CASE REPORT

Management of a borderline ovarian tumor in a pregnant woman in a rural hospital: a case report

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Abstract

Borderline ovarian tumors (BOTs) are neoplasms with benign and malignant characteristics, affecting young women in childbearing age. Finding incidental adnexal mass in pregnancy is more common with the use of ultrasound, incidence is about 2% to 10% of pregnancies. A great majority of adnexal masses excised during pregnancy are in fact BOTs. Treatment varies depending of gestational age: before 24 gestational week is usually conservative and surgical staging. Radical management is reserved to patients with suspected malignancy and satisfied parity. A 38-years-old woman presented to external consultation in a rural hospital with 36 gestational weeks of her fourth pregnancy, without antenatal control and asymptomatic. Obstetric ultrasound reported: right ovarian tumor with cystic and solid areas. Laboratory data were normal. She underwent elective cesarean and exploratory laparotomy, surgical findings were: a term female baby with no obstetric complications and a right ovarian tumor with trans-operatory report of mucinous epithelial cells with atypia, suggestive of ovarian borderline tumor. Based on this, a hysterectomy with bilateral oophorectomy was performed. No complications were reported. Post-operatory evolution was normal. Definitive histopathological study reported a borderline ovarian tumor.

Key words

Pregnant, Borderline, Ovarian, Tumors, Mucinous

1 Introduction

Borderline ovarian tumors (BOTs) are defined as an entity with histopathological characteristics between benign and malignant neoplasm [1]. These tumors account for almost 10%-20% of ovarian neoplasms [2]. There are often seen in young women whom are in childbearing age. They have a good prognosis in early stages and in absence of peritoneal implants [3]. There are described three subtypes: serous, mucinous and clear cells, being the first the most common (65%). When an invasive carcinoma is identified, usually is associated with poor prognostic [4]. Finding incidental adnexal mass in pregnancy is more common with the use of ultrasound and incidence can vary based on study population, use of sonography, and gestational age at presentation. It is reasonable to estimate that clinicians can expect to encounter adnexal masses in 2% to 10% of all pregnancies [5]. Around 2% to 3% of masses removed during pregnancy are found to be

malignant and this is a key issue to be considered when counseling the patient. Despite this fact, the great majority of high suspicion adnexal masses excised during pregnancy are in fact BOTs [6]. We present a case of a pregnant woman with a borderline ovarian tumor in a Rural Hospital.

2 Case presentation

A native 38 years old woman presented to external consultation in a Rural Hospital (rural hospital of PROSPERA, a social program of Federal Government and Instituto Mexicano del Seguro Social) with 36th gestational week of her fourth pregnancy (G4P3C0A0), without antenatal control and with satisfied parity. She was asymptomatic and physical exploration was normal. Obstetric ultrasound reported: right ovarian tumor, 8 cm of diameter, heterogeneous, with cystic and solid areas, no calcifications and diffused and non-defined borders (see Figure 1). Laboratory data and tumor markers were normal. She could't be referred to other hospital because of lack of economic resources. At 38th gestational week, she underwent elective cesarean and exploratory laparotomy with trans-operatory study, surgical findings were: a term female baby with no obstetric complications and a right ovarian tumor measuring 9 cm × 8 cm × 7 cm, heterogeneous whit cystic and solid components, citrine liquid on peritoneal cavity (see Figure 2), trans-operatory study reported mucinous epithelial cells with atypia, suggestive of ovarian borderline tumor. Based on this report, a hysterectomy with bilateral oophorectomy and omental biopsy was performed. No complications were reported. Post-operatory evolution was normal. Patient was discharged at third post-operatory day. Following was at 3, 6 and 12 post-operative months with laboratory and ultrasound, showing no evidence of recurrence. Definitive histopathological study reported an ovarian tumor with capsular integrity; neoplastic cells delimited by a fibroconjuntive and vascularized wall, coated with cylindrical cells with irregular nucleus, without evidence of stromal invasion, with papillary formations that bulge through the oviduct lumen (see Figures 3, 4).

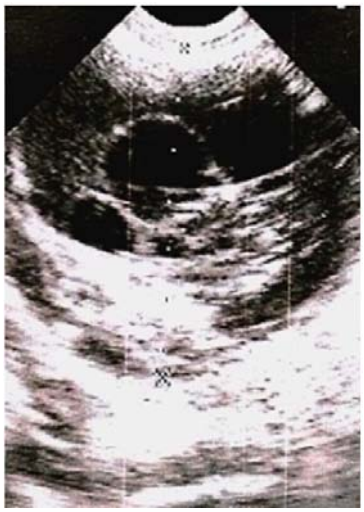

Figure 1. Simple pelvic ultrasound. Ovoid lesion (8 cm × 6.5 cm) with heterogeneous quistic and solid densities delimited by a difuse round bordered capsule.

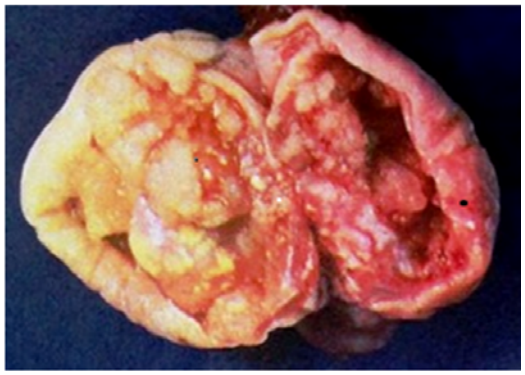

Figure 2. Surgical specimen. Right ovarian tumor measuring 9 cm × 8 cm × 7 cm, heterogeneous whit cystic and solid components.

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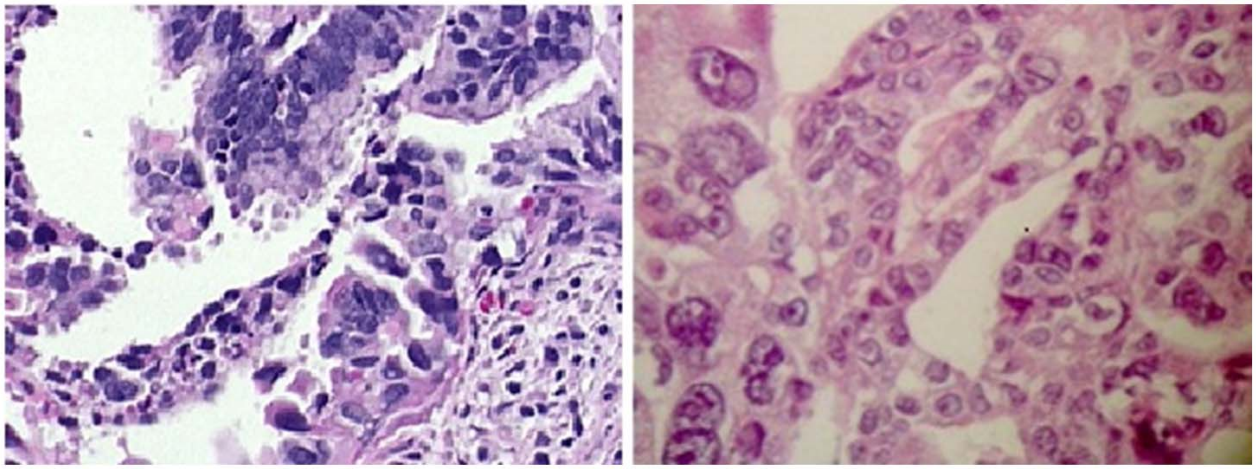

Figure 3. Hematoxylin and eosin-stained section. Shows the cylindrical cells with irregular nucleous delimited by wall of vascularized fibroconjuntive tissue.

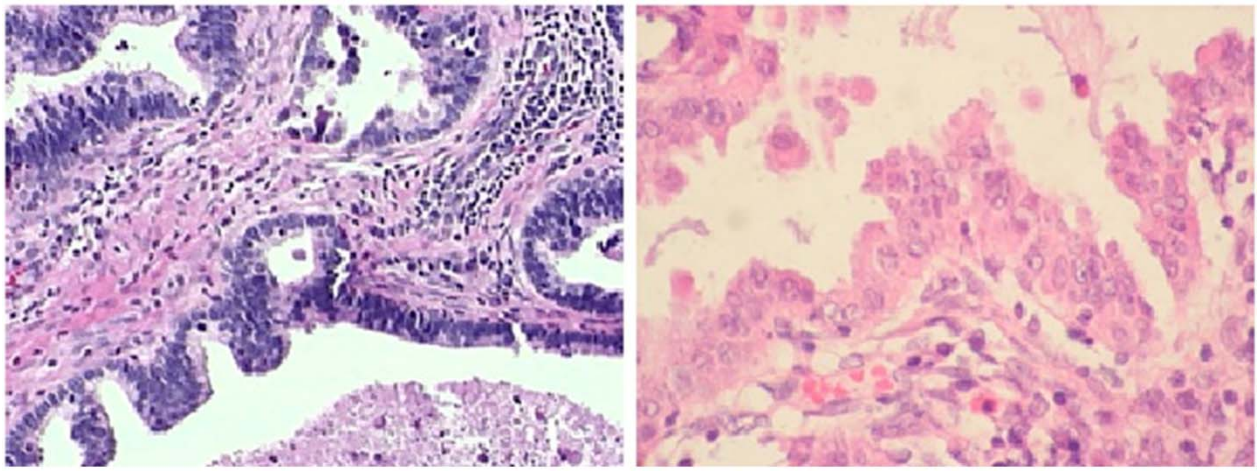

Figure 4. Hematoxylin and eosin-stained section. Papilar formations protruding towards the lumen are observed without evidence of stromal invasion o extraovaric implants.

3 Discussion

BOTs are an intermediate histological entity between benign and invasive ovarian tumor; representing almost 10%-20% of all ovarian epithelial tumors [7]. Approximately one-third is diagnosed in young women (< 40 years); however there is lack of knowledge about the epidemiology and management of BOTs diagnosed during pregnancy and even less information of treatment in rural and marginal areas. Previous studies in pregnant patients with adnexal masses have reported an incidence of BOTs of 0.15% to 3% [6]. BOTs are frequently diagnosed during the first trimester and usually they are detected in routine imaging studies. When symptomatic, patients may refer to unspecific abdominal pain [7].

Histologically, these tumors are defined as neoplasms with cytological atypia and proliferative patterns of growth cribriform and glandular patterns as well as goblet cell shape can be found depending on the subtype, both in the absence of estromal invasion. The subtypes described in literature have significant differences among them referent to histology, molecular biology and response to treatment and should be always determined by an expert pathologist who can define the precise diagnosis and discard the presence of extraovarian metastases [8]. Mucinous tumors are sub-classified in two main types: intestinal or endocervical (Müllerian). Although the epithelial cells found in these tumors resemble those in the

gastrointestinal tract or endocervical carcinomas, the histopathological criteria for diagnosis have generated controversy. In addition, there had been series of cases which haven't observed a "pure" endocervical subtype, and has also been associated with Brenner's tumor by the findings of transitional cells in mucinous tumor [9]. BOTs have been described as a unilateral, solid or cystic tumors filled with mucinous material; can be multiloculated and present papillary excrescences, which are delimited by a white smooth capsule. Its size can be very variable and common presentation ranges between 8-20 centimeters, but it has been reported much bigger. Solid areas should be studied with special attention in search of any invasive carcinoma [10]. Mucinous epithelium and glandular complex formations can be identified in the benign presentation of ovarian mucinous tumor, but some histological features associated with the borderline presentation might include: epithelial stratification (more 3 layers), cytological atypia, microinvasion (< 5 mm) in 10%-20%, or necrosis; however, only the stromal invasion greater than 5 mm has been associated with a poorer prognosis and must be catalogued as an invasive carcinoma. Peritoneal implants have not been associated to mucinous borderline neoplasms, a marked difference with serous neoplasms [11, 12]. The concept defined as low-grade intraepithelial neoplasm (grade 1) is applied when there is absence of marked cytological atypia, and it is associated with tumors originated from mutation of genes like KRAS, BRAF, PTEN and Beta Catenin. K-RAS mutation can be found in almost 50% of grade 1 tumors. On the contrary, high-grade potential tumors (grade 2) are defined as premalignant lesions with genetical instability, usually associated to mutation of the TP53 gene [13, 14].

There are several theories regarding the progression from the benign mucinous adenoma to invasive carcinoma in which the molecular biology of these tumors plays an important role depending on the site of the initial mutation and it is similar among histological subtypes including: PTEN, CTNN-B1, PI3CA and ARID1A. The actual information on immunohistochemical and genetic study of mucinous ovarian tumors supports that there is a progression from mucinous cistoadenoma to mucinous borderline neoplasm to mucinous adenocarcinoma [15].

Diagnostic workup of BOT's include transcutaneous and transvaginal pelvic ultrasound, an essential and reliable technique that could determine the origin of the mass, as well as its location, size and internal structure (existing vegetation or septa) and classify it into one of the following five categories: unilocular, unilocular-solid, multilocular, multilocular-solid, or solid [16]. In our case just was permorfed trans-abdominal ultrasound. Color Doppler imaging should also be performed to obtain a vascular road map of the ovarian mass [17]. Pelvic MRI with gadolinium injection can be performed after the first trimester. This drug is classified as a category C drug by FDA. Borderline tumors show a greater degree of complexity, with thickened walls or septae and internal solid components [18]. MRI has advantages of depicting more distant findings, such as widespread ascites, peritoneal implants, and pelvic or retroperitoneal adenopathy, and of being more accurate overall than sonography in the distinction of benign from malignant ovarian masses [19]. Pelvic CT scanning is not indicated during pregnancy. These studies could not be obtained because of economical limitation of the unit and the patient. As CA 125 is found at high levels during the first trimester and then returns to normal, it is not really useful, but remains interesting for follow-up [20]. The "ADNEX" index is a model with three clinical predictors (age, serum CA-125 level, type of centre) and six ultrasound predictors (maximal diameter of lesion, proportion of solid tissue, more than 10 cyst locules, number of papillary projections, acoustic shadows, and ascites). Serum CA-125 level and proportion of solid tissue were the strongest predictors. This prediction model is able to discriminate between five types of adnexal tumor (benign, borderline, stage I cancer, stage II-IV cancer, and secondary metastatic cancer), while still showing excellent overall discriminative capacity between benign and all malignant tumors, resulted in sensitivity of 96.5% and specificity of 71.3%. Unfortunately this index is not still validated for pregnant women [21]. In patients with suspicious ultrasound of malignant ovarian tumor, the surgical staging procedure is threefold. Diagnosis and histopathological grade of the tumor provide useful information to be discussed depending on the age of pregnancy and to perform initial treatment (surgery or chemotherapy) [16].

These tumors can be treated conservatively by adnexectomy and peritoneal cytology and exploration with biopsies, never lead to the end of the pregnancy and should be performed without rupture [16]. It is mostly done by laparotomy, but laparoscopic surgery may be an option before 24 weeks. Tumor rupture is significantly more frequent during laparoscopy

compared to laparotomy (29.5% *vs*. 13.1%) [21]. Cystectomy is associated with a higher recurrence rate (up to 31%) [23]. It should be performed only for patients with bilateral tumors and/or only one ovary; it was associated with a higher rate of intraoperative cyst rupture [24], and with the knowledge that is not safe in patients with mucinous borderline tumors because is associated with an increased risk of recurrence in the form of invasive carcinoma [25], but is an acceptable option for women who plan further pregnancies [26]. If borderline tumor is revealed by the histology of a surgical specimen, it seems reasonable to defer surgical treatment until after delivery and the surgical staging should be completed 3-6 weeks after delivery [16]. Spontaneous conception is reported after conservative surgery in 50% of patients without any deterioration in the survival rate [27]. The available data suggest that the rate of recurrence is higher after conservative surgery (10% to 20% *vs*. approximately 5% for radical surgery) [22]. Nevertheless, the psychological impact of waiting for relapse is considerable and there is still a risk for development of invasive ovarian tumors, for this reason its recommend definitive surgery after family planning is completed [24]. There is no clear evidence that chemotherapy can decrease relapse rates or improve survival in any subset of patients with this diagnostic [24].

These tumors when treated with adjuvant chemotherapy or radiotherapy showed high persistent or recurrent disease (up to 40%) [23]. In the case of relapse on the remaining ovary after conservative surgery, cystectomy may be proposed to preserve fertility, or salpingoophorectomy with or without hysterectomy is performed. When extraovarian recurrence or invasive disease occurs, extensive cytoreductive surgery, in line with the surgical management of primary ovarian cancer, is the treatment option of choice [24]. The overall recurrence rate for patients previously treated is estimated to be up to 11%. The absolute rate for malignant transformation is about 2%-4% [23].

Follow-up is usually a combination of clinical examination, ultrasound, and CA125 levels. During the initial two years, follow-up evaluation is performed every three months. Patients are then evaluated biannually for 3-5 years after surgery, and then annually thereafter [28, 29]. Transvaginal and transabdominal ultrasound are the optimal techniques for the surveillance because of their high ability to detect discrete intraovarian abnormalities as well as extraovarian implants [30].

4 Conclusions

Current guidelines for diagnosis and treatment of BOTs is mainly focused to urban centers and despite the evidence supporting those, characteristics between urban populations, rural and extremly poor areas, make not feasible the appliance of these guides in marginal zones. We consider the importance of this case is to reaffirm the diagnostic criteria and therapeutic to be taken account in a pregnant woman in extremly poverty conditios with suspicious findings in ultrasound and intraoperative report borderline ovarian tumor. Although current publications refer to a conservative surgery in women who want to conserve fertility, there is clear evidence that radical surgery offers the lowest rates of recurrence, therefore we consider that treatment in a patient with satisfied parity, poor prenatal care and without adequate diagnostic tools and in the third trimester of pregnancy, should be candidate to perform caesarean section with a radical surgery.

References

[1] Karseladze AI. WHO histological classification of ovarian tumors. Arkh Patol. 2005; Suppl: 1-64. PMid: 16108150.

[2] Lorusso D, Ratti M, Ditto A, *et al*. High-risk borderline ovarian tumors: analysis of clinicopathological features and prognostic impact of different follow-up strategies. Oncology. 2014; 87(3): 183-92. http://dx.doi.org/10.1159/000360990

[3] Hannibal CG, Vang R, Junge J, *et al*. A nationwide study of serous "borderline" ovarian tumors in Denmark 1978-2002: centralized pathology review and overall survival compared with the general population. Gynecol Oncol. 2014; 134(2): 267-73. http://dx.doi.org/10.1016/j.ygyno.2014.06.002

[4] Seidman JD, Kurman RJ. Pathology of ovarian carcinoma. Hematol Oncol Clin North Am. 2003; 17(4): 909-25, vii. http://dx.doi.org/10.1016/S0889-8588(03)00061-3

[5] Schwartz N, Timor-Tritsch IE, Wang E. Adnexal masses in pregnancy. Clin Obstet Gynecol. 2009; 52(4): 570-85. http://dx.doi.org/10.1097/GRF.0b013e3181bea9d7

[6] Sherard GB, Hodson CA, Williams HJ, *et al*. Adnexal masses and pregnancy: a 12-year experience. Am J Obstet Gynecol. 2003; 189(2): 358-62; discussion 362-3. http://dx.doi.org/10.1067/S0002-9378(03)00731-2

[7] Fauvet R, Brzakowski M, Morice P, *et al*. Borderline ovarian tumors diagnosed during pregnancy exhibit a high incidence of aggressive features: results of a French multicenter study. Ann Oncol. 2012; 23(6): 1481-7. http://dx.doi.org/10.1093/annonc/mdr452

[8] Hart WR. Mucinous tumors of the ovary: a review. Int J Gynecol Pathol. 2005; 24(1): 4-25. PMid: 15626914.

[9] Lee KR, Scully RE. Mucinous tumors of the ovary: a clinicopathologic study of 196 borderline tumors (of intestinal type) and carcinomas, including an evaluation of 11 cases with «pseudomyxoma peritonei». The American Journal of Surgical Pathology. 2000; 24(11): 1447-1464. http://dx.doi.org/10.1097/00000478-200011000-00001

[10] Young RH, Gilks CB, Scully RE. Mucinous tumors of the appendix associated with mucinous tumors of the ovary and pseudomyxoma peritonei. A clinicopathological analysis of 22 cases supporting an origin in the appendix. Am J Surg Pathol. 1991; 15(5): 415-29. PMid: 2035736. http://dx.doi.org/10.1097/00000478-199105000-00001

[11] Riopel MA, Ronnett BM, Kurman RJ. Evaluation of diagnostic criteria and behavior of ovarian intestinal-type mucinous tumors: atypical proliferative (borderline) tumors and intraepithelial, microinvasive, invasive, and metastatic carcinomas. Am J Surg Pathol. 1999; 23(6): 617-35. PMid: 10366144. http://dx.doi.org/10.1097/00000478-199906000-00001

[12] Ronnett BM, Kajdacsy-Balla A, Gilks CB, *et al*. Mucinous borderline ovarian tumors: points of general agreement and persistent controversies regarding nomenclature, diagnostic criteria, and behavior. Hum Pathol. 2004; 35(8): 949-60. PMid: 15297962. http://dx.doi.org/10.1016/j.humpath.2004.03.006

[13] Kurman RJ, Shih IeM. Pathogenesis of ovarian cancer: lessons from morphology and molecular biology and their clinical implications. Int J Gynecol Pathol. 2008; 27(2): 151-60. http://dx.doi.org/10.1097/PGP.0b013e318161e4f5

[14] Mayr D, Hirschmann A, Löhrs U, *et al*. KRAS and BRAF mutations in ovarian tumors: a comprehensive study of invasive carcinomas, borderline tumors andextraovarian implants. Gynecol Oncol. 2006; 103(3): 883-7. PMid: 16806438. http://dx.doi.org/10.1016/j.ygyno.2006.05.029

[15] Catasús L, Bussaglia E, Rodrguez I, *et al*. Molecular genetic alterations in endometrioid carcinomas of the ovary: similar frequency of beta-catenin abnormalities but lower rate of microsatellite instability and PTEN alterations than in uterine endometrioid carcinomas. Hum Pathol. 2004; 35(11): 1360-8. PMid: 15668893. http://dx.doi.org/10.1016/j.humpath.2004.07.019

[16] Marret H, Lhommé C, Lecuru F, *et al*. Guidelines for the management of ovarian cancer during pregnancy. Eur J Obstet Gynecol Reprod Biol. 2010; 149(1): 18-21. http://dx.doi.org/10.1016/j.ejogrb.2009.12.001

[17] Marret H, Vinatier L, Sauget S, *et al*. Power Doppler Index for preoperative ovarian tumors discrimination. Gynecol Obstet Fertil. 2007; 35(6): 541-7. PMid: 17540606. http://dx.doi.org/10.1016/j.gyobfe.2007.04.009

[18] Telischak NA, Yeh BM, Joe BN, *et al*. MRI of adnexal masses in pregnancy. AJR Am J Roentgenol. 2008; 191(2): 364-70. http://dx.doi.org/10.2214/AJR.07.3509

[19] Kurtz AB, Tsimikas JV, Tempany CM, *et al*. Diagnosis and staging of ovarian cancer: comparative values of Doppler and conventional US, CT, and MR imaging correlated with surgery and histopathologic analysis--report of the Radiology Diagnostic Oncology Group. Radiology. 1999; 212(1): 19-27. PMid: 10405715. http://dx.doi.org/10.1148/radiology.212.1.r99jl3619

[20] Spitzer M, Kaushal N, Benjamin F Maternal. CA-125 levels in pregnancy and the puerperium. J Reprod Med. 1998; 43(4): 387-92. PMid: 9583073.

[21] Van Calster B, Van Hoorde K, Valentin L, *et al*. International Ovarian Tumour Analysis Group. Evaluating the risk of ovarian cancer before surgery using the ADNEX model to differentiate between benign, borderline, early and advanced stage invasive, and secondary metastatic tumours: prospective multicentre diagnostic study. BMJ. 2014; 15: 349:g5920. http://dx.doi.org/10.1136/bmj.g5920

[22] Trillsch F, Mahner S, Ruetzel J, *et al*. Clinical management of borderline ovarian tumors. Expert Rev Anticancer Ther. 2010 Jul; 10(7): 1115-24. http://dx.doi.org/10.1586/era.10.90

[23] du Bois A, Ewald-Riegler N, de Gregorio N, *et al*. Gynäkologische Onkologie (AGO) Study Group. Borderline tumours of the ovary: A cohort study of the Arbeitsgmeinschaft Gynäkologische Onkologie (AGO) Study Group. Eur J Cancer. 2013; 49(8): 1905-14. http://dx.doi.org/10.1016/j.ejca.2013.01.035

[24] Fischerova D, Zikan M, Dundr P, *et al*. Diagnosis, treatment, and follow-up of borderline ovarian tumors. Oncologist. 2012; 17(12): 1515-33. http://dx.doi.org/10.1634/theoncologist.2012-0139

[25] Koskas M, Uzan C, Gouy S, *et al*. Prognostic factors of a large retrospective series of mucinous borderline tumors of the ovary (excluding peritoneal pseudomyxoma). Ann Surg Oncol. 2011; 18(1): 40-8. http://dx.doi.org/10.1245/s10434-010-1293-8

[26] Yinon Y, Beiner ME, Gotlieb WH, *et al*. Clinica outcome of cystectomy compared with unilateral salpingo-oophorectomy as fertility-sparing treatment of borderline ovarian tumors. Fertil Steril. 2007; 88(2): 479-84. PMid: 17408624. http://dx.doi.org/10.1016/j.fertnstert.2006.11.128

[27] Morice P. Borderline tumours of the ovary and fertility. Eur J Cancer. 2005; 42(2): 149-58. PMid: 16326097. http://dx.doi.org/10.1016/j.ejca.2005.07.029

[28] Zanetta G, Rota S, Lissoni A, *et al*. Ultrasound, physical examination, and CA 125 measurement for the detection of recurrence after conservative surgery for early borderline ovarian tumors. Gynecol Oncol. 2001; 81(1): 63-6. PMid: 11277651. http://dx.doi.org/10.1006/gyno.2000.6099

[29] Ramirez PT, Slomovitz BM, Soliman PT, *et al*. Total laparoscopic radical hysterectomy and lymphadenectomy: the M. D. Anderson Cancer Center experience. Gynecol Oncol. 2006; 102(2): 252-5. PMid: 16472844. http://dx.doi.org/10.1016/j.ygyno.2005.12.013

[30] Testa AC, Ludovisi M, Mascilini F, *et al*. Ultrasound evaluation of intra-abdominal sites of disease to predict likelihood of suboptimal cytoreduction in advanced ovarian cancer: a prospective study. Ultrasound Obstet Gynecol. 2012; 39(1): 99-105. http://dx.doi.org/10.1002/uog.10100