoperative images showing normal uterus and right adnexa and 20x18x10 cm, uninoculated left ovarian cyst with fallopian tube stretched over it

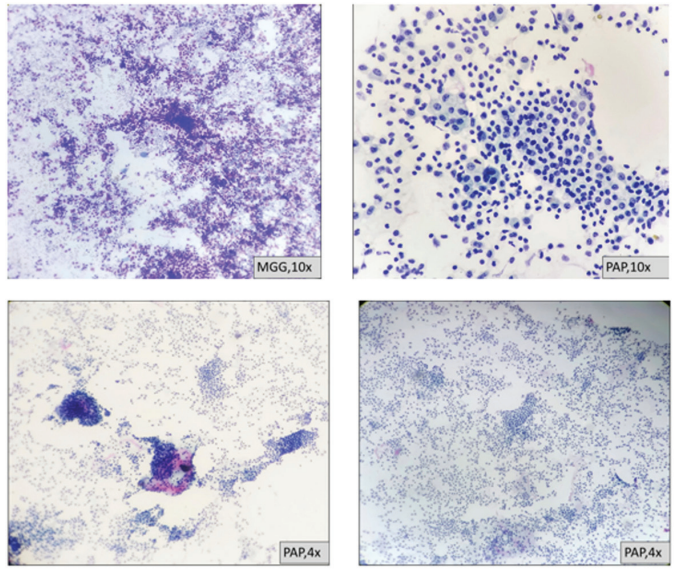

Figure 4. Ascitic fluid cytology negative for malignant cells

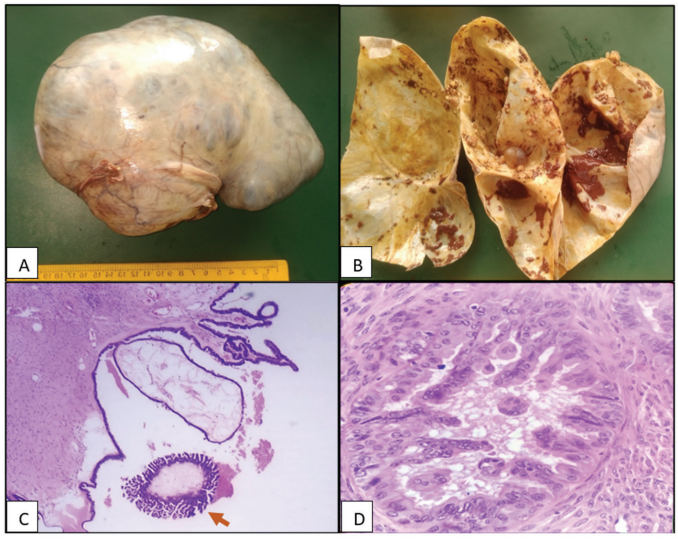

Figure 5. Large cystic lesion of the ovary with a smooth external surface (A) with unilocular cyst with a few papillary excrescences (B). Microscopically elongated "snakes" of epithelial cells without fibrovascular cores arising from papillae, resembling a Medusa-head (C). Tufted micropapillae in the large bulbous papillary structure (D). C and D are magnified at x100 and x400, respectively

Answer

A staging laparotomy was performed through a midline vertical incision. There was minimal straw-colored peritoneal fluid present which was sent for cytopathological examination. A left ovarian, unilocular, cystic mass, measuring 20x18x11 cm and weighing 2.25 kg, with an intact capsule and tube stretching over it was seen occupying the pelvic cavity (Figure 3). The uterus was average size and the right fallopian tube and ovary were healthy. There were no suspicious areas on the omentum, liver, or under the surface of the diaphragm. Total abdominal hysterectomy was performed with bilateral salpingo-oophorectomy (BSO) with pelvic and para-aortic lymphadenectomy and omental and peritoneal biopsy.

A pathologist with more than ten years experience in gynecologic pathology performed the histopathologic examination. The ascitic fluid was negative for malignant cells (Figure 4). Gross analysis of the ovary showed a thin-walled, cystic lesion with a smooth outer surface. The cut section showed an uninoculated cyst filled with viscous hemorrhagic fluid with incomplete septations and multiple papillary excrescences studded on the inner aspect of the wall (Figure 5). No solid component was noted. Histology showed that a single-layered, tubal columnar epithelium lined the cyst. The papillary growths were entirely exophytic, with no invasion at the base of the fronds. Micropapillae arose from the large bulbous papillary structures, lacking a fibrovascular core and were entirely comprised of large eosinophilic cells with distinct cell borders. The height of these micropapillary structures was more than five times the width. There was no evidence of stromal invasion; nuclear atypia and mitosis were inconspicuous. There were no macroscopic or microscopic implants over the fallopian tubes or on the contralateral ovary. Omentum, lymph nodes, and peritoneum were free of tumor. Based on the characteristic micropapillary pattern, the diagnosis of micropapillary serous carcinoma was made, which is a subset of borderline serous tumors, pT1aN0M0. The patient refused any further molecular or genetic testing due to economic constraints. The patient has now been on regular follow-up with pelvic examination, transvaginal USG, and monitoring of CA-125. There is no evidence of recurrence at the time of writing.

Discussion

With an annual prevalence of 1.8-4.8/100,000, borderline ovarian tumors (BOTs) account for approximately 15% of all epithelial ovarian cancers (1,2). BOTs were first described in 1929 by Taylor (3) as a "semi-malignant ovarian tumor". In 1971, the International Federation of Obstetrics and Gynecology identified BOTs as a "low-grade malignant tumor" completely different from ovarian cancer. In the World Health Organization classification of female genital tumors in 2014, the word "low-grade malignant tumor" was replaced by "borderline tumor" or "atypical proliferative tumor" (4).

BOTs are enigmatic neoplasms, and apprehension in the patient and the treating doctor is understandable. Although USG, in combination with color and power Doppler, is one of the best imaging modalities in differentiating benign from malignant ovarian masses with a specificity reaching up to 90% in expert hands (5), its ability to accurately diagnose an adnexal mass as borderline is limited. The sonographic appearance of BOTs range from unilocular cysts to masses with solid and fluid components, and papilla formation is typical (6,7). A retrospective study analyzing 383 ovarian tumors, including 27 borderline ones, found that BOTs have more similarity on USG to malignant lesions (absence of anechoic pattern, presence of diffuse internal echoes, and intra-cystic papillae) than to benign tumors (absence of septa, absence of solid or heterogeneous pattern) (8). However, papillary projections are known to be the most typical USG features of non-invasive (borderline and low-grade) malignant serous tumors. In contrast, solid components but no papillations favor invasive disease (9,10). Studies have shown that USG holds promise for differentiating varieties of BOTs, serous borderline ovarian tumors (SBOTs) from mucinous borderline ovarian tumors (MBOTs). Fruscella et al. (11) found that SBOTs and endocervical-type MBOTs had very similar sonographic features and usually presented as unilocular-solid lesions with a higher color score than intestinal-type MBOTs. Intestinal-type MBOTs were usually multilocular (with >10 locules) when compared with endocervical-type

MBOTs (11). The value of computed tomography and magnetic resonance imaging features in differentiating BOTs from malignant tumors is also relatively limited. Still, characteristics, such as papillary growth pattern with internal branching, higher signal intensity on T2-weighted images, and higher apparent diffusion coefficient values may be considered characteristic features of solid components in BOTs (12-14).

The predominant treatment is surgery. For patients who do not desire future fertility, complete resection with surgical staging, including total hysterectomy and BSO, peritoneal washing, omentectomy, and resection of grossly visible metastases, is the surgery of choice. As these tumors tend to occur in a younger age group, fertility-sparing surgery, rather than complete surgical staging, may be considered for patients desiring to maintain future fertility, as this has shown favorable outcomes in recurrence and disease-free survival (15). However, the National Comprehensive Cancer Network advises considering completion surgery after childbearing for patients with a remaining ovary (16). Routine lymphadenectomy and chemotherapy do not have a significant role in managing BOTs. The studies regarding adjuvant chemotherapy have contradictory results, with some showing benefits while others showing none.

Micropapillary features in BOTs are associated with an increased likelihood of invasive peritoneal implants, lymph node metastasis, and recurrence. However, using this as an independent factor to predict survival in BOTs remains controversial (12,13). Our patient did not have any risk factors for the development of BOT, as there was no history of intake of either ovulation-inducing drugs or hormone replacement therapy. The prognosis of BOTs, even at the advanced stage, is usually good, with a 5-year survival of more than 75%, even at stage 4 (17). The risk of malignant transformation is still unclear, and progression to invasive cancer may represent true transformation or even de novo development of ovarian or peritoneal cancer.

BOT presenting as asymptomatic ovarian cyst is not uncommon. The present case was, however, unique as the chief complaint was dyspareunia in the sexual partner. Since the genito-urinary examination of the husband was completely normal, the most probable cause was the ovarian cyst, bulging into the vagina, causing difficulty in penetration during intercourse. The present case is probably the first reported case of BOT presenting as dyspareunia for the sexual partner. Publishing such rare clinical features of a relatively common condition is essential to make clinicians aware that patients can sometimes present with these unusual presenting signs.

Borderline tumors pose a diagnostic challenge as they lack characteristic radiologic criteria compared with benign or malignant tumors. In this case, the patient was a post-menopausal female and thus the decision to undertake a complete staging laparotomy with BSO was straightforward. The dilemma of deciding the best treatment and surgery arises if the same tumor occurs in a young, reproductive age woman. A preoperative suspicion that the tumor may be borderline could be beneficial for fertility preservation. Healthcare providers should also be aware that specific histopathologic subtypes, such as micro-papillary variants, as in the presented case, are associated with an increased risk of recurrence and therefore determine poorer prognosis. Such patients should be monitored closely with regular comprehensive follow-up.

Mishu Mangla[1], Sumitra Sivakoti[2], Spandana Gabbeta[1], Naina Kumar[1], Somalwar B. Shrinivas[2], Annapurna Srirambhatla[3]

[1]Department of Obstetrics and Gynecology, All India Institute of Medical Sciences (AIIMS), Hyderabad, India

[2]Department of Pathology and Lab Medicine, All India Institute of Medical Sciences (AIIMS), Hyderabad, India

[3]Department of Radiodiagnosis, All India Institute of Medical Sciences (AIIMS), Hyderabad, India

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