

# Colonic mucinous adenocarcinoma causing intussusception and distant metastasis

## A case report

Xiaohui Xu, MS\*, Zhiyuan Kong, BS, Ke Yi, BS, Bing Wang, MS, Qingjun Lei, MS, Yi Wang, MS\*

### Abstract

**Rationale:** Cases of intussusception caused by mucinous carcinoma have been rarely reported, and those caused by colonic mucinous adenocarcinoma (MAC) with distant metastasis were even fewer.

**Patient concerns:** A 60-year-old woman who complained of severe pain around the navel with nausea and vomiting for a week was admitted on November 28, 2017. There were multiple watery stools and abdominal pain was worsened over the prior week.

**Diagnosis:** She was diagnosed by abdominal computed tomography, current medical history, and abdominal signs. Her initial diagnosis was acute abdomen, intussusceptions, and intestinal obstruction. The final diagnosis was MAC, which was based on postoperative pathology.

**Interventions:** The patient received emergency laparotomy, followed by 5 courses of chemotherapy with oxaliplatin plus capecitabine, and then 6 courses with 5-fluorouracil + oxaliplatin + calcium leucovorin.

**Outcomes:** The patient was in good nutritional condition, and no obvious tumor recurrence or metastasis was found until July 9, 2018.

**Lessons:** Even though the prognosis of colonic MAC is poor, being able to receive timely surgical treatment, good nutritional status and reasonable postoperative chemotherapy are the key factors to prolonging patient's survival.

**Abbreviations:** CT = computed tomography, EUS = endoscopic ultrasound, FOXM1 = forkhead box M1, MAC = mucinous adenocarcinoma, MRI = magnetic resonance imaging.

**Keywords:** colon, distant metastasis, intussusception, mucinous adenocarcinoma

Editor: N/A.

XX, KZ, and YK contributed equally to this work.

This work was supported by the National Natural Science Foundation of China (81703022) and the Jiangsu Province Key Youth Talents Project (QNRC2016262).

All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. And the study was approved by the Ethics Committee of the First People's Hospital of Taicang (Ethical approval number: KY20181128).

Informed written consent was obtained from the patient for publication of this case report and accompanying images.

The authors have no conflicts of interest to disclose.

Department of General Surgery, The First People's Hospital of Taicang City, Taicang Affiliated Hospital of Soochow University, Suzhou, China.

\* Correspondence: Xiaohui Xu, Department of General Surgery, The First People's Hospital of Taicang City, Taicang Affiliated Hospital of Soochow University, No.58 Changsheng South Road, Taicang, Suzhou, 215400, China (e-mail: Xhxu\_tc1988@suda.edu.cn); Yi Wang, Department of General Surgery, The First People's Hospital of Taicang City, Taicang Affiliated Hospital of Soochow University, No.58 Changsheng South Road, Taicang, Suzhou, 215400, China (e-mail: wangyi\_1966@126.com).

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Medicine (2019) 98:21(e15740)

Received: 19 December 2018 / Received in final form: 11 April 2019 / Accepted: 26 April 2019

<http://dx.doi.org/10.1097/MD.00000000000015740>

## 1. Introduction

Mucinous adenocarcinoma (MAC) occurs in a variety of human organ systems, including the digestive system,<sup>[1]</sup> respiratory system,<sup>[2]</sup> urinary system,<sup>[3]</sup> gynecological system<sup>[4]</sup> and even the integumentary system.<sup>[5]</sup> The histological diagnostic criterion for MAC is that more than 50% of the tumor tissue is composed of extracellular mucin.<sup>[6]</sup>

MAC accounts for approximately 10% of colon cancers and is usually more aggressive than non-MAC colon cancer.<sup>[7-9]</sup> MAC is also more frequent in female patients which occurs mostly in the right colon. Distant metastasis of colonic MAC often involves the ovaries. Niteck et al<sup>[10]</sup> have reported 23 cases of equivocal MAC tumors with 13 cases of ovarian metastasis. MAC of the colon has also been reported to have isolated splenic metastases.<sup>[11]</sup> There are related documentations of mucinous appendiceal tumors leading to intussusception<sup>[12,13]</sup>; however, a single ileocecal MAC without appendiceal MAC-leading to intussusception has been rarely reported.

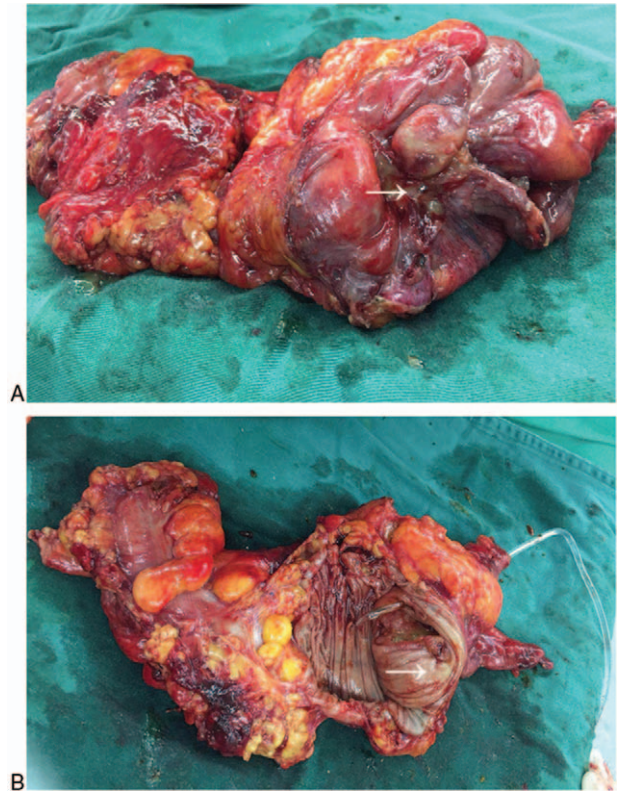
## 2. Case report

This study was approved by the Human Ethics Committee of The First People's Hospital of Taicang City. Informed written consent was obtained from the patient for publication of this case report and accompanying images. A 60-year-old female patient was suffering from pain around the navel 1 week prior. Her abdominal pain was a paroxysmal spasmodic pain accompanied by nausea and vomiting, and it was not relieved after vomiting. In addition, there had increased defecation of mostly watery stools. On November 28, 2017, the patient was initially admitted to the



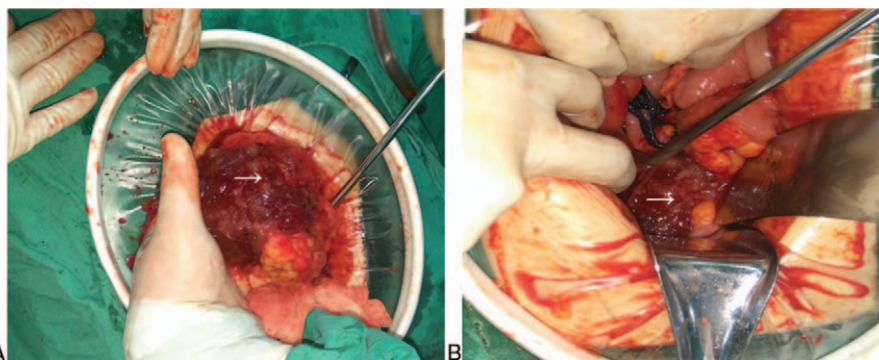
**Figure 1.** Preoperative enhanced CT: A. ileocecal intussusception, B. appendix, C. omental tumor, D. pelvic and right ovarian tumors. CT = computed tomography.

Department of Gastroenterology, and a computed tomography (CT) examination of the abdomen revealed a concentric ring-like change, swelling, exudation, and peritoneal effusion in the ileocecal region. A subsequent enhanced abdominal CT examination revealed that an ileocecal tumor might be the cause of the intussusception and peritoneal effusion (Fig. 1). After surgical consultation, the patient was treated with emergency surgery on November 30, 2017. When we opened the abdominal cavity, we found a large amount tan gelatinous liquid. A hard mass was found at the root of the appendix that was trapped in the cecum. We also found that the right ovary, the pelvic cavity, and the right upper quadrant of the omentum were all adhered with gelatinous fluid (Fig. 2a and 2b). A diagnosis of MAC was made based on a rapid pathological analysis of the gelatinous fluid and the right accessory. Finally, based on recommendations from both general surgeons and gynecologists the patient underwent a right hemicolectomy and complete hysterectomy double uterine exci-

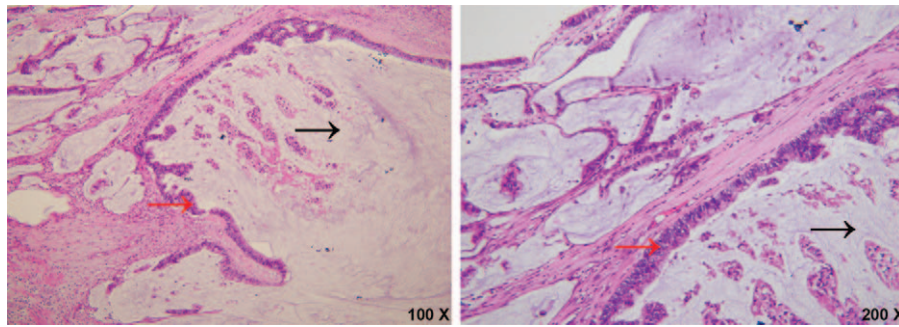


**Figure 3.** Resected specimens: A. Outside the lesion, the arrow points to the intussusception. B. Inside the lesion, the arrow points to the intussusception.

sion. The anatomy of the postoperative specimens revealed that the cecum and the appendix were invaginated, and a mucinous mass that involved the entire wall of the intestine and invaded the serosal layer and intestine without significant stenosis was seen within the cecal cavity (Fig. 3). Gross pathology suggested that an ileocecal ulcer-type MAC invaded and penetrated all the layers of the intestine and the serosa and that there was a disseminated MAC in the mesentery, chronic appendiceal inflammation, an omental adenocarcinoma, and a right ovarian MAC. HE staining of the tumor tissues showed that the tumor was derived from digestive tract tissue (Fig. 4). The patient's postoperative recovery was uneventful, and she was successfully discharged; she then went to the oncology department for medical treatment.



**Figure 2.** Intraoperative observations: A. Tumors on the greater omentum, B. Tumors in the pelvic cavity and right ovary.



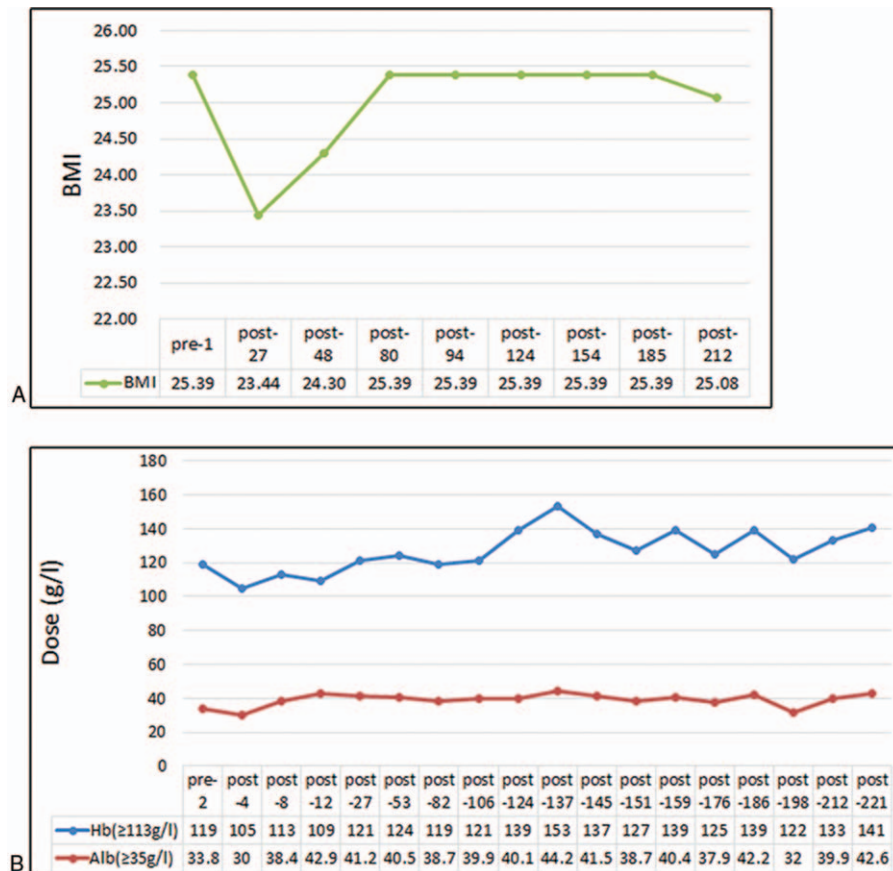
**Figure 4.** Postoperative pathology: Red arrows indicate cancer cells, and black arrows indicate mucus.

Postoperatively, the patient underwent 5 courses of chemotherapy with oxaliplatin plus capecitabine, followed by 6 courses of 5-fluorouracil + oxaliplatin + calcium leucovorin. Her postoperative nutritional status recovered well. The last time the patient was followed up was July 9, 2018. And it is exactly 212 days after the operation. The patient still had good nutritional status, although his serum albumin concentration was below normal at 198 days post operation (Fig. 5A and B). 194 days after the operation an enhanced magnetic resonance imaging (MRI) and CT showed no significant tumor recurrence or metastasis. Postoperative tumor markers including carcinoembryonic antigen levels gradually returned to normal, with the

exception of glycoprotein antigen 724 (CA724) levels, which remained high (Fig. 6) but were much lower than the levels before surgery. During follow-up, we will continue to monitor the patient’s recovery.

### 3. Discussion

MAC is an independent risk factor for poor prognosis.<sup>[14]</sup> Similarly, the prognosis of colonic MAC is also poor, and chemoradiotherapy remains less effective. Mucinous rectal adenocarcinoma was an indicator for a poor response to preoperative chemoradiotherapy; there was a decrease in overall



**Figure 5.** Postoperative nutritional status of the patient (pre: preoperative; post: postoperative; the units are given in days): A. BMI: body mass index. B. Hb: hemoglobin concentration; Alb: albumin concentration.

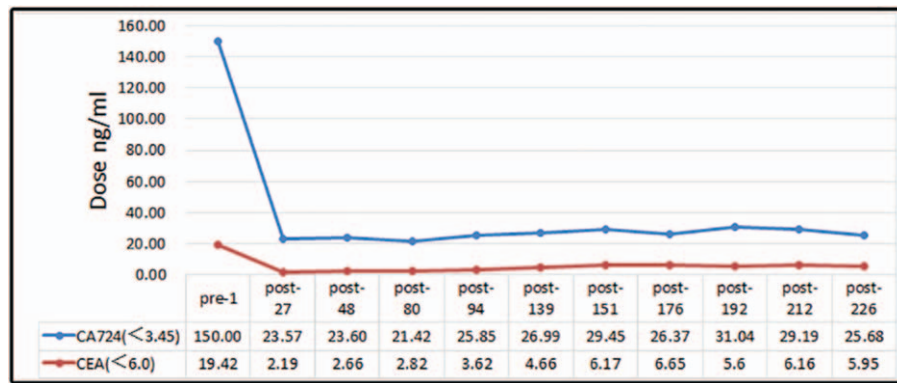


Figure 6. Trends in tumor indicators: CA724: glycoprotein antigen 724; CEA: carcinoembryonic antigen.

survival in patients with mucinous compared with nonmucinous locally advanced rectal cancer treated with neoadjuvant chemoradiotherapy and curative resection.<sup>[15]</sup> The prognosis of distant metastasis of colonic MAC is even worse, and it has been reported that the survival time of patients with sigmoid MAC metastasis to the hepatobiliary duct is only approximately 6 months.<sup>[16]</sup> In addition, patients with advanced mucinous colon cancer have a poorer response to fluorouracil-based first-line chemotherapy and reduced survival than patients with non-mucinous colon cancer.<sup>[17]</sup> Therefore, it is necessary to better understand the pathogenesis, diagnosis and treatment options of MAC in order to improve its clinical management.

### 3.1. Pathogenesis

MAC exhibits a higher frequency of DNA mismatch repair (MMR) defects, microsatellite instability (MSI) and RAS/RAF/MAPK pathway mutations, and a lower incidence of p53 mutations than non-MACs. MAC also more frequently exhibits a CpG island methylation phenotype (CIMP). This is characterized by CpG island hypermethylation in the promoter regions of carcinogenesis-related genes, resulting in epigenetic silencing.<sup>[8]</sup> Milewski et al found that the transcription factor Forkhead box M1 (FOXM1) is an essential gene for the progression of lung cancer to MAC. Inhibition of either FOXM1 or anterior gradient 2 (AGR2) in human pulmonary invasive MAC inhibited mucinous characteristics.<sup>[18]</sup> Thus, MAC seems to be the result of further development of adenocarcinoma, and the process can be regulated by certain genes such as FOXM1. In this context, the formation of MAC may be reversible even though evidence for the reverse has not been available. Lungulescu et al found that mucin acids and sulfomucin from mucinous rectal carcinoma are more frequent in younger patients, and the degree of differentiation and neoplastic stage are inversely related to the ratio of sulfomucin content.<sup>[19]</sup>

### 3.2. Diagnosis

The preoperative diagnosis of mucinous tumors is rare because of the low incidence of these tumors, the nonspecific symptoms and the relatively few significant biochemical parameters and imaging findings.<sup>[20]</sup> Ultrasound and abdominal and pelvic CT can be useful to identify swelling in the right iliac fossa or thickening of the wall of the cecum, but these findings may be common with other diseases, such as adenocarcinoma of the

cecum, Crohn's disease, or ileocolonic intussusception. Thus, these findings are not conducive to the early detection and treatment of MAC.<sup>[20,21]</sup> It has been reported that endoscopic ultrasound (EUS) has a unique advantage for the diagnosis of MAC associated with ascites; EUS frequently identifies ascites missed by other imaging studies, including abdominal CT. This study also demonstrated that EUS-guided paracentesis could identify malignancy in ascetic patients.<sup>[22]</sup> Because pelvic MRI can be used for accurate tumor staging, it is essential to use this modality in patients with rectal cancer.<sup>[23,24]</sup> The mean apparent diffusion coefficient of MRI was higher in rectal MAC than in rectal adenocarcinoma; there was a significant difference in the signal intensities between rectal MAC and rectal adenocarcinoma.<sup>[25]</sup> In addition, in some cases, preoperative pet-CT examinations were performed to assess whether there was local infiltration or distant metastasis.<sup>[26]</sup>

### 3.3. Treatment

Studies have shown that the response of colonic MAC to neoadjuvant radiotherapy and chemotherapy is poor. In addition, some authors believe that cell adhesion to mucin is strongly associated with the high aggressiveness of this tumor, although there are different points of view.<sup>[27]</sup> However, neoadjuvant chemoradiotherapy has been shown to increase the sphincter preservation rate and reduce local recurrence, thus being beneficial for locally advanced rectal MAC patients.<sup>[23]</sup> Guan et al found that both preoperative and postoperative radiotherapy can improve clinic outcome of patients with phase II and III rectal adenocarcinoma.<sup>[28]</sup> Stewart et al found that patients with mucinous tumors of the pancreas initially treated with folinic acid, fluorouracil, irinotecan, and oxaliplatin (FOLFIRINOX) continue to have stable primary and metastatic disease.<sup>[29]</sup> Therefore, preoperative neoadjuvant chemo-radiation therapy is a very important treatment option to improve the prognosis of MAC patients; however, this regimen is not appropriate for patients with advanced tumors, which is a common scenario for various malignancies.

In this specific case, we removed the right ovary, the left ovary, and the uterus together. It has been recommended that in mucinous ovarian cancer, an abnormal appearing appendix should also be excised. However, if the appendix is grossly normal, which is the case for this patient, performing an appendectomy as part of the surgical staging procedure seems not to be necessary.<sup>[30]</sup> Whether or not our surgical procedure is a

better option will be eventually determined by the patient's survival period.

#### 4. Conclusions

In summary, surgical treatment is still the main choice of treatment for colonic MAC. In this case, we found that preoperative nutritional status and postoperative chemotherapy may be important factors leading to a good prognosis. Although there have been some previous reports of the diagnosis and treatment of colonic MAC, more basic and clinical studies are needed in order to improve clinical management of the malignancy.

#### Acknowledgments

The authors would like to thank American Journal Experts (www.aje.cn) for providing linguistic assistance during the preparation of this manuscript.

#### Author contributions

**Conceptualization:** Xiaohui Xu, Yi Wang.

**Data curation:** Zhiyuan Kong, Qingjun Lei.

**Formal analysis:** Zhiyuan Kong, Bing Wang.

**Investigation:** Qingjun Lei.

**Methodology:** Xiaohui Xu, Bing Wang.

**Project administration:** Xiaohui Xu, Zhiyuan Kong, Ke Yi, Yi Wang.

**Resources:** Ke Yi.

**Software:** Zhiyuan Kong, Ke Yi.

**Validation:** Bing Wang, Qingjun Lei.

**Visualization:** Ke Yi, Bing Wang, Qingjun Lei.

**Writing – original draft:** Xiaohui Xu.

**Writing – review & editing:** Xiaohui Xu, Zhiyuan Kong, Ke Yi, Yi Wang.

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