Ovarian tumors – Ancillary methods

Ovarian tumor course – Oslo, 24-25/11/14

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Ancillary methods in ovarian pathology

- Genetic/genomic approaches – not in routine use
- Ploidy – limited applications, not widely accepted
- HPV analysis – for suspected cervical ca. metastasis
- Immunohistochemistry

- Morphology is the basis for correct diagnosis
Ploidy

- Flow cytometry vs. image analysis
- Suggests higher risk, not diagnostic
- Current indications at NRH:

Sex cord/stromal tumors (Granulosa, Sertoli-Leydig)
Borderline tumors (all types)
Stage I ovarian carcinoma
Ploidy

Diploid

Aneuploid
Main differentials

- Epithelial tumor (mainly adenocarcinoma) histotype
- Primary vs. metastatic adenocarcinoma
- Adenocarcinoma vs. germ cell tumor vs. sex cord stromal tumor
- Rare entities
Main differentials

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Differentiating ovarian AC of various histology

- **ER**: positive in the majority of SC + EC, negative in MC and CCC
- **WT1**: positive in the majority of SC, negative in EC, MC and CCC
- **p53**: aberrant expression in the majority of HGSC and TCC and in some EC, variable in CCC, negative in LGSC and MC
- **p16**: diffuse expression in SC and TCC, patchy in EC, variable in CCC
- **mCEA**: positive in MC, may focally stain EC, negative in SC and CCC
- **CDX2**: positive in MC, may focally stain EC, negative in SC and CCC
Differentiating ovarian AC of various histology

- **HNF1\(\beta\):** positive in CCC, may stain some EC, negative in SC and MC
- **Napsin A:** positive in CCC, negative in EC, SC and MC
- **ARID1A:** lost in CCC and in EC, positive in SC and MC
- **PTEN:** lost in EC, positive in CCC, SC and MC
- **GATA3, S100P and p63:** Brenner tumor markers (also Uroplakin III and Thrombomodulin?)
- **Chromogranin A:** positive in neuroendocrine adenoca. and small cell ca.
- **Synaptophysin:** positive in neuroendocrine adenoca. and small cell ca.
HGSC + undifferentiated carcinoma
Retroperitoneal metastasis – origin?

mCEA  CK8  Ber-EP4

PAX8  WT1
CCC vs. HGSC

WT1

HNF1β

WT1

HNF1β
CCC lung met.
Brenner borderline tumor
Brenner borderline tumor

- WT1
- PAX8
- CK7
- CK20
Neuroendocrine carcinoma
Neuroendocrine carcinoma

- CK7
- Villin
- Chromogranin A
- Synaptophysin
Main differentials

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Case 1

• A 41-year old female, medical history unknown
• Right-sided ovarian mass (30 cm, 4.5 kg)
• Pre-operative right-sided pleural effusion: Reactive
• Operated October 2010
Histology - ovary
Histology - ovary
Histology - ovary
IHC

CK7

CK20

ER

CDX2

CEA

Villin
Other findings

- Metastasis in right pericolic area
- No tumor in left ovary, fallopian tubes, uterus, appendix, 19 intestinal and 22 abdominal lymph nodes
Case 2

- A 70-year old female
- Right-sided colectomy 2010
- Tumor in left ovary (3.5 cm)
- Operated June 2011
Histology - ovary
Histology - colon
IHC

CDX2

CK20

CEA

CK7
Case 3

- A 63-year old female
- Sarcoma in corpus uteri in curettage, leiomyosa. and rhabdomyosa. (cacinosa.?)
- Enlarged right ovary (4.5 cm)
Histology - uterus
Histology - ovary
Histology- ovary
IHC

CK7

CK20

ER

CDX2

CEA
Breast carcinoma metastasis

- GCDFP-15
- Mammaglobin
- Her2 SISH
- WT1
- PAX8
Main differentials

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Most useful markers

• EMA (carcinoma)
• Inhibin (sex cord stromal tumors)
• Calretinin (sex cord stromal tumors)
• FOXL2 (sex cord stromal tumors)
• SF-1 (sex cord stromal tumors)
• Melan A (Sertoli-Leydig cell tumors)
• SALL4 (germ cell tumors)
• D2-40 (dysgerminoma)
• c-Kit/CD117 (dysgerminoma)
• OCT3/4 (dysgerminoma)
• AFP (yolk sac tumor)
• HCG (choriocarcinoma)
Granulosa cell tumor

Calretinin

Inhibin
Immature teratoma

SOX2

SOX2
Dysgerminoma

c-Kit

Oslo universitetssykehus
Mixed germ cell tumor

- AFP
- PLAP
- HCG
Mixed germ cell tumor

OCT3/4

D2-40
Mixed germ cell tumor

Glypican-3

Glypican-3
Main differentials

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Entities

- Mesenchymal tumors (sarcomas and other)
- Hematological cancers
- Melanoma
- Mesothelioma
- Unclassifiable malignant tumors
Spindle cell tumor panel

- Actin
- Desmin
- SMA
- S100
- EMA
- Pan-cytokeratin
- CD31
- CD34
- CD68
- CD99
DLBCL

CD20

CD10

Bcl-2
DLBCL
Mesothelioma

- D2-40
- CK7
- WT1
- Calretinin
Ovarian tumor
Omentum
Immunohistochemistry- referring lab

- Cytokeratin (AE1/AE3): negative
- CK8: negative
- NSE: positive
- Calretinin: negative
- Chromogranin: negative
- Synaptophysin: negative

OVARY WITH EPITHELIAL TUMOR WITH NEUROENDOCRINE DIFFERENTIATION, M/P PRIMARY OMENTAL METASTASIS
New IHC

AE1/AE3

Vimentin

Synaptophysin

HMB-45

Melan A
Final diagnosis

OVARY AND OMENTUM WITH MALIGNANT MELANOMA, PROBABLY METASTASES
Non-classifiable
Non-classifiable

Vimentin

AE1/AE3

PGR

ER
Summary

- Morphology is basis
- IHC is the main adjunct
- Large panels are not a good starting point
- Primary and metastatic tumors should be considered
- Not all cases can be decisively classified
Thank you for your attention