

Borderline ovarian tumor in adolescence: report of two cases and review of the literature

Abstract

Borderline ovarian tumors are a subtype of epithelial tumors which present a high mitotic index and nuclear atypia without stromal invasion, with a better prognosis than ovarian cancer. They usually affect young patients, even in adolescence. The reproductive prognosis is compromised as a consequence not just of the pathology itself, but also diagnostic, staging and treatment techniques. In the last decade, new alternatives have been developed in the management of these tumors, with emphasis on fertility sparing procedures, even in advanced stages. We analyze two clinical cases assisted at Centro Hospitalario Pereira Rossell and review the latest literature, with focus on prognosis and treatment possibilities.

Keywords: ovarian neoplasms, adolescent, fertility preservation

Volume 5 Issue 3 - 2018

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Received: March 21, 2018 | **Published:** May 24, 2018

Introduction

Borderline ovarian tumors were described in 1971 by FIGO, referring to a subtype of tumors with a better prognosis than ovarian cancer.¹ From the histological point of view, they present nuclear atypia and a high mitotic index that differentiates them from benign tumors, but unlike malignant tumors they have absence of stromal invasion.^{2,3}

Borderline tumors correspond to 10 - 15% of ovarian epithelial tumors, and are more frequent in reproductive age. The average age of presentation is between 20 and 46 years, and 25% of patients are under 35 years of age, which has consequences on reproductive prognosis.² The most frequent subtype is the serous. In more than 20% of cases, they are bilateral. They can present implants.¹ In the past, non-invasive and invasive implants were described, currently the term "implants" is reserved for those that do not show elements of invasion of the underlying tissue. The invasive sectors behave like low-grade serous carcinoma.

They may present recurrences, which may be in the form of a new borderline tumor or an invasive ovarian tumor.⁴ This phenomenon occurs in about 0.5-1% of borderline ovarian tumors.^{1,5,6} Borderline ovarian tumors (OBT) can be histologically serous, mucinous, endometrioid, clear cell, Brenner and seromucinous.^{7,4} The staging of borderline ovarian tumors is the same as the classification of ovarian cancer, as indicated by FIGO.⁸

Regarding the etiopathogenesis of these tumors, in the case of borderline serous tumors, it is suggested that they may correspond to precursor tumors of low-grade carcinoma or ovarian carcinoma type I. In these tumors, a tubal metaplasia is generated in the mesothelium of the ovarian surface, where they settle. On the other hand, type II ovarian carcinomas or high-grade carcinomas are thought to originate in the tube.⁴

The main clinical guidelines, National Comprehensive Cancer Network (NCCN), SEGO oncoguides, recommend surgery as standard treatment for borderline tumors.^{7,5,9} Given that 1 in 3 of the TBO are

diagnosed in women under 40 years of age, alternatives have been developed in the treatment in the last decade in order to preserve fertility even in advanced stages. The fertility treatment options are those that preserve the uterus and at least one of the ovaries functionally. A unilateral cystectomy or salpingo-oophorectomy may be performed, the former with a higher risk of recurrence than the latter.^{5,9} It is recommended to perform staging surgery, which includes a detailed examination of the abdominal cavity, cytology of ascites fluid or lavage, multiple peritoneal biopsies, inframesocolic omentectomy, and appendectomy in mucinous tumors. Lymphadenectomy is not recommended, since lymph node involvement does not influence subsequent therapeutic behavior or improve survival.^{5,7,9} There are no clinical guidelines or randomized studies or systematic reviews regarding a specific behavior to be followed in adolescent patients with borderline tumors, in which the parity wishes have not been satisfied. We present two clinical cases attended in the service of the "A" Gynecological Clinic of the Pereira Rossell Hospital Center of adolescent patients with borderline ovarian tumors, their treatment and follow-up considerations.

Report of cases

Case I

Patient of 17 years, with no personal or pathological family history, with a previous normal vaginal delivery. Consultation for abdominal pain of 48 hours of evolution. The right parauterine tumor presents 8 cm in diameter, intensely painful on palpation.

The transvaginal ultrasound informs in right adnexal topography a cystic image of 79 x 69 mm, with homogeneous content, with small incisions in the wall, without vascularization with Doppler. The rest of the paraclinical was normal. Tumor markers are obtained (CA 19-9, CA 125, CEA, LDH, -FP, HCG) with normal values. With diagnosis of adnexal torsion, emergency therapeutic laparoscopy is performed.

During the intraoperative period, a cystic tumor of the right ovary measuring 9 cm in diameter was observed. The tumor is punctured and drained, with aspiration of citrine fluid. There is a minimal

leakage of the contents into the peritoneal cavity. Right adnexectomy is performed without complications.

The pathological anatomy informs borderline serous tumor of the right ovary, without invasion of the capsule. Clinical and paraclinical follow-up is performed with gynecological ultrasound and tumor markers every 6 months. The follow-up at 6 and 12 months showed the asymptomatic patient, with negative tumor markers and gynecological ultrasound without pathological images in adnexal topographies.

Case 2

Patient of 18 years, nuligesta, with a personal history of laparotomic resection of serous cystadenoma at the level of the left ovary in 2011 and laparoscopic resections of functional cysts in the right ovary in 2013 and 2014. Consultation taking a picture of acute abdominal pain of 12 hours of evolution. A right parauterine tumor measuring 6 cm in diameter was found on the physical examination, intensely painful on palpation, with elements of peritoneal irritation.

The transvaginal gynecological ultrasound informs at the right adnexal level a cystic image of 60x59mm, with a homogeneous content, with thin septa within it of less than 2mm, without vascularization with Doppler. With diagnosis of adnexal torsion, therapeutic laparoscopy is performed. Right adnexal torsion is evident and a cystic lesion measuring 6 cm in diameter is identified. A cystectomy is performed with drainage of mucinous material.

The pathological anatomy reported borderline ovarian seromucinous tumor with torsional necrosis, without stromal or capsular invasion. The tumor markers were within normal limits (CA 19-9, CA 125, CEA, HE4). Clinical and paraclinical follow-up was performed, with tumor markers and gynecological ultrasound every 6 months, without evidence of elements of relapse.

Discussion

Borderline ovarian tumors account for 10-15% of ovarian epithelial tumors.^{1,2} They do not present stromal invasion, but may present implants.^{1,4} Given that 25% of the patients who present them are younger than 35 years old,² the preservation of fertility in the treatment is a central issue.

In relation to the clinical manifestations, they appear of varied forms, being the abdominal pain the most common symptom, followed by the abdominal distension, although they can be asymptomatic. Adnexal torsion, as in the case of our two patients, is not a frequent manifestation.^{2,10,11}

With regard to the diagnosis of the nature of the tumor in the extemporaneous histology sample during surgery, its performance is varied. The agreement varies between 49.9%¹¹ and 78.6%.¹² An extemporaneous sensitivity of 71.1% and a positive predictive value of 84.3% was demonstrated.¹³ In the case of our patients, there was no extemporaneous study for the diagnosis due to emergency surgery.

The value of CA 125 at the time of diagnosis may be normal or slightly elevated (above 35IU/mL), especially in serous-papillary and mucinous tumors. In any case, it is not useful for the diagnosis of borderline ovarian tumor, nor to assess the risk of recurrence. There is a statistically significant association between its elevation and the presence of peritoneal implants of any type.¹⁴ In the case of our patients, the values of the tumor markers were normal.

In relation to the treatment of BOT, fertility-conserving surgery, defined as that which conserves the uterus and at least one of the ovaries functionally, is a viable alternative in most of the studies analyzed.^{5,6,9,11,12,15-20} Survival is not greatly affected. The overall survival rate is greater than 94% for all jobs,^{12,15-17} in which conservative treatment of fertility was performed in at least 35.6% of the patients. The largest multicentric retrospective series, which analyzes 950 cases treated with surgery for BOT, presents a survival of 96.4% at 3 years and 94.6% at 5 years. The only retrospective study that discriminates the survival rate according to the treatment performed, reports a rate of 100% for those treated with complete surgery and 98.2% for those treated with non-complete initial surgery.¹⁶ Our two clinical cases did not receive staging surgery, and they have been managed with conservative treatment and evolutionary control, evidencing up to now the non-appearance of recurrent lesions.

Conservative surgery is the main way of preserving fertility in these patients. Other options include cryopreservation of embryos, cryopreservation of oocytes with subsequent *in-vitro* fertilization, or cryopreservation of ovarian tissue with subsequent reimplantation, which theoretically would have a greater risk of recurrence.^{21,22}

The follow-up prescribed in the NCCN guidelines for patients with incomplete staging will depend on whether the desire for conception is satisfied or not. If this is not the case, as in the case of our patients, the absence or lack of knowledge of the presence of invasive implants makes it possible to offer observation or surgery with preservation of fertility and surgical staging. The observation includes control every 3 to 6 months for 5 years and then annually, with physical examination, gynecological ultrasound, tumor markers for the epithelial lineage if they were initially elevated.^{9,23} After completing a desire for conception, you should consider performing staging surgery complete, because between 12 and 47% of patients can change their status as a result of it.^{5,9,16}

The TBO can present relapses that are described between 3.3 and 12%.^{6,15,17} Up to 30% of them may be due to malignant transformation of the borderline tumor.¹⁷ The elements of poor prognosis are: not performing staging surgery, serous lineage, initial stage IB or greater, bilateral tumor, invasive peritoneal implants and elevated levels of CA 125.^{12,17,18} These patients should be carefully selected for conservative fertility surgery, and short-term pregnancy should be suggested, and then complete staging surgery.²⁰ In the case of our patients, none presented bilateral tumors or elevated tumor markers. In any case, no staging surgery was performed in either of the two cases.

The appearance of relapses after conservative surgery is more frequent in serous OBS, which usually do so, with no impact on the survival of the patient. On the contrary, in mucinous TBO, recurrence is rare, but it usually occurs as invasive mucinous carcinoma with greater frequency.¹⁹

Regarding the population to which our patients belong (adolescents), in a series 29 cases of borderline tumors are analyzed in patients under 20 years of age, of which 25 patients were of reproductive age. All of them underwent conservative treatment of fertility (cystectomy, oophorectomy or unilateral adnexectomy). Of all the patients, there was a recurrence of a mucinous borderline tumor and a recurrence in the form of a mucinous cystadenocarcinoma.¹¹ According to a systematic review of 2012, this treatment can be performed safely without compromising long-term survival.¹⁹

In a 2014 Cochrane review, 7 controlled clinical trials were included regarding the management of borderline ovarian tumors. Only one of them compared management through conservative surgery (oophorectomy and contralateral cystectomy) versus ultraconservative management (bilateral cystectomy) for the management of bilateral borderline tumors in patients under 35 years of age with unmet parity. In this study there were no significant differences in recurrence between these two groups, but the relapse was earlier in the ultraconservative management group (16 months) than in the conservative management group (48 months). On the other hand, there was a significant difference in reaching pregnancy, in favor of ultraconservative management. There are no studies comparing conservative surgical treatment of fertility versus radical treatment. In this review there was no evidence in favor of the use of adjuvant therapy (chemotherapy or radiotherapy).²³

Conclusion

The borderline ovarian tumors are epithelial tumors with low risk of malignant transformation. It is possible to perform conservative treatment and control. In patients adolescents, with unsatisfied parity, there is evidence in favor of treatment using conservative fertility surgery (understood as the preservation of the uterus and at least one functioning annex), with safety and good long-term survival.

Sources of financing

The authors did not receive funding for the present work.

Acknowledgements

None.

Conflict of interests

The authors do not present a conflict of interest

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