

Incidental diagnosis of squamous cell carcinoma transformation in mature cystic teratoma of the ovary: A case report and review of literature

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Abstract

Malignant transformation in a mature cystic teratoma of the ovary is a rare complication. Herein, we report a case of a 62-year-old woman who was diagnosed with squamous cell carcinoma in a mature cystic teratoma of the ovary in the histopathology examination. This case report highlights the importance of suspecting malignant transformation in an elderly woman with a large mature cystic teratoma of the ovary with a thickened wall so that proper surgical and adjuvant treatments are planned.

Keywords

Squamous cell carcinoma, mature cystic teratoma of ovary, malignant transformation

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Introduction

Mature cystic teratoma of the ovary (MCTO) is a benign tumor that may develop in 10%–20% of women during their lifetime.¹ Malignant transformation of MCTO was noted in only 1.4%.² Squamous cell carcinoma (SCC) constitutes 0.3% of malignant transformation³ which accounts for 80% of malignant transformation in MCTO.⁴ SCC arising in MCTO is commonly observed in postmenopausal women.⁵ The other histological types include adenocarcinoma, small cell carcinoma, sarcoma, malignant melanoma and mixed type.⁶

The clinical presentation of SCC transformation in MCTO is not specific. The early-stage tumors are often detected incidentally during the abdominal examination or postoperative histological examination,⁷ while the advanced case might present with abdominal bloating, pain and palpable mass.^{3,8} Acute abdominal pain may be due to torsion of tumor or rupture or intra-cystic hemorrhage.⁹ The preoperative imaging studies and tumor markers are not specific to predict malignant transformation.³ The prognosis is usually poor which depends on complete cytoreduction, age and stage of the disease. Adjuvant treatment with platinum-based chemotherapy has been shown to improve the survival.³

Herein, we report a case of SCC arising in MCTO in a 62-year-old woman who was diagnosed postoperatively in the histopathological examination of the resected ovarian

tumor. The objective of this case report is to raise awareness among clinicians, radiologists and pathologists about the possibility of malignant transformation, especially if the woman is an elderly with big sized tumor with irregular thickening or solid foci in the walls so that complete surgical staging laparotomy is performed to accurately stage the disease and plan adjuvant treatment.

Case presentation

A 62-year-old-woman from a remote village in Bhutan, who had delivered six children vaginally at home, presented to the gynecology outpatient department (GOPD) at Jigme Dorji Wangchuck National Referral Hospital (JDWRH) with progressive distension of the abdomen over a 6-month period. There was no associated abdominal pain, bladder and bowel symptoms, or change in appetite or weight loss. She was menopausal for the last 20 years without any history of postmenopausal bleeding. She had no significant medical

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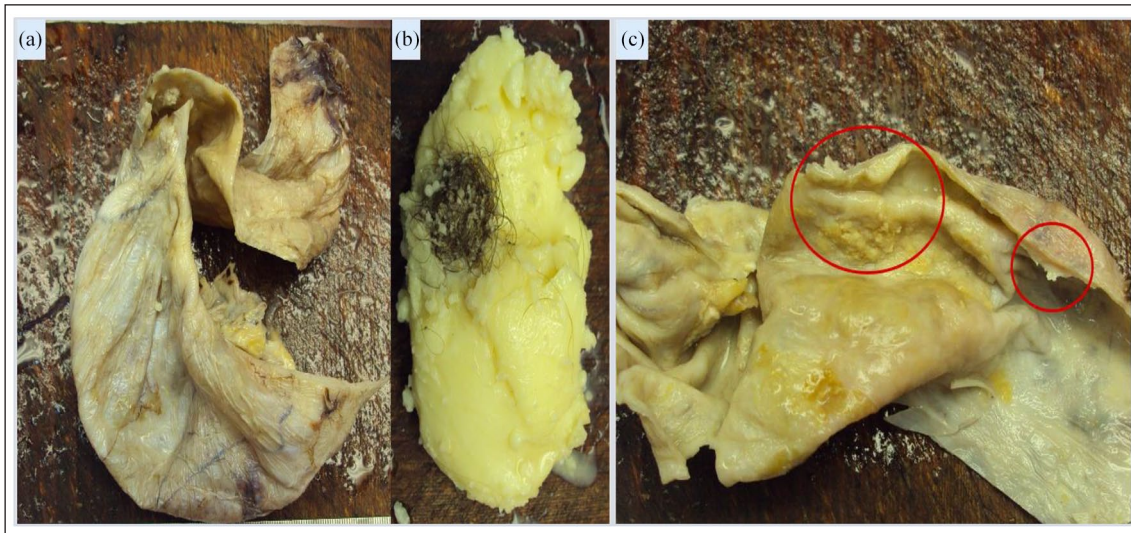


Figure 1. Gross image of the cyst: (a) external surface, (b) cystic content and (c) inner surface of the cyst (red circle: thickened part of the wall).

disorders. However, she was diagnosed to have hypertension during her recent visit to the hospital, and she was started on losartan 50mg once daily (OD) which has controlled her blood pressure. Her performance status according to the Eastern Cooperative Oncology Group (ECOG) scale¹⁰ was 0.

On abdominal examination, there was a huge abdominopelvic mass corresponding to 18 weeks of gravid uterus size. It was soft cystic in consistency, non-tender and mobile from side to side. Speculum examination of the vagina revealed healthy cervix and vagina. Bimanual examination findings corresponded with per-abdominal examination. There were no enlarged accessible lymph nodes in left supraclavicular and inguinal regions.

Ultrasound examination revealed a right adnexal cystic mass measuring 12 × 11 cm. Serum tumor markers were cancer antigen (CA) 125 of 21.24 g/L (normal <35 g/L) and CA 19-9 of 256.1 g/L (normal <37g/L). With the clinical diagnosis of benign ovarian tumor, an exploratory laparotomy was planned. Informed written consent was obtained for the surgery. Midline incision extending from above umbilicus to above symphysis pubis was made. There was a huge right ovarian mass (15 × 10 cm in size) with a small solid component on its wall with normal-looking bilateral tubes, uterus and contralateral ovary. There was no ascites or tumor deposit in the pelvic and abdominal cavity, and the pelvic and para-aortic lymph nodes were not palpable. Total abdominal hysterectomy (TAH), bilateral salpingo-oophorectomy (BSO) with intact capsule and infra-colic omentectomy were performed in the standard steps. As the ovarian tumor was assumed to be a benign one, intraoperative frozen section was not performed. Frozen section is not performed routinely for every case because of shortage of manpower in this institute. Even if the need for frozen section is felt during surgery, it is not practical as the pathology department needs to be informed 1 day ahead and

machines kept ready. She made an uneventful postoperative recovery.

Grossly, the right ovary showed a uniloculated cyst (Figure 1), measuring (15 × 11.5 × 7 cm) without a capsular breach. The cystic wall was irregularly thickened, ranging from 0.2 to 0.8 cm in thickness, and was filled with abundant grumous sebaceous material and hair. No definite solid component was noted. However, the inner surface of the cyst showed a focal tan yellow granular area along the thickened part of the wall (which turned out to be squamous cell carcinoma microscopically). Right fallopian tube was compressed by the ovarian cyst. Left adnexa, uterus cervix and omental tissue were unremarkable grossly.

Microscopically (Figure 2), a keratinizing squamous epithelium with underlying skin adnexa, respiratory-type epithelium, mature adipose tissue, smooth muscle, choroid plexus and brain tissue were identified. The thickened part of the cystic wall with a granular inner surface showed squamous cell carcinoma arising from the dysplastic epithelium. The malignant squamous cells were arranged in nest and sheet patterns in the stroma with desmoplastic reaction. Keratin pearls and mitotic figures were seen frequently, and a focus of lymphovascular invasion (LVSI) was noted.

However, the ovarian surface and omentum were free of tumor deposits. The right fallopian tube was uninvolved by tumor cells and the sections of left adnexal structures were unremarkable. The endometrium showed atrophic changes with focal cystic dilatation of endometrial glands. The cervix showed atrophy with focal transitional and immature squamous metaplasia. No dysplasia or malignancy was seen in sections of the cervix. A final diagnosis of well-differentiated squamous cell carcinoma arising from a mature cystic teratoma of left ovary was made. In accordance with the International Federation of Gynecology and Obstetrics (FIGO),¹¹ tumor stage was labeled as stage IA.

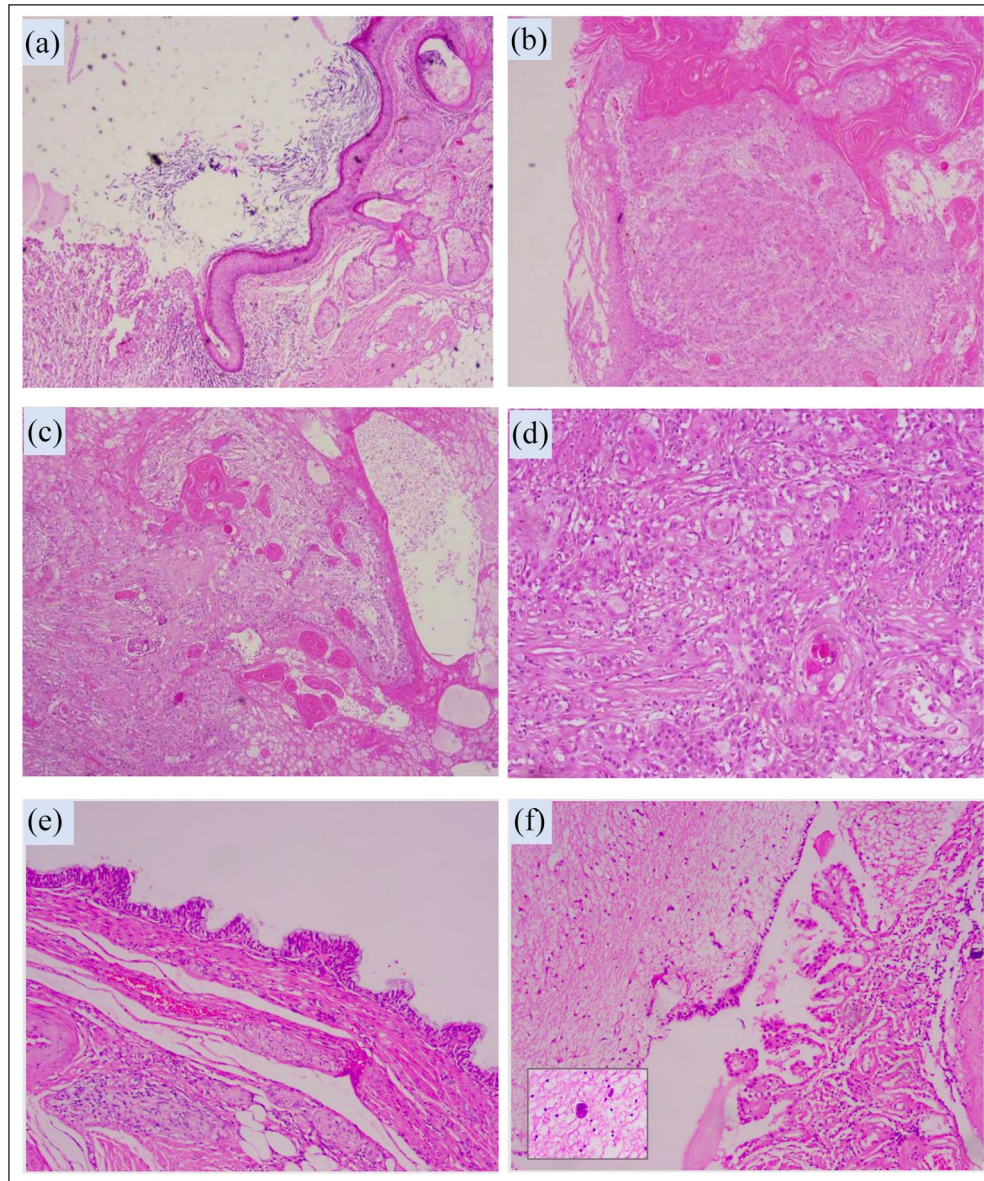


Figure 2. Microscopic images of the cyst (H&E stain): (a) non-dysplastic squamous lining, 40 \times ; (b) squamous cell carcinoma arising from dysplastic squamous epithelium, 40 \times ; (c and d) infiltrating squamous cell carcinoma exhibiting keratin pearls (40 \times and 100 \times); (e) another cyst lined by respiratory epithelium (100 \times); (f) brain (glial) tissue with choroid plexus (100 \times), corpora amylacea (inset).

Computed tomography (CT) scan which was done post-operatively did not reveal residual disease, enlarged pelvic and para-aortic lymph nodes, or liver deposits. After discussion with the patient and her family members, they opted not to receive adjuvant chemotherapy.

On follow-up at 3, 6 and 12 months, she remained symptom free with normal tumor markers (CA 125, carcinoembryonic antigen (CEA), CA 19-9) and normal ultrasound and CT scan.

Discussion

Squamous cell carcinoma is the most common type of malignant transformation arising in MCTO.⁴ In a retrospective

multicenter Italian study, the other histological variants seen were thyroid carcinoma, carcinoid, papillary renal cell carcinoma, medulloblastoma and intestinal-type mucinous adenocarcinoma.¹² The etiology of SCC transformation in MCTO is unknown. SCC transformation in MCTO may be due to a continuous process of squamous metaplasia, atypical hyperplasia, carcinoma in situ, interstitial infiltration and invasive cancer.¹³ A study in Taiwan has shown an association of SCC in MCTO with high-risk human papillomavirus (HPV) infection.¹⁴ Malignant transformation is reported to occur in 1.4%, especially in an elderly woman with unilateral tumors and rapid growth.^{2,15} Our case is a 62-year-old woman with a right-sided tumor which is consistent with other study findings.^{3,16,17} Therefore, it is logical to have a

high degree of suspicion of malignant transformation in women aged above 40 years with MCTO. Patients with malignant transformation aged >45 years have worst prognosis ($p < 0.01$) than those aged <45 years.³

MCTO usually remains asymptomatic, discovered incidentally during routine abdominal examination. The diagnosis is made on histopathological examination. Common symptoms include abdominal pain, distension, pelvic mass or swelling. Some cases are diagnosed during cesarean section and laparotomy for ectopic pregnancy.^{2,3,5,17,18} There is no specific symptoms and signs for early-stage malignant transformation. Advanced stages might have constitutional symptoms like weight loss, loss of appetite, early satiety and cachexia. Our case presented with gradual abdominal distension over 6 months without any constitutional symptoms, which is consistent with previously reported cases. In a systematic review of SCC transformation in MCTO, 47.3% presented with abdominal pain and 26.0% with abdominal mass.³

Tumor size, old age and solid components are the predictor of malignant transformation in MCTO. Our patient was an elderly woman with a solid area on the wall of a huge tumor which is consistent with other studies that have shown a positive correlation between the patient's age and tumor size.^{17,19} However, the surgeon did not think about the possibility of malignant transformation due to lack of awareness on the possibility of malignant transformation in such cases. In a systematic review, tumor size ≤ 10 cm and > 10 cm did not show any survival differences.³

The role of tumor markers for diagnosis and surveillance of SCC transformation in MCTO is not well established. SCC antigen was found raised in 16 out of 24 cases of SCC arising in MCTO in a study in Taiwan. SCC antigen was found elevated during recurrence in the serial monitoring.²⁰ In a systematic review, median preoperative SCC antigen was 7.4 ng/mL, CA 125 was 64.4 U/mL, CA 19-9 was 144.0 U/mL and CEA was 6.9 ng/mL.³ In our case, CA 125 was within normal range, and CA 19-9 was raised. SCC antigen facility is not available in our hospital, whereas CEA was not done as the reagent was out of stock at that particular time. In the serial postoperative monitoring of CA 19-9, it was 70.55 g/L on postoperative day 10 and 24.59 g/L on day 30. Serum SCC antigen and CA 125 levels are not related to stage of the disease, but a higher concentration is associated with adverse outcome.¹⁷

Doppler imaging studies revealing vascularization is a useful indicator of malignant transformation.^{18,21} CT showing adnexal mass with fat/fluid level and fat droplets would suggest dermoid cyst.¹⁶ However, CT scan and magnetic resonance imaging (MRI) have no role in detecting malignant transformation. In this case, Doppler study was not done as the ovarian mass was not suspected to have malignant transformation.

Although comprehensive staging laparotomy is standard care for ovarian cancers, a systematic review has found that

hysterectomy and omentectomy have shown survival benefit, but lymphadenectomy was not shown to improve survival in cases of SCC transformation in MCTO. However, the authors recommended lymphadenectomy as there were certain limitations regarding lymphadenectomy in their review.³ In another systematic review, omentectomy did not show survival benefits, whereas lymphadenectomy improved chances of survival in advanced cancers.¹⁷ In young patients with early-stage disease, fertility-sparing surgery is feasible.³ In our case, TAH and BSO with an intact capsule with omentectomy were performed. Histology showed well-differentiated SCC with LVSI. There was no malignancy seen in the other resected structures. Postoperative CT scan showed no residual tumor. Therefore, the FIGO stage¹¹ in this case is stage IA.

Frozen section was found to be a useful assessment during operation of such cases.²² During the intraoperative consultation or frozen section, cyst content is removed and the cyst wall is inspected for architectural complexity or solid nodules. Sections from solid areas are most helpful in identifying the presence of variety of tissues derived from three germ cell layers. The presence of markedly dysplastic epithelium associated with underlying stromal invasion confirms the malignant nature of the lesion.

Bleomycin/etoposide/cisplatin (BEP) and paclitaxel/carboplatin (TC) are recommended initial chemotherapy for germ cell and epithelial ovarian cancers, respectively. Although adjuvant chemotherapy has survival benefits in an advanced stage, there is no prescribed first-line chemotherapy regime for SCC in MCTO. A study by Hackethal et al. showed that adjuvant chemotherapy with alkylating agents was associated with increased survival in stages greater than IA. However, multifactorial analysis did not support this finding.¹⁷ In another study, alkylating agents did not show overall survival benefits in patients with stages II, III and IV. The authors recommended for individualized and integrated treatment based on platinum-based chemotherapy.³ Considering LVSI positive and non-assessment of peritoneal fluid, the option of adjuvant chemotherapy and its associated benefits and complications was explained to the patient and her family, but they opted to remain under surveillance. Adjuvant radiotherapy was not associated with survival benefits.^{3,17}

A systematic review showed that the 5-year overall survival was 85.8% for stage I but less than 40% for II, III, and IV. Stages II, III, and IV were associated with a worse prognosis ($p < 0.01$) compared with stage I disease. However, there was no association between survival and histology grade.³ Similar to epithelial ovarian cancers, the FIGO stage¹¹ is an independent prognostic factor in SCC in MCTO.^{3,17}

Patients with stage I disease was found to have a significantly better prognosis than stages II, III and IV.^{3,12} As our patient is 62 years with good performance status, well-differentiated SCC and FIGO stage IA disease, her survival status can be confirmed upon long-term follow-up only.

Conclusion

In a resource-poor setup with minimum facilities for investigation, it is challenging to come to a definite preoperative diagnosis of malignant transformation in MCTO. Therefore, clinicians should be aware of this rare entity and should have high suspicion of malignant transformation when a postmenopausal woman presents with a large tumor size with irregularly thickened cystic wall or solid foci on the tumor wall.

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Ethical approval

Our institution does not require ethical approval for reporting de-identified individual case report.

Informed consent

Written informed consent was obtained from the patient for her anonymized information to be published in this article. This informed consent is available with the principal author.

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