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Prognostic indicators in ovarian serous borderline tumours

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Summary

There have been great strides in our understanding of the serous group of borderline and malignant pelvic epithelial neoplasms in the past decade. While most serous borderline tumours have a favourable prognosis, recurrences and progression to carcinoma occur, often following a protracted clinical course. Clinical and pathological risk factors tend to co-vary, but the presence and type of extraovarian disease is the most important predictor for progression. Progression usually takes the form of low-grade serous carcinoma, although transformation to high-grade carcinoma is occasionally seen. A serous borderline – low-grade serous carcinoma pathway analogous to neoplastic transformation pathways seen in other organ systems has been proposed, based on global gene expression profiling, shared mutations in *KRAS* or *BRAF*, and in most cases, the presence of serous borderline tumour in *de novo* low-grade serous carcinoma. This discussion focuses on the key prognostic factors that predispose to disease progression and/or transformation to carcinoma in serous borderline tumours.

Key words: Ovary; serous borderline tumour; prognosis; implants; low-grade serous carcinoma.

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INTRODUCTION

Ovarian serous borderline tumour represents the most common type of borderline tumour arising in the ovary.[1] This neoplasm tends to be associated with a serous cystadenoma or adenofibroma,[2] is usually confined to the ovary and has an indolent course;[3] nevertheless, up to 6.8% can progress to low grade serous carcinoma.[4] Certain features of this type of tumour, such as bilaterality,[5] surface involvement,[5] capsular rupture,[5] presence of a micropapillary/cribriform pattern,[4,6–8] microinvasion,[4,9] advanced stage at presentation,[3,4,10,11] implant type[4,5,12] and residual disease[5] have been commonly linked to a more aggressive disease; however, tumours without these features can be associated with recurrences or low-grade serous carcinoma.[4,5,13] In this review, we present a summary of the prognostic indicators for this type of tumour, including under-recognised and recently described features.

PATHOLOGY FEATURES

FIGO stage

Based on a meta-analysis of the literature, the disease specific survival for serous borderline tumours has been estimated to be >95% for patients with low-stage (stage I) disease and approximately 65% for patients with high-stage (stage II–IV) disease.[10] However, since late recurrences do occur, and follow-up is limited in many of the studies analysed, these are conservative estimates of risk of recurrence and the risk is likely to be higher. As is the case with serous carcinoma, surface involvement (Fig. 1) and bilateral ovarian involvement appear to further stratify risk for disease recurrence and progression amongst patients who present with low-stage disease.[12] However, even when high-stage disease, the disease tempo of serous borderline tumours is characteristically indolent and protracted, often lasting years and there may be prolonged periods of dormancy and even spontaneous regression.

Micropapillary/cribriform pattern

Approximately 5–10% of all serous borderline tumours contain foci of significant micropapillary architecture, defined as non-hierarchical branching of slender, elongated papillae that are at least five times as long as they are wide (Fig. 2).[7] A second, less common form of this variant consists of a sieve-like cribriform pattern (Fig. 3). In most cases, the constituent cells in this pattern of serous borderline tumour exhibit a more uniform, hyperchromatic and monomorphous appearance than the usual serous borderline tumour. Pink cells, ciliated cells and tufting are not as frequent in tumours exhibiting a micropapillary or cribriform growth. Also, the degree of cytological atypia is often higher than that which is typically seen in serous borderline tumours and may border on that seen in low-grade serous carcinoma (Fig. 2 and 3). Small nucleoli are often present as well as mitotic figures, but the latter are not atypical and usually not significantly increased over that in the usual serous borderline tumour. By definition, the micropapillary or cribriform elements must occupy a continuous 5 mm linear extent in order to be designated as a micropapillary variant.[6]

Serous borderline tumours with micropapillary architecture are more frequently associated with bilateral ovarian involvement, exophytic ovarian surface involvement, microinvasive serous carcinoma and extraovarian implants.

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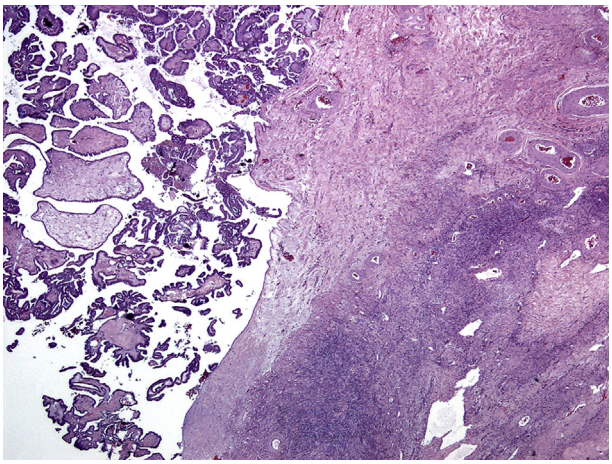

Fig. 1 Serous borderline tumour involving the ovarian surface.

In some series, the micropapillary variant has also been more frequently associated with low-grade serous carcinoma in the extra-ovarian implants (invasive implants); however, the poorer survival observed in earlier studies of micropapillary tumours is likely due to the presence of low-grade serous carcinoma in the extra-ovarian implants (invasive implants) rather than due to the micropapillary features in the ovarian neoplasm itself.[4,8,14,15] A recent population-based study demonstrated that the presence of serous borderline tumours with micropapillary architecture was also associated with increased risk of development of serous carcinoma when compared to usual stage I serous borderline tumours.[12] Although most micropapillary tumours exhibit diffuse micropapillary features, the extent of micropapillary architecture present in serous borderline tumours may vary (e.g., 15%, 40%, etc.) and although there are no specific outcome data linked to the extent of micropapillary and/or cribriform architecture, it seems reasonable to provide that information in the comment section of the pathology report.

Stromal microinvasion and microinvasive carcinoma

Approximately 10–15% of serous borderline tumours feature stromal-epithelial patterns that resemble stromal invasion in other organ systems, but do not elicit a significant destructive stromal response.[9] Five patterns of stromal microinvasion have been described: individual eosinophilic cells and cell clusters (so-called 'classic' microinvasion)[9,16] (Fig. 4); simple and non-complex branching papillae; inverted macropapillae; cribriform glands; and micropapillae (Fig. 5). The classic pattern of microinvasion is the most common, followed by simple papillary and inverted macropapillary patterns. Often, several patterns are present, particularly single cells, cell clusters and simple papillae. Cribriform stromal microinvasion is uncommon and experience is very limited. The micropapillary stromal-epithelial pattern is also very uncommon. Classic microinvasion occurs disproportionally in patients presenting with serous borderline tumours during pregnancy, usually with low-stage disease, and does not appear to be associated with any risk of progression in that setting. Unlike the classic pattern of stromal microinvasion, the presence of elongated and/or complex branching micropapillae, with or without background micropapillary ovarian histology, may confer a comparatively higher risk, particularly when multiple foci are present in the primary ovarian tumour.

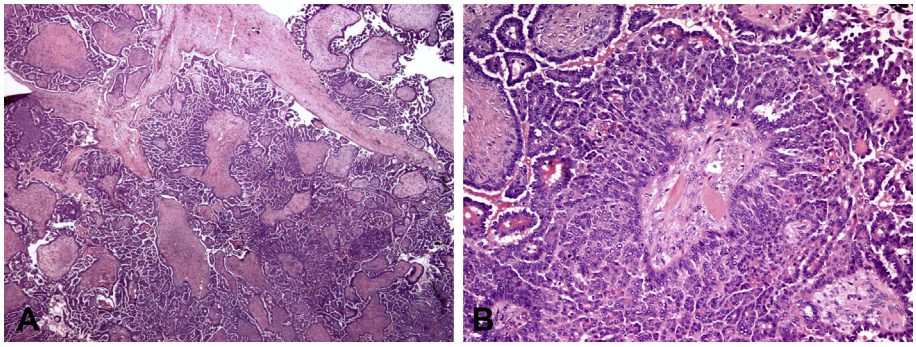

Fig. 2 Ovarian serous borderline tumour with a micropapillary pattern. (A) Low magnification, medusa head appearance; (B) higher magnification, nuclei are larger than those seen in the epithelial component of a classic type serous borderline tumour.

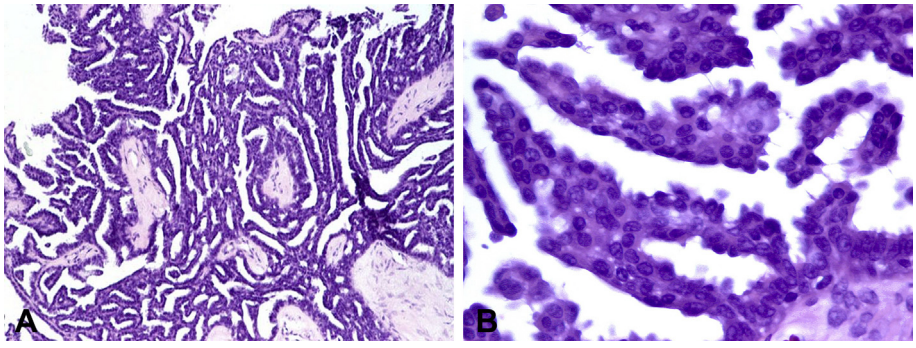

Fig. 3 Ovarian serous borderline tumour with a cribriform pattern. (A) Low magnification, sieve-like appearance; (B) higher magnification, nuclei are larger than those seen in the epithelial component of a classic type serous borderline tumour.

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