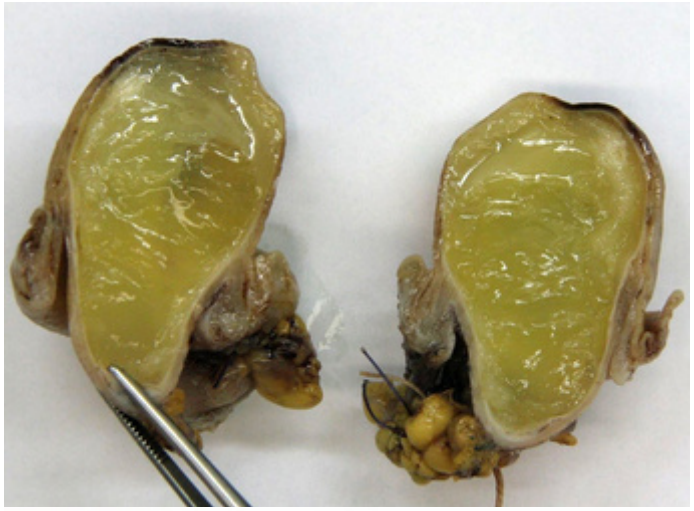
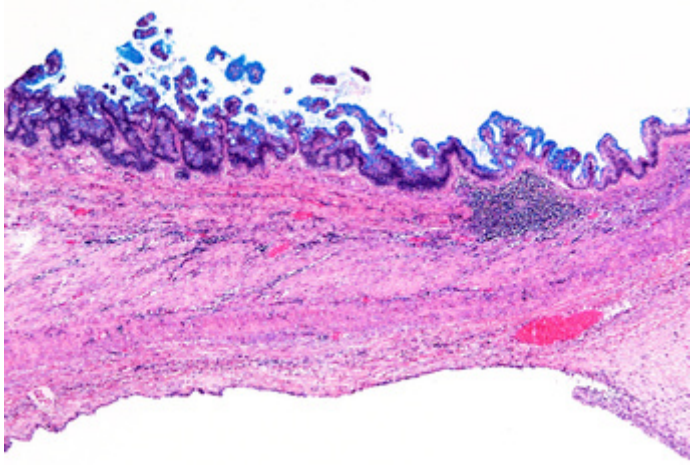
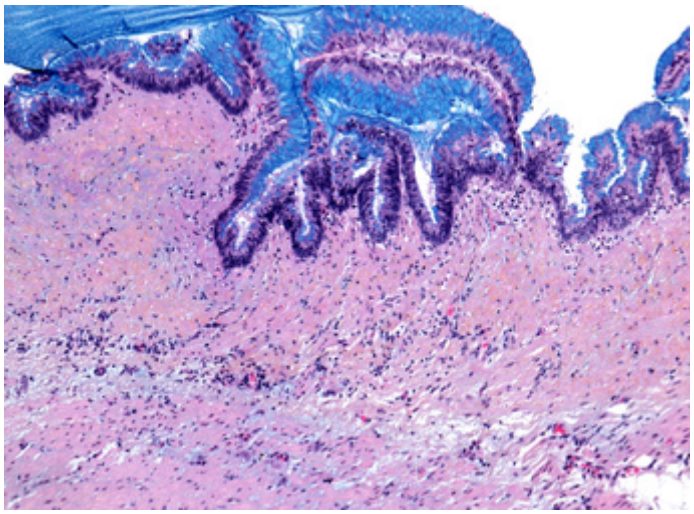
January 2017

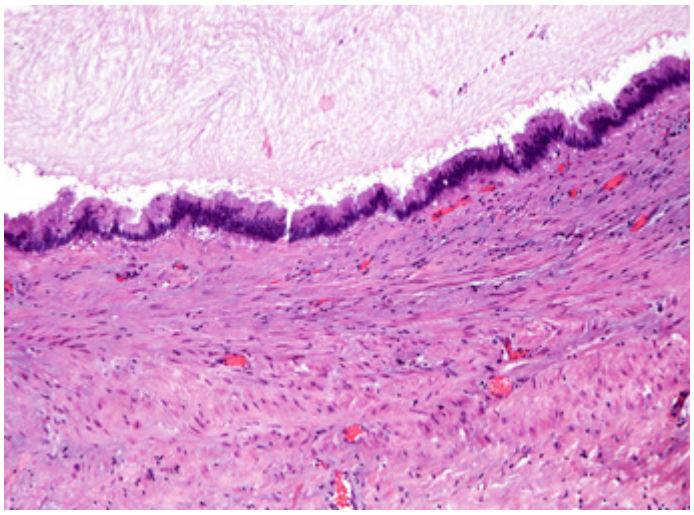
Appendix of a 60-year-old woman with clinical diagnosis of mucocele.

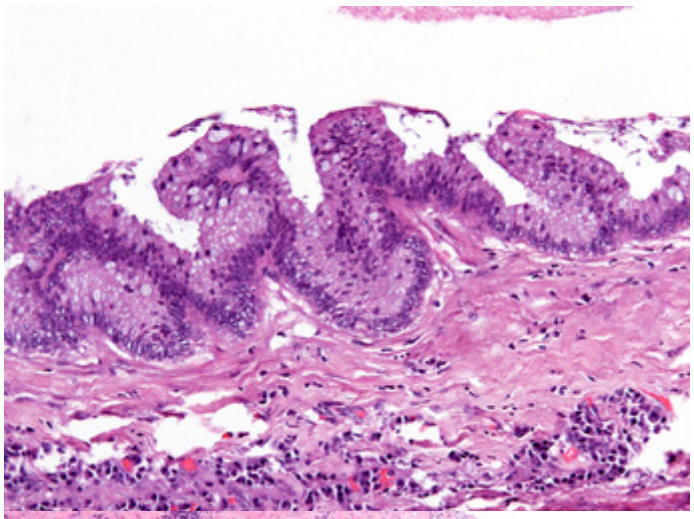
What is your diagnosis?

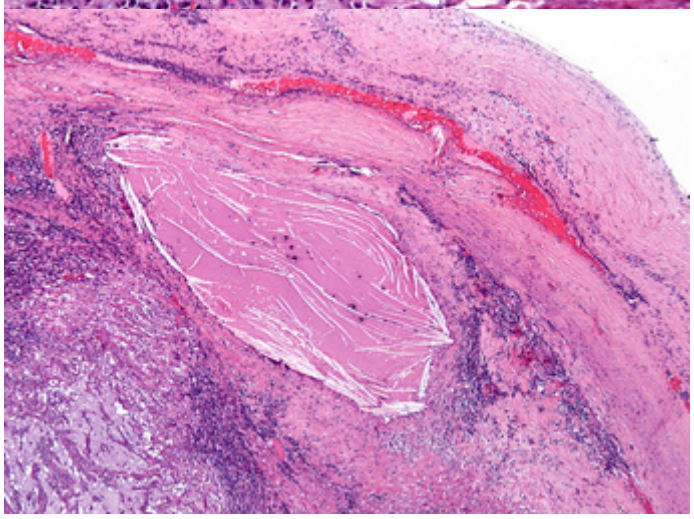












Diagnosis:

Low grade appendiceal mucinous neoplasm (LAMN).

Comment:

A 60-year-old female underwent laparascopy for suspected adnexal tumour. During surgery mucocele of the appendix was found and appendix was resected. Grossly, appendix was distended, measuring 8 cm in length and 2.8 cm in diameter. Serosal surface was smooth and shiny. Appendiceal wall was thin, with smooth inner surface, lumen was filled with gelatinous material (Panel 1). Microscopically, mucosa was circumferentially replaced by partially flat and partially undulating epithelial proliferation with small intracytoplasmic mucin vacuoles. The underlying lymphoid tissue was atrophic, muscularis mucosae was absent, submucosa and

some segments of muscularis propria were replaced by hyalinised fibrotic tissue. Epithelial cells had hyperchromatic nuclei showing nuclear stratification without significant mitotic activity or prominent nucleoli (Panels 2-5). Pools of acellular mucin were present in the deeper layers of the appendiceal wall, but without evident perforation (Panel 6).

LAMNs comprise less than 0.5% of malignancies of the gastrointestinal tract. They usually present in the sixth decade with predilection for females. Their classification and nomenclature have been controversial, largely because of the ability of a subset of LAMNs to disseminate to the peritoneal cavity as pseudomyxoma peritonei, despite their cytologically benign appearance.

According to WHO classification, LAMNs are characterised by pushing invasion of mucin and/or epithelium through the appendiceal wall. Their villous, undulating or flat epithelium shows low-grade dysplasia, often associated with atrophy of lymphoid tissue. The abundant cytoplasmic and luminal mucin may compress cells, rendering them cytologically bland. Lamina propria is frequently absent and neoplastic epithelium is lying atop fibrotic or hyalinised stroma. The muscularis propria is often fibrotic or hyalinised, but may be attenuated or even absent. Dystrophic calcifications can be present. Neoplastic epithelium may push into or through the wall, but features of infiltrative type invasion are absent. When the wall is entirely breached, mucin can be found in the peritoneal surface, with or without epithelial cells.

The prognosis of LAMN depends on the stage of the tumour. Tumours confined to the appendix can be cured by appendectomy. LAMNs associated with acellular mucin confined to the right lower quadrant carry a very low risk of recurrence or progression to pseudomyxoma peritonei, whereas those associated with mucin and neoplastic epithelium recur in about 50%. Tumours widely disseminated in the peritoneum pursue a progressive clinical course.

Therefore, in the evaluation of appendices with LAMN, the entire specimen should be submitted for histology. The presence and the extent of extra-appendiceal mucin, of mucinous epithelium within the extra-appendiceal mucin and the degree of cytologic atypia of the epithelium in the extra-appendiceal mucin should be reported, since the histologic grade of the mucinous appendiceal primary and the peritoneal metastases may differ. The pathology report should include the status of the surgical margin, although its involvement by neoplastic epithelium or acellular mucin does not predict recurrence of the disease according to a recent study.

Differential diagnosis of LAMNs includes adenoma where muscularis mucosae is intact, and adenocarcinoma characterized by an infiltrative rather than pushing invasion. Endometriosis with intestinal metaplasia can mimic LAMN, particularly when stromal component is scant. Mucin extrusion onto the serosal surface may also be caused by appendiceal diverticular disease, furthermore, the tangential sectioning and reactive changes in this setting may be mistaken for neoplasia.

For further reading:

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- Misdraji J. Mucinous epithelial neoplasms of the appendix and pseudomyxoma peritonei. Mod Pathol. 2015; 28, S67–79.
- Arnason T, Kamionek M, Yang M, et al. Significance of proximal margin involvement in low-grade appendiceal mucinous neoplasms. Arch Pathol Lab Med. 2015; 139: 518-21.
- Carr NJ, Cecil TD, Mohamed F, et al. Peritoneal Surface Oncology Group International. 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. Am J Surg Pathol. 2016; 40: 14-26.

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