Clin J Gastroenterol (2016) 9:203–207
DOI 10.1007/s12328-016-0660-9

CASE REPORT

Acute appendicitis with a neuroendocrine tumor G1 (carcinoid): pitfalls of conservative treatment

Hiroyuki A. Watanabe[1,6] · Taketoshi Fujimoto[2] · Yo Kato[3] · Mayumi Sasaki[4] · Toshikazu Ikusue[5]

Received: 11 August 2015 / Accepted: 31 May 2016 / Published online: 16 June 2016

Abstract A man in his early thirties presented to our clinic with right lower abdominal pain. Computed tomography (CT) and ultrasonography (US) revealed a swollen appendix and an appendicolith. Abscess formation was not observed but ongoing appendiceal rupture was not ruled out. Three months after successful conservative therapy, the lumen of the apical portion was kept dilated and laparoscopic interval appendectomy was performed. No tumorous findings were observed macroscopically. However, histology revealed many tiny nests infiltrating the submucosa, muscular layer, and subserosa at the root of the appendix. An appendiceal neuroendocrine tumor G1 (NET G1; carcinoid) was diagnosed immunohistologically. Neither CT nor US visualized the tumor because of its non-tumor-forming but infiltrative growth. In conclusion, after successful conservative treatment, interval appendectomy should be considered to uncover a possible appendiceal NET G1 (carcinoid), particularly when dilatation of the distal lumen is kept under observation.

Keywords Appendicitis · NET G1 (carcinoid) · Interval appendectomy

Introduction

Appendectomy is widely accepted as the first-line treatment for acute appendicitis in the absence of abscess formation and peritonitis [1]. However, controversy remains over the therapeutic options after conservative treatment [2–8]. Here, we describe a case of a neuroendocrine tumor G1 (NET G1; carcinoid) that was found by performing interval appendectomy after successful conservative treatment.

Case report

A man in his early thirties visited the Yokohama Clinic at Kanagawa Dental University (Yokohama, Japan) three - months before surgery with right lower abdominal pain of previous day onset. His family and medical history were not contributory. On physical examination, his body temperature was 37.1 °C, blood pressure was 114 mmHg systolic and 66 mmHg diastolic, and pulse rate was 98 beats/min. His abdomen was flat and soft, but there was tenderness at the right lower quadrant.

He showed no symptoms of skin flushing, erythema, bronchospasm, diarrhea, or right-sided valvular heart disease.

Laboratory results revealed leukocytosis at 14,990/μL, with a neutrophil proportion of 80.6 % (normal range

✉ Hiroyuki A. Watanabe
aozora1@himawarifukushi.or.jp

1 Department of Gastroenterology, Yokohama Clinic, Kanagawa Dental University, 3-31-6 Tsuruya-cho, Kanagawa-ku, Yokohama, Japan

2 Department of Surgery, Hiratsuka Gastroenterological Hospital, Tokyo, Japan

3 Department of Pathology, Nikko Medical Center, Dokkyo Medical University, Nikko, Japan

4 Department of Radiology, Shiseikai Daini Hospital, Tokyo, Japan

5 Department of Internal Medicine, Showa University Northern Yokohama Hospital, Yokohama, Japan

6 Present Address: Kohnan Aozora, Facility for the Elderly, 2187-1 Noba-cho, Kohnan-ku, Yokohama 234-0056, Japan

42.0–74.0 %), and an elevated C-reactive protein level of 5.93 mg/dL (normal range 0.00–0.30 mg/dL). Contrast-enhanced computed tomography (CT) revealed a retrocecal appendix with a thickened wall, an appendicolith, periappendiceal fluid collection, and fatty tissue enhancement in the ileocecal region. Abscess formation was not observed but ongoing appendiceal rupture was not ruled out (Fig. 1). Ampicillin sodium (3 g) and levofloxacin hydrate (500 mg) were administered for 2 and 8 days, respectively. He had no symptoms and no abnormal laboratory findings after completion of the treatment.

One month later, the patient visited Hiratsuka Gastroenterological Hospital (Tokyo, Japan) and requested laparoscopic appendectomy. Ultrasonography (US) showed a swollen vermiform appendix maintaining the layered structure of the wall and an appendicolith. The appendicolith that was expelled from the lumen measured 8 mm in diameter (Fig. 2a). The lumen of the apical portion was dilated (Fig. 2b). Interval appendectomy was performed three months after conservative treatment. The excised appendix measured 6 mm in width at the root, while the apical portion was enlarged up to 13 mm in diameter. An appendicolith was found outside the appendix without any evidence of rupture (Fig. 3). No findings of acute appendicitis were revealed histopathologically. However, many tiny nests were seen infiltrating the submucosa, muscular layer, and subserosa at the root of the appendix. The infiltrative area measured 11 mm in maximum diameter. The tiny nests consisted of uniform small round cells with a small round hyperchromatic nucleus and granular cytoplasm by hematoxylin and eosin (H&E) staining (Fig. 4a, b). The granular cytoplasm showed positive for chromogranin A staining (Fig. 4c, d). The mitotic count using MIB-1 antibody revealed <1 % and an appendiceal NET G1 (carcinoid) was diagnosed immunohistologically [9]. The patient has been well for 30 months

Fig. 1 Contrast-enhanced computed tomography scan revealing thickening of the appendiceal wall and an appendicolith measuring 8 mm in diameter. Abscess formation is not observed but ongoing appendiceal rupture is not ruled out

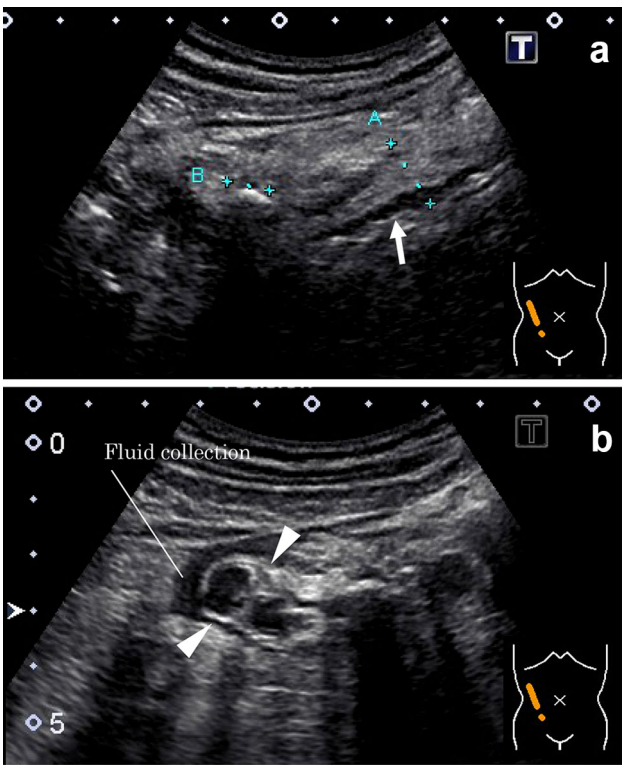

Fig. 2 **a** Ultrasonogram revealing a swollen vermiform appendix measuring 13 mm in width behind the cecum and maintaining the layer structure of the wall, as well as an appendicolith measuring 8 mm in diameter that was expelled from the lumen. There is no obvious lump of the appendix between the appendicolith and the root (*arrow*). **b** Ultrasonogram revealing a dilated lumen of the apical portion (*arrowhead*) of the appendix. A small amount of fluid collection is noted around the apical portion

Fig. 3 Macroscopic findings of the excised appendix which measured 5 cm in length and 6 mm in width at the root (*lower right side*), while the apical portion (*lower left side*) was enlarged up to 13 mm in diameter. The appendicolith, shown above the excised appendix, was broken and fragmented during the surgical procedure

since discharge and has undergone periodic health examinations at Hiratsuka Gastroenterological Hospital.

Discussion

In our case, acute appendicitis and an appendicolith were treated successfully by conservative therapy. Three months later, laparoscopic interval appendectomy was performed, which revealed a NET G1 (carcinoid).

The patient had no carcinoid syndrome (skin flushing, erythema, bronchospasm, diarrhea, or right-sided valvular heart disease). The syndrome is rarely observed in NET G1 (carcinoid) of the appendix [10].

Appendicoliths are reported to be associated with severe appendicitis [11–15]. However, in this case, appendiceal rupture occurred insidiously without abscess formation and

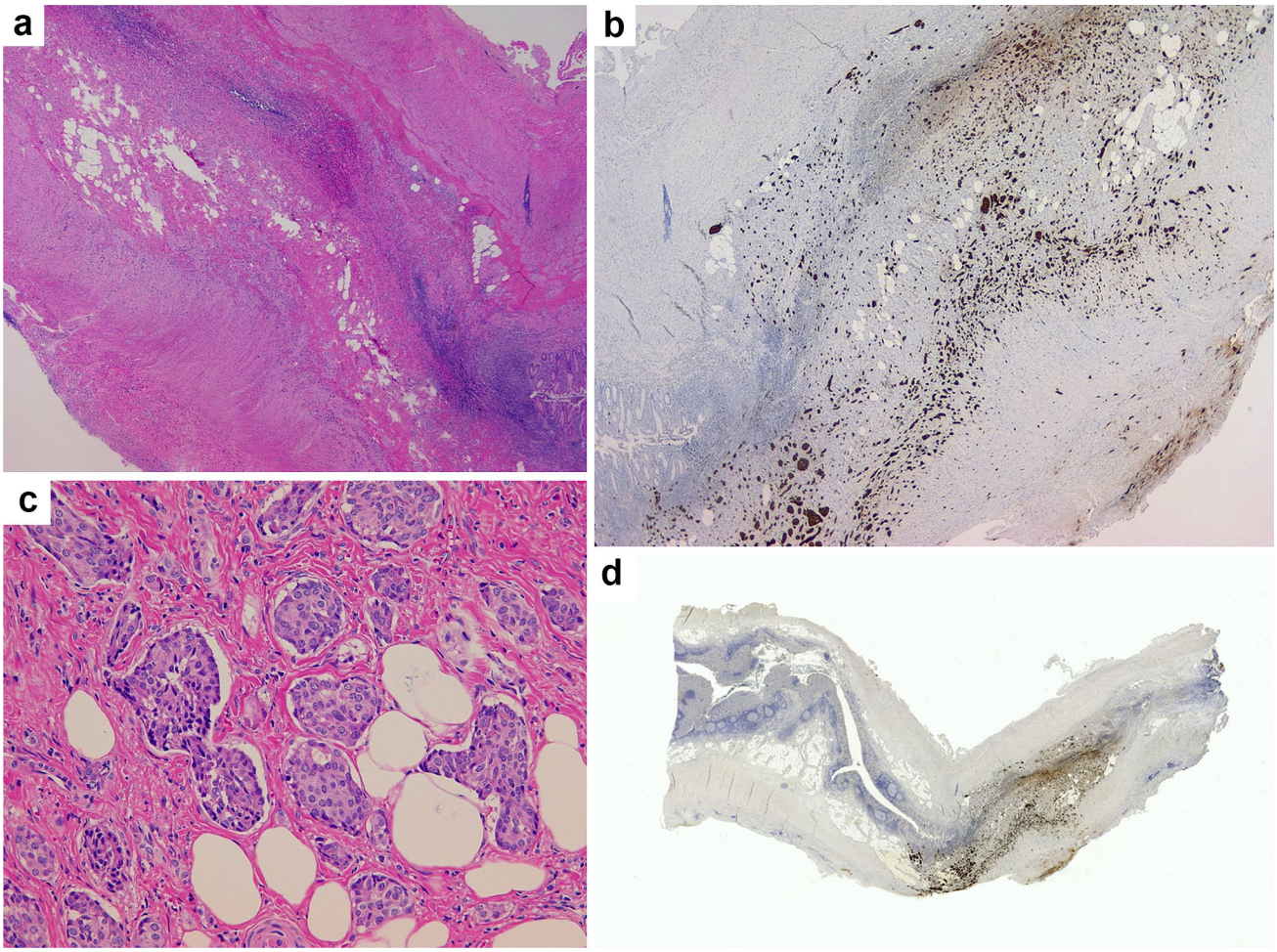

Fig. 4 **a** Histopathologic feature showing many tiny nests infiltrating the submucosa, muscular layer, and subserosa (H&E staining, magnification ×20). **b** Histopathologic feature showing many tiny nests consisting of uniform small round cells with a small round hyperchromatic nucleus and granular cytoplasm (H&E staining, magnification ×200). **c** Histopathologic feature showing the nests testing positive for chromogranin A (chromogranin A staining, magnification ×20). **d** Loupe view of half of the excised appendix. The right end is the cut-end of the appendix. The tumor shows non-tumor-forming but infiltrative growth (chromogranin A staining)

was repaired successfully by conservative treatment, because an appendicolith was found outside the appendix during surgery. On the other hand, pathology could not demonstrate drilling sites of the excised appendix. Although the patient has a risk of dissemination, he has been well and neither CT nor US has revealed abnormal findings for 30 months since discharge.

US revealed a swollen vermiform appendix maintaining the layer structure of the wall three months after conservative therapy. We sometimes see swollen appendix after conservative therapy of acute appendicitis; however, an appendiceal tumor is not suspected unless a hypoechoic mass is revealed [16–18].

There are no reports of an appendiceal NET G1 (carcinoid) measuring ≤1.5 cm being identified on preoperative CT [19]. On the other hand, hypoechoic masses measuring 10 mm × 10 mm visualized by US were diagnosed as NET G1 (carcinoid) histologically [16]. This shows that US is more suitable for diagnosis of an appendiceal tumor than CT. In our case, the appendiceal NET G1 (carcinoid) was 11 mm in maximum diameter and neither CT nor US visualized the tumor because of its infiltrative growth, but US depicted persistent luminal dilatation of the apical portion. When the tumor is located in the body or root of the appendix, acute appendicitis is liable to be complicated because of luminal obstruction [20, 21]. An appendectomy is indicated whenever US reveals persistent dilatation of the appendiceal lumen, even if the patient shows clinical improvement [17]. In our case, it is suspected that the NET G1 (carcinoid) induced acute appendicitis. Fortunately, the risk of recurrent appendicitis was avoided by interval appendectomy.

The incidence of an appendiceal NET G1 (carcinoid) has been reported to be 0.3–1.1 % of appendectomy specimens; 76–78 % are <1 cm in diameter [10, 19, 21]. In a long-term study of 150 unselected patients with appendiceal NET G1 (carcinoid), none of the 127 tumors measuring <2.0 cm in diameter showed metastasis. Therefore, appendectomy is considered to be adequate treatment for NET G1 (carcinoid) measuring <1 cm [19]. Furthermore, in a study of 18 conservatively managed patients with acute appendicitis who underwent interval appendectomy, an appendiceal NET G1 (carcinoid) was found in one patient [22].

In conclusion, after successful conservative treatment, interval appendectomy should be considered to uncover possible appendiceal NET G1 (carcinoid), particularly when dilatation of the distal lumen is kept under observation.

Compliance with ethical standards

Conflict of Interest: Hiroyuki A.Watanabe, Taketoshi Fujimoto, Yo Kato, Mayumi Sasaki and Toshikazu Ikusue declare that they have no conflict of interest.

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 1964 and its later amendments.

Informed Consent: Informed consent was obtained from all patients for being included in the study.

References

1. Fitz RH. Perforating inflammation of the vermiform appendix with special reference to its early diagnosis and treatment. Am J Med Sci. 1886;92:321–46.
2. Vons C, Barry C, Maitre S, et al. Amoxicillin plus clavulanic acid versus appendectomy for treatment of acute uncomplicated appendicitis: an open-label, non-inferiority, randomised controlled trial. Lancet. 2011;377:1573–9.
3. Varadhan KK, Neal KR, Lobo DN. Safety and efficacy of antibiotics compared with appendicectomy for treatment of uncomplicated acute appendicitis: meta-analysis of randomized controlled trials. BMJ. 2012;344:e2156.
4. Varadhan KK, Humes DJ, Neal KR, et al. Antibiotic therapy versus appendectomy for acute appendicitis: a meta-analysis. World J Surg. 2010;34:199–209.
5. Simillis C, Symeonides P, Shorthouse AJ, et al. A meta-analysis comparing conservative treatment versus acute appendectomy for complicated appendicitis (abscess or phregmon). Surgery. 2010;147:818–29.
6. Kobayashi S, Ohshima R, Katayama M, et al. Treatment outcomes for laparoscopic interval appendectomy (LIA) in the treatment of abscess-forming appendicitis. Jpn J Gastroenterol Surg. 2012;45:353–8 **(in Japanese, with English abstract)**.
7. Teixeira PG, Demetriades D. Appendicitis: changing perspectives. Adv Surg. 2013;47:119–40.
8. Mason RJ. Appendicitis: is surgery the best option? Lancet. 2011;377:1545–6.
9. Komminoth P, Arnold R, Capella C, et al. Neuroendocrine neoplasms of the appendix. In: Bosman FT, Carneiro F, Hruban RH, Theise ND, editors. WHO classification of tumours of the digestive system. Lyon: International Agency for Research on Cancer; 2010. p. 126–8.
10. Anton R, William CW, Leslie WO. Carcinoid tumors of the appendix. Ann Surg. 1993;217:385–90.
11. Ishiyama M, Yanase F, Taketa T, et al. Significance of size and location of appendicoliths as exacerbating factor of acute appendicitis. Emerg Radiol. 2013;20:125–30.
12. Yeung KW, Chang MS, Hsiao CP. Evaluation of perforated and nonperforated appendicitis with CT. Clin Imaging. 2004;28:422–7.
13. Ein SH, Langer JC, Daneman A. Non operative management of pediatric ruptured appendix with inflammatory mass or abscess: presence of an appendicolith predicitis. J Pediatr Surg. 2005;40:1612–5.
14. Kondo NI, Kohno H. Retained appendicolith in an inflamed appendix. Emerg Radiol. 2009;16:105–9.
15. Shindoh J, Niwa H, Kawai K, et al. Predictive factors for negative outcomes in initial non-operative management of suspected appendicitis. J Gastrointest Surg. 2010;14:309–14.
16. Rioux M, Duchesne N, Langis P. Carcinoid tumor of the appendix: ultrasound findings in two cases. J Clin Ultrasound. 1994;22:129–33.
17. Hermans JJ, Hermans AL, Risseeuw GA, et al. Appendicitis caused by carcinoid tumor. Radiology. 1993;188:71–2.
18. Deeg KH, Reisig A, Seitz G. Sonographic diagnosis of a carcinoid tumour of the appendix in a 14-year-old boy. Ultraschall Med. 2003;24:120–2.

19. Courtney AC, Bendon CN, Ricardo DM, et al. Carcinoid tumors of the appendix: are these tumors identifiable prospectively on preoperative CT? Am Surg. 2010;76:273–5.
20. Pickhardt PJ, Levy AD, Rohrmann CA Jr, et al. Primary neoplasms of the appendix: radiologic spectrum of disease with pathologic correlation. Radiographics. 2003;23:645–62.
21. Moertel CG, Weiland LH, Nagorney DM, et al. Carcinoid tumor of the appendix: treatment and prognosis. N Engl J Med. 1987;317:1699–701.
22. Carpenter SG, Chapital AB, Merritt MV, et al. Increased risk of neoplasm in appendicitis treated with interval appendectomy: single-institution experience and literature review. Am Surg. 2012;78:339–43.