

Risk factors and significance of lymph node involvement in serous borderline ovarian tumors

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ABSTRACT

Borderline ovarian tumors represent a particular category of ovarian neoplasms characterised by a more favourable outcome, lower risk of recurrence and association of long term survival rates. Although in up to one third of cases lymph node metastases are present, they seem that they do not affect significantly the survival. The aim of the current paper is to identify the most important risk factors for lymph node invasion in serous borderline ovarian tumors and to study their influence on survival.

Keywords: borderline ovarian tumors, lymph node metastases, risk factors, prognostic

INTRODUCTION

Initially described in 1929 as semi-malignant tumors, borderline ovarian tumors represent epithelial ovarian lesions exhibiting an atypical proliferation at this level – aspect which is not found in benign ovarian lesions – but which, differently from malignant ovarian lesions, does not associate local stromal invasion (1,2). Although these tumors have been widely described in all the age groups, it seems that a significant number of cases are diagnosed in young, fertile women and therefore the issue of fertility sparing should be widely discussed (3). When it comes to the most commonly encountered histopathological subtypes, they are represented by serous and mucinous ovarian tumors (3).

RISK FACTORS OF LYMPH NODE INVOLVEMENT IN BORDERLINE OVARIAN TUMORS

It has been demonstrated that lymph node involvement in borderline ovarian tumors at the level of the regional lymph nodes is to be expected in less than 10% of cases while distant lymph node metastases are seen in less than 1% of cases diagnosed with advanced stage of disease (4). Meanwhile it seems that distant lymph node metastases might be encountered as part of recurrent disease in certain cases with previous diagnose of borderline ovarian tumors (5). When it comes to the mechanisms conducting to the lymph node involvement in borderline ovarian tumors, two patterns have been proposed: the first is the classical one and is represented

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by the lymphatic spread to the surrounding lymph nodes while the second one takes into consideration the possibility of a synchronous malignant transformation of nodal endosalpingiosis; however, the presence of KRAS mutation in both lesions in most cases come to support the first hypothesis. Meanwhile the presence of this mutation is also associated with a poorer outcome of patients with borderline ovarian lesions (6).

The hypothesis of association between borderline ovarian tumors and endosalpingiosis was also underlined by Camatte et al.; in their study which included 42 patients submitted to surgery for borderline ovarian tumors and which associated lymph node dissection the rate of endosalpingiosis was of 26% (11 out of the 42 cases presented the association of the two pathological conditions) (7). Meanwhile, eight patients with endosalpingiosis also associated nodal involvement; another interesting correlation was the one between the histopathological subtype, the presence of peritoneal implants and the association of lymph node metastases; therefore it seems that nodal involvement is strongly associated with the presence of peritoneal implants and with the serous histopathological subtype (none of the cases with mucinous lesions presenting lymph node metastases) (7).

RECOMMENDATIONS REGARDING THE ROLE OF LYMPH NODE SAMPLING/DISSECTION IN BORDERLINE OVARIAN TUMORS

When it comes to the role of lymph node sampling or lymph node dissection in borderline ovarian tumors, this issue has been widely studied. However, most papers come to demonstrate that routine lymph node dissection should not be routinely associated as part of the surgical therapy for borderline ovarian tumors; therefore, in the study conducted by Matsuo et al. and published in 2017 the authors included 4,943 with this diagnostic, in 14.9% of cases lymphadenectomy being associated and in other 11.3% of cases both lymphadenectomy and hysterectomy being performed. The authors demonstrated the fact that neither hysterectomy nor lymph node dissection did not significantly influenced the cancer specific survival especially in cases diagnosed in early stages of the disease (8).

Meanwhile, other papers come to demonstrate that although in isolated cases lymph node dissection might upstage the disease, this fact does not significantly influence the long term prognostic in terms of survival (9,10). However, other authors underlined the fact that not the qualitative status of the lymph nodes but their quantitative assessment (the magnitude of the tumoral deposits) influences the rates of survival in such cases (11).

A recently published French Guideline underlined the fact that all macroscopic lesions – defined as peritoneal/omental implants or lymph nodes should be excised at the time of the initial surgery (12). An interesting study which has been conducted by Zilliox et al. included 14 patients diagnosed with borderline ovarian tumors during pregnancy; at the time of the initial diagnostic, during pregnancy, most cases were submitted to unilateral cystectomy or unilateral adnexectomy, a single case being submitted to per primam bilateral cystectomy (13). Meanwhile all cases were submitted to random omental and peritoneal biopsies; peritoneal cytology was also retrieved. At the end of pregnancy, restaging surgery was performed in 12 cases and, depending on the local conditions pelvic lymph node dissection alone or in association with para-aortic lymph node dissection was associated. Although at the histopathological report no positive lymph node was found, after restaging surgery 57.1% of cases were upstaged due to the presence of other tumoral implants (13). These data come to demonstrate once again that lymph node metastases are not commonly encountered in borderline ovarian tumors; even though, restaging surgery is particularly important, up to half of cases being in fact diagnosed in a more advanced stage of the disease but not due to the presence of lymph node metastases.

THE INFLUENCE ON THE LONG TERM OUTCOMES OF LYMPH NODE METASTASES IN BORDERLINE OVARIAN TUMORS

Maybe the most important discussion which should take place in regard to the status of the lymph nodes in borderline ovarian tumors is related to the influence of these histopathological findings on the long term outcomes.

In the recently published French Guideline, regarding the epidemiology, biopathology, imaging and biomarkers of borderline ovarian tumors, the authors came to demonstrate that the status of the lymph nodes does not influence the long term outcomes of these patients (defined by the recurrence rate/survival rate), this information having a level 3 of evidence (12).

An interesting systematic review conducted on this issue has been recently published and demonstrated that although lymph node involvement seems to be present in up to 10% of cases diagnosed with borderline ovarian tumors, this extension does not affect cancer specific survival or this risk of recurrence. As mentioned before, this meta-analysis underlines again the fact that not the qualitative status of the lymph nodes should be taken in consideration but the quantitative one; therefore, cases presenting lymph node metastases in more than

13% of the examined lymph nodes should be considered to be at risk to have a poorer oncological outcome (14).

CONCLUSIONS

Lymph node involvement in borderline ovarian tumors is not frequently encountered; even in cases

in which this finding is reported, it seems that it does not significantly influence the long term outcomes. Therefore, systematic lymphadenectomy is not justified especially in cases in which the diagnostic is established in an early stage of the disease.

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