

# Contrast-enhanced ultrasound improves accurate identification of appendiceal mucinous adenocarcinoma in an old patient

## A case report

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### Abstract

**Background:** Adenocarcinoma of appendiceal origin is far rarer than other colorectal carcinomas and its preoperative diagnosis is challenging. To our knowledge, utility of contrast-enhanced ultrasound (CEUS) to diagnose it is much less.

**Method:** A 61-year-old man presented with abdominal pain in the right lower quadrant for 20 days. In order to fulfill an accurately preoperative diagnosis, he received laboratory and imaging tests such as carcinoembryonic antigen (CEA), computer tomography (CT), CEUS and endoscope.

**Diagnosis and Intervention:** He was initially suspected of suffering appendicitis, while his white blood cell count was normal and carcinoembryonic antigen (CEA) in serum was remarkably increased. Both routine ultrasound and computer tomography (CT) examinations supported suppurative appendicitis. The overall data, however, failed to excluded neoplastic pathology thoroughly. Therefore, CEUS was carried out and showed an inhomogeneous enhancement intra the lesion located in the body of the appendix, which made our consideration of neoplasm. The result of the follow-up biopsy guided by endoscope was consistent with appendiceal tumor. The patient received laparoscopic right hemicolectomy. Histopathology confirmed as well differentiated mucinous adenocarcinoma of appendix origin. His postoperative course was uneventful, and he had a regular diet again without any complaint.

**Result:** Serum CEA was remarkably increased (12.00 ng/mL). Both routine ultrasound and CT examinations supported suppurative appendicitis. However, CEUS examination showed an inhomogeneous enhancement intra the lesion located in the body of the appendix, which made our consideration of neoplasm. The follow-up biopsy guided by endoscope and surgical specimens confirmed as well differentiated mucinous adenocarcinoma of appendix origin.

**Conclusion:** Most mucinous adenocarcinoma mimicking appendicitis results in difficult diagnosis preoperatively. Clinician and radiologist should be aware of it when old patient presented with appendicitis especially along with high level of CEA.

**Abbreviations:** ALT = alanine transaminase, AST = aspartate aminotransferase, CA199 = carbohydrate antigen 199, CEA = carcinoembryonic antigen, CEUS = contrast-enhanced ultrasound, CT = computer tomography, DBIL = direct bilirubin, HE = hematoxylin-eosin, LP = laparoscope, US = ultrasound.

**Keywords:** Appendiceal tumor, Appendicitis, CEA, CEUS, Mucinous adenocarcinoma

## 1. Introduction

Primary appendiceal adenocarcinomas is very rare malignant neoplasm accounting for 0.05% to 0.2% of all appendectomies and only 6% of all malignant tumors of appendix.<sup>[1]</sup> It is hard to be diagnosed since adenocarcinoma of appendix usually presents as acute appendicitis. Moreover, appendicitis resulting from ileocecal

tumor and inflammatory mass secondary to appendicitis are also hard to distinguish in clinic.<sup>[2]</sup> To clarify aforementioned situation is of great importance for clinical management because abscesses may sometimes require surgical or percutaneous drainage guided by ultrasound (US) or computer tomography (CT) whereas tumor usually needs appendectomy or even right hemicolectomy.

Contrast-enhanced ultrasound (CEUS) is a new technique that can provide information about blood perfusion for the lesion in real-time through intravenous injection of ultrasound contrast agent. For example, the difference in bowel wall microvasculature between healthy and diseased intestines can be determined by CEUS.<sup>[3]</sup> However, to our knowledge, applying CEUS to diagnose appendiceal tumor is rarely discussed except for Wakui's report.<sup>[4]</sup> Our current report describes a rare case of mucinous adenocarcinoma in appendix presenting with appendicitis, which is accurately identified with CEUS, rather than CT, owing to the inhomogeneous enhancement in the lesion located in the body of the appendix.

## 2. Case report

A 61-year-old man with a speeding up pain in the right lower quadrant for 20 days was admitted to our hospital. He reported no chills, fever, anorexia nausea, or vomiting. Two years ago, the patient first suffered abdominal pain and then recovered after

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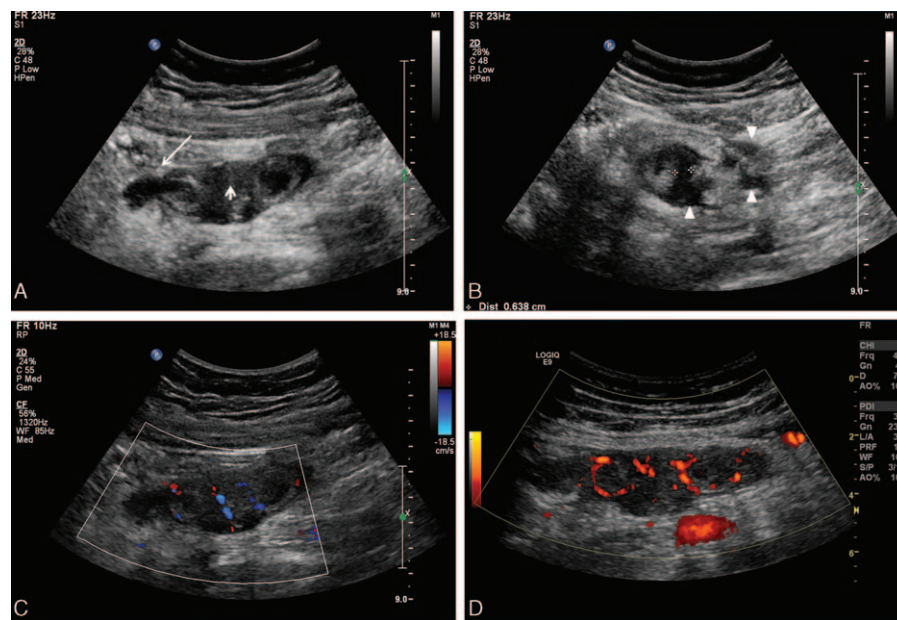
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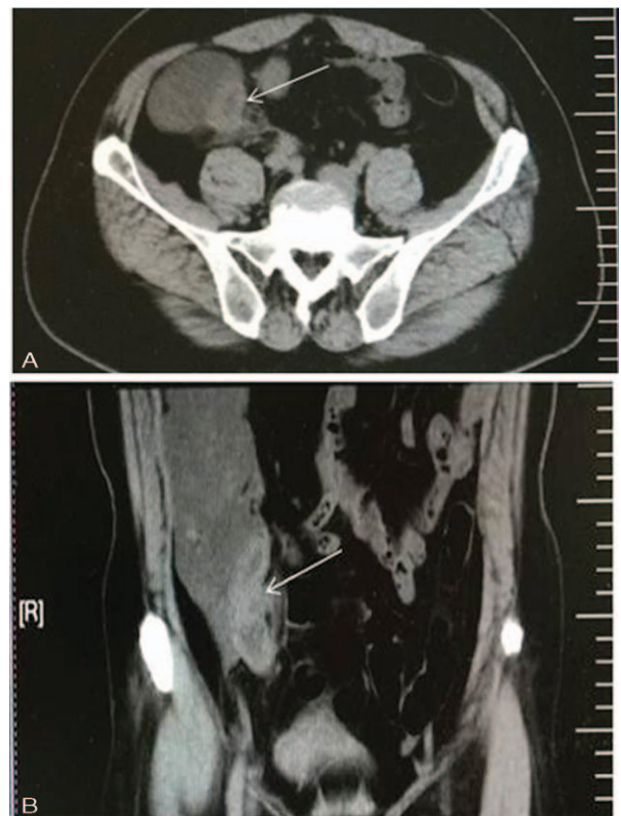
**Figure 1.** The longitudinal view of abdominal ultrasound (A) of reveals a suspected lesion (arrow) in the body of the appendix. Its characteristics are inhomogeneous, hypoechoic, ill-defined. Appendiceal ostium is marked by the arrowhead. Its transverse scanning (B) showing the posterior wall of the lesion is locally broken measuring about 6 mm in width and a smaller area of fluid surrounding the lesion and the appendix is marked as triangle sign. Color Doppler (C) and Power Doppler (D) show plenty of linear blood signals intra-lesion.

antibiotic therapy bases on the diagnosis of chronic appendicitis in a community hospital. Thereafter, the patient experienced the symptom interruptedly and moderately. Before admission to our hospital, he administrated cephalosporins of himself at home, which resulted in failure to relieve.

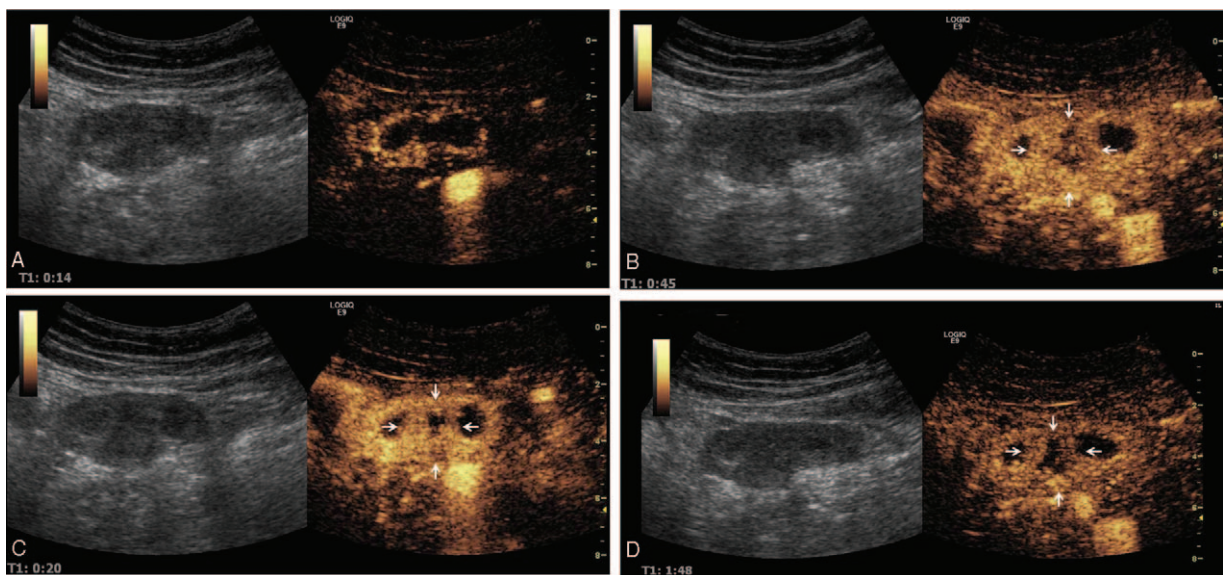
On physical examination for abdomen showed there was no rebound tenderness or muscular rigidity as well as any palpable mass apart from tenderness in the right lower quadrant. He denied family history of cancer and any co-morbidities such as cardiopulmonary diseases. Laboratory investigation revealed no left shift in leukocyte counts ( $5.07 \times 10^9/L$ , N:  $4-10 \times 10^9$ ), elevated carcinoembryonic antigen (CEA) (12.00 ng/mL, N: 0-3.4) and carbohydrate antigen 199 (CA199) (39.63 U/mL, N: 0-39) as well as slightly raised transaminase (alanine transaminase 58.00 U/L, N: 9-50; aspartate aminotransferase 43.00 U/L, N: 15-40) accompanied by increased direct bilirubin ( $9.80 \mu\text{mol/L}$ , N: 0-3.4).

On the first day of his hospitalization, abdominal US was performed using convex and linear transducers (C1-5 and 9L) of the GE Logic E9 scanner. US found appendix (size: 69 mm  $\times$  15 mm) had swollen wall up to 5 mm and dilated as well as fluid-filled lumen (diameter: 10 mm) on both ends of the appendix. A few amount of fluid surrounding the lesion and the appendix were seen, while no enlarged lymph node surrounding the lesion was detected. A heterogeneous area (20 mm  $\times$  20 mm) in the body of the appendix (Fig. 1A) was close to the posterior of the site where the distal wall of appendix was locally broken (range: 6 mm) (Fig. 1B). The abnormal area with ill-defined shape displayed plenty of vascular signal by Color Doppler and Power Doppler (Fig. 1C and D, respectively).

Subsequently, the patient received serial CT scans both of the abdomen and pelvis (Fig. 2). The abdominal CT showed cystic-solid shadow at the site corresponding to the appendix surrounded with scanty effusion. Besides, the cystic wall was thickened and separated. The lesion had no clear border



**Figure 2.** Axial (A) and coronal (B) CT images show cystic-solid shadow (arrowhead) at the site corresponding to the appendix surrounded with a small amount of effusion. Additionally, the cystic wall is thickened and separated. There is no accurate depiction of the diseased appendix and the cecum tissue. It is at last misdiagnosed as Purulent appendicitis by CT scan. CT=computer tomography.



**Figure 3.** Contrast-enhanced ultrasound images evaluating the lesion at 14 seconds, 20 seconds, 45 seconds, and 1 minute past 48 seconds are shown in the figures of A, B, C, and D, respectively. The heterogeneous lesion (arrowhead) displays mildly delayed and inhomogeneous enhancement compared with the normal appendiceal wall. The central part of the lesion largely shows low enhancement except for little non-enhancement and this low-enhanced area gets larger and larger gradually after 30 seconds. It is diagnosed as cystadenoma of the appendix other than Purulent appendicitis by CEUS. CEUS=contrast-enhanced ultrasound.

compared with cecum. At last, CT findings revealed suppurative appendicitis, while malignancy could not be excluded.

It remained challenged to determine whether the diseased appendix was an abscess or a neoplasm after US and CT scanning. Therefore, CEUS examination was suggested and performed by the same sonographer since the abnormally heterogeneous area yielded an easy diagnosis of suppurated appendicitis. A C1–5 convex probe was used in the examination at a low mechanical index (MI=0.15). According to the non-liver CEUS guideline,<sup>[5]</sup> the contrast agent SonoVue (Bracco, Milan, Italy) was injected as a bolus in units of 2.4 mL through a 20 gauge catheter into an antecubital vein, immediately followed by injection of 5 mL of normal saline solution (0.9% NaCl). The CEUS examination was recorded from the start of the bolus and for a 120 seconds period. The healthy appendiceal wall started to enhance at 14th second (Fig. 3A) and the enhancement was absent at the broken site of the far wall in the body of appendix and the outer area of the lesion presented mildly delayed iso-enhancement about 20 seconds (Fig. 3B), and its central part largely displayed hypo-enhancement except for a small amount of non-enhancement and the hypo-enhanced area got larger and larger gradually after 30 seconds (Fig. 3C and D). Generally, the heterogeneous area (22 mm × 21 mm measured with CEUS) presented mildly delayed and inhomogeneous enhancement. Appendiceal abscess was excluded and cystadenocarcinoma of appendix was highly suspected by the experienced sonographer because the typical characteristic of periappendicular abscess is absence of enhancement.

In order to exclude indeterminate tumor of colorectum, a follow-up electronic colonoscope was performed. A solid neoplasm with red and smooth surface exactly located on the appendicular ostium was detected (Fig. 4). There is no lesion such as ulcer, uplift in adjacent bowel in other part of colorectum. Meanwhile, the patient received biopsy guide by endoscope. It was then diagnosed pathologically as tubulovillous adenoma.

Finally, the patient received a laparoscopic right hemicolectomy. Macroscopically, the excised appendix sized about

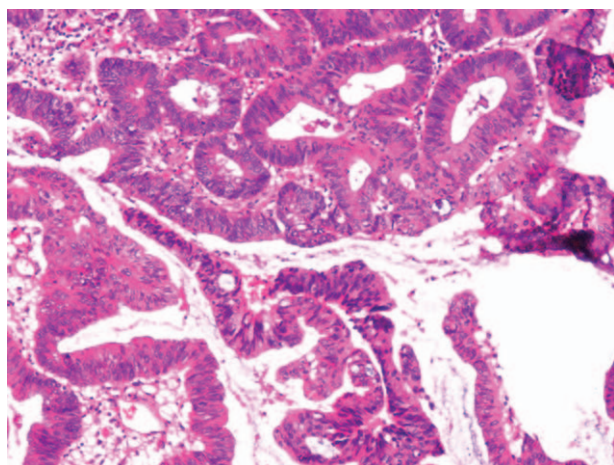
9 cm × 3 cm × 2.5 cm had reddish-gray and rough surface and gray-white mucus in the cavity of appendix. The mass (3.5 cm × 4.5 cm × 1.5 cm) invaded to the muscularis of appendix and adhered but not yet spread to surrounding connective tissue.

None of 11 excised lymph nodes showed disease involvement. The histology of hematoxylin-eosin (H&E) staining confirmed primary mucinous adenocarcinoma with well differentiation in appendix (Fig. 5). The low-grade mucinous adenocarcinoma of the appendix was determined to be stage of T2N0M0.

The postoperative course was smooth and his abdominal pain diminished. He was discharged 9 days after the operation. Due to early stage of the tumor, the patient did not get further chemotherapy. Currently, the patient finished initial reexamination that both abdomen CT finding and the serum level of CEA were normal at 1 month follow-up.



**Figure 4.** Electronic colonoscope shows a neoplasm with red and smooth surface is exactly located at the exit of the appendix.



**Figure 5.** A 100 times magnification hematoxylin-eosin (H&E) stained for specimen of the removal appendix reveals well-differentiated mucinous adenocarcinoma.

The timeline of the major progress of the patient was depicted in the Table 1. Written informed consent was obtained from the patient, and data had been de-identified.

### 3. Discussion

Acute appendicitis is the most common surgically abdominal emergency, while several other disease such as appendiceal adenocarcinoma, cecal carcinoma can still mimic it.<sup>[6]</sup> Our old male patient had right lower quadrant pain and elevated CEA as well as bilirubin, while mass palpation and inflammatory sign was unobvious. As we know, CEA levels can be elevated in a spectrum of medical conditions such as pancreatic, gastric, colon, and lung disease. However, its association with appendiceal pathology is rare except for 2 case reports.<sup>[7,8]</sup> The recent case report remind our careful investigation so as to exclude malignancy when enlarged appendix is associated elevated CEA levels.<sup>[7]</sup> Additionally, hyperbilirubinaemia was also

regarded as a predictive factor for complicated acute appendicitis such as perforation.<sup>[9]</sup> Besides, our patient had a 2-year history of uncertain appendicitis. Due to different management for complicated appendicitis or appendiceal tumor, comprehensively preoperative imaging modalities such as ultrasound, CT, CEUS as well as colonoscope are essential.

CT has largely become standard of diagnosing appendicitis at the expense of increased radiation exposure, cost, and time to surgical intervention,<sup>[10]</sup> whereas ultrasound is becoming more and more popular and is recommended as an appropriately initial test to evaluate patients such as children and pregnant women with suspected acute appendicitis in emergency by virtue of quickness, flexibility, cheapness, and free of ionizing radiation.<sup>[11,12]</sup> It is critical that the experienced sonographer found the posterior wall of oedematous appendix is regionally broken without accompanied with highly tensive tube and recommended CEUS to clinical doctor. In fact, the accuracy of ultrasound in diagnosing appendicitis is easily influenced by many factors coming from patient (obesity, pain, bowel gas) or operator (experience, skill), which results in false-negative diagnosis of appendicitis.<sup>[13]</sup> CEUS, a cheaper and nonradioactive technique compared with CT, can provide important information about blood perfusion in the diseased region in a real-time way. It is already recommended to evaluate disease activity and distinguishing between fibrous and inflammatory strictures for Inflammatory Bowel Disease in the EFSUMB Guidelines<sup>[5]</sup>. According to previous research in colon's disease, CEUS explored the diagnosis of phlegmon was made when intralesional enhancement was seen, while abscesses showed absence of enhancement in the hypoechoic mass.<sup>[14,15]</sup> However, applying CEUS into appendix is less discussed except for a literature about distinguishing between phlegmon and abscess in acute appendicitis.<sup>[16]</sup> The patient's lesion in site of appendix showed fast and inhomogeneous mode of enhancement, which helped us to exclude periappendicular abscess.

Although we had already got biopsy before surgery, the neoplasm from exit of appendix, or ileum, or caecum, or ascending colon is still explicit. Hence, laparoscope was chose for careful exploration before excision. Laparoscopic (LP) technique is typically used for uncomplicated appendicitis, while some

**Table 1**

**The timeline of the major progress of the patient diagnosed as appendiceal mucinous adenocarcinoma.**

Time	Items
February 2014	The patient was onset of abdominal pain on the right lower quadrant and then diagnosed as chronic appendicitis in a community hospital. His abdominal pain diminished after antibiotic therapy
2014–2016	He experienced the symptom interruptedly and his symptom relieved after taking anti-inflammatory drug by himself
January 2016	He suffered abdominal pain heavily and failed to control under the management of acute appendicitis in other hospital
February 1, 2016	He was admitted to our hospital with complain of abdominal pain. Physical test showed tenderness on the right lower quadrant. Blood test showed increased CEA, CA199, ALT, AST, and DBIL
February 2, 2016	Abdominal US revealed dilated and fluid-filled lumen on both ends of the appendix with swollen wall and a heterogeneous area in the body of the appendix
February 3, 2016	Abdominal CT showed cystic-solid shadow at the site of the appendix surrounded with scanty effusion without clear border to cecum
February 4, 2016	CEUS displayed the heterogeneous area presenting with mildly delayed and inhomogeneous enhancement compared with healthy appendix wall. Appendiceal abscess was excluded and cystadenocarcinoma was highly suspected
February 5, 2016	Electronic colonoscope showed a solid neoplasm with red and smooth surface exactly located on the appendicular ostium
February 6, 2016	The pathological result for biopsy guided by colonoscope was tubulovillous adenoma
February 8, 2016	He received a laparoscopic right hemicolectomy. The tumor invaded to the muscularis of appendix was determined to be stage of T2N0M0
February 9, 2016	Postoperative pathology confirmed appendiceal mucinous adenocarcinoma with well differentiation
February 17, 2016	He was discharged without complain of abdominal pain
March 19, 2016 (first time of follow up)	CT showed no postoperative complications finding, and the serum level of CEA was normal

ALT = alanine transaminase, AST = aspartate aminotransferase, CA199 = carbohydrate antigen 199, CEA = carcinoembryonic antigen, CEUS = contrast-enhanced ultrasound, CT = computer tomography, DBIL = direct bilirubin, US = ultrasound.

mimicking entities require an oncologic surgical approach and still others, such as benign dilation in cystic fibrosis, should not undergo surgery.<sup>[6]</sup>

Primary appendiceal adenocarcinomas are extremely rare malignancy making up only 6% of all malignant tumors of appendix.<sup>[1]</sup> The mean age at presentation for mucinous adenocarcinoma is about 50 years with a men predominance of 4:1,<sup>[17]</sup> and it is quite hard to be diagnosed since it often presents as acute appendicitis or as a palpable abdominal mass and some even without symptom. The traditional treatment for mucinous adenocarcinoma confined to the appendix is right hemicolectomy.<sup>[18]</sup> But in case of intra abdominal metastasis the treatment consists of aggressive debunking followed by adjuvant chemoradiotherapy along with it.<sup>[19]</sup> Therefore, histopathological examination of all appendicectomy specimens is mandatory to rule out malignant pathology.<sup>[20]</sup>

After careful study of our case and other related literatures, it remind us the investigations should be careful to exclude malignant lesion when we met old male patients presenting with appendicitis accompanied by elevated CEA. Most importantly, please do not forget to refer to CEUS, if possible.

#### 4. Conclusions

Malignancy of the appendiceal presenting with appendicitis is easily misdiagnosed in clinical. Therefore, comprehensive examinations including US, CEUS, CT, endoscope, and LP are essential, which avoid the events of appendectomy at the first stage and then excise of right hemicolectomy at the second stage procedure. This rare case we reported is inspiring because we made a more rewarding strategy in light of CEUS findings instead of CT or US. CEUS is also an alternative to evaluate old patient mimicking appendicitis with increased CEA especially when abscess and neoplasm are indeterminate by US and CT.

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