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Evaluation of Interobserver Agreement in the Classification of Peritoneal Implants in Ovarian Serous Borderline Tumors and Low-Grade Serous Carcinomas: A Multi-Reviewer Study

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INTRODUCTION & AIM

The diagnosis of non-invasive implant versus metastasis has significant prognostic and therapeutic implications. Non-invasive implants are associated with an excellent prognosis, while invasive LGSC metastasis demonstrate increased progression and more aggressive behavior.

There are no definitive diagnostic criteria to enable accurate diagnosis of these lesions, which is a frequent reason for differing opinions among pathologists regarding whether metastases of LGSC and non-invasive implants of SBT are distinct entities. Accurate classification significantly affects surgical planning, staging, and fertility preservation, especially for young patients, and the need to evaluate and improve diagnostic consistency is critical.

The aim of this study was to evaluate interobserver agreement in the classification of these implants.

METHOD

Twenty-four cases of ovarian SBT and LGSC with 33 samples of extraovarian implants were independently reviewed by three gynecologic pathologists and three general pathologists. Diagnostic criteria included destructive invasion, micropapillary architecture, and retraction clefts. The Fleiss' Kappa statistic was used to measure interobserver agreement, with consensus diagnoses determined by the majority of gynecologic pathologists. To avoid circularity in assessing the level of agreement between each gynecologic pathologist and the consensus, the leave-one-out approach was used.

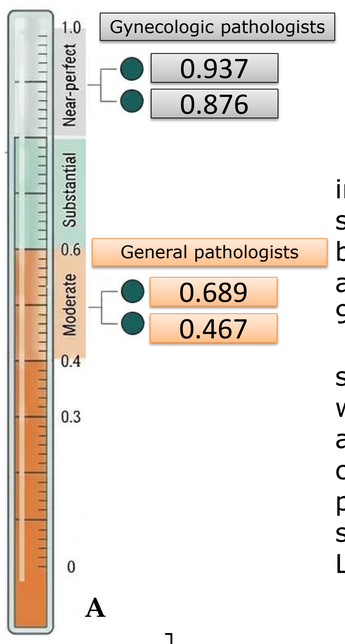
destructive invasion

micropapillary architecture

retraction clefts

RESULTS & DISCUSSION

On the basis of the abovementioned morphological features, 42.4% (14/33) of biopsies were classified according to the consensus diagnosis as metastases of LGSCs and 57.6% (19/33) as non-invasive implants of SBTs. Interobserver reproducibility for distinguishing non-invasive implants and metastasis was carried out with independent review results by six pathologists with different experience in the gynecological field. The Fleiss' kappa value for the assessment of invasion was 0.61 (95% CI 0.50–0.71), indicating substantial interobserver agreement.



When interobserver reproducibility was measured, gynecologic pathologists showed substantial to near-perfect agreement (κ=0.876–0.937), while general pathologists showed moderate agreement (κ = 0.467–0.698). Overall reproducibility was substantial (κ=0.61).

Patients in the SBT group were younger than patients in the carcinoma group but these differences were not statistically significant. FIGO staging showed that most cases in both groups were advanced (stage III-IV) with 75.0% in SBTs and 91.0% in LGSC. Stage II was rare, accounting for 15% and 9% for each group, respectively.

Prognosis analysis was performed on the disease-free survival (DFS) time of 23 patients (for 13 SBT and for 10 LGSC), with a median follow-up period of 45 months. The log-rank test and Kaplan–Meier survival curve were employed to evaluate the correlation between the type of extraovarian lesion and DFS of patients. Analysis of disease-free survival did not identify any statistical differences between extraovarian lesions of SBTs and LGSC (p = 0.08).

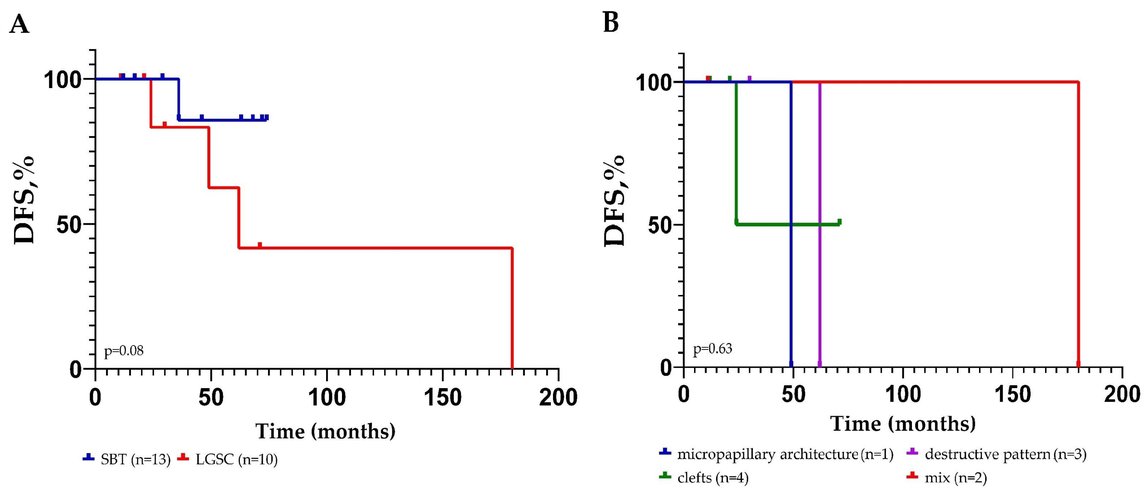


Figure 1. Univariable analysis of disease-free survival (DFS). (A) DFS of patients with SBT (n = 13) and LGSC (n = 10). (B) DFS of 10 patients with different morphological patterns of metastasis.

Histoarchitectural assessment of of 14 metastases of LGSC revealed several invasive growth patterns that were found alone or in combination. One of the most commonly detected single patterns of omentum and peritoneum metastases was a destructive variant with glands and clusters of tumor cells percolating through the stroma (A). In two biopsies, differential diagnosis included foci of endometriosis (B). Another frequent type of metastasis was clefts in fibrotic stroma with nests of epithelial cells surrounded with retraction artifacts (C). In contrast, non-invasive implants showed multiple miropapillary structures confined within an epithelium-lined space (D). Also, in cases of SBT, endosalpingiosis was found (E). In total, 7.1% (1/14) metastases demonstrated pure micropapillary architecture (F). The mixed architecture was identified in five cases, with three samples demonstrating a combination of micropapillary and destructive patterns; the other two showed both micropapillary structures and retraction artifacts.

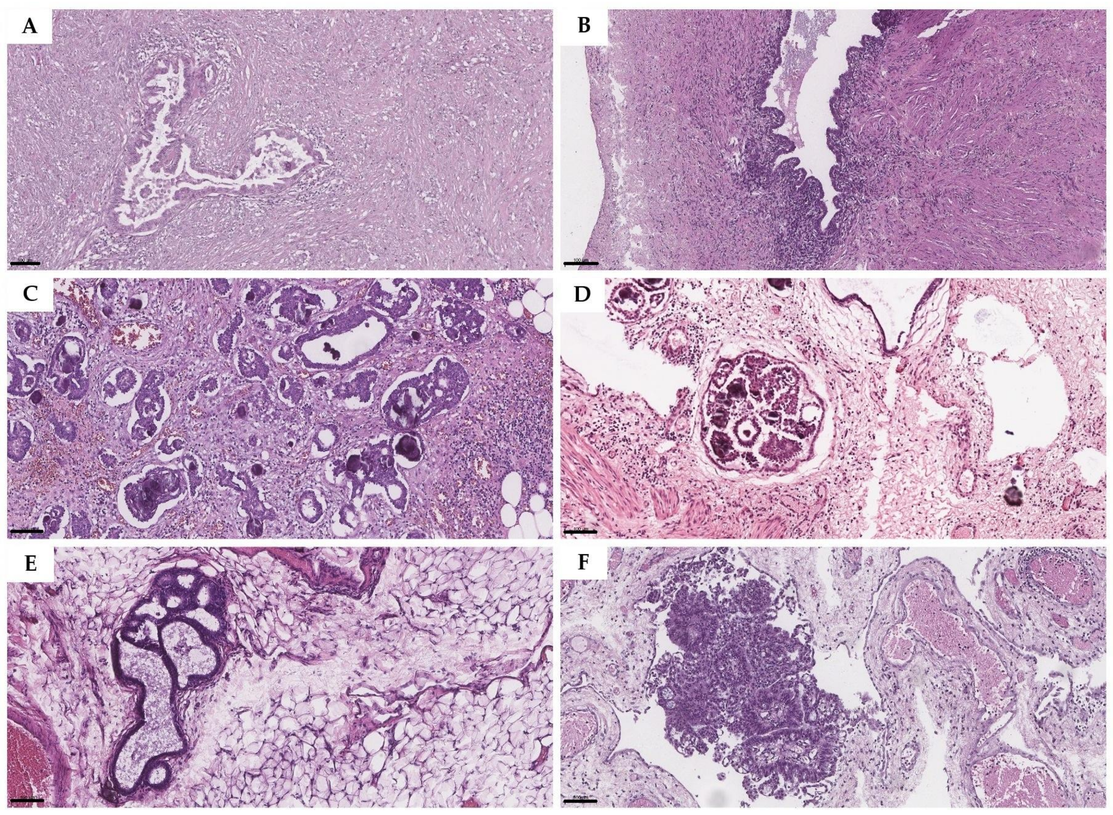


Figure 2. Histological lesions of omentum and peritoneum biopsies in SBT and LGSC groups. (A) Destructive pattern of invasion with glands and clusters of tumor cells percolating through the stroma; (B) endometriosis with ectopic located endometrial glands and endometrial type stroma; (C) metastasis with small isolated papillas within clear lacunar spaces (retraction artifacts); (D) non-invasive implant of SBT with micropapillary structures within epithelium lined space; (E) endosalpingiosis; (F) metastasis with micropapillary architecture.

CONCLUSIONS

The results showed that current diagnostic reproducibility remains suboptimal, particularly among general pathologists, underscoring the need for improved training and standardized criteria. Ultimately, a multidisciplinary approach combining morphological expertise, immunohistochemical validation and molecular stratification will be essential for optimizing the diagnosis and treatment of peritoneal implants to ensure tailored therapies that balance oncological safety and quality of life, especially for young patients who wish to preserve their fertility.

FUTURE WORK

A multidisciplinary approach combining morphological expertise, immunohistochemical validation and molecular stratification will be essential for optimizing the diagnosis and treatment of peritoneal implants to ensure tailored therapies that balance oncological safety and quality of life, especially for young patients who wish to preserve their fertility. Moreover, reliance on less predictive morphologic patterns should be minimized, and standardized training should be implemented with improved training programs for pathologists, particularly to distinguish subtle histological features.

CONTACTS

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