Case Report

Malignant transformation of ovarian mature teratoma: 04 cases report, review of the literature

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ABSTRACT

Mature ovarian teratomas or dermoid cysts are the most common ovarian germinal tumors and account for 20 to 25% of ovarian organ tumors. The malignant transformation of a mature teratoma is a rare event (1 to 3%), mainly found in the post-menopausal period. This is carcinomatous degeneration (80% of cases) or sarcomatous differentiated tissues of the dermoid cyst. The diagnosis of certainty is established by anatomopathological study of the surgical piece. Treatment of carcinoma teratomas is surgical and same to ovarian malignant epithelial tumors. We report four cases we managed in our health care center with a review of the literature.

Keywords: Hassan II Teaching Hospital of Fès, Management, Mature teratoma, Malignant transformation, Ovarian cancer, Ovarian cysts

INTRODUCTION

Ovarian dermoid cysts, also known as mature cystic teratomas, are characterized pathologically by the presence of elements from at least two of three germ cell layers; ectoderm, mesoderm, and endoderm. Radiologists similarly identify dermoid cysts by their diverse contents, including fat, hair, and teeth.[1] Mature cystic teratoma of the ovary (MCTO) may occur in 10-20% of women during their lifetime.[2] It may occur at any age, with highest incidence during the reproductive period.[3] More than 80% of mature cystic teratomas (MCTs) develop during the reproductive years.[4] The clinical course of MCT is typically indolent, and its prognosis depends on age, stage and optimal cytoreduction. However, it can be complicated by a malignant transformation with squamous cell carcinoma (SCC) accounting for 80-90% of the transformed histology.[5] Malignant transformation of mature cystic teratoma is extremely difficult either to predict or to detect early. Moreover, the mechanism of malignant transformation has not yet been elucidated.[6]

Mature cystic teratomas with malignant transformation (malignant teratomas) constitute 1% of all ovarian carcinomas. They typically affect patients older than 45 years and larger than 9.9 cm diameter. Malignant transformation may occur in any of the three germ cell layers including the ectoderm, mesoderm and endoderm. Squamous cell carcinoma arising from the squamous lining of the cyst, is the most common type of malignant transformation, accounting for 80% of the reported cases.[5,7-9]

The diagnosis of certainty is established by the anatomopathological study of the surgical piece. We report four cases of malignant transformation of mature ovarian teratomas we managed in our health care center and a review of the literature.

CASE REPORT

Patient 1

Mrs. BF, 54 years old, multiparous without regular monthly bleeding for 6 years, with no notable pathological history, who consulted for an increase in abdominal volume evolving in a context of deterioration of the general state, in which the clinical examination found a hard abdominopelvic mass exceeding the umbilicus, painless and whose limits with the uterus were not well defined.

Pelvic ultrasound found a solid-cystic image taking all the screen, suspicious of malignancy, probably ovarian origin, the 2 ovaries were not seen. Magnetic resonance imaging (MRI) was not performed due to lack of means.

Thoracic-abdominal-pelvic computed tomography (CT-TAP) showed a solid cystic mass, measuring 120/120/280 mm, suggestive of an ovarian tumoral process suspected of malignancy and intimate contact with the colon, pelvic wall and uterus without evidence of invasion. There were no deep lymphadenopathies or peritoneal effusion. The liver, pancreas and kidneys were normal.

A laparotomy was decided for the patient. The surgical exploration found an ascites of low abundance, a huge right mass being 25 cm at the expense of the right ovary with spontaneous release of a gelatinous liquid that. The uterine right trump, the left appendix and the uterus were free of any damage, no peritoneal carcinosis, the liver was smooth, the extemporaneous anatomopathological examination of the mass returned in favor of a mucinous tumor at the limit of the malignancy of where the decision to perform a total hysterectomy with bilateral adnexectomy, omentectomy, appendectomy and multiple biopsies. The definitive anatomopathology study of the mass concluded that there was a multisystem carcinoma teratoma. The total hysterectomy, left appendix, omentectomy, appendectomy and peritoneal biopsies were non-tumorous. The tumor was classified pT1c stage. The postoperative follow up was simple. The patient was resumed for pelvic and lomboaortic lymphadenectomy which objectified 12 negative lymph nodes/12 nodes. After discussion in a multidisciplinary consultation meeting, an indication of adjuvant chemotherapy was selected (bleomycin, etoposide and cisplatin (BEP) type).

Patient 2

Mrs. BH, 41 years old, multiparous with regular monthly bleeding, without any particular pathological history who consulted for pelvic pain that had been evolving for 6 months, for which she had laparotomy in a private clinic with a right ovarian kystectomy and anatomopathology result in favor of an ovarian dermoid cyst with partial squamous cell carcinoma lesions in situ with micro-invasive areas. Then the patient was sent to us for

additional treatment. The physical examination was unremarkable.

Abdominal-pelvic ultrasound did not notice pathological abnormality.

Thoracic-abdominal-pelvic computed tomography did not found suspicious lesions on the abdominal and pelvic floor with absence of residue; absence of suspicious lesion in the thoracic stage. The patient's folder was discussed in a multidisciplinary consultation meeting and the decision was a surgical repeat. The surgical exploration did not found ascites, cytological sampling done; uterus of normal size, the 02-appendix seen without particularity, the rest of the exploration of the abdominal cavity also without particularity. Performing a total hysterectomy associating bilateral adnexectomy, infra-gastric omentectomy and pelvic lymph node and lombo aortic lymphadenectomy. The anatomo pathological study found inflammatory cytology, absence of tumor cells, total hysterectomy, bilateral adnexectomy and omentectomy were free of tumor proliferation; pelvic lymphadenectomy: 35 nodes negatives on 35, and lomboaortic: 42 nodes negative on 42. The tumor was classified pT1a stage. The case was discussed again in multidisciplinary consultation meeting with a decision to clinical and radiological monitoring.

Patient 3

Mrs G. R. aged of 45, multiparous, still with regular monthly bleeding without significant pathological history admitted for pelvic pain without other associated signs.

Clinical examination found a uterine cervix macroscopically normal, presence of a right pelvic mobile mass measuring 10 cm.

Pelvic ultrasound was in favor of cystic mass sus and right lateral uterine of 8.5 cm with finely echogenic contours and partially vascularized partitions and burgeons of 16 mm.

Thoracic-abdominal-pelvic computed tomography described the aspect of a pelvic malignant tumor probably ovarian origin.

The patient underwent a laparotomy with surgical exploration which revealed a cystic mass with a thick wall, bumpy without exo-cystic vegetations of the right ovary, left appendix, liver and appendix without particularities, no peritoneal carcinosis. During the procedure, a first cytology was performed followed by a right adnexectomy and a biopsy of the left ovary as well as peritoneal biopsies (Epiploon, right and left parietocolic gutters).

Anatomo pathological study found histological appearance of a carcinoma of the right ovary in the form of adenocarcinoma moderately differentiated grade II.

cytology, peritoneal biopsies and left ovary were free of disease. Surgery was performed again for cytology, total hysterectomy, left adnexectomy, omentectomy and pelvic and lombo aortic lymphadenectomy. The second anatomopathological study found: inflammatory cytology, hysterectomy parts with left adnexectomy and omentectomy returned free from any tumor proliferation; pelvic lymphadenectomy 18 nodes negatives / 18 and lombo aortic lymphadenectomy: 17 nodes negatives on 17. The tumor was classified pT1a stage. The postoperative period was simple. Decision of clinical and radiological surveillance.

Patient 4

Mrs. F.E 47 years old, without significant pathological history, multiparous, with regular bleeding period, admitted for management of an abdominopelvic mass evolving since 09 months. On physical examination: presence of a huge abdominopelvic mass of 28 cm exceeding the umbilicus. Pelvic ultrasonography described a voluminous multilocular mass predominantly cystic with multi partition, thick wall of 8.9 mm not vascularized. Parietal nodule of 23/16 mm with effusion. There was difficulty to specify the right or left seat.

Thoracic-abdominal-pelvic computed tomography described a large sus right uterine abdominopelvic cystic formation of $130 \times 200 \times 215$ mm of origin most likely multiloculated ovarian with cystic component majority calcic and fat containing a parietal nodule recalling the protuberance of ROKITANSKI without regional local extension or lymphadenopathies: the possibility of a mature teratoma (dermoid cyst) was to be mentioned first). Decision to schedule the patient for laparotomy to perform adnexectomy, contralateral ovarian biopsy ± lymphadenectomy if palpable lymph nodes.

The patient underwent a laparotomy during which exploration found: ascites of low abundance, which was sampled for cytological study; discovery of an enormous right solido-cystic mass of 30/28 cm, left appendix without particularity with a uterus of normal size; no peritoneal carcinosis; liver and stomach smooth, no palpable lymphadenopathy. Achievement of a right adnexectomy without capsular intrusion + multiple biopsies

The anatomopathological study showed histological appearance of a carcinoma of the right ovary in the form of mucinous adenocarcinoma, cytology, peritoneal biopsies and healthy left ovary were free of any tumoral invasion.

After discussion in multidisciplinary consultation meeting, we repeated the surgery for total hysterectomy, left adnexectomy, omentectomy and pelvic and lumbo aortic lymphadenectomy. (Clips were put near to the mesenteric root and at the left renal vein).

The second anatomopathological study after the second surgery found the Hysterectomy free from any tumoral lesion. The parameters, the paracervix, the fallopian tubes and the ovaries are free from any tumor infiltration. Lombo aortic lymphadenectomy: 17N- / 17N; Pelvic lymphadenectomy: 30N- / 30N.

DISCUSSION

Mature cystic teratoma, which is a commonly observed benign ovarian tumor in young women, is a germ cell tumor containing fat, hair, teeth, cartilage, and so forth. It is the most common type of benign ovarian tumor accounting for approximately 20% of all ovarian tumors according to Hurwitz et al.[10,11]

It is the most common germ cell neoplasm, typically affecting young adult females in their second and third decades of life.[12] According to Hackethal A and al, it represent the most common ovarian neoplasms in patients younger than 20 years.[5] Mature cystic teratoma is known to occasionally become malignant, and the majority of such transformations result in squamous cell carcinoma (SCC). Malignant transformation was reported by Hurwitz et al, to occur in 1% to 2% of patients with a mature cystic teratoma.[11] Kim et al, observed in a serie of 560 patients who underwent surgery for a mature cystic teratoma at their facility 4 cases of malignant transformation with a rate of 0.6%.[2] The age of the patient is a risk factor for malignancy, as squamous cell carcinoma in mature cystic teratoma (SCC in MTC) typically occurs in postmenopausal women.[5,13] Although 80% of MCTs are diagnosed during reproductive age, malignant transformation is typically detected during postmenopausal age.[5,13] In a study made by Chen et al, the mean age at diagnosis was 55±14.4 years.[14] Hackethal et al, reported a mean age at diagnosis of 55 years. Chiang et al, also reported a mean age of 52 years in their study made on 52 patients.[15] In our present report, all the patients were more than 40 years old with the average of 46-75 years. Which is smaller than what the precedents authors reports. That small average may be related to the small size of our sample made of only 4 patients. However, malignant transformation of MCT generally occurs after 40 years old with a great incidence in pre and post-menopausal period.[15] The great frequency of malignant transformation is reported to be between 45 and 60 years old.[13,16,17]

The diagnosis of malignant transformation of mature cyst teratoma is difficult in preoperative. No diagnosis criteria can confirm the malignancy before the anatomopathological study. There are certain clinical biological and radiological signs predictive of malignancy. The main criteria leading to the malignant transformation are the patient age and the tumor size.[13,16,17] In general, malignant teratoma has a more aggressive clinical course than mature cystic teratomas.[18] Due to the rarity of MT to SCC and the complex components of MCTs, preoperatively distinguishing

between these 2 conditions is extremely difficult.[15] Diagnosis of malignant transformation of MCTs poses difficulties to clinicians. It is commonly accepted that all ovarian tumors should be considered as potentially malignant, until proven otherwise.[5] In order to detect the malignant transformation of MCTs, there are some risk factors that contribute to the transformation, such as the patient age, the size of tumor, the serum tumor markers and the imaging characteristics of the tumor.[5]

Despite all, the symptoms are not specifics and vary according to different stages of the disease and is like ovarian benign cysts including weigh and pelvic pain, abdominal distension, dyspareunia, transit and urinary disorder and ascites.[13] 02 of our patients consulted for pelvic pain and the 02 others for an increase of abdominal volume. In Chang et al study, the most common presenting symptoms were a palpable abdominal mass, abdominal distension, and lower abdominal pain.[15] Other minor symptoms included voiding difficulty, low back pain, and weight loss. A study made by Park SB et al on a large series of 1325 patients where 12 patients were confirmed as having malignant teratomas, the clinical presentation was dominated by an abdominal pain, a pelvic or abdominal mass and weight loss.[19]

On the radiological side, ultrasound has a special place in the detection, diagnosis and monitoring of dermoid cysts.[20]

According to some authors, in spite of very variable radiological aspects, the sensitivity of the ultrasound does not make it possible to distinguish a malignant degeneration from a mature teratoma. The ectodermal component of the cyst is constant and corresponds essentially to a pilosebaceous mixture. According to some authors this is at the origin of a pathognomonic echographic symptomatology resting in rule on a strong hyperechogenicity and the posterior attenuation.[21,22] The presence of fat component or organoid elements (teeth, hair, bone) are fairly sensitive signs in favor of teratoma. But certain imaging features of the tumor may contribute to the diagnosis of malignant transformation. The use of transvaginal -doppler- ultrasound for the measurement of the blood flow resistance in the intratumoral vessel may be an accurate method to distinguish benign from malignant MCTs. Interestingly, Emoto et al, reported that the doppler detection method was a more useful indicator than serum SCC antigen levels.[23] In case of diagnostic difficulty, a CT scan or at best an MRI will be able to visualize a tumor with greasy content having an irregular solid component taking the contrast. This solid component is relatively large and is associated with transmural extension with invasion of neighboring organs. The use of contrast medium by the protrusion of Rokitansky must make evoke the possibility of a malignant transformation.[21] Concerning the clinical use of magnetic resonance imaging in SCC diagnosis, the presence of a solid component that extends transmurally and invades the adjacent structures is highly suggestive of

malignancy.[8] In the clinical use of CT in diagnosis of SCC, the formation of an obtuse angle between the border of the soft tissue component and the cyst wall is a sign of malignancy.[24] MRI (or failing that, CT scan) will identify fat within the lesion characterizing dermoid cysts or mature cystic teratomas. Despite the great importance of MRI in the diagnosis it is also not specific. Mori et al first differentiated malignancy from benignancy by preoperative MRI then they found in there study that, of the preoperatively diagnosed benign cases, 1.1% of the cases were in fact borderline and 0.3% of the cases were malignant.[24] For Umemoto et al preoperative ultrasonography and CT are insufficient in detecting the solid portion of the tumor because of the inferior imaging quality of these techniques in comparison to MRI.[25] Even a small solid area can be malignant. They recommend that in emergency surgery to pay particular attention to a possible occult malignancy that may be revealed postoperatively. The key diagnosis is obtained after anatomopathological study of the tumor.

The management of malignant transformation of mature cyst teratoma might be the same way to any other ovarian tumor.

The first stage of its management is the surgery either laparoscopy or laparotomy. Surgery is the standard treatment for ovarian cancer. It can be performed according to the disease stage with a complete removal.

In our study we started by laparotomy with the aim of exploration and adnexectomy of the side concerned by the tumor and a second surgery when the hystological study return in favor of malignancy. The second surgery was a complete one associating hysterectomy, adnexectomy, infrgastric omentectomie and pelvic and lumbo aortic lymph nodes dissection. We choose laparotomy so that to avoid the spillage of the tumor which could have changed the prognosis of the patients.

Even if laparoscopic surgery has gained in popularity for the management of benign ovarian teratoma, the use of laparoscopic surgery to manage malignant transformation has been described as risky by some authors in different studies and is not recommended due to the higher risk of tumor spillage of dermoid contents during laparoscopic procedures. In other hand laparoscopic surgery should be made with a successful removal without spilling the content of the tumor.[26] So a laparotomy should be performed to prevent inadvertent tumor upstaging by iatrogenic intraperitoneal tumor rupture.

Wen et al, described in their study a rapid postoperative progression after intraoperative spillage of the tumor contents.[27] Regardless of whether tumor dissemination is linked with intraoperative tumor rupture they insisted that in any patient with a preoperative diagnosis of MCT, the tumor should be removed completely intact to avoid possible iatrogenic complications and catastrophic events such as peritoneal dissemination of the tumor.

Pelvic/para-aortic lymph node dissection is controversial because the tumor spreads by direct extension and/or peritoneal seeding, and metastatic lymph nodes are described in the literature.[15]

Only 1 of our 4 patients benefited of chemotherapy or radiotherapy. We opted for surveillance after the optimal surgery and our patients did not relapse during the follow up. The clinical and radiological exams were without any particularity during the 2 following years after surgery. There is no consensus regarding adjuvant treatment and the effectiveness of chemotherapy or RT for MT of MCTs. But some authors recommend the use of chemotherapy. A large systematic review made by Congcong Li et al showed that the recommend initial chemotherapy regimen for ovarian germ cell tumor and for epithelial ovarian cancer is bleomycin/etoposide/cisplatin (BEP) and paclitaxel/carboplatin (TC), respectively.[28] Currently there is no recognized first-line adjuvant therapy for SCC transformation in MCTO, though chemotherapy can improve prognosis of patients with SCC transformation in MCTO of advanced stage. Hackethal et al, also suggested that chemotherapy with alkylating agents is related to better prognosis in patients with SCC transformation in MCTO, Dos S et al, proposed whole-pelvis radiation and platinum-based chemotherapy for stage I-II patients because SCC is a radiosensitive tumor.[5,29]

The prognosis depends mainly on the stage. Survival at 5 years is 77% for stage I and only 11% for advanced stages.[30] Other prognostic factors at to look for are grade, vascular invasion, break-in capsular and the histological type of the component malignant. A mature teratoma carcinized into carcinoma epidermoid is more favorable prognosis than transformation in sarcoma or melanoma.[29,30] The presence or not of tumor residue is also a factor to take in consideration; 5 years survival is 79% without tumor residue and 10.1% with a tumor residue.[31]

CONCLUSION

Malignant transformation of mature cyst teratoma is a rare event. It can occur even in a woman during a period of genital activity as it is the case in 3 of our 4 patients. There is no specific clinical symptomatology. In spite of the diagnostic orientation made by the image, the accurate diagnosis is based on anatomopathological study.

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