Effusion cytology of a mucinous borderline ovarian tumour: Pitfall or controversy? A case report with insight into the newly proposed International System for Reporting Serous Fluid Cytology

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1 | INTRODUCTION

Fluid from peritoneal effusions (ascites), with a history of a pelvic mass is frequently submitted to cytology to assess for malignancy. Cytology of mucinous epithelium from adenomatous or borderline tumours exfoliated into serous cavities is challenging, not well described and can be mistaken for adenocarcinoma.

2 | CASE REPORT

A 43-year-old woman presented clinically with a pleural effusion, ascites and a palpable pelvic mass. An abdominopelvic computed tomography scan confirmed a large cystic pelvic mass, probably of ovarian origin and free fluid along the paracolic gutters with suspected peritoneal dissemination (Figure ). Pre-operative ascitic fluid cytology was reported as adenocarcinoma while the pleural fluid cytology displayed only reactive changes.

A staging laparotomy revealed a left ovarian mass, necessitating a total hysterectomy, bilateral salpingo-oophorectomy and omentectomy. Histology of tumour sections showed a mucinous borderline ovarian tumour (MBOT) with capsular involvement. The absence of omental and peritoneal invasive disease prompted a review and amendment of the original malignant ascitic cytological diagnosis. Review of the pleural fluid remained reactive. At 6 weeks post-surgery follow-up, our patient was clinically well and her pleural effusion had radiologically resolved.

3 | DISCUSSION

MBOTs are also known as mucinous tumours of low malignant potential or atypical proliferative mucinous tumours.1,2 They have an excellent overall survival and prognosis when confined to the ovary and are not associated with peritoneal or omental invasion.1,2 Neoplastic epithelium from capsular involvement or a ruptured MBOT can, however, be dislodged into the serous cavity and elicit a peritoneal effusion. This does not render the tumour invasive.

The literature on effusion cytology for MBOTs are limited. Discerning borderline neoplastic deposits from malignant cells is problematic. Only serous borderline ovarian tumours have been addressed in this regard.3-5 Recognisable malignant criteria from adenocarcinomatous effusions include: cohesive spherical cell clusters with a smooth community border (cannonballs), eccentric location of nuclei, increased nuclear to cytoplasmic ratios, nuclear pleomorphism with overlap, hyperchromasia, irregular nuclear membranes and chromatin distribution.6,7 A retrospective review of our patient’s ascitic fluid displayed unequivocal presence of epithelial cells, but, besides eccentric nuclei, cells lacked the other nuclear malignant features.
Instead, careful cytological evaluation of the cell groups in the fluid revealed a spectrum of mucinous neoplasia, ranging from benign (Figure 1B,C) to borderline (Figure 1D-F). These morphological features were extrapolated from known histological criteria used for diagnosing mucinous cystadenomatous (Figure 2A) and borderline (Figure 2B) changes in ovarian pathology. The cytology showed cystadenomatous cell groups arranged in an elegant fanned out array, with monolayered epithelium and basal, rounded nuclei, occupying less than half the cell (Figure 1B,C). These cells mirror the ovarian cystadenomatous component (Figure 2A). Cytological borderline transition showed complexity, stratification with nuclear crowding and elongated nuclei, extending to more than half of the cell (Figure 1D). Polarity was still maintained, nuclei showed moderate atypia and cytoplasmic mucin indenting the nucleus to the base of the cell was still identified (Figure 1D-F). This borderline cytology is comparable to the borderline ovarian histomorphology (Figure 2B). The pitfall here is misinterpreting these mucinous epithelial cells as well-differentiated mucinous adenocarcinoma. The low nuclear to cytoplasmic ratios, absence of malignant nuclear features and a neat apical mucinous rimmed border in complex groups should caution against this oversight.

Histologically, the MBOT was of intestinal phenotype. It showed multiloculated cystic spaces lined by goblet cells containing mucinous epithelium, involving the ovarian surface (Figure 2A). Most of the tumour showed cystadenomatous features with a monolayered cyst lining (Figure 2A). Stratification and complexity represented

**FIGURE 1**  (A) Computed tomography scan image (abdominal window) demonstrates the enhancing septae in the large cystic pelvic mass with free fluid tracking along the paracolic gutters. Omental nodularity is suggestive of omental dissemination. (B) Peritoneal effusion cytology showing features from the ovarian mucinous cystadenomatous component. Note monolayered epithelium with round eccentric nuclei occupying less than half the height of the cell. The nucleus is depressed by abundant cytoplasmic mucin (Papanicolaou [Pap] stain, 1000×). (C) Peritoneal effusion cytology of ovarian mucinous cystadenoma component with apical mucin and basally located nuclei. Malignant nuclear features are absent (Pap stain, 1000×). (D) Peritoneal effusion cytology showing transition from mucinous cystadenoma with basal rounded nuclei on the right, to borderline with elongated nuclei on the left (Pap stain, 400×). (E) Peritoneal effusion cytology of mucinous borderline ovarian tumour component showing complexity and stratification with enlarging nuclei that are starting to crowd. Cells show tall, elongated nuclei extending to more than two thirds of the cell (Pap stain, 1000×). (F) Peritoneal effusion cytology of mucinous borderline ovarian tumour exhibiting honeycombing, with a peripheral border of apical mucin and moderate nuclear atypia. Overt malignant features are lacking (Pap stain, 1000×)
borderline transformation, comprising about 30% of the tumour (Figure 2B). Sections from the peritoneum and omentum showed loose lying extraovarian neoplastic deposits in the form of detached cells and glands within fibrin meshworks, but no invasion (Figure 2C,D). These latter cells represent the exfoliated ovarian tumour cells in the fluid. Peritoneal or omental invasion was absent. The nature of these exfoliated cells is debatable and adds to the evolving concepts associated with MBOTs. Current literature negates the occurrence of extraovarian MBOTs, yet rarely addresses exfoliated deposits from the ovarian surface. Given that these exfoliated cells are barely attached to the omentum (Figure 2C,D), we concede that the term implants, as applied to serous borderline ovarian tumours may also be problematic.

Reasons cited for refuting extraovarian MBOT are metastasis and sampling bias. These possibilities were both excluded in this case. Metastasis from the breasts, gastrointestinal and pancreaticobiliary tracts were confidently excluded either intraoperatively, radiologically or histologically. Possible gynaecological sources were excluded with normal microscopy of the right ovary, endometrium and endocervix. Ovarian surface involvement is also an indicator of metastasis. Immunohistochemistry (ICC) on tumour tissue and fluid cell-block sections exhibited strong and diffuse positive staining with cytokeratin 7 and PAX8, with negative cytokeratin 20 and SATB2 staining in the tumour and neoplastic deposits; supporting the ovary as the primary tumour site. This immunoprofile mitigates against an intestinal primary and ratifies this tumour as a pure MBOT without accompanying teratoma or Brenner components. Unilaterality and size exceeding 130 mm also endorses an ovarian origin.

The challenge of sampling large heterogeneous tumours is a recognised limitation. The tumour and omentum were adequately sampled with an excess of 2 sections per 10 mm of tissue, according to guidelines. Evidence of intraepithelial carcinoma, microinvasion, expansile pattern or infiltrative carcinoma, Brenner tumour, or teratoma was absent. Invasion of the omentum or peritoneum could not be identified. The nature of neoplastic deposits supports the histological diagnosis of MBOT in that they are sparse and indolent in appearance. The histological illustrations depicted here were, indeed, the only deposits found (Figure 2C,D) after extensive sampling prompted by the prior discrepant cytological diagnosis.

Does it matter? The mainstay of treatment for MBOT, irrespective of stage, is surgical debulking. If imaging portrays omental invasion, as in this case, an erroneous diagnosis of adenocarcinoma on cytology would upstage the tumour. This can lead to misguided preoperative cytoreductive chemotherapy for irresectable tumours, which an extraovarian MBOT can mimic.

According to the currently proposed International System for Reporting Serous Fluid Cytology, borderline tumours are designated the atypia of undetermined significance (AUS) category.
This seems contradictory to the aims of the system, as the main focus of the system is to minimise the indeterminate categories. The AUS category accommodates for cells where morphology is compromised, or acts as a placeholder, until ancillary studies can better characterise the nature of the cells. Neither of these possibilities applies to our case. Morphology was clearly epithelial and mucinous. ICC would not differentiate between borderline or malignant. Advice to exclude neoplastic and preneoplastic conditions before applying the AUS category also conflicts with a diagnosis of borderline lesions, as they are regarded as precursor lesions to low grade ovarian carcinoma. Effusions classified as AUS are usually expected to have a benign outcome with the aid of ICC, in contrast to suspicious for malignancy (SFM), where a malignant process is anticipated. In our case, SFM would be the most suitable category for the choices currently available, albeit inaccurate. Borderline tumours are neoplasms intermediate between benign and malignant. This highlights the need to refine the indeterminate categories. Seeing that clinical management for SFM and malignant categories are similar, broadening the SFM to incorporate neoplastic entities seems more plausible. Future case reports demonstrating similar issues are encouraged to assist in making the International System for Reporting Serous Fluid Cytology more inclusive.

4 | CONCLUSION

This case highlights rare cytomorphology of a mucinous neoplasm comprising adenomatous and borderline features in an effusion sample arising from a pure MBOT. Careful morphological examination of effusion cytology specimens is essential to avoid a false positive diagnosis of metastatic carcinoma, which can result in overtreatment. Awareness of diagnostic pitfalls of mucinous tumours improves diagnostic accuracy of fluid cytology. The educational value of multidisciplinary discussion and retrospective review with cytological-histological correlation cannot be overemphasised.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

R.R. was the project leader and responsible for the design, concept and preparation of the manuscript. P.B., M.M.M. and P.T.S. made conceptual contributions and were involved in the manuscript preparation and final editing.

ETHICAL APPROVAL

The Human Research Ethics Committee of Stellenbosch University approved the present report (SU ethics # C20/06/01).

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REFERENCES


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