INTRODUCTION
Brenner tumor (BT) of the ovary is a relatively uncommon neoplasm. It constitutes 1.4-2.5% of all ovarian tumors [1]. Most of them are benign and less than 2-5% are proliferating or borderline [2]. MBT pose a real problem making therapeutic management share their extreme rarity and their relatively poor prognosis. In this observation we report the case of MBT diagnosed in a 62-year-old woman with a review of the literature of different histological clinical and therapeutic aspects of this rare neoplasm.

CASE PRESENTATION
A 62-year-old woman was presented to the emergency in August 2011 for recurrent postmenopausal bleeding. The patient reported a 1-year history of vaginal bleeding and abdominal pain. She had a medical history (the antecedents) of hypertension (high blood pressure) without treatment, a vaginal delivery and the deceased child of Duchenne muscular dystrophy, menopausal from 8 years without hormone replacement therapy. The magnetic resonance imaging (MRI) revealed a large right ovarian mass with endometrial proliferation extended to the uterus and bladder. Total hysterectomy with bilateral salpingo-oophorectomy with pelvic lymphadenectomy was performed. Disease was classified pT3cN1R1, FIGO (Federation of Gynecology and Obstetrics) stage IIIC. To the extent of the disease the first-line of the chemotherapy was validated with the subsequent surgery eventual.

RESULTS: The patient received 7 courses of chemotherapy with carboplatin-paclitaxel. But the cyto-reduction was insufficient for surgery. Surveillance to 2 months objectified progression of the disease in abdominal lymph node. The patient received consecutively 5 lines of systemic therapy. The patient had an altered general condition and died at 33 months of diagnosis.

CONCLUSION: MBTs ovary are extremely rare and there is no consensus on the therapeutic management of metastatic forms. Taking charge of systemic unfortunately rare cases reported has not been detailed. It seems necessary to identify all cases diagnosed in a database, and in order to harmonize the treatment of this rare disease.
Laparotomy was performed, and total hysterectomy with bilateral oophorectomy and pelvic lymphadenectomy were excised which were classified disease pT3cN1R1, stage Figo IIIC. Surgical staging includes removal of the uterus, fallopian tubes, and ovaries; peritoneal cytology; and intraoperative assessment of the pelvic and para-aortic lymph nodes. Pathological examination was in favor of invasive carcinoma with giant multi-nucleated cells and with a pseudo-papillary appearance or brennerien high grade (3 grade architectural and 4 grade cyto-nucléaire). Additional immuno-histochemical tests were carried out. Malignant cells were negative vis-à-vis the antibodies CK5/6 P63, HNF1β, Beta HCG, HPL, alpha fetoprotein and Glypican PLAP (Figure 2). It was noted a strong estrogen receptor positivity (90%) and progesterone (50%). These aspects have confirmed the diagnosis of MBT. In the pelvic lymphadenectomy, only one right iliac lymph node had been invaded and peritoneal cytology was negative. The proposed treatment strategy was that systemic treatment with platinum salts. The patient received intravenous 7 courses of chemotherapy with paclitaxel (175 mg/m²) and carboplatin (AUC5) every 21 days with a reduction in tumor volume insufficient to allow the closure of surgery. Surveillance to 2 months objectified progression of the disease in para-aortic lymph node and bilateral iliac levels.

Figure 2. Stratified epithelium of transition with marked nuclear polymorphism, p16-, Rb-, p53-, Cycline D1+, Ras +, EGFR +.

The patient then received a second-line treatment by topotecan then a 3rd line by caelyx to a new node-local progression. At 19 months of diagnosis, after collegial discussion, fourth-line chemotherapy by gemcitabine and paclitaxel was started. Systemic treatment had achieved a stabilization of the neoplastic disease which remains localized to abdominal but very broad level to undertake surgery. In November 2013, the radiological evaluation was objectified a disease progression in the lung, liver and pelvis with enlarged mediastinal lymph nodes, pelvic and abdominal. A fifth line chemotherapy capecitabine was started but the patient presented a rapid deterioration of the general condition and died in May 2014, to 33 months of diagnosis.

DISCUSSION

BT was described for the first time by Macnaughton-Jones in 1889 [3], and by Brenner in 1907 who had compared the Graaf follicle because of strong resemblance epithelial nests and suspecting origin from granulosa cells [4]. The BTs are designated in the WHO classification 2003 by the group of transitional cell tumors. The BTs or transitional cell carcinomas represent 1-2% of all ovarian tumors and are divided into benign, borderline or malignant [1]. They are composed of epithelial elements that resemble histologically urothelium and cancers that develop there [8]. In most cases the tumors are benign. However, 2-5% of TBs are malignant, posing the problem of diagnosis and therapeutic management [2,6]. Histologically, the MBT is characterized by the presence of typical homes in transitional carcinoma pseudo-papillary high-grade cells, often low grade, which may be associated with a component of benign or borderline TB bathing in the fibroid stroma [8]. Invasive implants are characterized by uncontrolled proliferation tumor infiltrating peritoneal serous or adjacent organs whose appearance is identical to that of the secondary locations serous adenocarcinomas. The prognostic significance of these invasive peritoneal implants remains controversial, but it is generally accepted that this is a pejorative factor that justifies a thorough and rigorous observation peritoneal during surgical
The differential diagnosis arises mainly with serous carcinoma high grade. Genetically joined this tumor epithelial carcinoma type I with the possibility of the presence of mutations in KRAS (Kirsten rat sarcoma viral oncogene homolog), Braf (v-raf murine sarcoma viral oncogene homologated B1) and PTEN (phosphate and tensin homolog deleted on Chromosome ten) [8]. However clinical trials histological screening is needed to clarify the molecular biology of this disease. Macroscopically, the MBT are usually unilateral, large and greyish-white appearance. The bilateral nature is rare that can meet in about 12% of cases [9].

MBT rather occurs in women post-menopause, between 50 and 70 years. Clinical signs are nonspecific: pelvic pain is usually the first associated or not with bleeding and/or pelvic mass. CA 125, which is an important serum marker in the assessment of ovarian carcinomas, contributes little to the diagnosis of this tumor type is not as specific. However, a high rate can be for their malignant nature [10]. Metastases have been described in 50% of cases and are usually of locoregional sites. The peritoneal involvement being the most common [9]. The therapeutic management is based on that of epithelial ovarian cancers and is mainly based on the complete cytoreductive surgery or in cases of advanced stage, consisting of a total hysterectomy with bilateral oophorectomy and omentectomy. No preoperative argument allows distinguishing between a borderline ovarian tumor (TOBL) and invasive malignant tumor. The only arguments that can be used are those directed towards malignancy or, more often, to a non-benign: age over 50 years, tumor size greater than 10 cm, ultrasound criteria (mixed lesion, partitions, vegetation endo- or exo cystic), CA 125 above normal. In these situations, surgical exploration by median laparotomy is recommended. The frozen section has the interest in this case, not so much to confirm the diagnosis of TOBL for which the risk is significant overestimation (actually benign lesion 10%) and underestimation (malignancy 18%), but to make the diagnosis of a true malignancy. In situations where doubt remains, it is better to wait for the final histological results to first, not to make unnecessary gestures or unnecessary mutilating the other and especially not to perform incomplete staging of invasive cancer. The patient will be informed of this possibility of reoperation [7]. On medical treatment, the use of chemotherapy is controversial according to the authors, because of the low objective response rates reported in the literature. Complete histological responses are exceptional and were observed mainly after poly-chemotherapy with platinum salts [8]. A classic pattern of carboplatin kind - paclitaxel is highly recommended [11].

In 1992, Platini had reported 2 cases of pathologic complete remission after poly-chemotherapy in patients operated for MBT stage FIGO IIIC each. The first patient received six courses of chemotherapy combining cisplatin and cyclophosphamide, and the second - 6 courses of carboplatin, cyclophosphamide and doxorubicin. In both cases the histological response was surgical

CONCLUSION

Malignant tumors of the ovary Brenner are extremely rare and there is no consensus on the treatment of metastatic forms. The surgical management of localized forms is required whenever possible. The indication of adjuvant chemotherapy remains controversial. It seems necessary to identify all cases diagnosed in a database, and in order to harmonize the treatment of this rare disease.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

