Appendiceal neoplasia and pseudomyxoma peritonei

Norman Carr
RCPath Update 2017
Appendiceal mucinous neoplasms are unusual

- ... but all of us see them from time to time
- Other conditions can mimic them, e.g. ruptured diverticula
- Correct diagnosis is important
  - prolonged follow-up
  - pseudomyxoma peritonei is now treated radically
- Contentious terminology addressed by recently published international consensus
A Consensus for Classification and Pathologic Reporting of Pseudomyxoma Peritonei and Associated Appendiceal Neoplasia

The Results of the Peritoneal Surface Oncology Group International (PSOGI) Modified Delphi Process

Norman J. Carr, FRCPath,* † ‡ Thomas D. Cecil, MD,* † Faheez Mohamed, MD,* † Leslie H. Sobin, MD,§ Paul H. Sugarbaker, MD,‖ Santiago González-Moreno, MD, PhD,¶ Panos Taflampas, MD,* † Sara Chapman, PhD,‡ and Brendan J. Moran, MD* †

Abstract: Pseudomyxoma peritonei (PMP) is a complex disease with unique biological behavior that usually arises from appendiceal mucinous neoplasia. The classification of PMP and its primary appendiceal neoplasia is contentious, and an international modified Delphi consensus process was instigated to address terminology and definitions. A classification of mucinous appendiceal neoplasia was developed, and it was agreed that

Scope of presentation

- Pseudomyxoma peritonei
- Appendiceal mucinous neoplasia
What is pseudomyxoma peritonei?

• A syndrome of mucinous tumour within the abdomen
  – tends not to invade/metastasise
  – grows relentlessly
  – death is usually by intestinal obstruction
Pseudomyxoma peritonei is characterised by the redistribution phenomenon

- Omentum
- Paracolic gutters
- Pouch of Douglas
- Falciform ligament
- Subphrenic spaces

stomata
Most PMP arises from an appendiceal mucinous neoplasm

- Other primary sites include:
  - colon
  - urachus
  - IPMN
The ovary and pseudomyxoma

Primary ovarian mucinous neoplasms rarely produce pseudomyxoma:

- cystadenomas -> acellular mucin
- mucinous adenocarcinomas -> conventional cancer

Exception: low grade mucinous neoplasia arising in a teratoma
A case of pseudomyxoma thought to be an ovarian primary...
Useful features in practice when there are enteric features

**Favouring appendix or colorectum:**
- Scalloping and retraction
- Infiltrative invasion
- Vascular invasion
- Dissecting mucin (pseudomyxoma ovari)
- Signet ring cells
- SATB2+

**Favouring ovary:**
- Back-to-back neoplastic glands with no intervening stroma
- Associated primary teratoma
- CK7+ CK20- CDX2-

Li Z et al 2017
Stewart CJ et al 2014
Pseudomyxoma peritonei: classification

1. Low grade mucinous carcinoma peritonei (disseminated peritoneal adenomucinosis – DPAM)

2. High grade mucinous carcinoma peritonei (peritoneal mucinous carcinomatosis – PMCA)

3. High grade mucinous carcinoma peritonei with signet ring cells (PMCA-S)

Acellular intra-abdominal mucin

- Can be a feature of PMP, but other causes exist (e.g. ruptured cystadenoma of ovary)
- In TNM8 for the appendix, acellular mucin within the abdominal cavity is classified pM1a
Cytoreductive surgery with heated intraperitoneal chemotherapy (HIPEC)
Surgical specimens
Survival of 2,298 patients with appendiceal PMP treated with cytoreductive surgery and HIPEC

C.f. Mayo results of <25% overall survival at 17 years

(Gough DB et al 1994)

Chua TC et al 2012
Appendiceal mucinous neoplasms
Low grade appendiceal mucinous neoplasm (LAMN)

Mucinous neoplasm with low grade cytological atypia and any of:

- loss of muscularis mucosae
- fibrosis of submucosa
- ‘pushing invasion’ (expansile or diverticulum-like growth)
- dissection of acellular mucin in wall
- undulating or flattened epithelial growth
- rupture of appendix
- mucin and/or cells outside appendix
LAMN: Pushing invasion
LAMN: Patterns of growth
LAMN: denuded epithelium

Sample adequately – submitting entire appendix is recommended
<table>
<thead>
<tr>
<th>Description</th>
<th>Stage</th>
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<tbody>
<tr>
<td>LAMN confined to appendix (acellular mucin or mucinous epithelium may extend into muscularis propria)</td>
<td><strong>Tis (LAMN)</strong></td>
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<tr>
<td>Tumour invades subserosa or mesoappendix</td>
<td><strong>T3</strong></td>
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<tr>
<td>Tumour perforates visceral peritoneum, including cells and/or mucin on the serosa</td>
<td><strong>T4a</strong></td>
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High grade appendiceal mucinous neoplasm (HAMN)

• No infiltrative invasion, but high grade cytology
Why distinguish HAMN from LAMN?

(1) In a series of 49 cases, subsequent PMP was more likely with high grade dysplasia (36%) than low-grade dysplasia (6%)

(2) patients with “noninvasive mucinous adenocarcinoma” (corresponding to HAMN) had decreased survival compared to LAMN (p<0.01)

1. Yantiss RK et al 2009
Mucinous appendiceal adenocarcinoma

- Infiltrative invasion
  - Well differentiated
  - Moderately differentiated
  - Poorly differentiated
  - Poorly differentiated with signet ring cells
Features of infiltrative invasion

• Desmoplastic stroma
• Tumor budding (discohesive single cells or clusters of up to 5 cells)
• Small, irregular/angulated glands
Fibrosis beneath LAMN
Serrated polyp

- Resemble colorectal sessile serrated lesion
- Muscularis intact
- Different genetics from colon (KRAS and GNAS, not BRAF or DNA MMR defects)
- With or without dysplasia
Tubular, tubulovillous or villous adenoma

- Rare
- Resemble typical colorectal type
Ruptured diverticulum
Favouring a diverticulum

1. Atrophy and crypt disarray, but preservation of essential mucosal architecture

2. Hyperplastic changes confined to the luminal portion of the mucosa

Hsu M et al 2009
Favouring a diverticulum

3. Neuromatous mucosal proliferation

- S100 positive and EMA negative
  - related to axial neuromas
  - not perineuriomas
References

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