Colon cancer with colovesical fistula: A report of four cases and a literature review

CHANGMING DONG[1,2*], XIANG PAN[1*], LIFU WEI[3], XIAOJUN MAN[2], ZHENGXI ZHOU[1], YANPING HUANG[1], XIAOXIANG WANG[1], LEZHONG QI[1], FENG XUE[3] and YIFAN LI[1]

[1]Department of Urology, Affiliated Hospital of Yangzhou University, Yangzhou University, Yangzhou, Jiangsu 225000; [2]Department of Urology, First Hospital of China Medical University, Shenyang, Liaoning 110001; [3]Department of General Surgery, Affiliated Hospital of Yangzhou University, Yangzhou University, Yangzhou, Jiangsu 225000, P.R. China

Received July 26, 2022; Accepted February 10, 2023

DOI: 10.3892/ol.2023.13744

Abstract. Colon cancer with colovesical fistula (CVF) is a rare complication of colon cancer that possesses an extremely poor prognosis. Surgical treatment can improve the prognosis. The current study presents four cases of CVF, in which the first two cases were treated conservatively and the other two were treated surgically. The first case presented with intestinal obstruction for 3 days, and computed tomography (CT) was performed. The patient refused surgery and still exhibited lower abdominal pain 11 months later. The second case presented with urinary frequency and urgency that lasted for 2 days, and CT was performed. The patient refused surgery and died 2 months later. The third case presented with fecaluria that lasted for 1 month, and CT, endoscopy and one-stage palliative surgery were performed. The patient was lost to follow-up 5 months later. The fourth case presented with acute urinary tract symptoms for 4 months, and CT, endoscopy and one-stage radical surgery were performed. The patient remained disease-free 10 months later. The four cases reported in the present study not only represent excellent examples of the disease spectrum, but also act as a reminder of the possibility of detecting CVF at an early stage of the disease. The present study discusses the epidemiology of CVF, and presents the pattern of CVF in terms of signs, symptoms and imaging examinations, including CT, cystoscopy and colonoscopy, as well as treatment in the early stage of the disease.

Correspondence to: Professor Yifan Li, Department of Urology, Affiliated Hospital of Yangzhou University, Yangzhou University, 368 Hangjiang Middle Road, Yangzhou, Jiangsu 225000, P.R. China
E-mail: yfli@bjmu.edu.cn

Professor Feng Xue, Department of General Surgery, Affiliated Hospital of Yangzhou University, Yangzhou University, 155 Nanjing North Road, Yangzhou, Jiangsu 225000, P.R. China
E-mail: fxue@yzu.edu.cn

*Contributed equally

Key words: colovesical fistula, enterovesical fistula, colon cancer, vesical fistula, ureteral fistula

Introduction

A colovesical fistula (CVF), a communication between the colon and bladder, is a known but rare complication of colon cancer (1-3), and it can occur secondary to other diseases (4). The prognosis of CVF is poor, and is often accompanied by uremia, septicemia and even renal failure (5). If CVF could be detected in the early stage of the disease, the poor prognosis of CVF may be changed. However, due to the rarity of CVF, the non-specificity of the symptoms (6), signs and imaging examination findings (7), and the poor prognosis, it is challenging and yet crucial to confirm CVF early. Currently, considerable debate exists in the literature on the choice of the initial diagnostic study (6); there is no single optimal test and the investigations employed vary. We recommend computed tomography (CT) as the primary imaging investigation in a suspected CVF. In the present study, the case database of Yangzhou First People's Hospital (Yangzhou, China) was reviewed, and out of a total of 39 suspected cases, four cases of CVF with different grades of disease and different prognoses were identified for discussion. The present study was approved by the Ethics Committee of Yangzhou First People's Hospital and written informed consent for future publication was obtained from all patients, including the patient who died.

Case report

Case one. A 59-year-old man presented to the Affiliated Hospital of Yangzhou University (Yangzhou, China) on 30 July 2020 with abdominal pain and distention accompanied by cessation of anal gas and defecation that had persisted for 3 days. The patient had recurrent colon cancer and had previously undergone a radical resection of colon cancer. The patient was afebrile with normal vital signs. A routine blood test showed a neutrophil level of 87.1×10^9/l (reference range, $0.04\text{-}0.5 \times 10^9$/l). A routine urine test showed a red blood cell level of 3/high-power field (HPF) (reference range, 0/HPF). A kidney function test showed a creatinine level of 130.2 μmol/l (reference range, 50-110 μmol/l). CT revealed recurrence of

the colon cancer, with invasion in the left posterior bladder wall, and gas in the ascending and sigmoid colon (Fig. 1). The diagnosis was colon cancer with a CVF. The patient refused surgical treatment and was treated with 0.5 g levofloxacin, once a day for 10-14 days. The symptom of lower abdominal pain remained 11 months later.

The final pathological diagnosis was sigmoid colon cancer. According to the American Joint Committee on Cancer Tumor-Node-Metastasis (AJCC TNM) classification (8), the patient was diagnosed with stage T4N0M0 disease, indicating intermediate-grade colon cancer.

Case two. An 84-year-old man presented to the Affiliated Hospital of Yangzhou University in April 2015, with urinary frequency and urgency that had persisted for 2 days. On presentation, the patient was afebrile with normal vital signs. A routine blood test showed a hemoglobin level of 84 g/l (reference range, 100-160 g/l) and a neutrophil level of $81.1x10^9$/l (reference range, 0.04-0.5$x10^9$/l). A routine urine test showed a red blood cell level of 2,452.2/HPF (reference range, 0-3/HPF) and a white blood cell level of 15,619.2/HPF (reference range, 0-5/HPF). CT revealed thickening in the sigmoid colon, rectum and bladder wall, which was considered to be colon cancer, and air in the bladder (Fig. 2). The diagnosis was colon cancer with a CVF. The patient refused surgical treatment and was treated with levofloxacin 0.5 g once, once a day, for 10 to 14 days. The subsequent clinical course was marked by deterioration, and the patient died due to the CVF 2 months later.

According to the AJCC TNM classification, the patient was diagnosed with stage T4N0M0 disease, indicating low-grade colon cancer.

Case three. A 45-year-old man presented to the Affiliated Hospital of Yangzhou University in June 2020 with fecaluria that had persisted for 1 month. The patient had a background of colon cancer. On presentation, the patient was afebrile with normal vital signs. A routine blood test showed a hemoglobin level of $57x10^{12}$ g/l (reference range, 100-160$x10^{12}$ g/l), neutrophils of $9.81x10^9$ g/l (reference range, 0.04-0.5$x10^9$ g/l). A routine urine test showed a red blood cell level of 3/HPF (reference range, 0-3/HPF). A liver function test showed a creatinine level of 380 μmol/l (reference range, 50-110 μmol/l) and urea nitrogen level of 42.65 mmol/l (reference range, 2.86-7.14 mmol/l). Cystoscopy showed cloudy urine and fecal scraps in the bladder. Enteroscopy revealed multiple tumors 10 cm above the anus. CT showed uneven thickening, with enhancement in the distal regions of the sigmoid colon and proximal regions of the rectum wall, which was colon cancer and a fistula (Fig. 3). The diagnosis was colon cancer with a CVF. The patient was treated with 0.5 g levofloxacin, once a day for 10-14 days. Due to the patient's good physical condition and lack of obvious manifestations of inflammation or intestinal obstruction, the patient underwent a palliative sigmoidectomy, proximal colostomy, partial small intestine resection and partial cystectomy, and was lost to follow-up subsequent to a period of 5 months.

The tumor was formed of infiltrating extra-muscular fibrous adipose tissue. A total of eight metastatic tumors were indicated in the peri-intestinal lymph node. The final pathological diagnosis was of sigmoid colon cancer. According to the AJCC TNM classification, the patient was diagnosed with stage T4N3M0 disease, indicating low-grade colon cancer.

Case four. A 55-year-old man presented to the Affiliated Hospital of Yangzhou University in December 2020 with urinary frequency, urgency and pain that had persisted for 4 months. The patient had a background of sigmoid cancer. On presentation, the patient was afebrile with normal vital signs. A routine blood test showed a neutrophil level of $87.1x10^9$ g/l (reference range, 0.04-0.5 $x10^9$ g/l), a hemoglobin level of $84x10^{12}$ g/l (reference range, 120-160 g/l). A routine urine test showed a red blood cell level of 3/HPF (reference range, 0-3/HPF) and a white blood cell level of 139.8/HPF (reference range, 0-5/HPF). The urine culture found *Escherichia coli*, and the fecal occult blood test was positive. CT showed sigmoid cancer with invasion and a fistula in the bladder wall. Cystoscopy revealed hyperemia, edema and thickening in the bladder wall. Colonoscopy confirmed colon cancer (Fig. 4). The patient was treated with 0.5 g levofloxacin, once a day for 10-14 days. Due to the patient's good physical condition and a lack of obvious manifestations of inflammation or intestinal obstruction, a laparoscopic palliative sigmoidectomy and a partial cystectomy were performed. The diagnosis was colon cancer with a CVF. The patient remained asymptomatic after 10 months.

The tumor measured 4.5x3.5x2.5 cm in size and the final pathological diagnosis was sigmoid colon cancer. According to the AJCC TNM classification, the patient was diagnosed with stage T4N0M0 disease, indicating low-grade colon cancer.

Discussion

A CVF is a communication between the colon and bladder that is caused by colon cancer, and it has a poor prognosis. The clinicopathological characteristics of CVF in the four cases presented in the current study are summarized in Table I. However, CVF is extremely rarely reported worldwide. As CVF as an abbreviation has many ambiguities, an electronic search of PubMed (https://pubmed.ncbi.nlm.nih.gov) was performed using the key words 'colovesical fistula', and reviewing the previous literature, only 17 cases were found. The characteristics of each case are shown in Table II (1-3,9-19). The leading cause of CVF is diverticulitis, accounting for 72-75% of cases, followed by colon cancer at 16% (3). Due to the differences in anatomy, the probability of a CVF in women is lower (20). Colon cancer invasion can lead to bladder wall ulceration and necrosis, and even CVF (21,22).

The chief complaints caused by a fistula are pneumaturia and fecaluria, and these non-specific symptoms can delay the diagnosis. Considering the risk of uremia, septicemia and renal failure, a patient with advanced colon cancer presenting with urinary tract symptoms should be considered for CVF and imaging examinations should be performed (5). In the four presented cases, CT, cystoscopy, colonoscopy and biopsy were performed to detect the fistulae. Clinically, CT is the first method selected to examine patients with CVF due to its non-invasiveness and high sensitivity. CT could provide information about the complexity of the fistula (23) and the surrounding anatomical structures (24), which could help the next treatment plan (5). An early, small bladder fistula caused

Figure 1. Computed tomography scan showing recurrent colon cancer invading the left posterior bladder wall (arrow).

Figure 2. Computed tomography scan showing air in the bladder (arrow 1), irregular thickening and enhancement of the sigmoid in the distal parts of the sigmoid colon and proximal parts of the rectal wall (arrows 2 and 4), and a fistula between the colon and bladder (arrow 3).

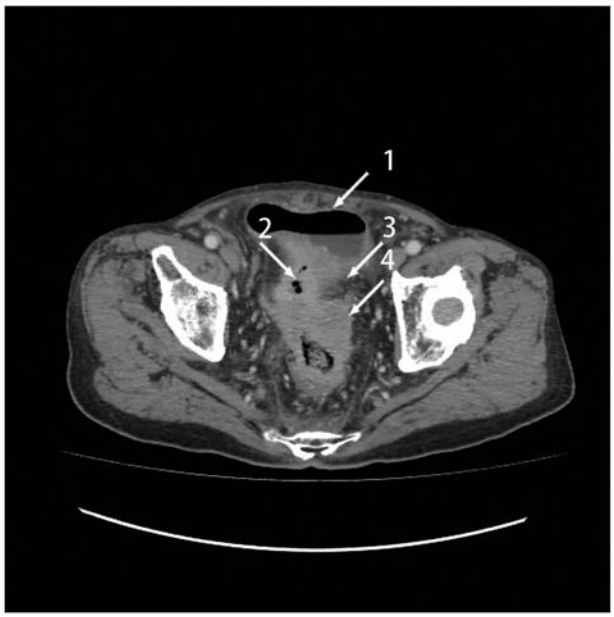

Figure 3. Computed tomography showing air in the bladder (arrow 1), thickening in the sigmoid colon, rectum and bladder wall (arrows 3 and 4), and a fistula between the colon and bladder (arrow 2).

Figure 4. Computed tomography showing air in the bladder (arrow 1), thickening in the sigmoid colon, rectum and bladder wall (arrows 2 and 4), and a fistula between the colon and bladder (arrow 3).

by colon cancer is not easy to diagnose, as compared with that of Crohn's disease or an intestinal diverticulum, the bladder fistula caused by colon cancer is usually smaller, mainly manifesting as inflammatory changes, and it is difficult to obtain an accurate biopsy. In colon cancer cases, it is difficult for feces to enter the bladder through the small fistula, so the fecal and urinary symptoms are not obvious, but this can become a source of bacterial cystitis, which is difficult to cure. Therefore, CT is a suitable primary choice for patients with a suspected CVF. Air in the bladder, uneven thickening in the sigmoid colon and rectal wall (1-3,25,26), a fistula in the bladder or colon wall (1), invasion in the bladder wall, and gas in the ascending and sigmoid colon are common findings on CT scans, which may indicate the diagnosis of a CVF. Due to inflammatory signs, it is not always possible to perform a cystoscopy or biopsy (7), and a cystoscopy cannot always find the fistula directly. Likewise, due to intestinal obstruction, a colonoscopy is not always available (7). In particular, an endoscopy is not suitable for patients who require urgent surgery. According to a previous study, the poppy seed test,

Table I. Clinicopathological characteristics of four cases of colovesical fistula.

Case no.	Age, years	Sex	Etiology	Presenting symptoms	Site of causative lesion	Air in bladder	Bladder and/or bowel wall thickening	Fistulous tract visualized	Invasion in the bladder wall	Extravesival mass that often contained air	Cytoscopy	Colonscopy	Clinical stage	Treatment	Prognosis
1	59	Male	Colon cancer	Abdominal pain and distention accompanied by cessation of anal gas and defecation	Sigmoid colon	N	N	N	Y	Y	Not performed	Not performed	T4N0M0	Refused surgery	Abdominal pain remained
2	84	Male	Colon cancer	Urinary frequency and urgency	Sigmoid colon	Y	Y	N	N	N	Not performed	Not performed	T4N0M0	Refused surgery	Died of CVF
3	45	Male	Colon cancer	Fecal urine	Sigmoid colon	N	Y	N	N	N	Cloudy urine and fecal scraps in the bladder	Multiple tumors 10 cm above the anus	T4N3M0	Underwent surgery	Lost to f ollow-up
4	55	Male	Sigmoid cancer	Urinary frequency, urgency and pain	Sigmoid colon	N	N	Y	Y	N	Hyperemia, edema and thickening of the bladder wall	Colon cancer	T4N0M0	Underwent surgery	Asymptomatic

Y, yes; N, no.

Table II. Reported cases of colon cancer with vesical fistula.

First author/s, year	Country	Age, years	Sex	Chief complaint	Tumor location	CT description	Ureteroscopy or cystoscopy/biopsy result	(Refs.)
Oda *et al*, 1984	Japan	50	Male	Hematuria, constipation, lower abdominal discomfort, fecaluria	Sigmoid colon	Deformity and a tumor mass in the bladder	A fistula in the posterior bladder wall, a mass at 35 cm from the anal margin	(15)
Kao *et al*, 1997	China	73	Male	Terminal gross hematuria, fecaluria, diarrhea and painful urination	Sigmoid colon	CT not performed	Colon adenocarcinoma	(14)
Repici *et al*, 2000	Italy	76	Female	Large bowel obstruction, severe anemia, fecaluria and pneumaturia	Sigmoid colon	A neoplastic mass infiltrating the entire pelvic cavity	A mass 7 to 8 cm from the anal margin; colon adenocarcinoma	(13)
Godbole and Loughridge, 2003	UK	75	Female	Painless hematuria	Sigmoid colon	A fistula between the ileum and bladder	A globular swelling at the fundus of the bladder	(12)
Yabuki *et al*, 2004	Japan	76	Male	Pain in urination, abdominal pain during defecation and fever	Sigmoid colon	CT not performed	A fistula in the bladder dome	(11)
Medlicott *et al*, 2007	Canada	69	Male	Recurrent urinary tract infections with pneumaturia	Right colon	Diverticulosis coli complicated by a CVF	Colon adenocarcinoma	(33)
Patel *et al*, 2009	USA	43	Female	Weight loss, nausea, vomiting, stool incontinence and tenesmus	Sigmoid colon	A sigmoid colon mass lesion invading the bladder	A sigmoid mass with ulceration, a fistula between the mass and the urinary bladder; colon adenocarcinoma	(34)
Ahmad *et al*, 2010	UK	62	Male	Recurrent urinary tract infections and fecaluria	Sigmoid colon	Progression of sigmoid cancer	Examinations not performed	(17)
Pineda and Maxwell, 2012	USA	82	Female	Left lower abdominal pain, pneumaturia and particulate in the urine	Sigmoid colon	Sigmoid colonic thickening and air in the bladder	Small cell carcinoma	(35)
Kim *et al*, 2015	Korea	70	Male	Asymptomatic	Sigmoid colon	Thickening of the sigmoid colon and a fistula of the colon and bladder	Examinations not performed	(19)
Nakazawa *et al*, 2015	Japan	84	Male	Hematuria, fecaluria, pneumaturia and micturitional pain	Sigmoid colon	CVF	Colon adenocarcinoma	(10)

Table II. Continued.

First author/s, year	Country	Age, years	Sex	Chief complaint	Tumor location	CT description	Ureteroscopy or cystoscopy/biopsy result	(Refs.)
Kachaamy *et al*, 2016	USA	56	Male	Vomiting and fecaluria	Terminal ileum	A rectal mass invading the terminal ileum and bladder, and air in the bladder	Fistula with distal obstruction	(16)
Li *et al*, 2017	China	54	Male	Urinary frequency, urge incontinence, urodynia, dysuria, hematuria and hypogastralgia	20 cm from the anal margin	Thickening in the bladder wall and a mass on the left anterior bladder wall	A mass in the sigmoid colon; tumor in sigmoid colon	(1)
Yang *et al*, 2018	Korea	71	Male	Weight loss with diarrhea	Sigmoid colon	Irregular thickening in the sigmoid colon	A mass in the sigmoid colon; colon adenocarcinoma	(3)
Skierucha *et al*, 2018	Poland	81	Female	Diarrhea	10 cm from the anal verge	A heterogeneous conglomerate of structures in the bladder	A mass and leakage in the sigmoid colon	(2)
Ashrafi and Sotelo, 2019	USA	72	Female	Passing gas in the urine	Sigmoid colon	A mass extending from the sigmoid colon to the bladder	Diverticulosis in the sigmoid colon; gas in bladder	(18)
Pineda and Maxwell, 2012	USA	63	Male	Burning and the passage of flatus with urination	Sigmoid colon	Diverticula, and bladder and sigmoid wall thickening	Irregularity of the dome of the bladder; colon adenocarcinoma	(35)

CVF, colovesical fistula.

which involves swallowing poppy seeds and detecting their presence in the urine, is recommended, as it is highly sensitive (100%), non-invasive and easy to perform (27). While the poppy seed test is indeed sensitive, it cannot provide much more information about etiology or location, and this test should be treated as a screening test only. Although magnetic resonance imaging is not used as a routine test, a number of previous studies have recommended it, due to its intrinsic soft-tissue resolution (6,28-31).

The present four cases, which underwent different therapies, including conservative treatment and surgery, were in stark contrast to each other. The cases of conservative treatment refused surgery and were prescribed antibiotics on a long-term low-dose basis. The cases of surgery underwent a palliative sigmoidectomy, proximal colostomy, partial small intestine resection and partial cystectomy, and a laparoscopic palliative sigmoidectomy and partial cystectomy, respectively. The patients who underwent surgery had better outcomes and quality of life compared with the patients who underwent conservative treatment. To the best of our knowledge, surgery is a favorable prognostic factor for CVF. According to a previous study, conservative treatment is usually reserved for patients who are unsuitable for major surgery, for patients with multiple complications and comorbidities, or for patients too old to tolerate general anesthesia (5). The present study is consistent with this in that the patient in case 2 accepted conservative treatment. Due to the potential risk of uremia and septicemia, surgery is often necessary, although some cases can heal with conservative management. Moreover, staged repairs may be reserved for patients with advanced malignancy, and could be performed as palliative surgery to manage complications from CVF (5,23).

When CVF is confirmed, one-stage radical surgery is recommended for patients without intestinal obstruction. According to a previous study, the outcome of staged surgery is not better than that of one-stage surgery (23). Palliative surgery, such as a partial colon resection and simple division of the fistula, leads to a greater probability of recurrence (26). In patients with a shorter expected life span, a colostomy often leads to discomfort and even death, especially in cases requiring urgent surgery (13). Laparoscopic surgery has been widely accepted to treat malignancy, due to its shorter hospital stay, better resulting postoperative quality of life and fewer complications (32). Some studies have recommended stent implantation surgery to help close the fistula; however, since this is not a common treatment for vesical fistulas, this hypothesis requires additional study (17,28). Among the four cases in the present study, the prognosis of the patients who received surgery was better, while the prognosis of the patients who refused surgery was associated with the clinical staging of the primary disease. Moreover, the patient in case one had difficulty in alleviating the symptoms and experienced a poor quality of life, as the fistula could not heal itself without surgery.

The major strength of the present study is the relatively large number of patients with CVF. However, the study has several limitations. First, the available imaging investigations in the Affiliated Hospital of Yangzhou University are less. Second, since treatment with laparoscopic surgery is rarely performed, valuable recommendations could not be provided for specific surgical approaches. Additional studies with a greater number of imaging investigation methods is needed to confirm any suggestions. Larger studies with longer follow-up times are also needed to conclude specific surgical methods.

In conclusion, CVF is a rare complication of colon cancer. The four CVF cases with a mix of favorable and poor prognoses are examples of the disease spectrum and act as a reminder that certain imaging evidence, including invasion and fistula in the bladder wall, gas in the colon and bladder, and uneven thickening in the colon and rectal wall, may indicate a CVF and point to the need for surgery.

Acknowledgements

The authors would like to thank Dr Hailiang Liang (Department of General Surgery, Affiliated Hospital of Yangzhou University, Yangzhou University, Yangzhou, China) for their valuable discussions with regard to the study.

Funding

This study was supported by the National Natural Science Foundation of China (grant no. 82002675), the Jiangsu Natural Science Research of Colleges and Universities-General Project (grant no. 20KJB320014), the Jiangsu Science and Technology Program-Youth Fund Project (grant no. BK2020938), the Yangzhou Key Research and Development-Social Development Project (grant no. YZ2020110), the Yangzhou Soft Science Research Program (grant no. YZ2020258), the Jiangsu Postdoctoral Research Funding Program (grant no. 2020Z268) and the Yangzhou University High-level Talent Research Start-up Fund (grant no. 2019LYF).

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

CD, XP, LW, ZZ, YH, XM, XW, YL, FX and LQ contributed to the acquisition, analysis and interpretation of the patient data presented in this case report. CD, XP, YL and FX drafted the manuscript. All authors made critical revisions. All authors read and approved the final manuscript. CD, XP, YL and FX confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The ethical approval and documentation for a case report was approved by the Ethical Committee of the Affiliated Hospital of Yangzhou University (Yangzhou, China; approval no. 2020-YKL03-G042).

Patient consent for publication

All patients provided written informed consent for the publication of this study. Informed consent for future publication was obtained before the patient in case two died.

Competing interests

The authors declare that they have no competing interests.

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