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Case Report

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OVARIAN MATURE CYSTIC TERATOMA WITH MALIGNANT TRANSFORMATION: TWO CASE REPORTS AND LITERATURE REVIEW

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ABSTRACT

Background: Malignant transformation of a mature cystic teratoma (MCT) is a rare complication that occurs in 0.17% to 2% of cases in usually postmenopausal women. The most common form of malignant transformation of a MCT is squamous cell carcinoma, accounting for more than 80% of malignant transformations. The frequency of malignant transformation of MCT to adenocarcinoma is just 6.8%. Case presentation: We report two Moroccan cases of mature cystic teratoma with two different malignant transformations arising from it; the first case was transformed into mucinous cystadenocarcinoma and the second into squamous cell carcinoma (SCC). Our both cases presented the same symptoms, including chronic abdominal pain and distention. The two patients underwent a complete staging surgery, the patient of case 2 required adjuvant chemotherapy given a positive peritoneal cytology unlike the patient of case 1 which was classified as stage IA and close follow-up has been proposed. To date, the two patients have not presented a recurrence of the disease during the past 4 years of follow up. Conclusion although the prognosis seems highly dependent on the stage of the disease, there is a lack of consensus in the literature regarding adjuvant treatment. In light of adjuvant Platinum-based chemotherapy used for epithelial ovarian cancer, its use in this kind of situation seems to be a reasonable option with interesting outcomes.

KEYWORDS: Mature cystic teratoma, Squamous cell carcinoma, Mucinous cystadenocarcinoma.

INTRODUCTION

Ovarian teratomas are the most common ovarian germ cell tumors.[1] and, in many series, the most commonly operated ovarian tumor, they constitute about 10-18% of all ovarian tumors. They usually occur during childbearing age (mean age, 27 years).[2] They include mature teratomas (cystic or solid), monodermal teratoma (struma ovarii, carcinoide and neural tumors) and immature teratomas.

Mature cystic teratoma (MCT), a term more appropriate than the commonly used term "dermoid cyst", is the most common form, accounts for 99% of all ovarian teratomas.[3] They most often occur at childbearing age (average age 34),[4] but they can be seen at any age between 3 months and 86 years old.[5] They grow slowly at an average rate of 1.8mm each year and are considered large when they are over 5cm in diameter and giant when they are over 15cm.[6]

Ectodermal tissue (derived from the skin and nervous system) is found almost constantly in the tumor. The mesodermal component (fat, bone, cartilage) is present in 90% of cases. The endodermal component (gastrointestinal mucinous epithelium, bronchial ciliated epithelium, thyroid tissue) is found in a majority of cases.[7]

Ovarian teratoma is usually asymptomatic until it reaches a considerable size and manifests as a pelvic or abdomino-pelvic mass. The most common symptoms are increased abdominal volume as well as abdominal pain.[3,8]

In its pure form, a mature cystic teratoma is always benign, but very rarely it can undergo malignant transformation of any of its components, squamous cell carcinoma (SCC) is the frequent malignancy arising from the ectodermal component of MCT followed by adenocarcinomas and carcinoid tumors.

At the present study, we report two cases of ovarian malignancies arising from mature cystic teratoma, the first case was transformed into mucinous cystadenocarcinoma and the second into SCC.

CASE PRESENTATION

Case 1

A 64-year-old patient, gravida 9 para 9, Moroccan women, presented in June 2017 to the gynecology

department at the university hospital in Rabat. She complained of abdominal pain with abdominal distention that had lasted for 3 months, the patient also presented postmenopausal metrorrhagia as well as pollakiuria, there was no history of constitutional symptoms as anorexia or weight loss. She was under treatment for arterial hypertension and type 2 diabetes, and she reported no history of smoking, drug abuse or alcohol consumption and no family history of cancer. In abdominopelvic examination, a mass was palpated above the pelvis from the midline to the lateral side, causing a mild compression effect against the rectum. An abdominopelvic ultrasound revealed left ovarian cyst of 9.1x9.5 x9.6 cm with no ascites. Abdominal CT scan was performed, showing a large solid-cystic mass involving the left ovary, measuring 10 cm with presence of fat and calcifications suggesting a mature teratoma. Routine blood tests were normal except the serum levels of CA125, CEA and CA19-9 which were slightly elevated (37,54 U/mL , 6,2 µg/l and 38 U/mL, respectively). The patient underwent an exploratory laparotomy and the surgeon proceeded to subtotal hysterectomy with unilateral adnexectomy and cystectomy. No surgical spill or capsule rupture happened. Microscopic examination revealed a mature cystic teratoma turned into mucinous cystadenocarcinoma, the result of the cytological assessment of peritoneal washing was negative for malignancy. The patient was referred to our oncologic hospital to complete the treatment, a multidisciplinary consultation meeting was held with the decision to carry out complete surgical staging. The result of thoraco-abdominopelvic CT scan were reported normal and tumor markers (Ca 125, Ca 19-9 and CEA) were in their normal range. The patient underwent second laparotomy with trachelectomy, omentectomy and appendectomy that were free of tumor according to microscopic examination; lymph node dissection could not be performed because of operating difficulties. We classified the disease as stage IA according to the International Federation of Gynecology and Obstetrics (FIGO's) classification as the tumor was limited to one ovary with capsule intact. The indication for adjuvant chemotherapy was not indicated in our patient. We closely followed up the patient the last 4 years by monitoring tumor markers and CT scan regularly, and fortunately, no recurrence had been occurred to date.

Case 2

A 52-year-old, gravida 4, para 4, post-menopausal Moroccan woman with a suspicion ovarian tumor was referred to our oncologic hospital in July 2018. She complained for about 5 months of chronic abdominal pain and discomfort with loss of appetite and weight loss. Bowel/bladder habits were normal. She had no significant clinical of family history. Abdominal examination revealed a palpable mass that was extended up to her umbilicus with no detectable ascites. External genitalia and cervix had a normal appearance. Abdominal ultrasound revealed a large solid mass with cystic changes of about 10x7 cm. Magnetic resonance imaging (MRI) revealed that the lesion consisted predominantly of a solid component with a small cystic area containing fat, suggestive of right ovarian teratoma. The routine blood laboratory tests were in their normal range, among the tumor markers, only the CA125 was elevated (52U/mL), the rest of the tumor markers were within normal limits including β HCG, AFP and LDH. The patient underwent laparotomy through a midline incision, which revealed a 12x7 cm solid right ovarian mass filled with hair shaft, bone and greasy brown material. Peritoneal washing was done for cytology and the surgeon performed a right salpingo-oophorectomy that was sent for frozen section. The results reported a mature solid teratoma, sections from the solid nodule showed moderately differentiated squamous cell carcinoma (SCC) arising in MCT with presence of tumor cells in peritoneal washing. The biopsies of ovarian serosa, uterus and left adnexa, omentum and lymph nodes, were free of tumor. The decision of multidisciplinary consultation meeting was to carry out complete surgical staging. The result of thoraco-abdominopelvic CT scan was reported normal and tumor marker CA 125 too. The patient underwent a total hysterectomy with left salpingo-oophorectomy, omentectomy appendectomy, lymph node dissection and multiple peritoneal biopsies. We staged the disease as IC3 according to the FIGO's classification as the tumor was limited to one ovary with presence of malignant cells in peritoneal washing. Five weeks after the surgery, the patient underwent 4 cycles of adjuvant chemotherapy (Paclitaxel 175mg/m² over 3 hours followed by Carboplatin AUC 5 IV). We closely followed up the patient by monitoring tumor markers and CT scan regularly. Three years after diagnosis, the patient has had no recurrence.

DISCUSSION

In its pure form, a mature cystic teratoma is always benign, but very rarely it can undergo malignant transformation of any of its components. It is a rare complication, reported in 0.17% to 2% of cases depending on the series.[4,9] and usually occurs in postmenopausal women in the 6th or 7th decade of life. Malignant transformation most often concerns mature cystic teratoma, and more rarely struma ovarii.

It is characterized by the malignant transformation of the squamous epithelium into differentiated tissues. Squamous cell carcinoma is the most common type of malignant degeneration, accounting for more than 80% of cases. Rarer adenocarcinoma, sarcoma and melanoma have also been described.[10,11,12]

The second case we described was about a SCC arising in MCT which is quite common in the literature, while in our first case, the malignant transformation resulted in mucinous adenocarcinoma which has been more rarely described in the literature.[13,14]

The main factor recognized by most authors favoring the malignant transformation of MCTs is the tumor size, MCT larger than 6 cm have an increased risk of malignant degeneration.[15,23] In the two cases we presented, the tumor size was quite large, measuring 9,6 cm and 12 cm respectively, which is linked to a greater risk of malignant transformation.

The fact that there are no specific tumor markers of malignant transformation or suggestive imaging makes the preoperative detection of malignant transformation of MCTs difficult,[16] often there is an increase in tumor markers (CA125, CA19-9 and CEA), as in the case of our two patients, and a larger solid component.[17]

Patients may be asymptomatic or present with symptoms such as pain and abdominal distention as was the case with our two patients.[18] In advanced stages, altered general condition can be seen as anorexia and weight loss.[19] The patient presented in the 2nd case presented a loss of appetite and weight loss secondary to her advanced disease.

The prognosis is linked to the stage of the disease, tumor grade, growth pattern, capsular rupture, and vascular invasion.[20,21] In a study published in 2008 by Chen et al,[22] the 5-year survival rate in cases of MCT transformed into SCC, all stages combined is 48.4%, the subgroup analysis showed survival rates at 5 years of 75.7, 33.8, 20.6 and 0% for stages I, II, III and IV, respectively. The two cases we described had a disease classified as stage IA and IC3 respectively, which correlates a good prognosis.

The treatment of choice is total abdominal hysterectomy and bilateral salpingo-oophorectomy.[23,24] However, it is justifiable to perform conservative treatment with unilateral salpingo-oophorectomy if the patient is nulliparous or young woman who wants to preserve fertility, especially in stage IA disease. Our two patients were able to benefit from optimal surgical treatment given their menopausal status.

The utility of node dissection is controversial since the mode of spread is generally by direct extension or peritoneal seeding, but it may influence treatment planning, especially in early-stage disease.[25,26]

Due to the rarity of this tumor, adjuvant treatment has not been prospectively evaluated, literature review had shown various postoperative treatment modalities such as chemotherapy or radiotherapy or combination of both.

Best adjuvant therapy for SCC arising in MCT has not been defined. The current recommendation of platinum-based chemotherapy is related to its activity in ovarian epithelial cancers and gynaecological squamous-cell carcinomas, and seems to be associated with better survival.[27] Combination of Paclitaxel and Carboplatine AUC 5 is the most common chemotherapy regimen used in this situation.

Alkylating drugs can also be considered for chemotherapy regimens. Whereas radiotherapy might actually lead to greater morbidity and adverse survival.[21,23,28]

In a series of 17 patients with SCC arising in a MCT,[29] there were no known recurrences in 6 stade IA patients regardless of whether they were conservatively managed or opted for adjuvant therapy.

Patni et al., similarly to our 2nd case, has used the combination of carboplatin and paclitaxel regimen for up to four cycles.[30] We used chemotherapy for this case because of the stage (IC3) due the presence of malignant cells in peritoneal washing.

The optimal management of mucinous cystadenocarcinoma arising from MCT has not been established. Adjuvant combination chemotherapy per 3 weeks using gemcitabine (700 mg/m^2) carboplatin (75 mg/m^2) paclitaxel (135 mg/m^2) seems to be effective.[31]

CONCLUSION

Malignant transformation of MCT is a rare situation; SCC is the histological type most often found. Postmenopausal women with large MCT are more likely at risk of developing malignancy.

The recommendations for surgical management are well defined and consistent in radical extensive surgery and optimal debulking, while the evidence for adjuvant therapy is poorly defined. The use of 4 cycles platinum-based cycles (paclitaxel and carboplatin) with or without alkylating agents is the protocol most often accepted by authors and seems to be correlated with long relapse-free survival, mainly for disease stage > IA.

ABBREVIATIONS

MCT: Mature cystic teratoma
SCC: squamous cell carcinoma
CEA: carcinoembryonic antigen
CA19-9/ CA125: cancer antigen 19-9/125
FIGO: International Federation of Gynecology and Obstetrics
IV: intravenously
β HCG : Beta human chorionic gonadotropin
AFP: Alpha-fetoprotein
LDH: Lactate Dehydrogenase

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