Peritoneal Malignancy Institute Basingstoke

Located at: Basingstoke and North Hampshire Hospital
Part of: Hampshire Hospital NHS Foundation Trust

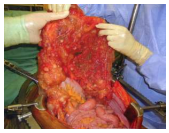
Appendiceal neoplasia and pseudomyxoma peritonei

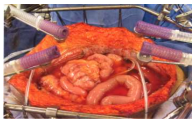
Norman Carr

Harrogate 2019

Correct diagnosis is important

- Patients may have prolonged follow-up
- PMP may be treated with cytoreductive surgery and heated intraperitoneal chemotherapy (HIPEC)





Classification has been confusing and inconsistent

- Recent 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

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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 mutinosis, respectively. A checklist for the pathologic reporting of PMP and appendiceal mucinous neoplasms was also developed. By adopting the classifications and definitions that were agreed, different centers will be able to use uniform terminology that will allow meaningful comparison of their results.

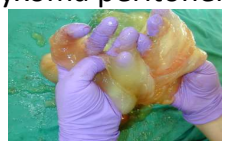
Key Words: appendiceal neoplasms, pseudomyxoma peritonei, appendix, peritoneum, Delphi technique

Content

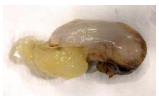
- Pseudomyxoma peritonei
- Mucinous appendiceal neoplasms
- Goblet cell carcinoid

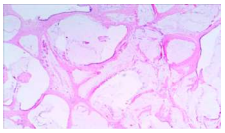
What is pseudomyxoma peritonei?

- A syndrome of mucinous tumour within the abdomen
  - tends not to invade/metastasise
  - grows slowly but relentlessly
  - death is usually by intestinal obstruction



Most PMP arises from an appendiceal mucinous neoplasm



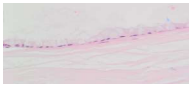


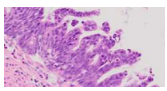
Other primary sites:

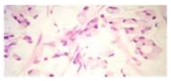
- ovarian teratoma
- colon
- urachus
- IPMN
- cervix
- renal pelvis

Pseudomyxoma peritonei: classification

1. Acellular mucin
2. Low grade mucinous carcinoma peritonei
3. High grade mucinous carcinoma peritonei
4. High grade mucinous carcinoma peritonei with signet ring cells



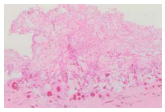




Davison JM et al 2014, Shetty S et al 2013, Sirintrapun SJ et al 2014

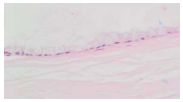
Acellular intra-abdominal mucin

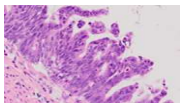
- Can be a feature of PMP
  - in TNM8 for the appendix, acellular mucin within the abdominal cavity is classified pM1a
  - better prognosis
- But other causes exist (e.g. ruptured cystadenoma of ovary)



Pseudomyxoma peritonei

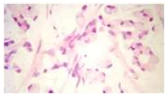
- Low grade mucinous carcinoma peritonei (disseminated peritoneal adenomucinosis – DPAM)
- High grade mucinous carcinoma peritonei (peritoneal mucinous carcinomatosis – PMCA)

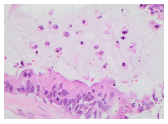




Pseudomyxoma peritonei

- High grade mucinous carcinoma peritonei with signet ring cells (PMCA-S)
  - worse prognosis
- 10% threshold
- Differential is degenerating cells





Davison JM et al 2014

Appendiceal mucinous neoplasms

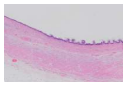
- Low grade appendiceal mucinous neoplasm (LAMN)
- High grade appendiceal mucinous neoplasm (HAMN)
- Mucinous adenocarcinoma

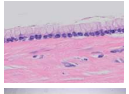
"Mucocoele = macroscopic description only
"Cystadenoma" should not be used

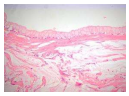
Low grade appendiceal mucinous neoplasm (LAMN)

Mucinous neoplasm with low grade cytological atypia and any of:

- loss of muscularis mucosae
- fibrosis of submucosa
- dissection of acellular mucin in wall
- 'pushing invasion' (expansile or diverticulum-like growth)
- undulating or flattened epithelial growth

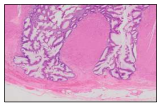
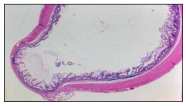
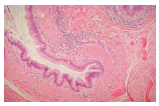




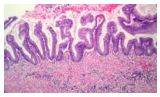
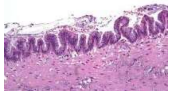
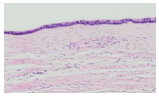


Carr et al 2017

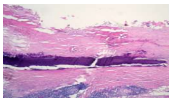
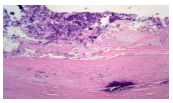
LAMN: Pushing invasion

Patterns of growth

LAMN: denuded epithelium

Sample adequately – recommended to all process

Risk of pseudomyxoma peritonei

- Confined to wall
  - risk of PMP is about 3%
- Acellular mucin outside appendix
- Neoplastic cells outside appendix
  - risk of PMP is about 40%

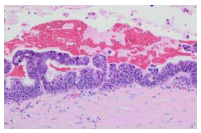
Appendiceal adenocarcinomas in TNM8

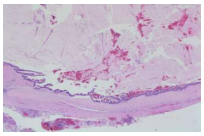
LAMN	
LAMN confined to appendix (acellular mucin or mucinous epithelium may extend into muscularis propria)	**Tis (LAMN)**
Tumour invades subserosa or mesoappendix *	**T3**
Tumour perforates visceral peritoneum, including cells and/or mucin on the serosa	**T4a**
Distant mets	
Intraperitoneal acellular mucin only	**M1a**
Intraperitoneal metastasis only, including mucinous epithelium **	**M1b**
Non-peritoneal metastasis	**M1c**

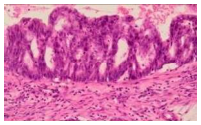
* Includes acellular mucin (Valasek 2018) ** Includes ovary and omentum

High grade appendiceal mucinous neoplasm (HAMN)

- No infiltrative invasion
- High grade cytology







Why distinguish HAMN from LAMN?

(1) Small series suggest worse prognosis if dysplasia is high grade

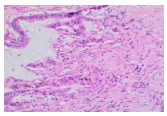
(2) Historically, some "HAMNs" would have been called "adenocarcinoma"

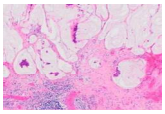
(3) Genetic studies (as yet unpublished) suggest intermediate genetic abnormalities

1. Yantiss RK et al, 2009
2. Misdraji J et al, 2003

Mucinous appendiceal adenocarcinoma

- Defined by infiltrative invasion
- Well differentiated tends to produce PMP
- Poorly differentiated may behave as conventional adenocarcinoma



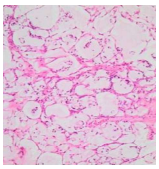
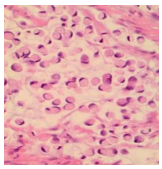


Valasek 2018

Mucinous appendiceal adenocarcinoma: grading

- G1
  - Well differentiated
- G2
  - Moderately differentiated
  - Poorly differentiated
- G3
  - Poorly differentiated with signet ring cells

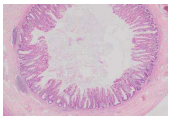
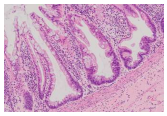
"Signet ring cell carcinoma" if >50% signet ring cells

Usually arises from goblet cell carcinoid

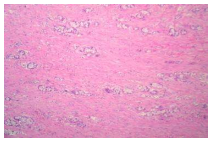
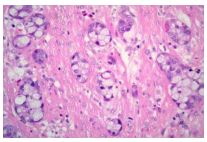
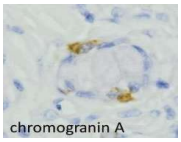
Serrated polyp should be distinguished from LAMN

- Resembles colorectal sessile serrated lesion
- Muscularis intact
- Different genetics from colon (*KRAS* and *GNAS*, not *BRAF* or DNA MMR defects)

Goblet cell carcinoid

- Rare, a type of adenocarcinoma

GCC: Adverse histological features

- Marked nuclear atypia
- Discohesive growth
- Sheets of signet ring cells
- Distortion of appendiceal architecture
- Desmoplasia
- Areas resembling conventional adenocarcinoma

Tang – groups A, B and C

Problem with "goblet cell carcinoid"

- Confusing name: they are a type of adenocarcinoma – *they are not carcinoids*
- TNM stage as adenocarcinoma
- Do not use NET criteria for grading
- ki67 index has not been shown to be prognostic
- Other names have been suggested (goblet cell adenocarcinoma is popular…)

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