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A Rare Case of Low-Grade Appendiceal Mucinous Neoplasm with Pseudomyxoma Peritonei Presenting with Ruptured Umbilical Hernia

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Abstract

Low-grade appendiceal mucinous neoplasm (LAMN) is a rare malignancy with symptoms varying depending on the clinical manifestations. The most worrisome complication of this particular neoplasm is seeding of mucin into the adjacent peritoneum, leading to pseudomyxoma peritonei (PMP). We present an unusual case of a 70-year-old female found to have LAMN with PMP who presented with ruptured umbilical hernia.

Keywords: Appendix, Low-grade appendiceal mucinous neoplasm, Mucin, Pseudomyxoma peritonei

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Introduction

Low-grade appendiceal mucinous neoplasm (LAMN) is a rare malignancy accounting for 1% of gastrointestinal (GI) neoplasms and is found in <0.3% of appendectomy specimens.[1,2] LAMNs are diverse and can be classified as colonic-type, mucinous adenocarcinoma, goblet cell adenocarcinoma, or neuroendocrine carcinoma.[3] Mucinous adenocarcinoma accounts for the majority of cases according to the literature.[2] This malignancy is commonly an incidental finding during operative exploration and is often diagnosed late.

Gross examination of LAMN may be unremarkable or may appear as a mucin-filled, cystically dilated tissue. The appendix wall may appear thin, fibrotic, hyalinized, or calcified with a smooth or granular appearance.[4] Similar to polyps found in the colon, LAMN can be classified as villous or flat with atrophied lymphoid tissue. Neoplastic tissue growth occurs in a "pushing" invasion pattern wherein no tumor budding or single-cell invasion is noted.[4]

LAMNs are associated with diverticula, herniations, dissections, and rupture.[4] The most feared complication is seeding of mucin into the adjacent peritoneum, leading to pseudomyxoma peritonei (PMP), associated with a high rate of mortality.[1,2] Seeding into the peritoneum occurs in the late stages of the disease. Even though LAMNs confined to the appendiceal lumen do not show definitive malignant features, they can proliferate outside the appendix in a malignant fashion and result in the development of PMP, a life-threatening complication with 45% 10-year survival.[5] Our case was unique due to the findings of periappendiceal acellular mucinous deposits, along with umbilicus hernia and subumbilical deposits.

Case Presentation

A 70-year-old female presented to the hospital with complaints of umbilical swelling and pain. The swelling had increased gradually for the past 6 months. The patient was brought to the emergency when the swelling ruptured and blood and mucin oozed out. On clinical examination, it was revealed that there is herniation at the umbilicus and abdomen is bloated. Ultrasonography (USG) abdomen revealed a defect of size 5.8 cm in the anterior abdominal wall in the umbilical and supraumbilical region, showing herniation of intestinal loops (obstructed hernia). Further, evidence of large hypoechoic collection with multiple septations in lower abdomen and pelvis measuring 11.8 cm × 11.2 cm × 7.8 cm. However, the bilateral ovaries were normal.

The patient underwent laparotomy, and during the surgery, it was revealed that there is an exophytic growth at the appendiceal site and numerous mucinous deposits were seen in periappendiceal areas as well as at subumbilical area. Mass was resected along with intestinal segment (right hemicolectomy) and mucinous deposits sent for histopathological evaluation to the department of pathology.

On gross, the right hemicolectomy specimen measured 30 cm × 12 cm × 5 cm with an exophytic growth measuring 9 cm × 7 cm × 2 cm seen arising from the appendix [Figure 1]. The growth was grayish-white, irregular, and hard in consistency. The cut surface of the tumor showed solid, homogenous gray-white areas. Many small, round, hard nodules were also noticed, few attached with the mass and rest were sent separately in a different container. Specimen from the umbilical site showed multiple mucin-filled loculations below the subcutaneous tissue.

Microscopic examination revealed a tumor arranged in glandular pattern, lining showing mildly atypical columnar epithelium which at places showed pseudostratification and apical mucin [Figure 2]. The tumor infiltrated the muscularis propria and extended up to serosa.

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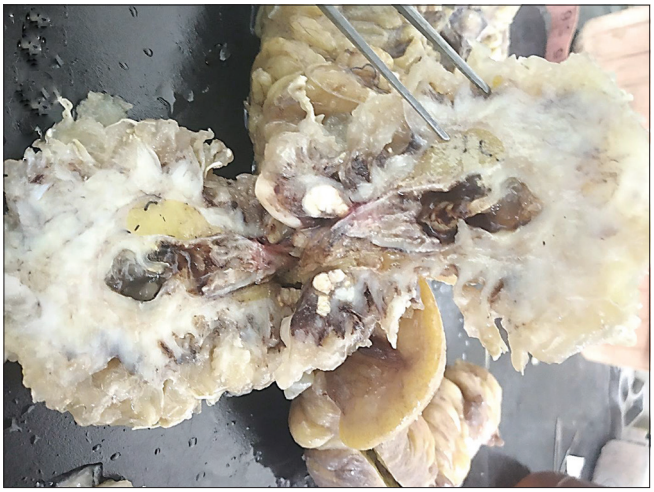

Figure 1: Gross image: Appendix with intestinal segment. Cut section of appendix shows thickened wall. Lumen of appendix is filled with hemorrhage. Wall of appendix is surrounded by solidified mucinous deposits and gray-white dense hard nodules

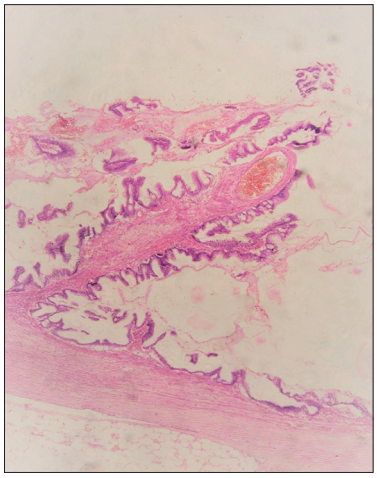

Figure 2: Appendiceal mucosa lined by mucinous epithelial cells with mildly atypical, at places pseudostratified and hyperchromatic nuclei and apical mucin (hematoxylin-eosin, 20×)

Few foci of organized mucin pools were also noted. Sections from the hard nodules also showed the organized mucin with areas of calcification [Figure 3]. Periodic acid–Schiff (PAS) stain done on the section from the hard nodules showed PAS-positive mucinous deposits [Figure 4]. Section studied from umbilical nodule shows lakes of mucin in the dermis and subcutaneous tissue [Figure 5].

Discussion

LAMNs are rare neoplasms in the appendix or the surrounding appendiceal mucosa wall. Most commonly seen in men, in the sixth decade of life. Patients with LAMN can present with abdominal pain, intussusception, and obstruction. However, LAMNs are often incidentally found in asymptomatic patients. Complications of LAMN include intussusception, ureteral obstruction, volvulus, small bowel obstruction rupture, herniation, and PMP.[1,2] Often, this malignancy is misdiagnosed as acute appendicitis, retroperitoneal tumors in the right iliac fossa, or an adnexal mass.[2]

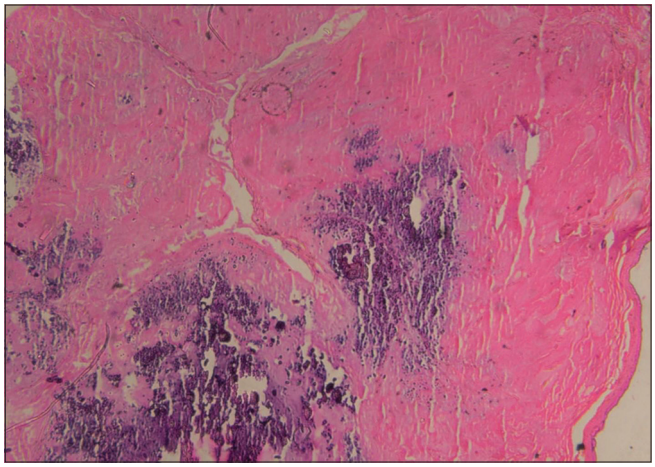

Figure 3: Section studied from hard nodules shows organized mucin with areas of calcification. (hematoxylin-eosin, 40×)

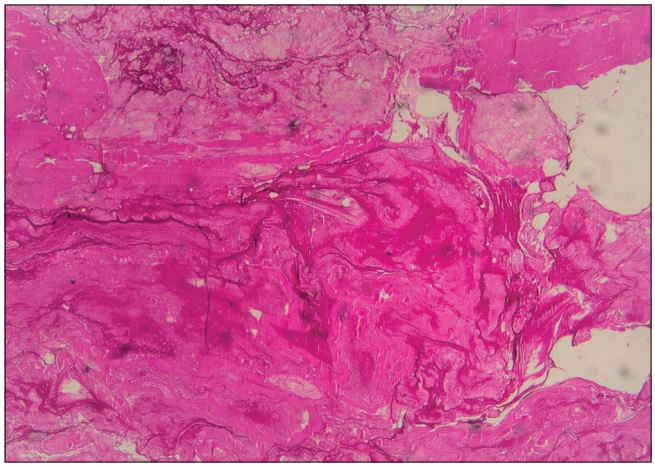

Figure 4: Special stain – periodic acid–Schiff-positive mucinous deposits in hard nodules (40×)

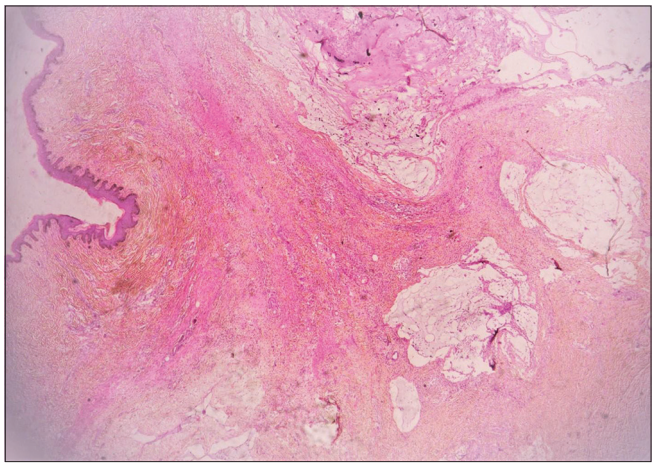

Figure 5: Umbilical nodule showing lakes of mucin in the dermis and subcutaneous tissue. (hematoxylin-eosin, 20×)

Grossly, specimens of LAMN include hyalinization and fibrosis of the appendiceal wall with a grossly swollen appendix secondary to mucinous accumulation.[1,2-4] LAMNs <2 cm are rarely malignant

and are classified as benign simple or retention mucoceles. Masses larger than 6 cm present with a higher risk of malignant cells, a higher risk of appendiceal perforation, and development of PMP.[2] Histological evidence of LAMN includes atypical glandular cells and epithelial cells with "pushing invasion" of malignant cells creeping into the appendiceal wall with possible diverticulum formation.[4] Mucinous, colonic, and goblet cells are also often identified within LAMN.[6] The spectrum of these lesions ranges from benign (appendiceal mucocele also known as retention cyst) to neoplastic. Mucinous neoplasms can be further classified on histopathology as adenomas, low-grade and high-grade neoplasms, and adenocarcinoma.[7,8]

Low-grade mucinous neoplasms are adenomatous tumors with mucin extending beyond muscularis mucosa. These can be associated with mural perforation causing low-grade PMP. Any invasion of underlying organs/serosa associated with hematogenous and nodal deposits suggest high-grade PMP which is commonly associated with mucinous adenocarcinoma.[7,8] Histopathology of PMP depicts epithelial cells and mucin in the peritoneum.[4]

Elevated carcinoembryonic antigen (CEA), carbohydrate antigen (Ca) 19-9, and Ca–125 may be detected in 56.1–67.1% of patients with LAMN.[9] There is also 35% risk of a concurrent GI malignancy in patients with LAMN.[6]

PMP is a complication of mucinous LAMN that can develop from peritoneal seeding in 20% of patients with a mucinous adenoma. It can be diagnosed using various modalities such as USG, computed tomography (CT) scan, and MRI depicting the presence of gelatinous mucinous nodules in the peritoneal cavity.[7]

Radiology plays a pivotal role in evaluation of appendiceal mucinous neoplasms (AMNs). Red flags on CT that helps in differentiating them from appendicitis are as follows: Appendiceal diameter of >15 mm, associated soft-tissue mass, wall thickening, and irregularity.[7] In these cases, search should be undertaken for associated extra-appendiceal mucin and PMP appearing as low-attenuation masses in peritoneal cavity, typically causing scalloping of solid abdominal viscera. Vice versa, in a case with PMP, one should actively search for mucinous tumors of the appendix. Occasionally, the initial presentation of these tumors is in the form of a large ovarian mucinous deposit with PMP; underlying primary AMN being disproportionately small and thus can be overlooked.[10] In patients with simultaneous ovarian and appendiceal mucinous masses on CT, appendix is always considered the primary site, based on molecular genetic studies.[4]

In patients with PMP, other less common primary sites can be ovary, urachus, colon, or pancreas. PMP associated with primary ovarian neoplasia is rare and probably restricted to mucinous tumors arising in mature cystic teratomas.[11] According to a study done by Stewart *et al*., all the ovarian mucinous tumors associated with mature cystic teratomas were morphologically similar to those secondary to appendiceal neoplasia. They comprised irregularly distributed glands and cysts lined by tall, mucin-rich epithelial cells exhibiting focal villoglandular architecture and low-grade cytological atypia. The immunophenotype of the teratoma-associated tumors and those secondary to appendiceal neoplasia was identical: There was strong and diffuse expression of CK20, CEA, CDX-2, MUC2, and MUC5AC with no reactivity for the other anti-sera tested.[12]

Besides this, these patients also have increased incidence of synchronous and metachronous colon polyps and masses.[6] However, these imaging modalities have only been shown to identify up to 29% of adenomas before surgical intervention.[9]

Further advances in biomarkers and molecular genetics demonstrate CDX2, MUC-2, CK 20, β- catenin, CEA, CA 19-9, and KRAS mutations identified in hopes of improving early identification.[1] The 5-year survival rate for PMP is 25%.[13]

Conclusion

Overall, further studies are needed for a more definitive method of diagnosis, treatment, and monitoring of LAMN. Histopathology remains the gold standard for the diagnosis. However, early detection to date varies by imaging modality and the tumor markers utilization. This case presents the importance of staging of the appendiceal neoplasm when there is association of PMP and also to rule out other common neoplasms associated with PMP.

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