

Is it an endometrioid carcinoma or mesonephric type adenocarcinoma?

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Mesonephric carcinoma is a rare and highly malignant tumour of the female genital tract. We report a case of mesonephric adenocarcinoma of cervix in a 76 years old lady presenting with recurrent post menopausal bleeding and thickened endometrial lining.

Presentation

This 76 years old lady presented with recurrent postmenopausal bleeding. Ultrasound scan revealed a normal sized uterus in which the endometrium was distended and heterogeneous with an AP measurement of 28.5mm towards the cervix, but comparatively thin at the fundus. The patient was para 2 and had normal vaginal delivery and one Caesarean section. Her cervical smears were normal until the age of 65. She has had a previous history of breast cancer (12 years back) which was treated with lumpectomy, radiotherapy and Tamoxifen.

Initial Investigation and Histology

The patient underwent a hysteroscopy and pipelle biopsy. The pipelle could not be advanced beyond 6cm and it was unclear if the tumour was arising from the cervix or the uterus.

The endometrial biopsy sample revealed a malignant tumour with villoglandular architecture (figure 1) and focal hyalinized stromal cores (figure 2). The cells displayed mild to moderate nuclear pleomorphism with numerous mitotic figures (figure 3). Micropapillary structures were also seen.

Immunohistochemistry showed diffuse strong positivity for PAX8 & GATA3 with patchy positivity for CK7 & vimentin and focal positivity for calretinin. p53 was wild type. p16, CEA, ER, PR, TTF1, CD10, AMACR and Napsin A were negative (representative examples in figure 5). The mismatch repair proteins were retained.

The features suggested either an endometrioid adenocarcinoma, probably G2 (although the immunoprofile is not entirely typical with completely negative hormone receptors) or mesonephric/mesonephric like carcinoma of cervix/endometrium (although the morphology is not classical).

The case was discussed at the multidisciplinary team meeting and decided for MRI with an examination under anaesthetic given the debatable histology.

The MRI demonstrated 4.2 x 3.6 x 4.2cm mass centred on the upper cervix/utero-cervical junction with extension into lower uterine segment. No clear extension into cervical stroma, myometrium or parametrium was seen and no evidence of metastatic disease within the abdomen or pelvis.

Examination under anaesthetic and further hysteroscopy revealed fronds of tissue extending from endometrial cavity down into endocervical canal with normal appearing exocervix (although enlarged). The endometrial curetting's showed villoglandular tumour fragments with similar morphological features to the previous biopsy (figure 4) and a similar conclusion of either G2 endometrioid carcinoma or mesonephric-like carcinoma.

Based on the recommendations from the tumour board it was decided to treat the case as an endometrial cancer. Therefore, the patient underwent laparoscopic hysterectomy with bilateral salpingo-oophorectomy and pelvic lymphadenectomy.

Resection specimen

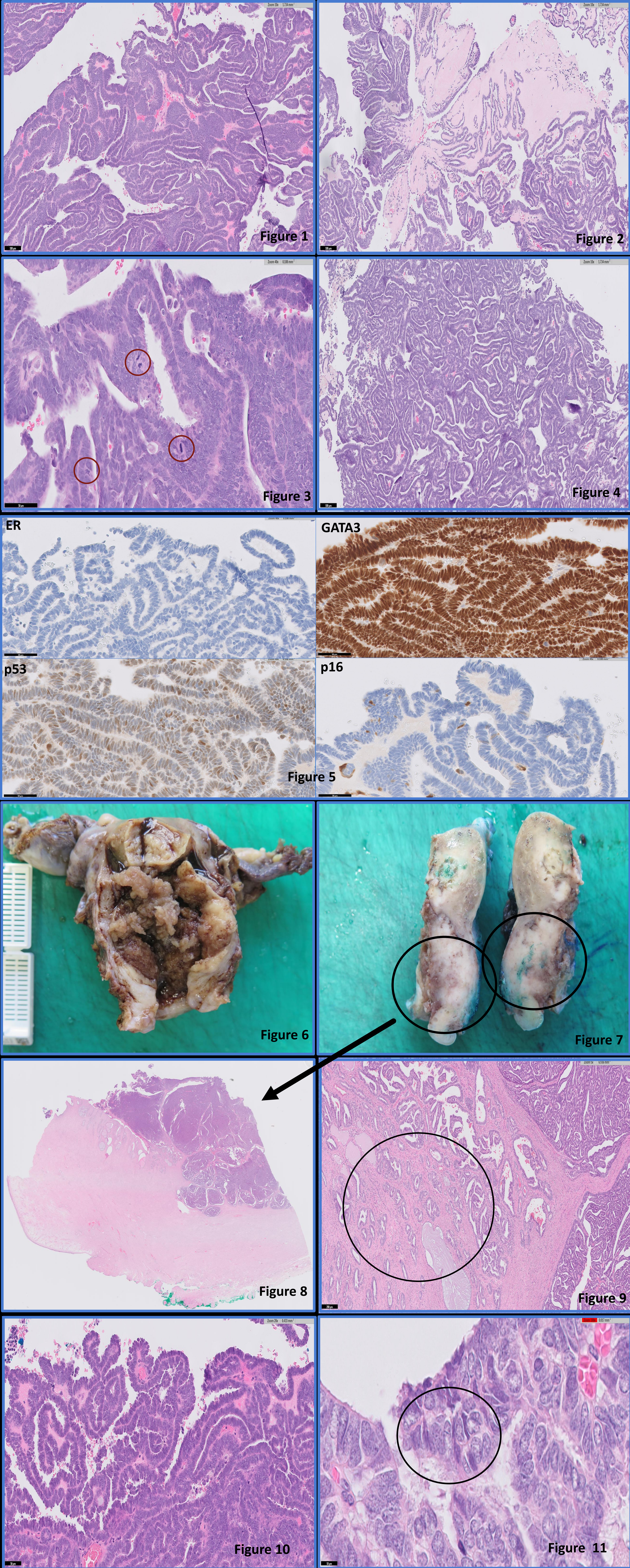
The specimen is an anteriorly opened uterus and cervix 85mm x 35mm x 30mm (figure 5). Right fallopian tube 45x6mm and right ovary 25x20mm. Left fallopian tube 60x7mm and left ovary 20x10mm. The opened uterus revealed uterine wall thickness of 15mm with some thickening of the endometrial lining. However, the endocervical canal showed the presence of an eroding tumour with papillary projections (50mm across) circumferentially involving most of the endocervical canal (figure 6 & 7).

Histological sections of the tumour revealed a predominant villoglandular and papillary architectures arising within the cervix (figure 8 and 10). The tumour cells are cuboidal to columnar with moderately pleomorphic angulated and grooved vesicular nuclei (reminiscent of papillary thyroid carcinoma) and scanty cytoplasm (figure 11 circle).

On immunostaining the tumour cells are diffuse and strongly positive for PAX8 and GATA3. P53 is wild type with no evidence of p16 overexpression. Negative staining is noted for ER, calretinin, TTF, CEA, Napsin A & AMACR.

The epicentre of the tumour was predominantly based within the endocervical canal with circumferential involvement of the cervical wall. There was an extension to the lower uterine segment with only superficial tumour invasion at the uterine body. No deep myometrial invasion or extension to the uterine fundus is noted. Mesonephric duct remnants are also identified deep to the tumour within the cervical wall (figure 9 circle).

The final histological diagnosis was that of HPV independent, mesonephric type adenocarcinoma of uterine cervix, with negative pelvic lymph nodes, FIGO stage IB3.



Discussion

Adenocarcinoma, HPV-independent, mesonephric type, of uterine cervix is an uncommon malignant neoplasm with mesonephric (Wolffian) differentiation that is thought to arise from vestiges of embryological male reproductive system (wolffian/mesonephric duct).¹

Histologically the tumour is characterised by a variety of architectural patterns such as glandular and tubular, glandular, and solid in various combinations. The glandular and tubular architecture is the most prominent pattern with some tubules containing luminal eosinophilic colloid-like material.²

In a multi-institutional study on mesonephric and mesonephric-like adenocarcinoma of the gynaecologic tract, only a small number of cases (22%) were correctly diagnosed by pathologists on initial biopsy. And it was suggested that this might be related to the uncommon nature of these neoplasms (i.e. pathologists are not very familiar with the morphologic features especially on small biopsy specimens) and the variety of the architectural patterns that this tumour can exhibit mimicking other neoplasms.³

Mesonephric adenocarcinoma has a broad differential diagnosis. On the benign spectrum, it should be differentiated from mesonephric remnants and hyperplasia. Ki-67 immunostaining may be helpful, since it has been reported to show positivity in only 1–2% of cells in mesonephric hyperplasia versus 5–20% or more in carcinoma. On the malignant spectrum, the ductal variant of the tumour should be differentiated from endometrioid adenocarcinoma, which is usually positive for ER, PR, and vimentin. Tumours with papillary and slit-like arrangements can be confused with serous carcinoma (most often represent metastasis from ovarian serous carcinoma) and foci of hobnail cells in mesonephric adenocarcinoma can resemble clear cell carcinoma. In contrast to mesonephric adenocarcinoma, both serous and clear cell carcinoma show high nuclear grade.⁴

Therefore, It is a morphologically challenging diagnosis since the tumour typically exhibits a mixture of morphologic patterns and is often confused with the more common types of adenocarcinomas.⁵

Conclusion

In conclusion, we present this case of mesonephric type adenocarcinoma of the cervix that was diagnostically challenging as it appeared endometrial on hysteroscopic examination and showed a predominant ductal/pseudo-endometrioid pattern histologically with lacking of the characteristic back-to-back tubules with intraluminal eosinophilic secretions.

References

- 1- WHO Classification of Tumours Editorial Board. Female genital tumours. Lyon (france): International Agency for Research on Cancer; 2020. (WHO classification of tumour series, 5th ed.; vol. 4).
- 2- Xie C, Chen Q, Shen Y. Mesonephric adenocarcinomas in female genital tract: A case series. *Medicine (Baltimore)*. 2021;100(35):e27174.
- 3- Pors J, Segura S, Chiu DS, Almadani N, Ren H, Fix DJ, Howitt BE, Kolin D, McGluggage WG, Mirkovic J, Gilks B, Park KJ, Hoang L. Clinicopathologic Characteristics of Mesonephric Adenocarcinomas and Mesonephric-like Adenocarcinomas in the Gynecologic Tract: A Multi-institutional Study. *Am J Surg Pathol*. 2021;45(4):498-506.
- 4- Montalvo N, Redrobán L, Galarza D. Mesonephric adenocarcinoma of the cervix: a case report with a three-year follow-up, lung metastases, and next-generation sequencing analysis. *Diagn Pathol*. 2019;14(1):71.
- 5- Dierickx A, Goker M, Braems G, Tummers P, Van den Broecke R. Mesonephric adenocarcinoma of the cervix: case report and literature review. *Gynecol Oncol Rep*. 2016;17:7–11.