A rare case of malignant transformation of mature cystic teratoma: A case report*

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ABSTRACT

Mature Cystic Teratomas of the ovary are the most common ovarian tumors in both adolescents and reproductive-age women. This case report shows a rare case of squamous cell carcinoma arising from a mature cystic teratoma in a 59-year-old postmenopausal woman. Malignant transformation occurs in 1% of all cases of mature cystic teratomas and due to its rarity, there is no established protocol regarding optimal diagnosis and management. Preoperative diagnosis was difficult due to non-specific symptoms such as abdominal mass and abdominal pain present in this patient. The surgery was planned based on the large size of the tumor on imaging, menopausal age and a family history of breast cancer in the family. She subsequently underwent Total Abdominal Hysterectomy with Bilateral Salpingo-oophorectomy, Frozen Section, Bilateral Lymph Node Dissection, Infracolic Omentectomy and Right Internal Iliac Artery Ligation. Final diagnosis was confirmed post operatively with the final histopathologic report. This report would show that proper risk assessment and preoperative planning would optimize management of even rare cases of malignant tumors.

Keywords: Malignant Transformation, Teratoma, Squamous Cell Carcinoma

INTRODUCTION

Germ cell tumors account for 25% of all ovarian neoplasms. Ninety percent of all germ cell tumors are mature cystic teratomas.[1] Malignant transformation of a Mature Cystic Teratoma occurs in 1% of all such cases and this was present in our patient. This is only the 2nd reported case of squamous cell carcinoma arising from mature cystic teratoma in our institution for the past 20 years.

These ovarian tumors are often not diagnosed preoperatively. Patients usually present with nonspecific signs and symptoms that pose a challenge to clinicians in making proper diagnosis and management. Final diagnosis is confirmed only postoperatively by official histopathologic reports hence assessment of the risk for malignancy should be established preoperatively to provide proper surgical management.

In addition, due to its rarity, postoperative management also posed another challenge since the standard chemotherapeutic regimen for squamous cell carcinoma arising from mature cystic teratoma has not been determined through clinical trials, but some studies reported that the treatment of this disease is similar to that of epithelial ovarian cancer.

Herein we report a case of a postmenopausal woman, preoperatively suspected with ovarian malignancy, intra-operatively diagnosed with mature cystic teratoma which was histologically confirmed postoperatively to have a rare squamous cell carcinoma arising from the mature cystic teratoma.

CASE REPORT

This patient is D.D., a 59 year-old G1P1 (1001), single, Filipino, Roman Catholic, from Parañaque City who came in with a chief complaint of abdominal mass.

She had left oophorectomy fora benign cyst in Japan in 1992 with no other known co-morbidities. She has a family history of hypertension on the paternal side and a sister who had breast cancer. There were no other heredofamilial diseases noted.

She is a college graduate that is presently unemployed but previously worked as a receptionist for 6 years. She is a nonsmoker, nonalcoholic beverage drinker with no history of illicit drug use.

She had her menarche at age 13, with regular intervals of 28-30 days, lasting for 4-5 days, consuming 4-5 moderately soaked pads per day. No accompanying signs and symptoms were noted with menses. Cessation of menses were noted when she was 51 years-old.

She had her first coitus at age 20 with 2 non-concurrent sexual partners with no report of postcoital bleeding, dyspareunia or leucorrhea. No papsmears were done and no history of contraceptive pill use. She is a G1P1 (1001) with her pregnancy carried to term delivered by spontaneous vaginal delivery in our institution without any complications.

History of her illness started 1 year prior to admission when she noted a soft, movable non-tender mass at the hypogastric area. There were no other associated

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symptoms. No consultation was done until 1 month prior to admission when the patient noted a sudden increase in the size of the mass associated with intermittent crampy hypogastric pain and constipation. This prompted consultation with a private doctor who requested for a Kidney Urinary Bladder ultrasound which revealed normal findings of the kidneys, ureters and urinary bladder. A transvaginal ultrasound was also done and revealed normal sized uterus with proliferative endometrium. There was note of a right ovarian cyst measuring 10.79 x 9.71 x 9.86 cm, predominantly cystic with solid nodular murals 0.6 cm thick with 0.2 cm septations and with a Sassone score of 10. She was then referred to our institution for surgical intervention due to financial constraints.

Patient was seen at the outpatient clinic in our institution. She was awake, conscious, coherent, not in cardiorespiratory distress with no pallor. She has normal body mass index of 20 kg/m^2. She has clear breath sounds with a dynamic precordium, no murmur with normal heart rate and rhythm. Physical examination of the abdomen revealed a flat, soft, with a 10 x 10 cm, doughy, nontender, movable, midline mass on the hypogastric area. Speculum exam and internal examination showed that the cervix was pink, smooth and deviated posteriorly to the right. The uterus cannot be assessed due to the abdomino pelvic mass which was about 16-18 weeks size, doughy, movable, and nontender. On rectovaginal examination, there was good sphincteric tone, intact rectal vault with a solid, movable mass palpated at the culde sac. Both parametria were smooth and pliable.

The admitting impression was Ovarian New Growth, Probably Malignant. Patient underwent Exploratory Laparotomy on the 2nd hospital day. Intraoperatively, there was no ascites. The omentum, spleen, liver, intestines, subdiaphragmatic area were grossly normal. The uterus was small with smooth serosal surface. The right ovary was converted to an 11 x 10.5 x 5 cm unilocular cystic mass with smooth thin walls. It was densely adherent to the posterior cul de sac and rectosigmoid. The cyst was inadvertently ruptured at the posterior area during adhesiolysis and was seen to contain sebum and hair and a solid necrotic area which measured 0.4 – 0.5 cm (Figure 1). The specimen was sent for frozen section and was read as Teratoma with Squamous Cell Carcinoma Degeneration. The team proceeded with Total hysterectomy with bilateral salpingo-oophorectomy, Bilateral Lymph Node Dissection, Infracolic Omentectomy and Right Internal Iliac Artery Ligation. She was also referred to surgery intraoperatively due to multiple dense adhesions noted between the ovarian mass and sigmoid colon as well as the proximal ileum. Enterolysis was done. There was also an 8 x 6 x 2 cm extraluminal mass adherent to the rectosigmoid area with dense adhesions 10 cm from the ileum as (Figure 2). The General Surgery service then proceeded with Hartmann's Procedure and Jackson Pratt Drain Insertion. On cut section, the colonic mucosa was pinkish, corrugated without appreciable lesions. The appendix was also noted to be congested hence appendectomy was done. Estimated blood loss was 1.7 liters. Patient was then transfused with 4 units fresh frozen plasma and 3 units packed red blood cells postoperatively. She also had hypokalemia postoperatively which was corrected. She was discharged on the 10th hospital day recovered.

Final histopathologic report showed Teratoma with Malignant Transformation, Squamous Cell Carcinoma, ruptured with involvement of the sigmoid serosa. Histologically, the tumor is characterized by the presence of keratinization. Keratinization may take the form of squamous pearls or individual cells with markedly eosinophilic dense cytoplasm (Figure 3). All 31 harvested pelvic lymph nodes were negative for involvement. There was note of lymphoid hyperplasia in the appendix (Figure 4), chronic cervicitis with nabothian cyst in the cervix (Figure 5) and senile atrophy of the endometrium (Figure 6).

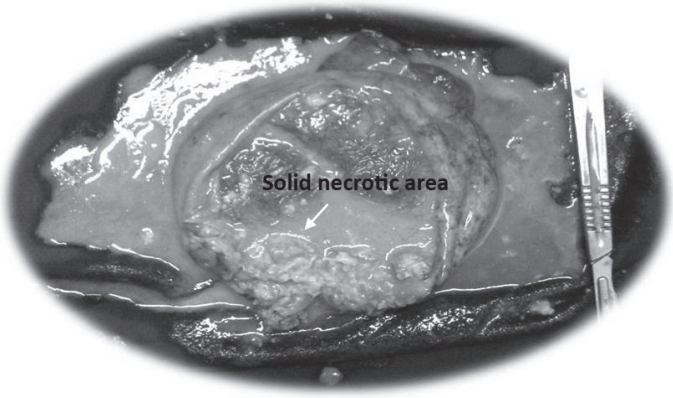

Figure 1: Right Ovaryconverted to a complex cystic mass containing necrotic debris, sebum, and hair with a solid necrotic area.

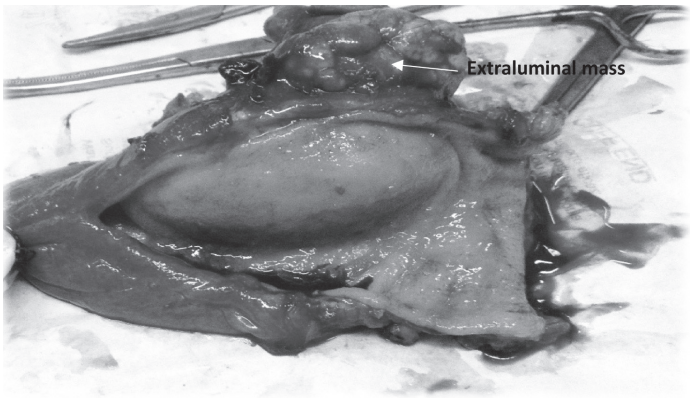

Figure 2: Colon attached to extraluminal mass with necrotic areas.

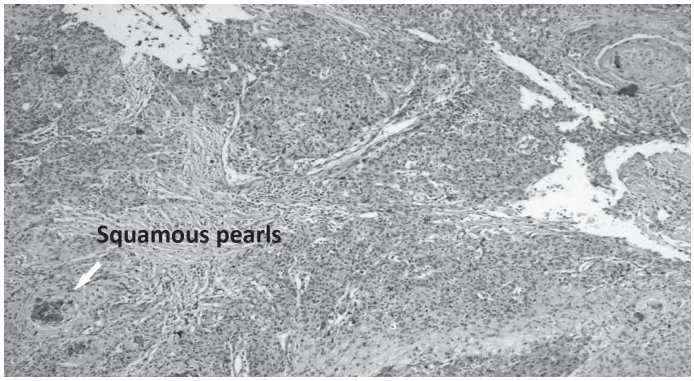

Figure 3: Scanner View of Malignant Teratoma showing keratinization in the form of squamous pearl with markedly eosinophilic dense cytoplasm. (H&E stain, 40x)

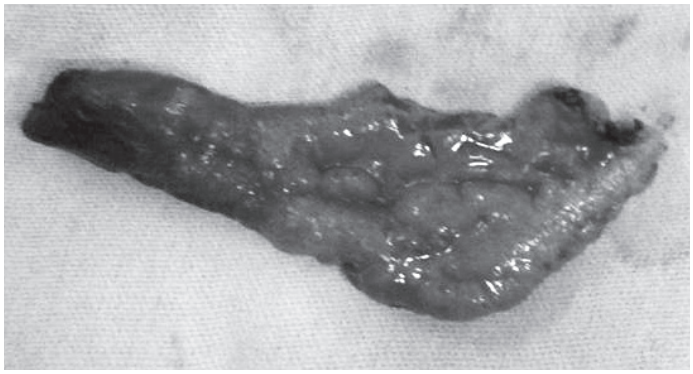

Figure 4: Congested Appendix

Patient was advised to have 4 cycles of adjuvant chemotherapy postoperatively. She underwent 1 cycle of chemotherapy with Bleomycin, Etoposide and Cisplatin but was lost to follow up.

DISCUSSION

Teratomas consist of tissues from all three layers of the developing embryo: the ectoderm, mesoderm, and the endoderm. One or more of the layers may be presented, and the tissues can be mature (benign) or immature (malignant).[2]

Mature Cystic Teratomas (MCTs) are among the most common ovarian neoplasms and account for 10 – 20% of all ovarian tumors in women of reproductive age. Malignant transformation in MCT of the ovary is rare, occurring in 1% of all cases. The most common malignancy is squamous cell carcinoma (SCC), which represents about 75% of malignant transformations, followed by adenocarcinoma and melanoma. Benign teratomas may contain a malignant component, usually in women older than 50 years.[3]

Benign Teratomas are usually unilateral, unilocular with smooth, shiny, opaque white outer walls. A combination of skin and skin appendages, including sebaceous glands, sweat glands, hair follicles, muscle

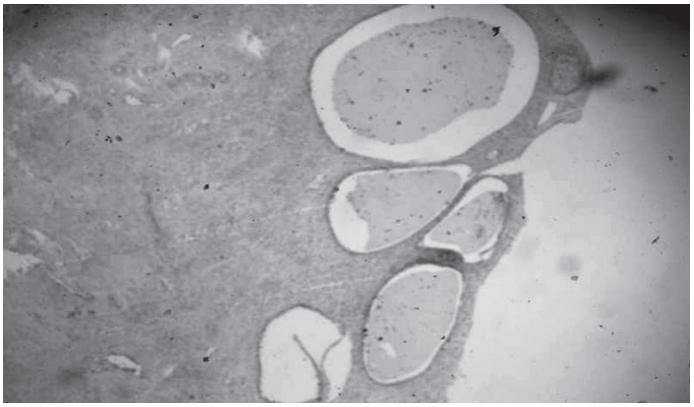

Figure 5: Scanner view of the cervix showing nabothian cyst. (H&E stain, 40x)

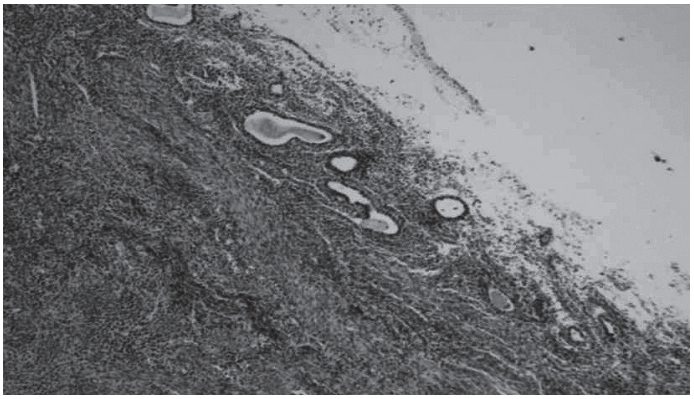

Figure 5: Scanner view of the proliferative senile atrophy of the Endometrium (H&E stain, 40x)

fibers, cartilage, bone, teeth, glial cells and epithelium of the respiratory and gastrointestinal tracts may be visualized. Several theories explained the pathogenesis of MCTs. They are believed to arise from a single germ cell after the first meiotic division. Therefore, they develop from totipotential stem cells, and they are a neoplastic sequelae from a transformed germ cell. MCTs or dermoid cysts have a chromosomal makeup of 46,XX. Linder and co-workers, in a series of experiments using chromosome banding techniques and electrophoretic variance, discovered that the chromosomes of dermoids were different from the host. They postulated that dermoids began by parthogenesis from secondary oocytes. An alternative hypothesis was that the dermoids arise from the second polar body with the oocyte. The studies by Linder and co-workers ruled out the possibility that the dermoids arise from somatic cells or from an oogonium before the first stages of meiosis. The first meiotic division occurs at approximately 13 weeks of gestation. Thus dermoids begin in fetal life sometime after the first trimester.[1]

Presenting symptoms of MCTs are nonspecific. The most common symptom is abdominal pain followed by abdominal or pelvic mass, but patients may be

asymptomatic or have various symptoms due to invasion of nearby organs like constipation, diarrhea, rectal bleeding or urinary frequency. [4]

Preoperative diagnosis of MCTs of the ovary can be done through ultrasound where bony tissues can be identitified. However, it is hard to differentiate malignant transformation clinically from a benign teratoma. Risk factors for malignancy in MCTs include age, tumor size, and serum tumor markers which should be assessed. In a systematic review and analysis of published data on squamous-cell carcinoma in mature cystic teratoma of the ovary done by Hackethal et al, they concluded that squamous-cell carcinoma in mature cystic teratoma was mainly found in women aged more than 50 years, with high concentrations of squamous-cell-carcinoma antigen and cancer antigen CA125, and with ovarian tumours more than 100 mm in size.[5] Kikkawa et al also emphasized that tumor diameter larger than 9.9 cm was 86% sensitive for malignancy. Whenever the size exceeds 10 cm or soft tissue plugs and cauliflower appearance with irregular borders are seen, malignant transformation should be suspected.[6]

The prognosis for these tumors has been reported to be very poor with a five-year survival rate of only 15 – 30%. Prognostic indicators of survival have been identified in various studies, but most of them agree that higher FIGO stages would carry a worse prognosis. [7]

The main therapeutic approach to an ovarian MCT with malignant transformation is surgical.[7] The goal of treatment is to have zero residual bycytoreductive surgery. Patients with FIGO stage IA tumors have better survival than those with more advanced disease. Complete resection together with hysterectomy, bilateral salpingo-oophorectomy and lymphadenectomy for patients with advanced disease, followed by adjuvant chemotherapy with an alkylating drug was associated with higher survival.[5] The best regimens for ovarian SCC-MCT have not been determined through clinical trials, but some researchers reported that the treatment of this disease is similar to that of epithelial ovarian cancer.[4] Cisplatin and alkylating drugs have recently been recommended, simply because of their activity in other histologic types of ovarian cancer and non-ovarian gynecological squamous cell carcinomas. [8]In our patient, we used Cisplatin in combination with Bleomycinand Etoposide for its action in germ cell tumors.

SUMMARY

Ovarian squamous cell carcinoma arising from Mature Cystic Teratoma is extremely rare, and is rarely diagnosed preoperatively. A high index of suspicion for malignancy using the tumor size, age of the patient and elevated tumor markers is of utmost importance. Measuring the squamous cell carcinoma antigen level is highly recommended as a diagnostic clue. An adequate staging surgery should be included in the standard treatment so therapy can be optimized.

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