

Background

- Mesonephric adenocarcinoma (MA) and mesonephric-like adenocarcinomas (MLA) are a distinct category of tumours of the gynaecological tract recently included in the WHO 2020 classification
- They exhibit diverse morphological patterns, often within the same tumour, and can be easily mistaken for other neoplasms; as a consequence, they may be misdiagnosed and under-recognized
- They are considered high grade and may show distant recurrence, especially to the lung
- We describe the morphological, immunohistochemical and molecular characteristics of six cases (1 MA of cervix; 1 MLA of uterine corpus and four MLAs of ovary)

Methods

- The cases were derived from the archives of South of Tyne and Wear Pathology, Northern Gynaecological Oncology Centre, Queen Elizabeth Hospital, Gateshead, United Kingdom
- All slides and reports were reviewed; clinical information was obtained from specimen request forms

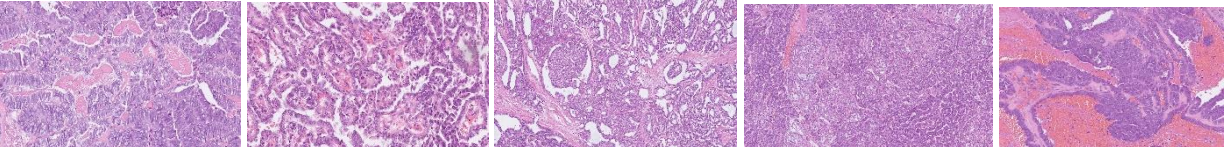
Results

- Mean patient age of 60y (range 38-78); 1 case of MA (cervix), 5 MLAs (4 ovary,1 uterus)
- All cases were characterised by marked architectural heterogeneity relative to the cytology (tubular, some with mucinous and eosinophilic colloid-like secretions, pseudoendometrioid, papillary, solid with spindled cells, trabecular, glomeruloid, tramtrack, angiomatoid; none showed mucinous differentiation)
- Nuclei showed marked overcrowding, were either hyperchromatic or vesicular but were relatively uniform in size despite the diverse architecture
- All cases showed strong diffuse positivity with PAX-8 and TTF-1, whilst being flat negative for hormone receptors (ER/PR) and wild type p53 staining pattern. GATA3 was variable and WT-1 was negative in all cases. We did not find calretinin or CD10 helpful
- Pathogenic KRAS variants were identified in all six cases
- Two of three MLA ovary showed metastatic disease (both have since died of disease) and one had recurrence

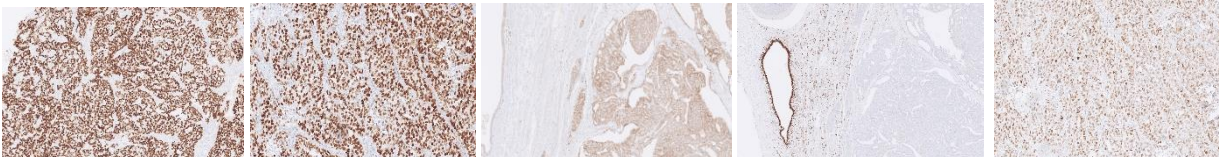
Summary of IHC and molecular findings

	Case 1 (Uterus)	Case 2 (Ovary)	Case 3 (Ovary)	Case 4 (Ovary- Recurrence)	Case 5 (Ovary)	Case 6 (Cervix)
CK7	+	+	+	+	+(patchy)	ND
CK20/CDX2	-	-	-	-	-	-
PAX8	+	+	++	+	+	+
GATA3	Focal	Focal	++	-	+	+
CD10 (luminal)	Patchy	Patchy	-	-	+	+
TTF-1	Diffuse++	Diffuse++	Focal ++	Diffuse++	+	+
ER/PR	Both -	Both -	Both -	Patchy weak +/-	Both -	Both -
WT-1	-	-	-	-	-	ND
p53	Wild	Wild	Wild	Wild	Wild	Wild
HNF1B/Nansin A	-	-	Patchy/-	-/+	ND	Patchy/-
KRAS variant assay	c.35G>T p.(Gly12Val)	c.35G> T p.(Gly12Val)	c.35G>C p.(Gly12Ala)	c.35G>C p.(Gly12Ala)	c.35G>A p.(Gly12Asp)	c.35G>T p.(Gly12Val)

Diverse architectural patterns



Pseudoendometrioid Papillary Glomeruloid Squamoid, tram-track Angiomatoid



TTF1 PAX8 GATA3 ER p53

Discussion and Conclusion

- Our case series has demonstrated that MLAs share morphological, immunohistochemical and molecular characteristics with MA of cervix
- MLAs are of probable Mullerian origin as three of four ovarian MLAs were associated with endometriosis
- Their architectural diversity and variable immunoprofile can cause diagnostic difficulties
- Immunopositivity with PAX8, TTF-1 and/or GATA3 with weak/flat negativity for ER/PR in a architecturally diverse gland-forming tumour should alert the pathologist to this rare diagnosis
- Despite their deceptively bland appearance, they are aggressive with a tendency towards earlier and distant recurrence and thus considered high grade neoplasms
- In theTCGA classification, most are ‘copy number low/no specific molecular profile
- HRD (Homologous Recombinant Deficiency) test performed on one ovarian MLA was found to be HR proficient with no evidence of tBRCA mutation

References

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