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## Case Report

# Appendiceal mucocele pathologically classified as appendiceal epithelial hyperplasia and preoperatively diagnosed by contrast-enhanced ultrasonography: A case report <sup>☆,☆☆</sup>

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## ARTICLE INFO

## Article history:

Received 28 October 2023

Revised 5 December 2023

Accepted 18 December 2023

Available online 4 January 2024

## ABSTRACT

We report a patient with a mucocele with diffuse wall thickening diagnosed by transabdominal ultrasonography and contrast-enhanced ultrasonography. Transabdominal ultrasonography showed diffuse thickening of the entire appendix wall and an anechoic area that appeared to be fluid collected throughout the appendix lumen. However, the “onion skin sign” was not detected. Contrast-enhanced ultrasonography combined with superb

Abbreviations: US, ultrasonography.

<sup>☆</sup> Acknowledgments: We thank Edanz (<https://jp.edanz.com/ac>) for editing a draft of this manuscript.

<sup>☆☆</sup> Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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<https://doi.org/10.1016/j.radcr.2023.12.033>

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**Keywords:**  
Appendix  
Mucocele  
Diagnosis  
Transabdominal ultrasonography  
Contrast-enhanced ultrasonography

microvascular imaging revealed abundant mucosal blood flow and no abnormal vascular network within the mucosa of the appendix wall. We preoperatively diagnosed a mucocele complicated by acute and chronic appendicitis, and ileocecal resection was performed. Macroscopic and microscopic findings of the resected specimens demonstrated that the appendiceal wall was diffusely thickened, with fibrosis and inflammatory cell infiltration, and that the appendiceal root lumen was narrowed with epithelial hyperplasia. No neoplastic changes were observed. The cause of the appendiceal mucocele was likely fibrosis and stenosis at the root of the appendix due to initial acute appendicitis.

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## Introduction

Appendiceal mucocele is a rare disease that occurs in 0.2%–0.7% of appendectomy patients. It is asymptomatic in approximately 50% of patients, and its most common symptom is abdominal pain [1]. Preoperative diagnosis can be difficult because the symptoms are similar to those of acute appendicitis. Some reports have shown that transabdominal ultrasonography (US) is useful for preoperative diagnosis of an appendiceal mucocele [2–7]. In patients with appendiceal diseases detected by transabdominal US, the detection rate of appendiceal mucocele was 6.6% [4]. The “onion skin sign” refers to the typical sonographic appearance of an appendiceal mucocele, the concentric layers of echogenic layering debris of which are seen within an enlarged and elongated appendix, and resemble the appearance of an onion in cross-section [4–7]. Herein, we present a patient with appendiceal mucocele with diffuse wall thickening without the ‘onion skin sign’ diagnosed by transabdominal US.

## Case report

A man in his 60s was hospitalized because of severe right lower abdominal pain. The symptoms had appeared suddenly at 2–3 hours before admission, after which the patient’s condition gradually deteriorated. Physical examination revealed tenderness in the right lower abdomen. Laboratory tests included a leukocyte count of 13,370 cells/mm<sup>3</sup> (normal 3500–9000 cells/mm<sup>3</sup>) and a C-reactive protein of 0.3 mg/dL (normal <0.3 mg/dL). His liver function, renal function, and platelet count were normal.

Transabdominal US (APLIO 500 TUS-A500; Canon Medical Systems, Otawara, Japan) showed diffuse thickening of the entire appendix wall (Fig. 1A) and an anechoic area that appeared to be fluid collected (Fig. 1B) throughout the appendix lumen. Contrast-enhanced US using perflubutane (Sonazoid; GE Healthcare, Oslo, Norway) showed a contrast effect at the root of the appendix (Fig. 1C, red arrow). Subsequent contrast-enhanced US combined with superb microvascular imaging revealed abundant blood flow in the mucosal layer and no abnormal vascular network within the mucosa of the appendix wall (Fig. 1D). Abdominal plain computed tomography showed diffuse appendiceal enlargement and diffuse wall thickening throughout the appendix wall, while the fatty tis-

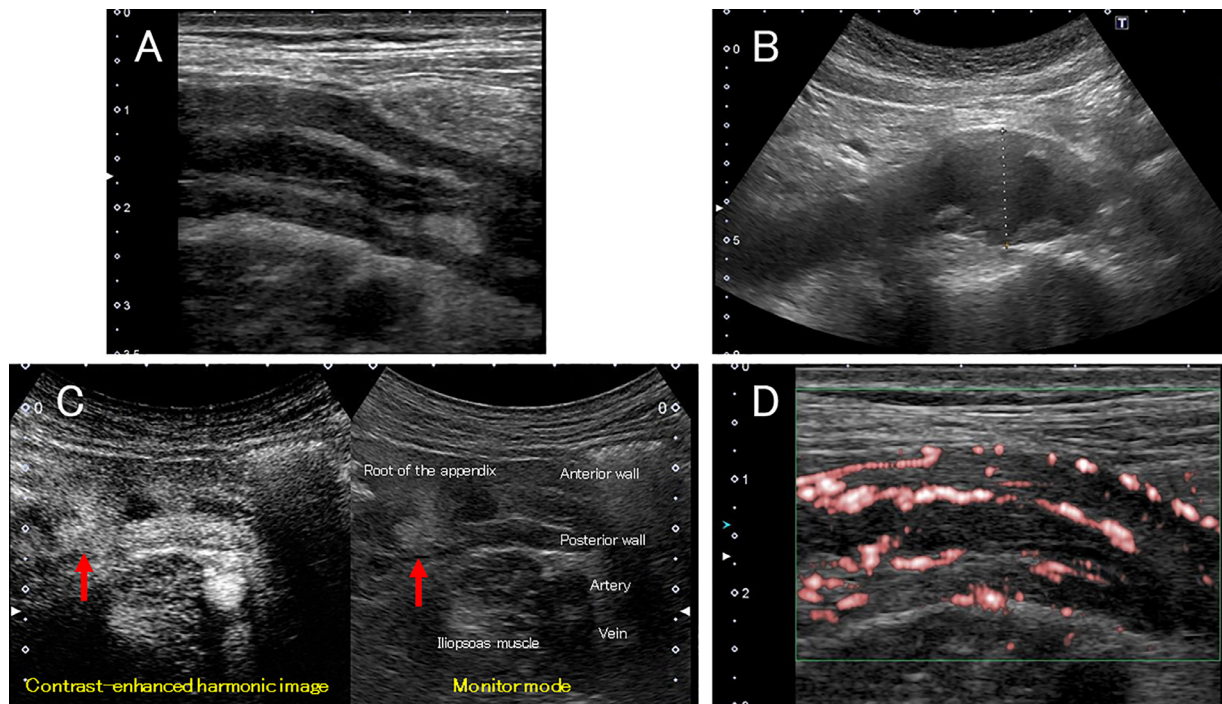
sue around the appendix was focally thickened. Neither extraluminal free air nor ascites was observed (Fig. 2A, B, red arrows). Colonoscopy showed a localized submucosal mass-like protrusion at the appendix orifice. No mucus leakage from the appendix orifice into the colon lumen was observed (Fig. 3).

We preoperatively diagnosed a mucocele complicated by acute and chronic appendicitis, and ileocecal resection was performed at 2 days after admission. The postoperative course was uneventful, and the patient was discharged on the 7th postoperative day. Macroscopic findings of the resected specimens demonstrated that the appendiceal wall was diffusely thickened, and the appendiceal lumen was dilated (Fig. 4A). The lumen of the root of the appendix was narrowed, and its surrounding area was fibrotic (Fig. 4A, red arrows). Microscopic findings demonstrated a thinned mucosal layer and a thickened muscle layer (Fig. 4B). Epithelial hyperplasia was observed at the root of the appendix (Fig. 4B, C). Fibrosis and inflammatory cell infiltration, which were predominantly lymphocytes, were observed in the appendiceal wall (Fig. 4B, D). No neoplastic changes were observed.

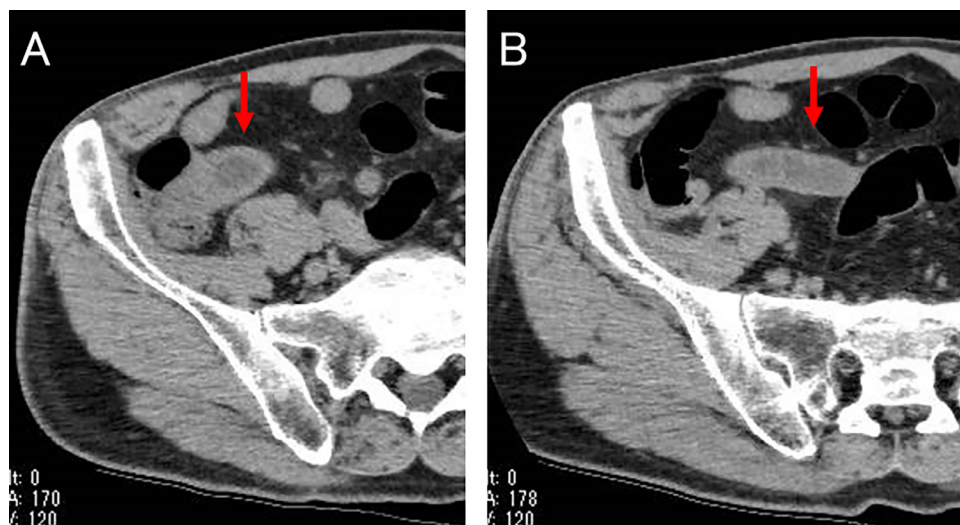
## Discussion

Appendiceal mucocele is pathologically classified into four groups: simple mucocele, epithelial hyperplasia, mucinous cystadenoma, and mucinous cystadenocarcinoma. Previous studies have reported rates of simple mucoceles in approximately 29% of appendiceal mucoceles, epithelial hyperplasia and mucinous cystadenoma in 31%–34% of appendiceal mucoceles, and mucinous cystadenocarcinoma in 5% of appendiceal mucoceles [1]. The present case exhibited epithelial hyperplasia.

On transabdominal US examination, the “onion skin sign” is considered a characteristic finding of an appendiceal mucocele. However, the cause of this imaging pattern has not been fully elucidated. Degani et al. reported a macroscopic view of the appendix that showed a heavy mucoid substance arranged in layers, and speculated that repeated sedimentation of the mucinous substance may cause the layered appearance [6]. Caspi et al. suggested that the gradual absorption of water and solutes may cause gelation of the mucin after secretion into the appendiceal cavity, and that the layering phenomenon may result from fluctuations in the secretion of mucin into the cavity or in the degree of excretion blockage from the cavity [7]. In the present case, there was no evidence



**Fig. 1 – Transabdominal ultrasonography findings.** Transabdominal ultrasonography findings included a diffuse thickening of the entire appendix wall (A) and an anechoic area with the appearance of fluid collection in the appendix lumen (B). Contrast-enhanced ultrasonography revealed a contrast effect at the root of the appendix (C, red arrows). Contrast-enhanced ultrasonography combined with superb microvascular imaging revealed an abundant mucosal blood flow and no abnormal vascular network within the mucosa of the appendix wall (D).

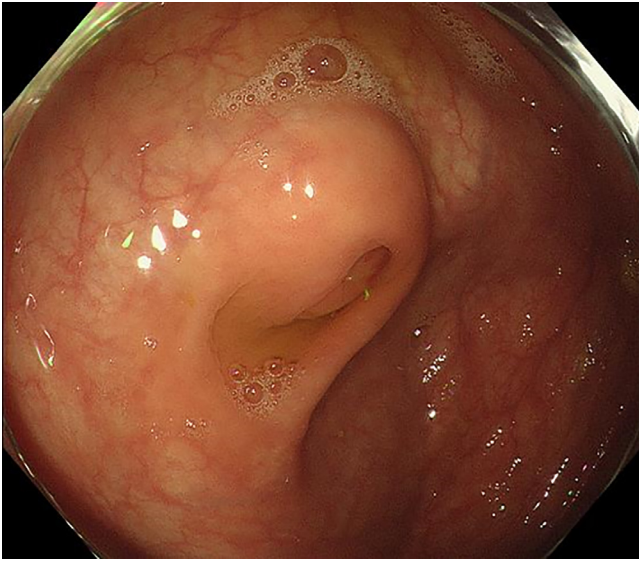


**Fig. 2 – Abdominal computed tomography.** Abdominal plain computed tomography showed diffuse appendiceal enlargement and diffuse wall thickening of the entire appendix wall, and the fatty tissue around the appendix was focally thickened (A, B, red arrows).

of the “onion skin sign” on transabdominal US. Bhagwanani et al. reported that mucin-filled appendices contain malignant cells [8]. Thus, in the present case, the mucin content may have been low in the fluid collecting in the appendiceal lumen because we found no tumor component on pathology in the resected specimen.

Transabdominal US is a valuable method for assessing various gastrointestinal diseases and clinical conditions [9,10]. Contrast-enhanced US is also useful for real-time assessment of local blood flow [11–13]. A prior case report demonstrated that appendiceal mucinous adenocarcinoma could be diagnosed preoperatively by evaluating blood flow in a focal





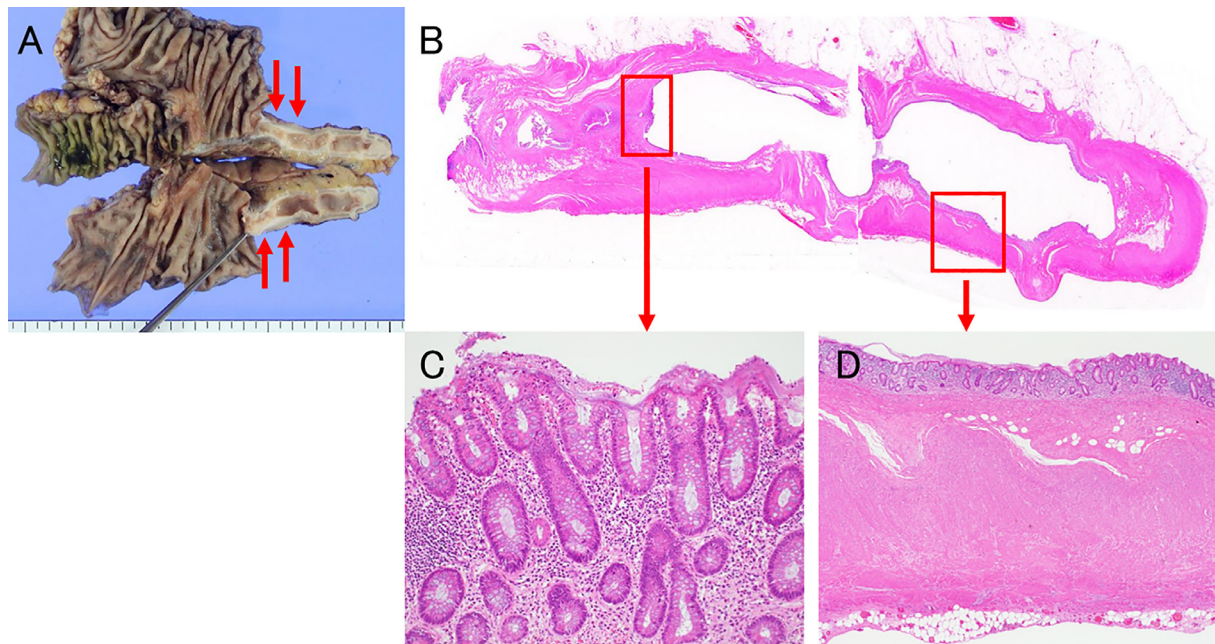
**Fig. 3 – Colonoscopy findings. Colonoscopy showed a localized submucosal mass-like protrusion at the appendix orifice.**

nodular lesion in the tumor cavity using contrast-enhanced US [12]. In the present case, contrast-enhanced US revealed a contrast effect at the root of the appendix. Contrast-enhanced US can also be used to evaluate vascular structure. For example, the microvascular structure in colon cancer was reported

to be irregular and characterized by large vessels, whereas acute inflammation was not observed [13]. In the present case, we found no vascular network abnormalities within the mucosa of the appendix wall, visualized by contrast-enhanced US. Therefore, we preoperatively ruled out a neoplastic lesion such as mucinous cystadenoma or mucinous cystadenocarcinoma. These findings were clearly confirmed without the need for contrast-enhanced computed tomography.

Appendiceal mucocele is a cystoid extension of the appendix caused by mucus accumulation in the appendix lumen. Kalmon et al. defined three factors that lead to the development of mucocele of the appendix: progressive narrowing of the valvular opening of the appendix, aseptically content, and sustained mucus production [14]. In the present case, macroscopic and microscopic findings of the resected specimen revealed diffuse thickening of the appendix wall, chronic inflammatory cell infiltration, epithelial hyperplasia in the appendix root, and stenosis of the appendix root with surrounding fibrosis. The occurrence of this appendiceal mucocele was likely caused by the following mechanisms. The initial appendicitis caused inflammation that spread to the root of the appendix, which resulted in a mild mucus drainage disorder. This was followed by chronic appendiceal inflammation and a persistent increase in internal pressure in the appendix, which resulted in fibrosis and hyperplasia of the appendix root.

In conclusion, we report a case of appendiceal mucocele with diffuse wall thickening diagnosed preoperatively using contrast-enhanced US. Transabdominal US and contrast-enhanced US are radiation-free, can be performed repeatedly, and have excellent real-time performance. These



**Fig. 4 – Macroscopic and microscopic findings of the resected specimen. Macroscopic findings demonstrated that the appendiceal wall was diffusely thickened, the appendiceal lumen was dilated (A), the lumen of the root of the appendix was narrowed, and its surrounding area was accompanied by fibrosis (A, red arrows). Microscopic findings demonstrated a thinned mucosal layer and thickened muscle layer (B). Epithelial hyperplasia was observed at the root of the appendix (B, C). Fibrosis and inflammatory cell infiltration were observed in the appendiceal wall (B, D).**

modalities are useful for the diagnosis of an appendiceal lesion.

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### Compliance with ethical standards

This study was conducted in accordance with the principles of the Declaration of Helsinki. This study was reviewed and approved by the Institutional Ethics Committee of Kawasaki Medical School (approval number: 6195-00). This article contains no studies involving human participants performed by any authors.

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### Patient consent

Written informed consent was obtained from the patient to publish this case report and any accompanying images.

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### REFERENCES

- [1] Rymer B, Forsythe RO, Husada G. Mucocoele and mucinous tumours of the appendix: a review of the literature. *Int J Surg* 2015;18:132–5. doi:10.1016/j.ijssu.2015.04.052.
- [2] Kim SH, Lim HK, Lee WJ, Lim JH, Byun JY. Mucocele of the appendix: ultrasonographic and CT findings. *Abdom Imaging* 1998;23:292–6. doi:10.1007/s002619900343.
- [3] Senturk M, Yavuz Y, Alkan S, Kafadar MT. The investigation of 14 appendiceal mucocele cases encountered in 4850 appendectomy patients. *J Gastrointest Cancer* 2021;52:701–5. doi:10.1007/s12029-020-00462-4.
- [4] Kameda T, Kawai F, Taniguchi N, Omoto K, Kobori Y, Arakawa K. Evaluation of whether the ultrasonographic onion skin sign is specific for the diagnosis of an appendiceal mucocele. *J Med Ultrason* (2001) 2014;41:439–43. doi:10.1007/s10396-014-0527-y.
- [5] Leshchinskiy S, Ali N, Akselrod D. The onion skin sign of appendiceal mucocele. *Abdom Radiol (NY)* 2018;43:2527–8. doi:10.1007/s00261-018-1489-0.
- [6] Degani S, Shapiro I, Leibovitz Z, Ohel G. Sonographic appearance of appendiceal mucocele. *Ultrasound Obstet Gynecol* 2002;19:99–101. doi:10.1046/j.1469-0705.2002.00510.x.
- [7] Caspi B, Cassif E, Auslender R, Herman A, Hagay Z, Appelman Z. The onion skin sign: a specific sonographic marker of appendiceal mucocele. *J Ultrasound Med* 2004;23:117–21 quiz 22–23. doi:10.7863/jum.2004.23.1.117.
- [8] Bhagwanani A, El-Sheikha J, Shah N, Thrower A, Carr NJ, Moran BJ. The appendix "mucocoele" misnomer: radiological terminology of "likely appendix mucinous neoplasm" better reflects pathology findings. *Clin Radiol* 2023;78:234–8. doi:10.1016/j.crad.2022.10.005.
- [9] Fujita M, Manabe N, Honda K, Murao T, Osawa M, Kawai R, et al. Usefulness of ultrasonography for diagnosis of small bowel tumors: a comparison between ultrasonography and endoscopic modalities. *Medicine (Baltimore)* 2015;94:e1464. doi:10.1097/MD.0000000000001464.
- [10] Manabe N, Kamada T, Hata J, Haruma K. New ultrasonographic evaluation of stool and/or gas distribution for treatment of chronic constipation. *Int J Colorectal Dis* 2018;33:345–8. doi:10.1007/s00384-018-2964-3.
- [11] Manabe N, Hata J, Haruma K, Imamura H, Kamada T, Kusunoki H. Active gastrointestinal bleeding: evaluation with contrast-enhanced ultrasonography. *Abdom Imaging* 2010;35:637–42. doi:10.1007/s00261-009-9588-6.
- [12] Wakui N, Fujita M, Yamauchi Y, Takeda Y, Ueki N, Otsuka T, et al. Mucinous cystadenocarcinoma of the appendix in which contrast-enhanced ultrasonography was useful for assessing blood flow in a focal nodular lesion in the tumor cavity: a case report. *Exp Ther Med* 2013;6:3–8. doi:10.3892/etm.2013.1094.
- [13] Onji K, Yoshida S, Tanaka S, Takemura Y, Oka S, Yoshihara M, et al. Microvascular structure and perfusion imaging of colon cancer by means of contrast-enhanced ultrasonography. *Abdom Imaging* 2012;37:297–303. doi:10.1007/s00261-011-9738-5.
- [14] Kalmon EH, Winningham EV. Mucocele of the appendix. *Am J Roentgenol Radium Ther Nucl Med* 1954;72:432–5.