Metastatic adenocarcinoma in ascitic fluid

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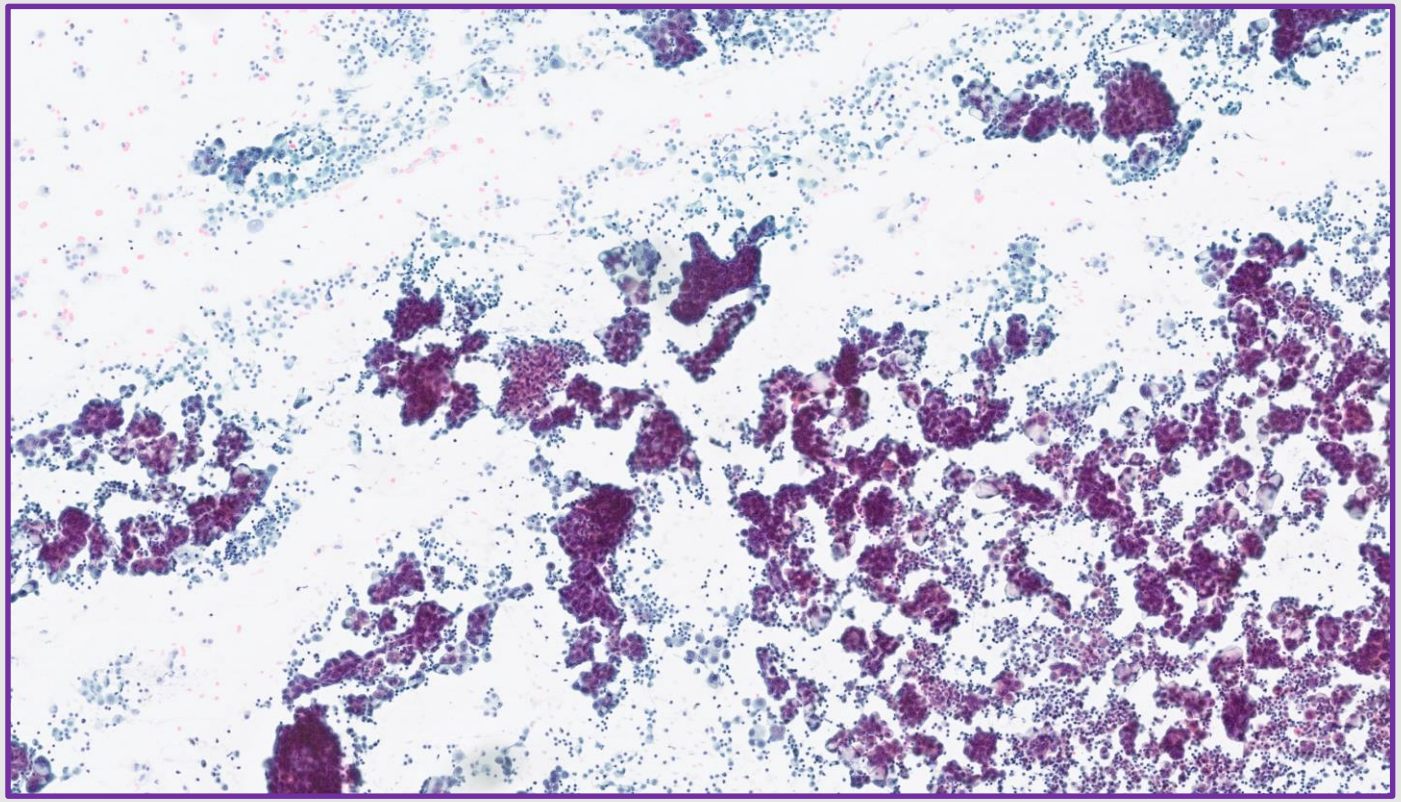
Clinical information

- Female, age 85.
- Presented with abdominal distension and loss of appetite.
- History of ischaemic heart disease, chronic kidney disease, type 2 diabetes.
- No previous history of malignancy.
- Ascitic fluid drained.

Ascitic fluid Cytology

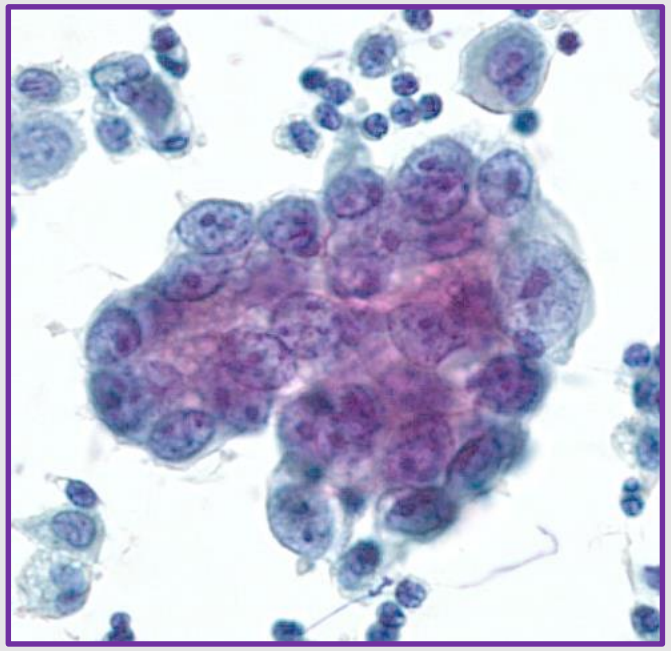
Cellular, 3D clusters and groups apparent even at low power.

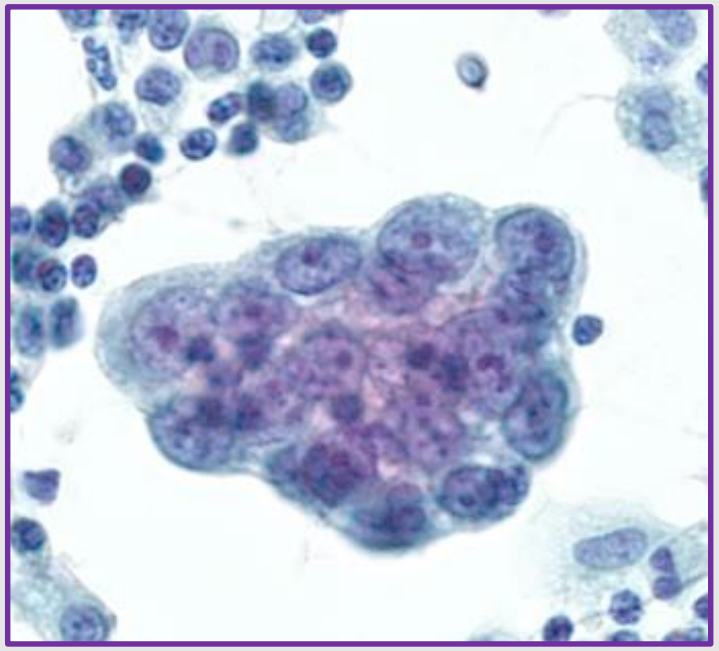


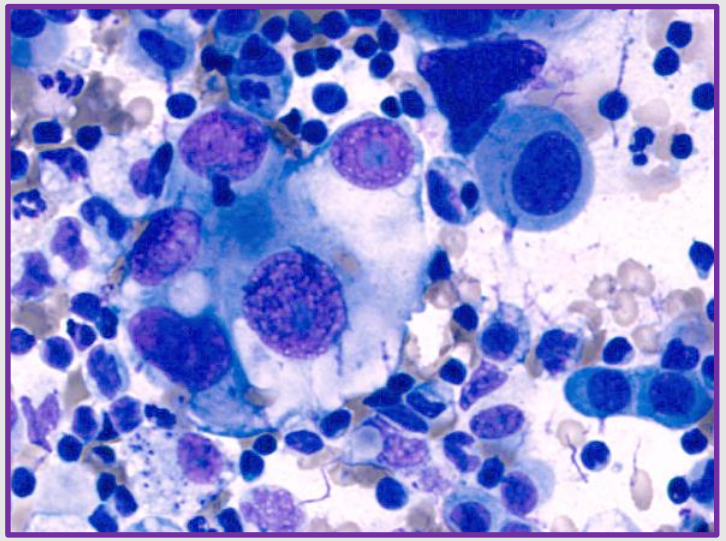
Ascitic fluid Cytology

Pleomorphic nuclei and raised nuclear cytoplasmic ratios.

Prominent nucleoli.



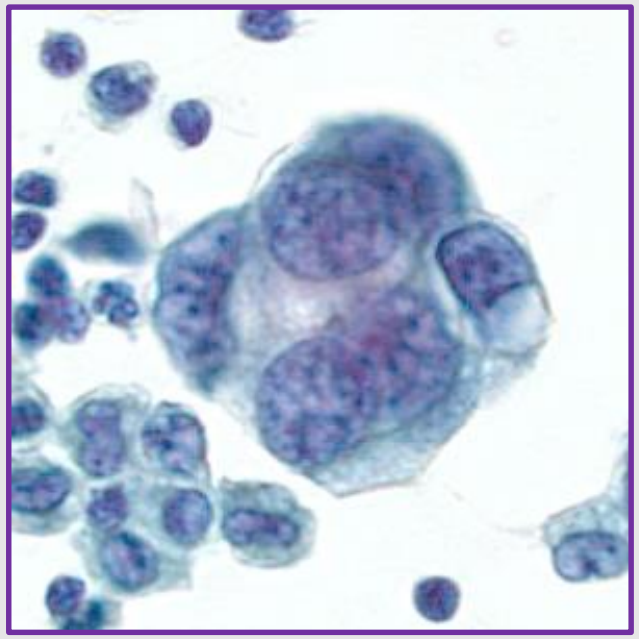


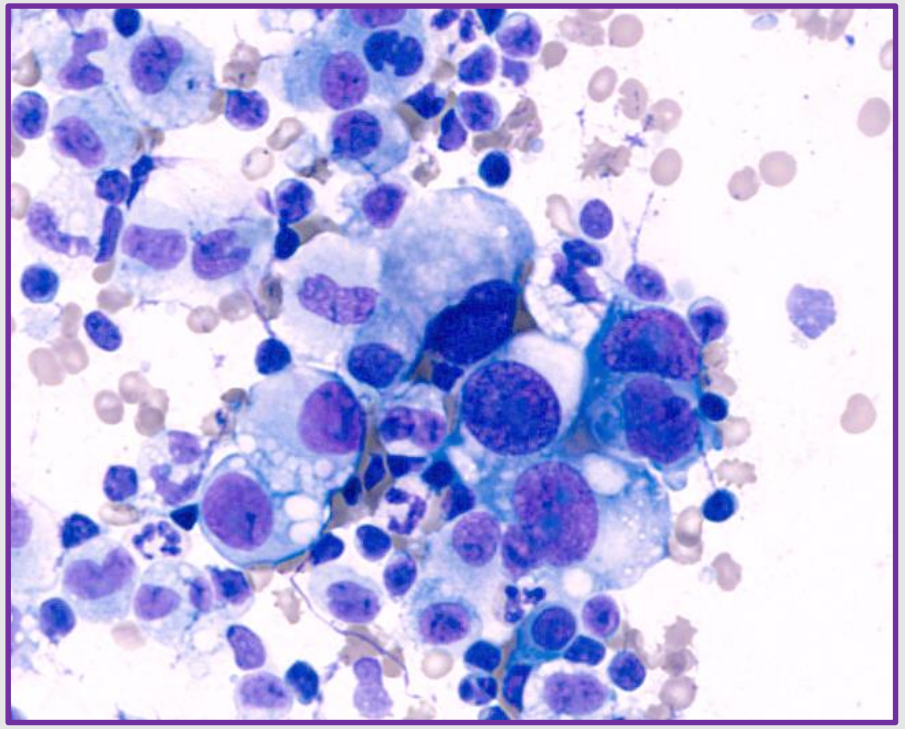


Ascitic fluid Cytology

Coarse chromatin and

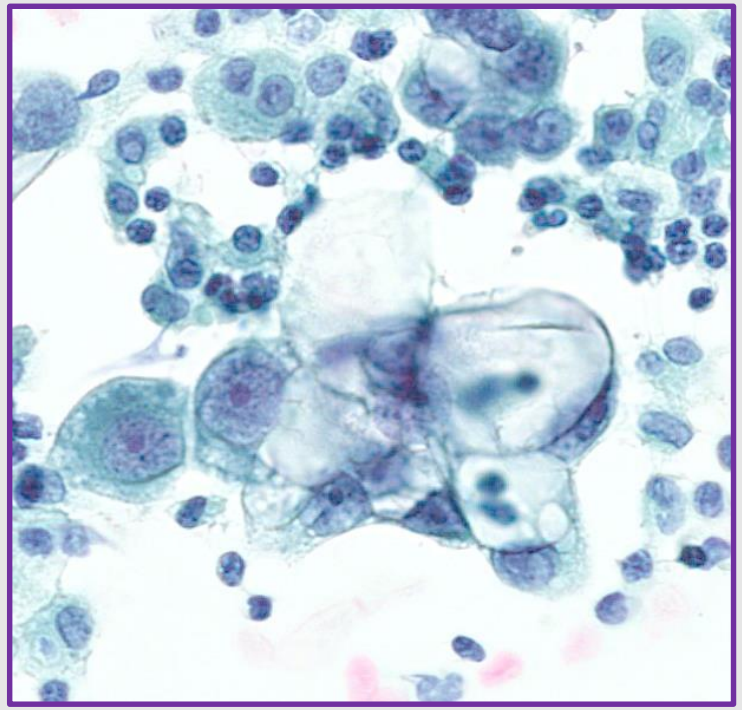
irregular nuclear membranes.

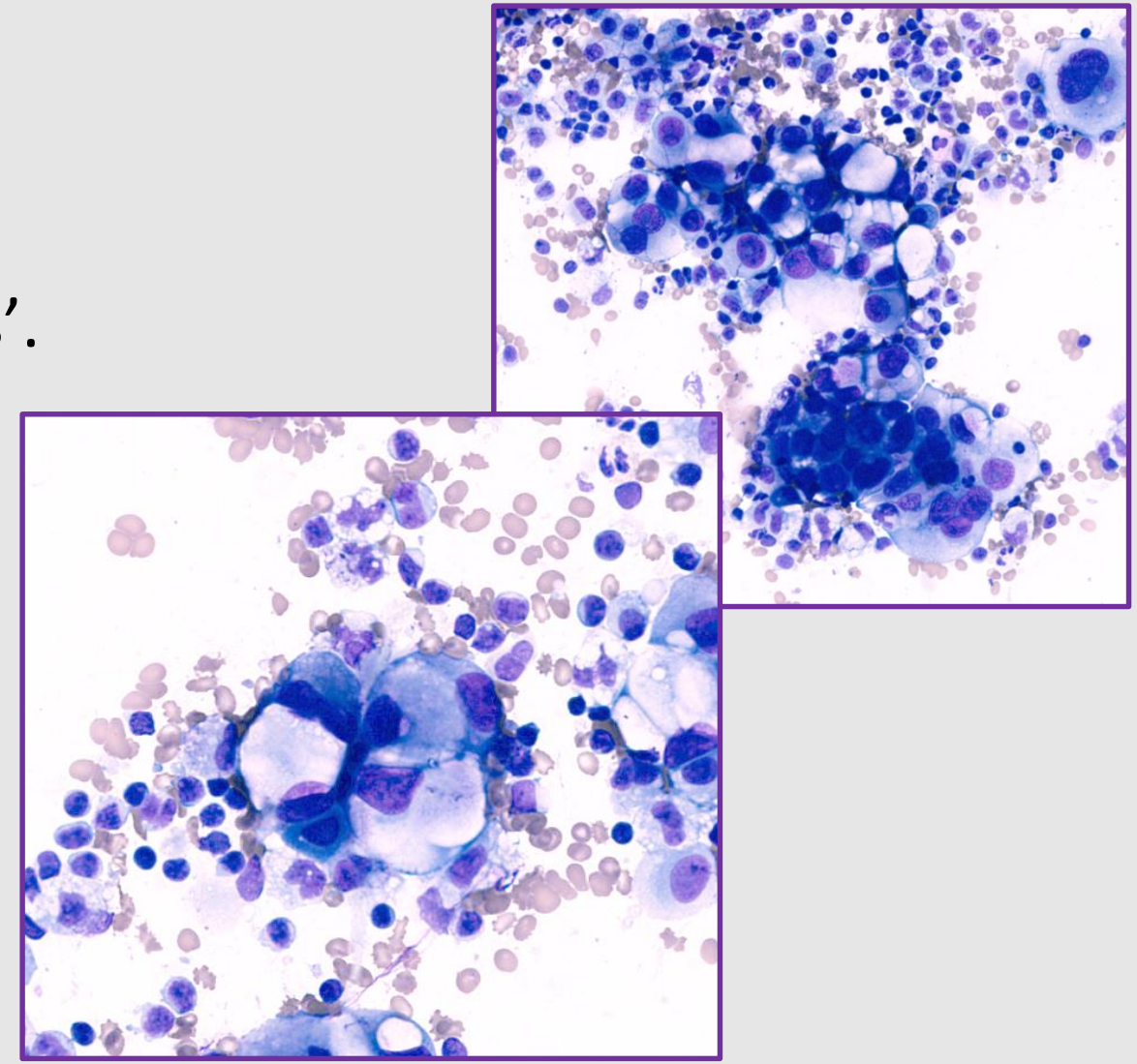




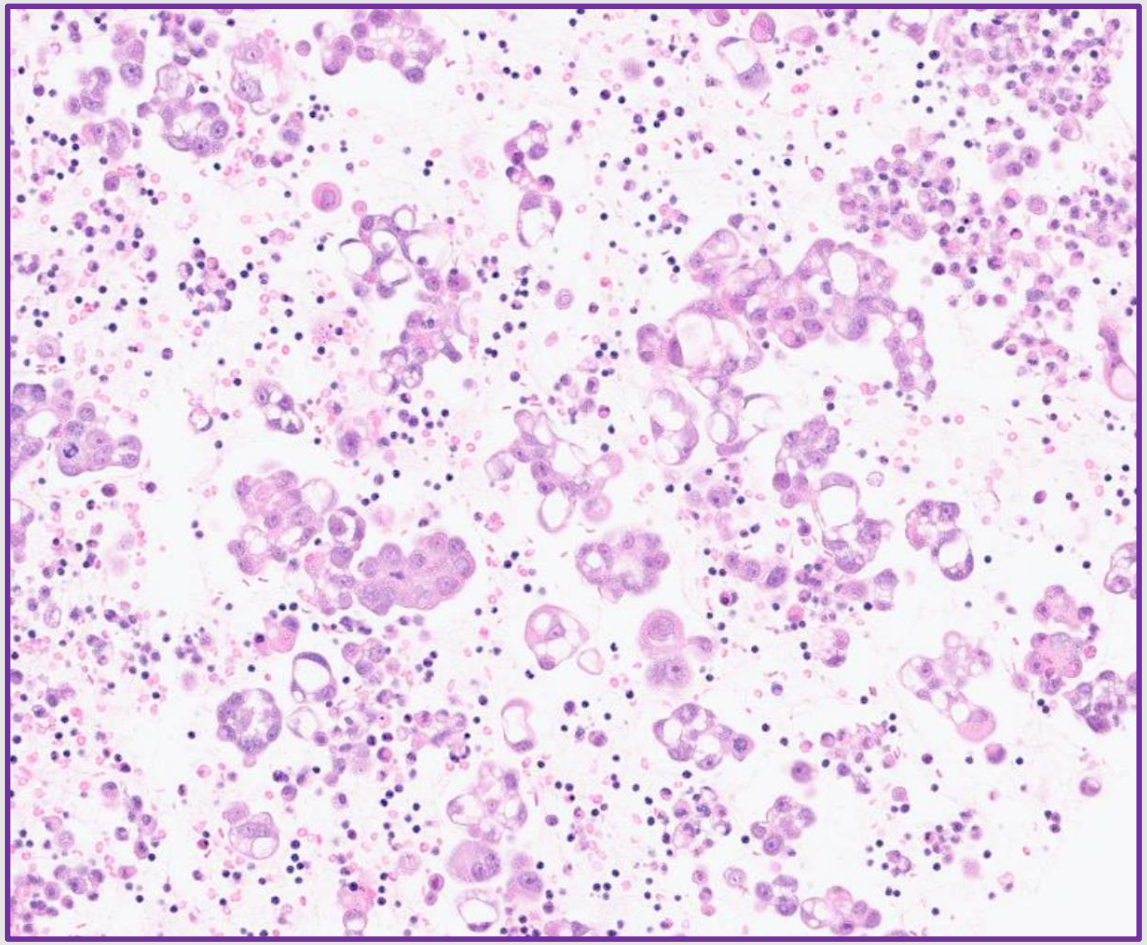
Ascitic fluid Cytology

Cytoplasmic vacuolation – single
or multiple. So called ‘soap bubbles’.





Ascitic fluid cell block



Cell block showing clusters of malignant glandular cells.

Sufficient cellularity for immunohistochemistry.

Immunohistochemistry

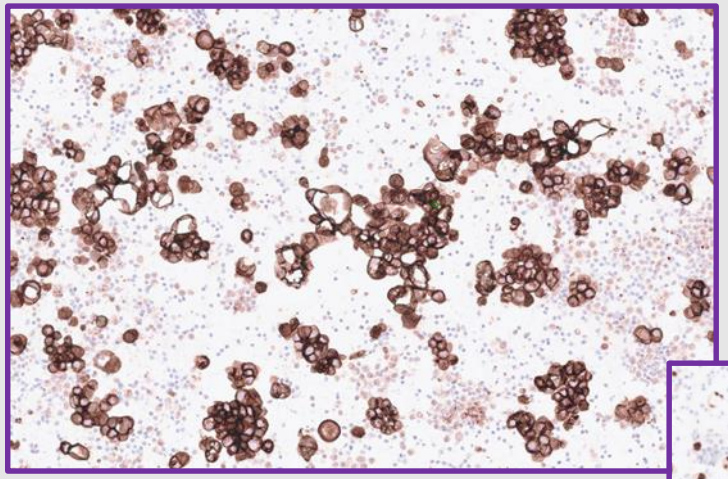
Common primary sites of malignancy in serous fluids[1]. Also utilise patient history, clinical and radiology to guide panel.

	Pleural	Peritoneal	Pericardial
Male	Lung Lymphoma Gastrointestinal tract Pancreas	Lymphoma Gastrointestinal tract Pancreas Genitourinary	Lung Lymphoma Gastrointestinal tract
Female	Breast Lung Ovary Lymphoma Gastrointestinal tract Pancreas	Ovary Uterus Breast Lymphoma Gastrointestinal tract	Breast Lung Lymphoma Gastrointestinal tract

First panel of IHC given the morphology

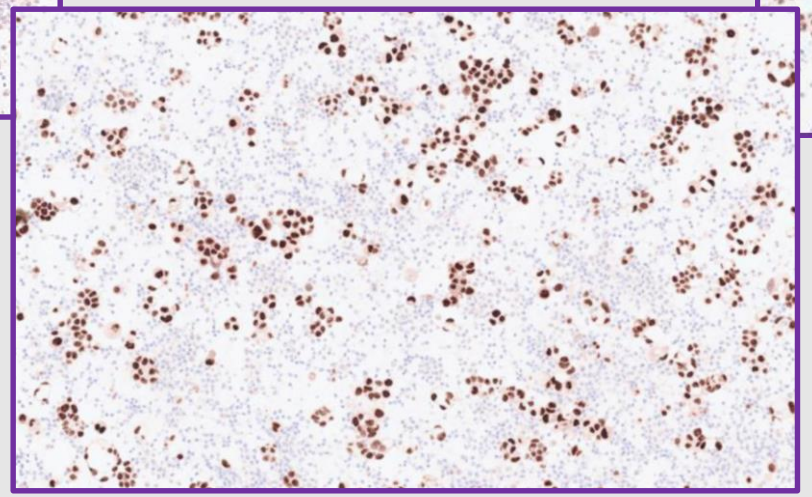
Immunocytochemistry

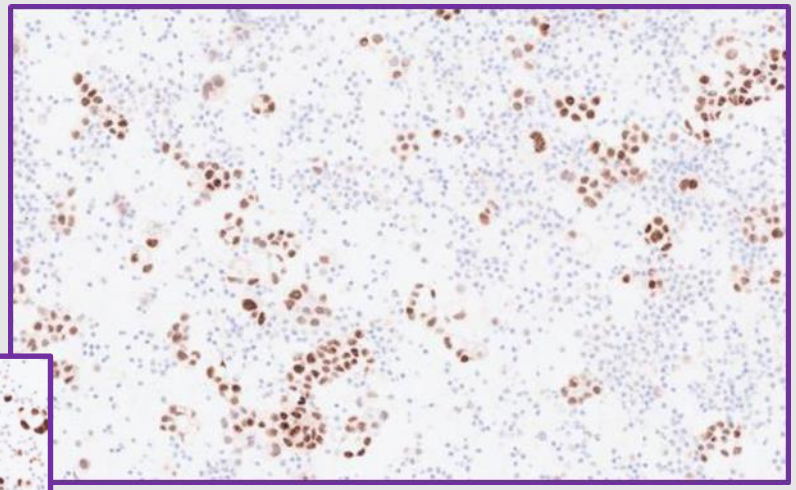
Positive for Claudin 4, CK7, Pax8, WT1 and ER.



Claudin 4 – epithelial marker

Pax8 – Nuclear staining – Female genital tract, thyroid and renal

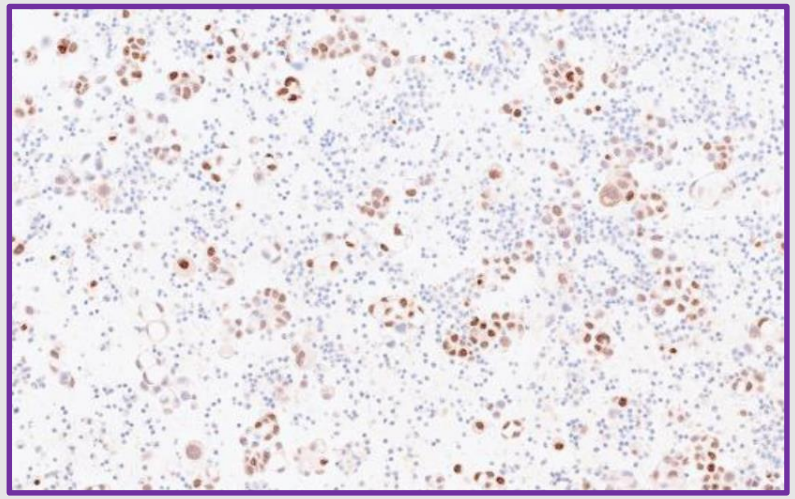




Oestrogen Receptor - nuclear staining

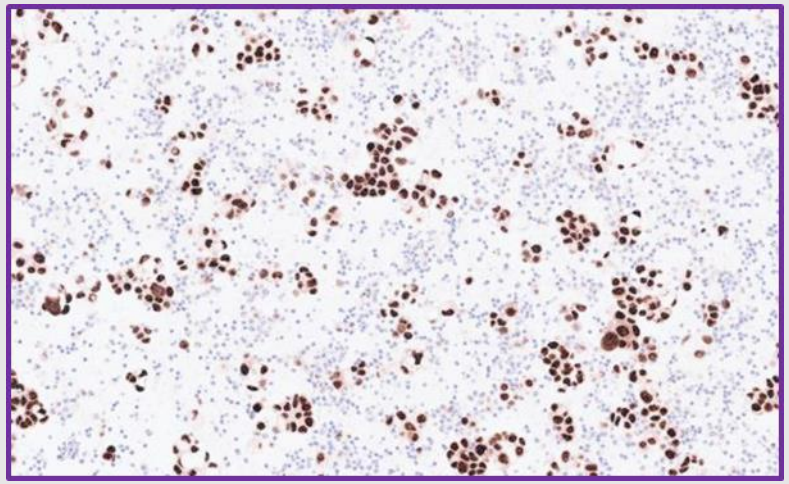
Immunocytochemistry

WT1 – Nuclear staining - Serous epithelium and mesothelium



Negative for CK20 & CEA (epithelial markers), TTF1 (lung adenocarcinoma), GATA3 (breast and bladder) and PR

P53 – Nuclear stain – mutation analysis. Mutational type staining



Given this IHC staining profile and the morphological characteristics the diagnosis is given as **metastatic tubo-ovarian high grade serous carcinoma**.

P53 staining patterns

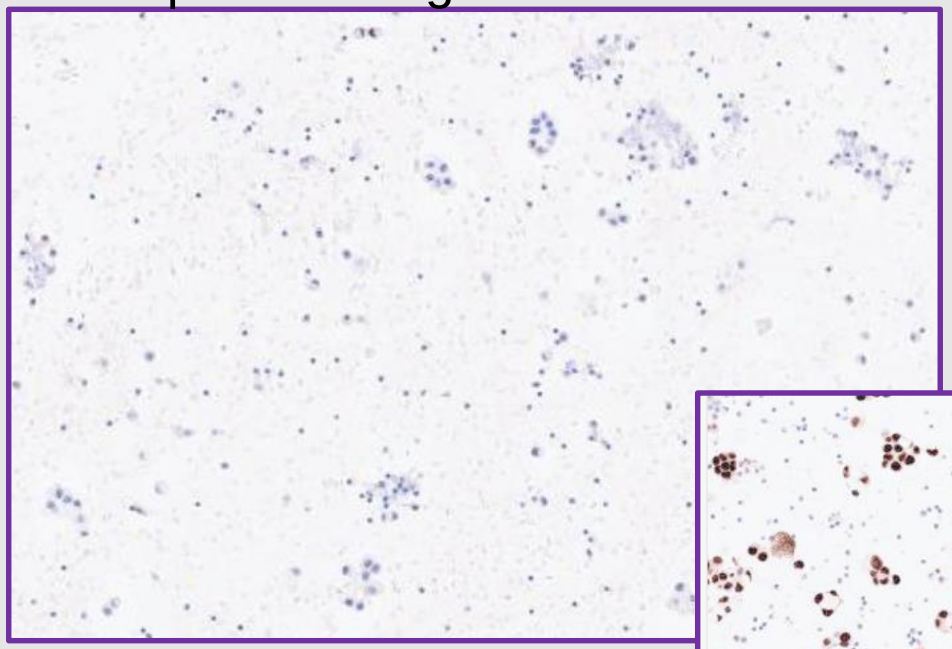
- p53 is a tumour suppressor gene. Mutations in the gene affect the regulation of the cell cycle causing uncontrolled cell division.
- Analysis of p53 staining to investigate p53 mutation status can provide information on the grade of tubo-ovarian carcinoma[2].
- High grade serous carcinomas ubiquitously harbour p53 mutations. 95% show abnormal p53 staining.
- Staining patterns are described as
  - Wild type (normal p53)
  - Overexpression (abnormal p53)
  - Null pattern (abnormal p53)
  - Cytoplasmic (abnormal p53)

P53 staining patterns

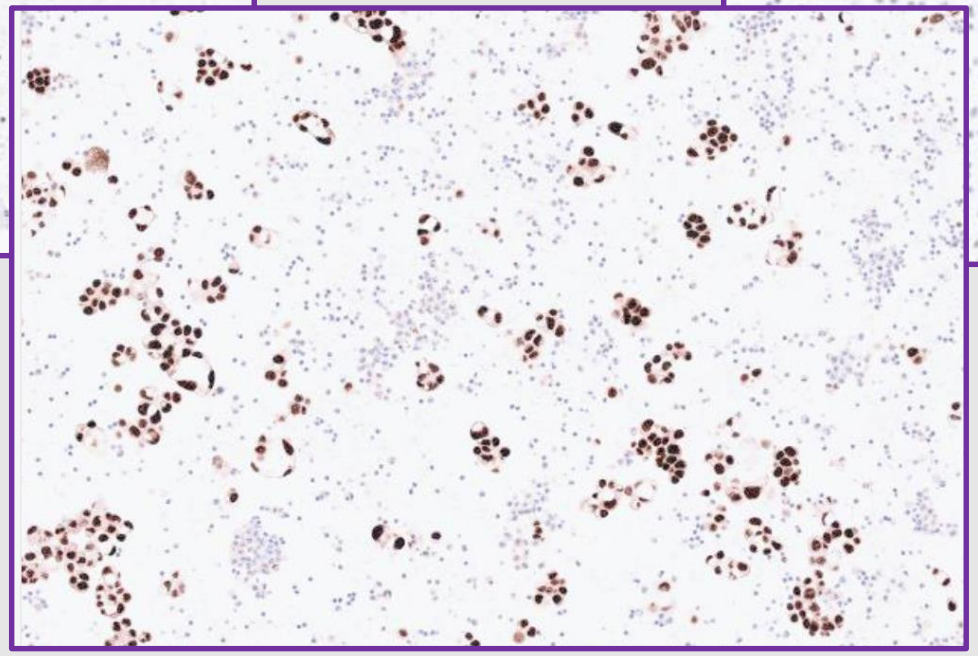
- Wild type staining (normal) – variable intensity of positive staining. Percentage of cells positive can range from a few to almost all cells.
- Overexpression (abnormal) – strong intensity staining in at least 80% of tumour cell nuclei.
- Null pattern (abnormal) – No staining in tumour nuclei. Background normal cells stain variably (wild type)
- Cytoplasmic staining (abnormal) – Cytoplasmic staining in the presence of weak (variable) or absent nuclear stain in more than 80% of tumour cell nuclei.
- Overexpression is most common mutational staining pattern, occurring in around two thirds of high grade serous carcinomas, followed by null pattern in one quarter of the same.

P53 staining patterns

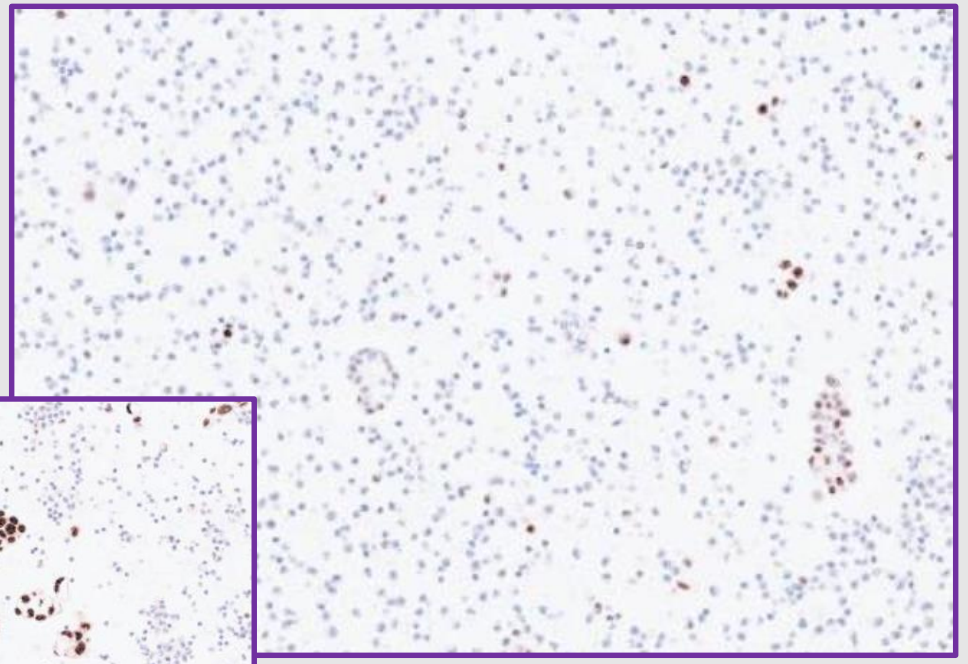
Null pattern mutational p53 staining



Overexpression mutational p53 staining



Wild pattern normal p53 staining



Summary

- Accounting for almost 75% of epithelial ovarian cancers, high grade serous carcinoma is aggressive and rapidly progressive.
- Studies now show many high grade serous carcinomas are derived from fallopian tube secretory epithelial cells[3].
- Mutations in p53 are an early event in transformation of secretory cells. They have been identified in precursor lesions (serous tubal intraepithelial carcinomas) and are necessary for high grade serous ovarian carcinoma development.

References

1. International Reporting System for Serous Fluid Reporting
2. Interpretation of p53 Immunohistochemistry in Tubo-Ovarian Carcinoma. Kobel,M British Association of Gynaecological Pathologists. Version 1.0 October 2016
3. Pathogenesis and heterogeneity of ovarian cancer. Kroeger PT Jr, Drapkin R. Current Opinion in Obstectrics and Gynaecology 2017 29(1):26-34