CLINICAL VIGNETTE

Appendiceal Tumor Presenting as Acute Appendicitis

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Case Summary

A 44-year-old female presented to the ER with right lower quadrant abdominal pain for 1 day. The pain was sharp, non-radiating and rated an 8 out 10. She had constant pain for 14 hours associated with 10-15 episodes of emesis. She reported a fever of 101.5, but denied recent travel, sick contacts, diarrhea, or a prior history of similar symptoms. She had no significant past medical history. On presentation, her vital signs were normal and her physical exam was notable for tenderness in the right lower quadrant, as well as a positive Rovsing sign and deep tenderness over McBurney's point, raising high suspicion for acute appendicitis. Her blood work included WBC 10.2 with 70% neutrophils, Hgb 12 and Plat 207 and normal comprehensive metabolic panel, urinalysis and negative pregnancy test.

A CT scan of the abdomen and pelvis with contrast showed a dilated appendix to 12mm which was fluid filled with a hyper enhancing wall. Marked periappendiceal stranding was seen. A ring of fluid density seen at the base of the appendix. Phlegmonous changes were seen, raising the possibility of a perforated appendix, though no free air was seen.

She was diagnosed with acute appendicitis and was taken to the operating room for a laparoscopic appendectomy. She was found to have a "dilated, broad-based, clearly inflamed appendix" without evidence of rupture or perforation.

Pathology from the surgical specimen revealed "Acute appendicitis and Appendiceal mucinous cystadenoma, the appendiceal mucinous cystadenoma is confined to the mucosa. No high-grade dysplasia or invasion is seen. Margin of resection is involved by mucinous cystadenoma."

Patient did well and was discharged on post operative day 1. The pathology was reviewed at her surgical follow up appointment and no further follow up was recommended.

Two years later, at the age of 46, the patient was referred for a gastroenterology consultation by her primary care doctor. The pathology from her surgery 2 years ago was reviewed and consultation was requested to see if any further management was required.

A CT scan of the abdomen and pelvis (Figure 1 and 2) was ordered which showed a filling defect along the cecal wall, raising suspicion for an intussuscepted appendiceal stump, recurrent soft tissue mass, or other lesion.

A colonoscopy was then completed, which was the patient's first colonoscopy. (Figures 3-5).

A biopsy was taken from the soft tissue lesion seen in the cecum.

Pathology revealed the following:

- Fragments of adenoma with tubulovillous architecture
- No high grade dysplasia or malignancy seen

***Comment: However, it is not possible to distinguish if this represents a recurrence of the patient's previous appendiceal adenoma or if this is a new lesion. Clinical correlation recommended.*

The patient was then referred to surgery and she underwent a laparoscopic resection of the cecum. (Figures 6-8). The gross surgical specimen revealed evidence of mucinous material (Figure 9).

The pathology from the surgical specimen revealed a low-grade appendiceal mucinous neoplasm (LAMN).

Discussion

Appendicular tumors are quite rare and account for about 1% of all appendectomy specimens.[1] They have been a source of confusion and debate for many years, especially among pathologists. Appendiceal mucinous tumors can spread to the peritoneum resulting in a distinctive syndrome called pseudomyxoma peritonei (PMP). They frequently lack classic, infiltrative invasion of the appendiceal wall, yet manage to seed the peritoneum. In the peritoneum, mucinous epithelial cells embedded in the abundant mucin are often bland, yet PMP is progressive and frequently fatal.

Historically, cystic mucinous tumors of the appendix were classified as "mucoceles", and when they showed hyperchromatic, elongated nuclei, they were called "cystadenocarcinomas". However, mucocele is simply a descriptive term and NOT a pathologic diagnosis, therefore its use was discontinued.[2]

In the 1960s and 70s, they were reclassified as "mucinous cystadenomas" or "villous adenomas of the appendix", in keeping with nomenclature for colorectal adenomatous polyps; doubts began to surface about the malignant nature of these seemingly noninvasive tumors. There continued to be controversy, as these same tumors were seen to seed the peritoneal cavity with neoplastic mucinous epithelium that resulted in death in more than 50% of patients due to bowel obstruction. For decades, there was disagreement between those who believed in the concept of a "ruptured adenoma" vs those who insisted that the presence of epithelium outside the appendix indicates that the primary tumor must be an invasive adenocarcinoma.

In 2010, a new term was introduced to reconcile the benign appearance of the appendiceal tumor and the peritoneal mucinous epithelium with the often fatal biologic behavior of PMP.[3] This term came about from a study done in 2003 by Misdraji, et al. They felt that because appendiceal tumors that are confined to the appendix (mucinous cystadenoma or villous adenoma) are indistinguishable from those that have spread to the peritoneum, a single term should be used to encompass them, whether they are confined to the appendix or if they have spread to the peritoneum. The new term was LAMN, or low-grade mucinous appendiceal neoplasm. This term described tumors that lack destructive invasion of the appendiceal wall. Adenocarcinoma is the term reserved for tumors with either high-grade cytology or destructive invasion.

The types of mucinous appendiceal neoplasms include adenoma, LAMN and adenocarcinoma.

Low-grade Appendiceal Mucinous Neoplasm (LAMN)

Clinical Features:

Abdominal pain is the most common clinical presentation, often presenting in the 6th decade. There is a female predominance and patients may present with an abdominal mass or abdominal distention, possibly due to the development of PMP. A ruptured LAMN may present with mucin in a hernia sac. In 20% of cases, it is found as an incidental finding in asymptomatic patients who have undergone appendectomy.

Pathology:

The appendix may appear grossly normal or can be dilated and filled with tenacious mucin. (Figure 12). The wall is often thin, fibrotic and calcified. Gross rupture may show mucin in the wall or on the serosal surface. Histologically they can appear similar to adenomas with a villous or flat neoplastic mucinous epithelium. A defining feature is "pushing invasion", a pattern of invasion of the underlying appendiceal wall. The wall may rupture with mucin filling onto the peritoneal surface, without or without mucinous epithelial cells growing freely in that mucin.

Natural History:

The prognosis is dependent on the stage of the tumor. When widely disseminated in the peritoneum, a progressive clinical course ensues (PMP). If limited to the appendix or rupture is localized to the RLQ, then the presence of neoplastic mucinous epithelium dictates the prognosis.

LAMNs associated with acellular mucin and confined to the RLQ carry a very low risk of recurrence or progression PMP. Those associated with mucin and neoplastic mucinous epithelial cells in the RLQ carry a high risk of recurring as disseminated disease.

Therefore in the evaluation of LAMNs, the entire specimen, should be examined to evaluate for the presence of mucin on the serosa, and more importantly, the presence or absence of mucinous epithelium within the extra-appendiceal mucin.[4]

Treatment:

For LAMN's that are confined to the appendix, without extra-appendiceal mucin, a simple appendectomy is performed. This is essentially curative. If margins are positive, then a cecectomy is generally performed, though data are lacking. If cellular epithelium is present and confined to the RLQ, a right hemicolectomy can be considered, but data are lacking.

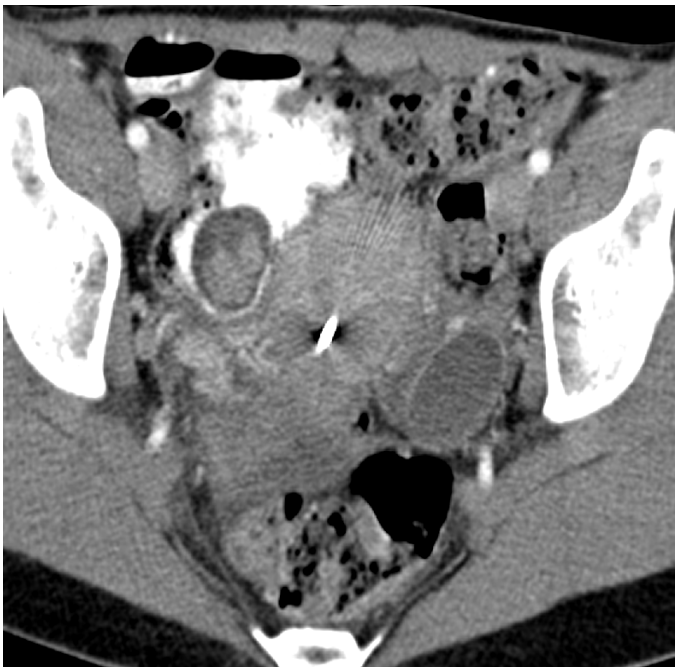
Tumors that have disseminated widely are treated for PMP.

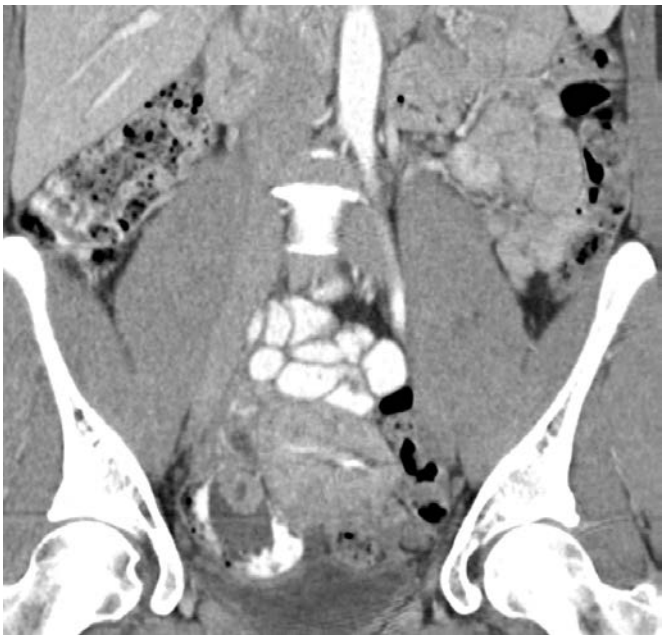
Conclusion

Appendiceal tumors are rare but are important because they can spread to the peritoneum leading to a potentially fatal disease. Adenomas, LAMNs and adenocarcinomas can be found on appendectomy specimens. Adenomas have intact muscularis mucosae, while LAMNs have pushing invasion. LAMNs are low-grade tumors but can still disseminate into the peritoneum.

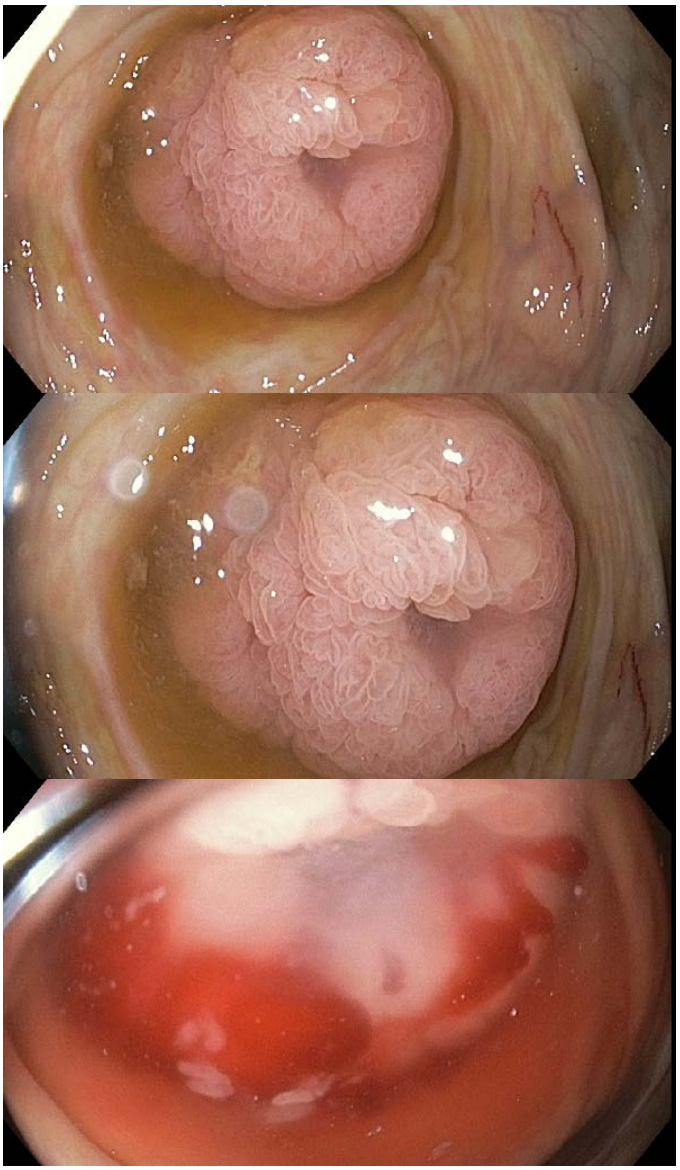
Treatment varies according to tumor invasion, but can range from a simple appendectomy to a right hemicolectomy.

Figures





Figures 1 and 2. CT Scan of the Abdomen and Pelvis. A filling defect is seen along the cecal wall, measuring approximately 3cm. Heterogeneous with air, fat and soft tissue components. Soft tissue components are most prominent at the base of the lesion.



Figures 3-5. Mass seen in the cecum with mucinous substance.

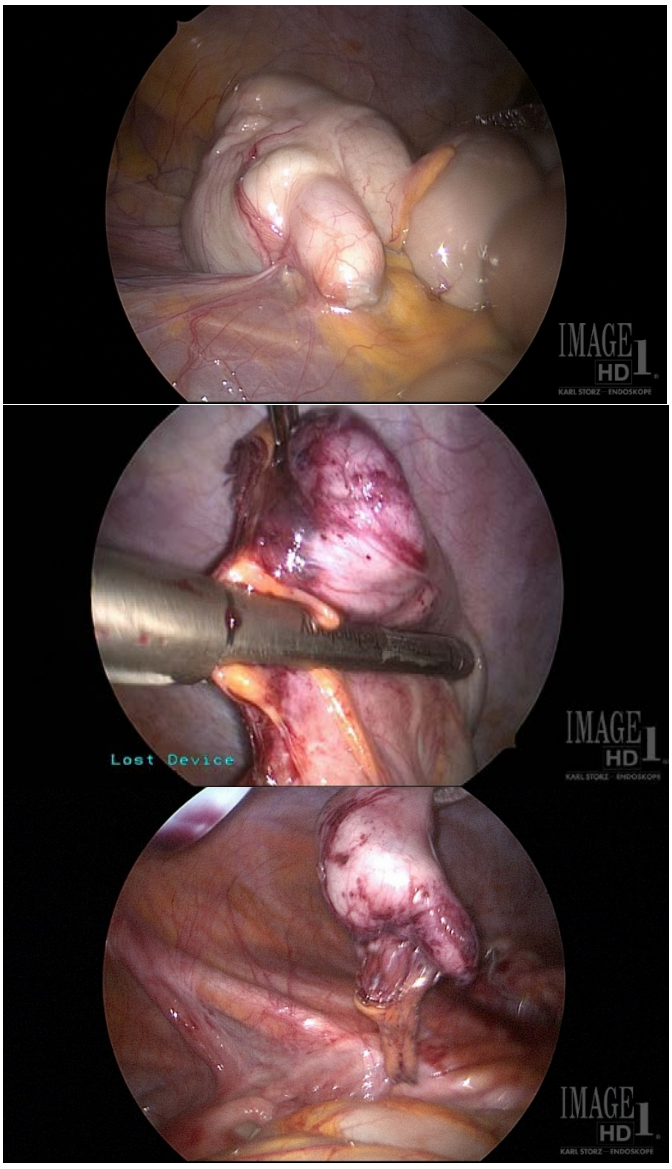


Figure 6-8. Laparoscopic surgical resection of the cecum.

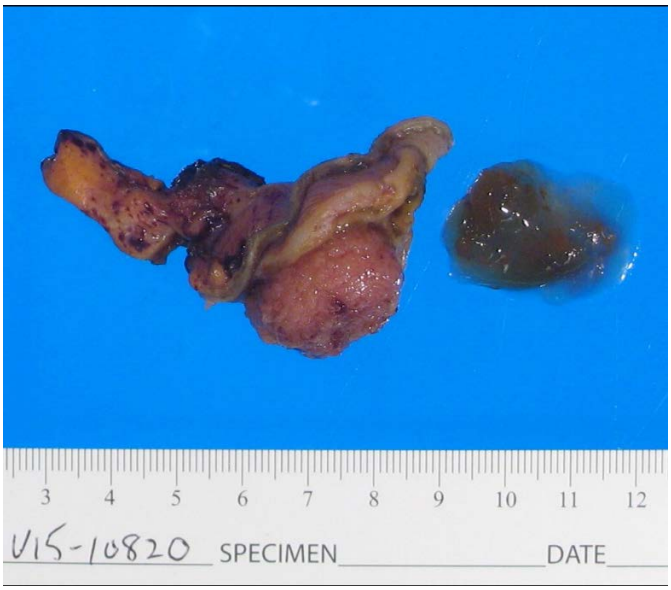
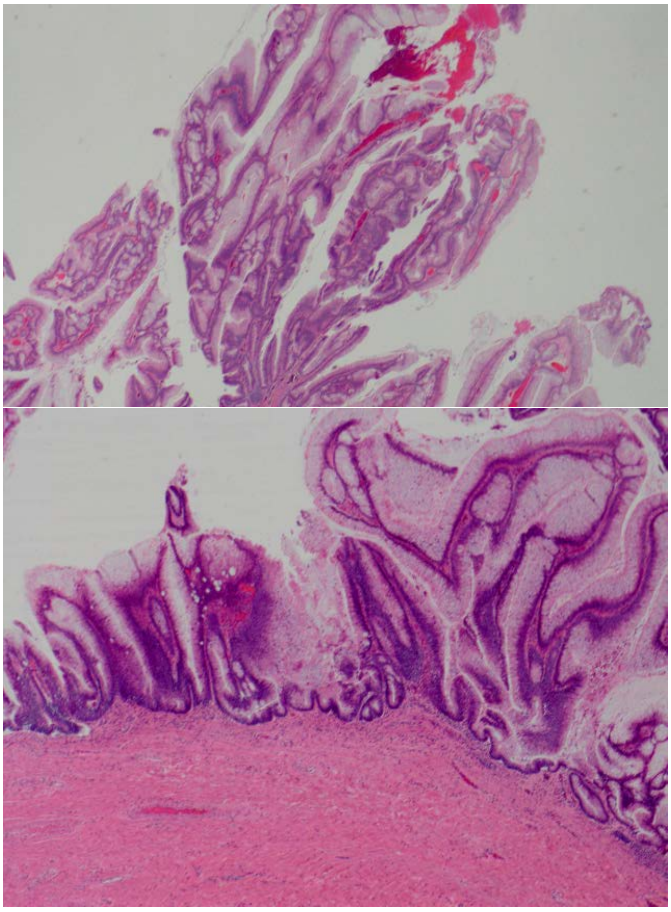


Figure 9. Surgical specimen revealing evidence of mucinous material.



Figures 10 and 11. Surgical pathologic specimen consistent with low-grade appendiceal mucinous neoplasm (LAMN). Most of the lesion resembles a tubulovillous adenoma (TVA) that is arising within the appendiceal orifice. However, there are areas with loss of lamina propria and atrophy of the muscularis mucosae.

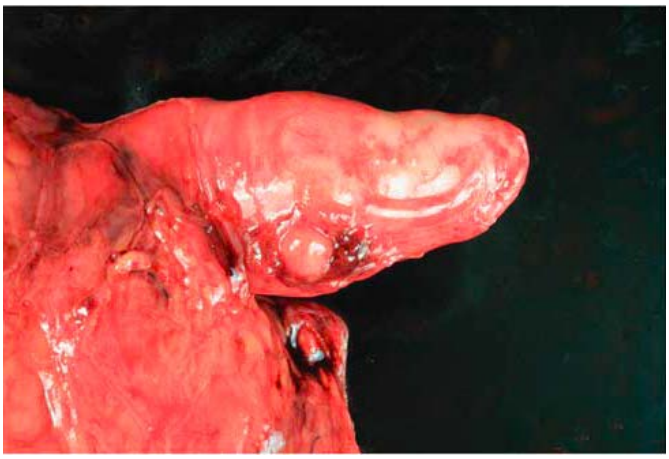


Figure 12. Gross appearance of a low-grade appendiceal mucinous neoplasm. The appendix is dilated and enlarged, although from external appearance alone, the differential includes benign and malignant conditions that can cause a dilated appendix. The serosa shows a mucoid hemorrhagic plug that, while innocuous in appearance, is the point of rupture of tumor epithelium into the peritoneum.

REFERENCES

1. **Tirumani SH, Fraser-Hill M, Auer R, Shabana W, Walsh C, Lee F, Ryan JG**. Mucinous neoplasms of the appendix: a current comprehensive clinicopathologic and imaging review. *Cancer Imaging*. 2013 Feb 22;13:14-25. doi: 10.1102/1470-7330.2013.0003. Review. PubMed PMID: 23439060; PubMed Central PMCID: PMC3582328.
2. **Misdraji J**. Mucinous epithelial neoplasms of the appendix and pseudomyxoma peritonei. *Mod Pathol*. 2015 Jan;28 Suppl 1:S67-79. doi: 10.1038/modpathol.2014.129. Review. PubMed PMID: 25560600.
3. **Misdraji J, Yantiss RK, Graeme-Cook FM, Balis UJ, Young RH**. Appendiceal mucinous neoplasms: a clinicopathologic analysis of 107 cases. *Am J Surg Pathol*. 2003 Aug;27(8):1089-103. PubMed PMID: 12883241.
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