CASE REPORT

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An appendiceal mucocele associated with inverted epithelium and submucosal hyperplasia at the appendiceal root: a rare case report

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ABSTRACT

A 54-year-old woman was referred to our hospital because of abnormal colonoscopic findings, including a submucosal protuberance at the appendiceal root. A biopsy showed no malignant findings. Computed tomography revealed a 20-mm cystic lesion with thick walls at the appendiceal root, suggestive of an appendiceal mucocele. Laparoscopic ileocecal resection was performed based on the preoperative diagnosis of a suspected mucinous appendiceal neoplasm. The resected specimen showed a closed appendiceal orifice surrounded by a mucus-containing submucosal tumor. Histopathologically, the appendiceal epithelium was circumferentially inverted in the appendiceal root, with hyperplasia of the submucosal connective tissue. No atypical epithelium was observed. We hypothesized that repeated partial invagination of the appendiceal root caused submucosal hyperplasia and drainage disturbance of the appendiceal content, leading to the development of a mucocele.

Keywords: appendix, mucocele, invagination, appendiceal mucinous tumor, ileocecal resection

Abbreviation:
CT: computed tomography

INTRODUCTION

The condition in which mucus is retained due to obstruction of mucus discharge from the appendiceal lumen is called appendiceal mucocele. Appendiceal mucocele refers to a mucinous mass observed in imaging rather than a distinct pathologic entity, as the underlying pathology can vary, ranging from non-neoplastic conditions (such as polyps and fecalith) to neoplastic ones (including low- and high-grade appendiceal mucinous neoplasms [LAMN and HAMN] and mu-

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cinous adenocarcinoma). It is a rare condition, accounting for 0.1–0.7% of all appendectomies,[1-3] often associated with a closed appendiceal orifice or hypersecretion of mucin by the appendiceal epithelium.[4-6] We report a rare case of appendiceal mucocele associated with inverted epithelium and submucosal hyperplasia at the appendiceal root, hypothetically caused by repeated partial invagination of the appendiceal root.

CASE REPORT

A 54-year-old female underwent periodic colonoscopy and visited our hospital for further evaluation of an abnormality detected during the procedure. She had a medical history of lumbar spinal stenosis, arrhythmia, and adenomatous goiter. She was well-nourished and did not have abdominal symptoms. Blood tests did not show any remarkable abnormality: white blood cell count: 3.7 × 10^3/μL; C-reactive protein level: 0.02 mg/dL; hemoglobin: 13.9 g/dL; carcinoembryonic antigen (CEA): 2.3 ng/mL; and carbohydrate antigen 19-9 (CA 19-9): 13.8 U/mL. Colonoscopy showed a submucosal protuberance with a central depression at the appendiceal orifice, where the mucosal architecture was preserved (Fig. 1a, b), and a biopsy showed no malignant findings. Colography using gastrografin showed a 20 mm-diameter opacifying defect in the cecum, and the appendix was not visualized (Fig. 2). Computed tomography (CT) revealed a 20 mm round cystic lesion with wall thickening at the appendiceal root and a thin appendiceal tip (Fig. 3a, b). We preoperatively diagnosed an appendiceal mucocele that presumably developed from a mucinous appendiceal neoplasm, and laparoscopic ileocecal resection was performed. The postoperative course was uneventful, and the patient was discharged from the hospital 8 days after the operation. A macroscopic examination of the resected specimen revealed a submucosal tumor containing mucus at the appendiceal root with a closed appendiceal orifice (Fig. 4a) and circumferentially inverted appendiceal epithelium (Fig. 4b, c). The appendiceal tip was thin and the lumen was occluded. Histopathologically, the appendiceal epithelium was inverted with hyperplasia of the submucosal connective tissue at the appendiceal root (Fig. 5a, b). Mucous accumulation was observed in the appendiceal lumen; however, no atypical epithelium was found (Fig. 5c).

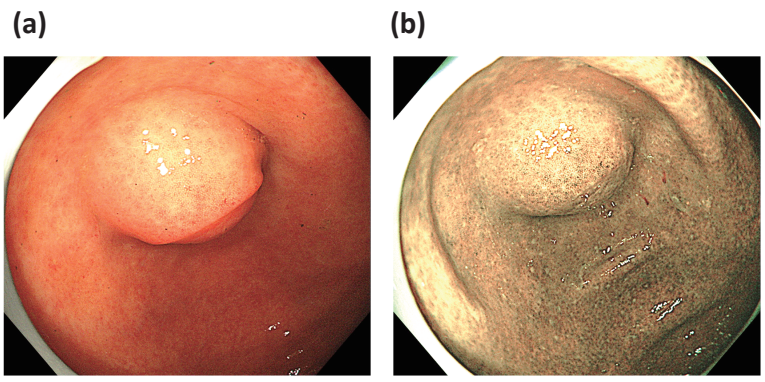

Fig. 1 Colonoscopy
White light image showing a submucosal protuberance with a central depression at the appendiceal orifice (a). Narrow band imaging showing preserved mucosal architecture (b).

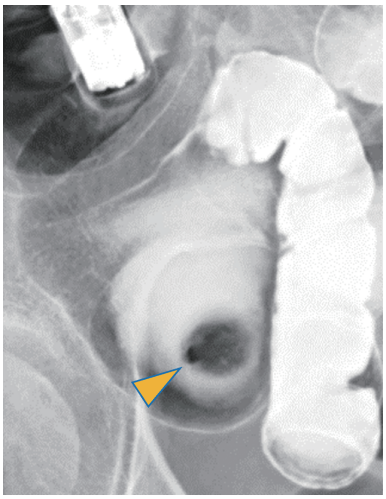

Fig. 2 Colography
A 20 mm-diameter opacifying defect (arrowhead) in the cecum without appendiceal visualization.

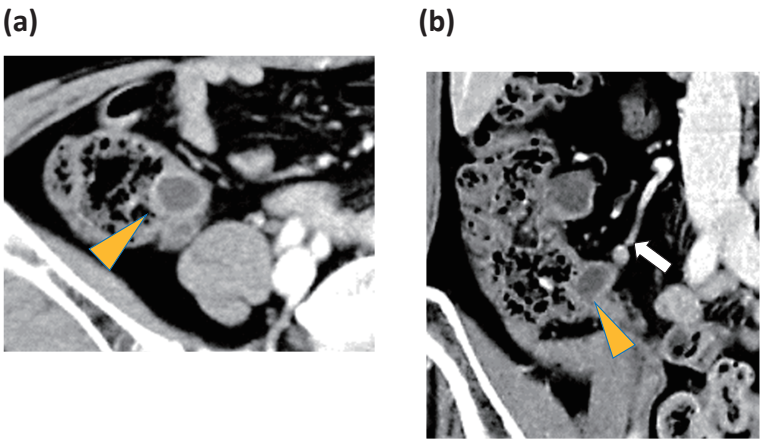

Fig. 3 Computed tomography
A 20 mm round cystic lesion with wall thickness at the appendiceal root (arrowhead) and a thin appendiceal tip (arrow), horizontal image (a), coronal image (b).

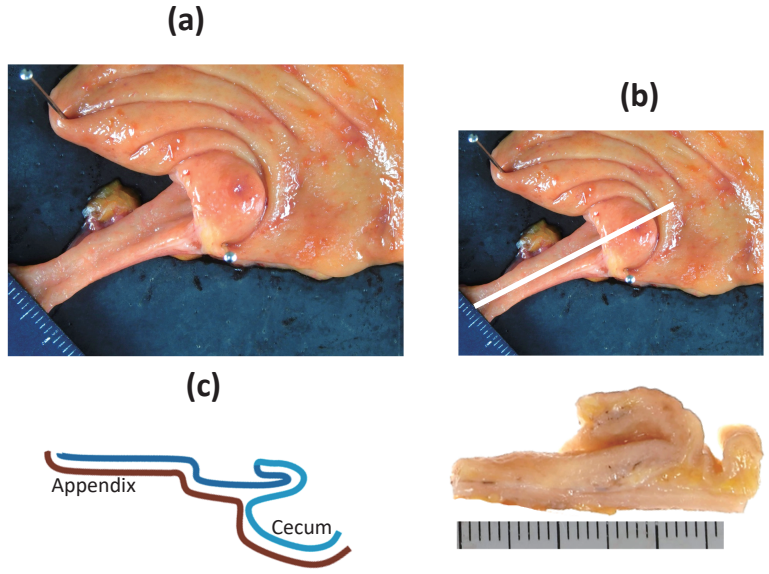

Fig. 4 Macroscopic finding of the resected specimen
A submucosal tumor containing mucus at the appendiceal root with a closed appendiceal orifice (a). Cut surface of the resected specimen (indicated by a white line) showing inverted appendiceal epithelium (b). Schema showing circumferentially inverted appendiceal epithelium (c).

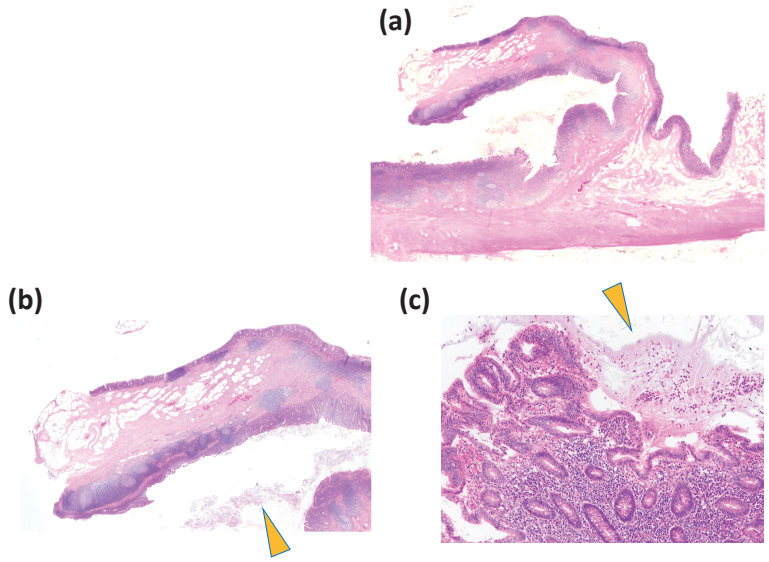

Fig. 5 Histopathological findings
Appendiceal epithelium was inverted with hyperplasia of the submucosal connective tissue (a, b), and mucous accumulation (arrowhead) was observed in the appendiceal lumen; however, no atypical epithelium was found (c). Loupe image (a), Hematoxylin and eosin (HE) x100 (b), HE x200 (c).

DISCUSSION

In this report, we describe a case of appendiceal mucocele associated with an inverted epithelium and submucosal hyperplasia of the appendiceal root. The appendiceal orifice was occluded by a circumferentially inverted epithelium.

Appendiceal mucoceles can develop in various conditions, including a closed appendiceal orifice or mucin hypersecretion of the appendiceal epithelium.[4-6] Histologic etiologies include retention cysts, mucosal hyperplasia, LAMN and HAMN, and mucinous adenocarcinomas. Among the 29 patients who underwent surgical resection for appendiceal mucocele in our department between 2011 and 2022, 26 (90%) had neoplastic lesions. On the other hand, Morano et al reviewed 276 cases of non-perforated appendiceal mucocele from the English literature and reported that malignant lesions were predominant in female patients. They also reported that 42% of cases were benign lesions, including retention cysts and mucosal hyperplasia.[4] Our case had distinctive feature of a circumferentially inverted epithelium and submucosal hyperplasia of the appendiceal root. Operative procedures for mucocele, including appendectomy, partial cecectomy, and ileocecal resection, are decided based on the preoperative diagnosis. Our preoperative diagnosis was a mucinous appendiceal neoplasm because of the size (20 mm in diameter) and thick walls of the cystic lesion.[5] The differential diagnosis should have included a simple cyst (retention cyst), mesenteric or duplication cyst, endometriosis, fecalith, and other chronic local processes leading to obstruction of the appendiceal orifice.[4,7-11]

In our case, macroscopic and histopathological examinations revealed a circumferentially inverted epithelium and submucosal hyperplasia at the appendiceal root without any atypical epithelium. We hypothesized two theories. First, repeated partial invagination of the appendiceal root, consistent with type III according to the McSwain classification of appendiceal intussusceptions[12] (Fig. 6), mechanically causes submucosal hyperplasia, obstruction of the appendiceal orifice, and disruption of appendiceal content drainage, resulting in mucin retention and the development of an appendiceal mucocele (Fig. 7a-d). Second, mucin hypersecretion by the appendiceal mucosa leads to mucocele development, inducing appendiceal invagination. Since mucin-producing epithelium was not found in the appendix, we prefer the first hypothesis.

Many studies have reported cases of appendiceal invagination secondary to a neoplastic appendiceal mucocele[4,13,14]; however, they are different from our case, which was a non-neoplastic mucocele that presumably developed secondary to repeated partial invagination of the appendiceal root.

King K et al reported a similar case, in which colonoscopy showed a submucosal protuberance at the appendiceal orifice. CT showed a cystic lesion adjacent to the appendiceal orifice, suggestive of an appendiceal mucocele. The resected specimen revealed an intraluminal polypoid mass that developed from a mucosal prolapse associated with mucosal hyperplasia.[6] Our case was similar to this in terms of imaging modalities, including colonoscopy and CT, but had different pathology and etiology.

Appendiceal invagination is a rare disease that is reportedly seen only in 0.01% of surgical specimens.[15] It can be diagnosed by identifying the "cup and ball" sign and multiple concentric ring sign on CT or ultrasonography (US),[16,17] and the coiled-spring sign on colonography.[18] Unfortunately, US was not performed in our case. A review of the preoperative CT could not detect partial invagination of the appendiceal root.

Mucinous appendiceal neoplasms have a slight female predominance and are often diagnosed in 50–60-year-old patients.[19,20] Anemia and elevated CEA and CA19-9 levels may be indicative of the disease.[21,22] CT images indicating wall thickening, calcifications, irregularity, and nodular enhancement are suggestive of a neoplasm.[23] Isolated, focal, and distal appendiceal dilatation are

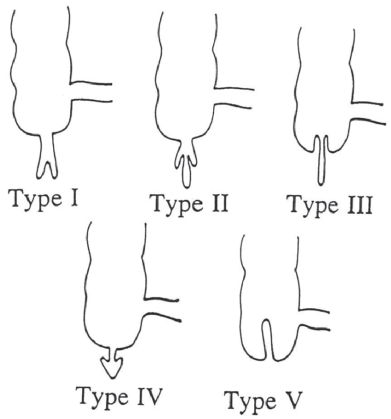

Fig. 6 A classification of appendiceal intussusceptions proposed by McSwain

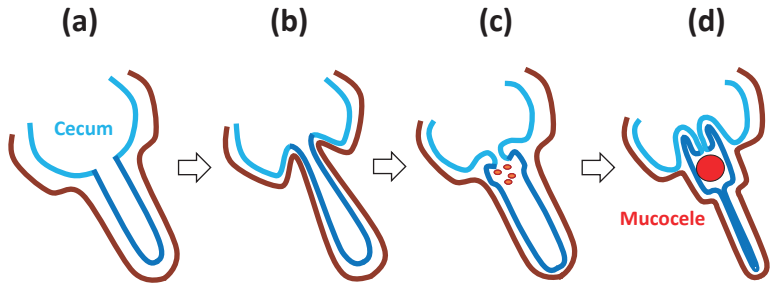

Fig. 7 Schematic representation of our hypothesis
Repeated partial invagination of the appendiceal root (b: type III McSwain classification) mechanically causes submucosal hyperplasia, obstruction of the appendiceal orifice, and drainage disturbance of the appendiceal content, resulting in mucin retention (c), as a result, an appendiceal mucocele be developed (d). (a–d, in that order).

often associated with mucinous appendiceal neoplasms.[24]

Differential diagnosis between non-neoplastic and neoplastic appendiceal mucoceles is challenging. Transabdominal ultrasonography or endoscopic ultrasonography, both of which were not performed in this case, can more precisely reveal anatomical architecture, which may have indicated partial invagination of the appendiceal epithelium.[19,20] Accordingly, less invasive surgical approaches, such as a partial cecectomy with preservation of the ileocecal valve, are adequate for non-neoplastic appendiceal mucoceles.

Although preoperative differentiation between non-neoplastic and neoplastic mucoceles is difficult, we hope for future progress in imaging modalities and the accumulation of more cases. Although rare, clinical suspicion of a non-neoplastic appendiceal mucocele, characterized by circumferentially inverted epithelium and submucosal hyperplasia at the appendiceal root, is necessary in cases of submucosal protuberance at the appendiceal orifice for appropriate treatment.

DISCLOSURES

Human/animal rights

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008(5).

Informed consent

Informed consent was obtained from the patient included in the study.

Authors' contributions

All authors contributed to the study conception and design. Material preparation and data collection were performed by Shuhei Asai, Hideo Miyake, Asayo Kato, Norihiro Yuasa, Rio Takada, and Masahiko Fujino. The first draft of the manuscript was written by Shuhei Asai, and all authors read and approved the manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

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