Gynecologic Pathology Evening Session
USCAP 2016
Case # 4

Anaís Malpica, M.D.
Professor of Pathology
Clinical History

- A 22 year-old female presented with a one-month history of pelvic pain

- Imaging studies showed a 9.0 cm left ovarian tumor
Clinical History

• The patient underwent
  – left salpingo-oophorectomy
  – removal of a lesion from the right ovary
  – omentectomy
  – left pelvic node sampling
  – multiple peritoneal biopsies

• The left ovary was received in fragments, measuring in aggregate 10 cm
Cystic spaces lined by gastrointestinal-type mucinous epithelium with nuclear stratification
Adjacent solid component with pleomorphic epithelioid and spindle cells
Left ovarian surface with a proliferation of mesothelial cells
Right ovary with serous adenofibroma and a marked proliferation of mesothelial cells
Omentum
1. Anaplastic carcinoma arising in a background of mucinous borderline tumor
2. Mesothelioma associated with a mucinous borderline tumor
Calretinin
Final Diagnosis

- Mesothelioma associated with a mucinous borderline tumor
What You Need Know

• Incidence:
  – Mesothelioma of the peritoneum is a rare disease
    • It accounts for 10%-15% of the 2,500 cases of mesothelioma dx each year in the United States
  – SEER data base
    • 44% of the cases of peritoneal mesothelioma are seen in women
Clinical Features

- **Age:**
  - Wide age range, 2 years to 92 years
    - Median age, 49 years (MDACC, 2014)
    - Mean age, 47.4 years (Baker P, et al, 2005)

- **Clinical Presentation**
  - Common:
    - Abdominal/pelvic pain or discomfort
    - Abdominal or pelvic mass
    - Abdominal distension
Clinical Presentation

– Less common:
  • Nausea
  • Anorexia
  • Weight loss
  • Changes in bowel habits
  • Bowel obstruction

– Uncommon:
  • Fever
  • Lymphadenopathy
  • Back/neck pain
Confounding Clinical Features

• Young age
• Incidental finding
• Elevated CA125
• Vaginal bleeding
  – Endometrial sampling with fragments of mesothelioma
Pathogenesis

- Asbestos exposure
  - However, peritoneal mesothelioma in women often occurs in the absence of asbestos exposure
- Erionite exposure
- Radiotherapy exposure
- Use of Thorotrast
- SV40
  - Causal relationship has been questioned
Pathogenesis

• BAP1 hereditary cancer predisposition syndrome
  – Inherited in an autosomal dominant pattern
  – Germline mutations of BAP1 confer increased susceptibility for the development of several tumors
    • Uveal melanoma
    • Epithelioid atypical Spitz tumors
    • Cutaneous melanoma
    • Mesothelioma
    • Other tumors
Pathogenesis

- BAP 1 somatic mutations can be seen in:
  - Uveal melanoma
  - Cutaneous melanocytic tumors
  - Mesothelioma
  - Clear cell renal cell carcinoma
  - Other tumors
Gross Features

Plaques

Nodules
Confounding Gross Features

- Adhesions
- Gelatinous nodules
- Mucinous ascites
Histologic Features
Variable Degree of Cytologic Atypia

Mild
Moderate
Severe
Variable mitotic index, usually low
Solid pattern

Trabecular pattern and clusters of cells
Cystic pattern
Deciduoid

Rhabdoid cells
Abundant Foamy Histiocytes
Malignant mesothelioma, biphasic type
Mesothelioma, spindle cells in solid, fascicular or storiform pattern

Mesothelioma, spindle cells in collagenous background (desmoplastic appearance)
Do we always need to see invasion?

9 cm cul de sac mass
Papillary tumor with the appearance of WDPM extensively involving the peritoneum
Focal invasion
Immunohistochemical Features

• The use of a panel is recommended
  • 2 positive markers for mesothelioma
    • Calretinin
    • Keratin 5/6
    • D2-40/Podoplanin
  • 2 negative markers for mesothelioma
    • PAX-8
    • Estrogen receptor
    • Ber-EP4
    • MOC-31 (or B72.3, this can be only focally positive)
Value of PAX8, PAX2, claudin-4, and h-caldesmon immunostaining in distinguishing peritoneal epithelioid mesotheliomas from serous carcinomas

Nelson G Ordóñez

Department of Pathology, University of Texas MD Anderson Cancer Center, Houston, TX, USA

MODERN PATHOLOGY (2013) 26, 553-562

PAX-8 and Claudin-4 appear to be the best positive markers for carcinoma

PAX8, Serous Ca

Claudin 4, Serous Ca
Malignant Mesothelioma
Confounding Immunohistochemical Features

Calretinin +
ER +
IHC in unsuspected mesothelioma
Electron Microscopy

Dilated intercellular spaces

Long, slender, undulating microvilli
Differential Diagnosis - Mesothelial Hyperplasia

- Gross description is important
- No evidence of invasion into the adipose, fibroconnective or fibromuscular tissue
Mesothelial Hyperplasia

• IHC
  – Mesothelial hyperplasia cells: desmin (+, 85%), and EMA (-, 80%), p53 (-, 100%), GLUT -1 (-, 87-97%), and IMP3 (-, 73-100%)
  – Malignant mesothelioma: desmin (-, 90%) and EMA (+, 80%), GLUT-1 (+, 60-67%), p53 (+, 45%), IMP3 (+, 53-73%)
  – However, exceptions to the these results occur, limiting the value of the studies
  – BAP-1 (IHC) and p16 (FISH)
    • Loss of either marker is in keeping with mesothelioma
Well Differentiated Papillary Mesothelioma

1. There is no infiltration of underlying tissue
2. No complexity of the papillary growth
3. Size and extent

Bland mesothelial cells with no mitosis or up to 1 mitosis per 10 HPFs
Multilocular Peritoneal Inclusion Cysts

- Thorough sampling is required to rule out invasion or the presence of different morphologic areas.
High Grade and Low Grade Serous Carcinoma
Clear Cell Carcinoma  
Metastatic Adenocarcinoma
Ectopic Decidua
Histiocytic reaction/aggregates

KP-1 (CD68) (+)
Differential Diagnosis

• Carcinosarcoma
• Sex cord stromal tumor (adult granulosa cell tumor or Sertoli-Leydig cell tumor)
• Other spindle cell lesions:
  – Leiomyomatosis peritonealis
  – Solitary fibrous tumor
  – Synovial sarcoma
Treatment

• Cytoreductive surgery is required to remove all gross peritoneal disease
• Residual microscopic disease is treated with hyperthermic intraperitoneal chemotherapy (HIPEC)
  – Adjuvant systemic chemotherapy can be added
Prognosis

- Malignant mesothelioma of the female peritoneum has a variable course
- Localized forms tend to behave in an indolent fashion
- Sarcomatoid mesothelioma is usually aggressive
Prognosis

• Features associated with a favorable outcome:
  – Younger age, <60 years
  – Complete or near complete resection
  – Low histologic grade

• Features associated with an aggressive behavior:
  – High nuclear grade
  – High mitotic index
  – Loss of p16
West Texas, between Marfa and Fort Davis
The more opinions you have, the less you see.

Wim Wenders