Fournier's gangrene due to rectal cancer: A case report

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Abstract. Fournier's gangrene (FG) is an extremely rare necrotizing fasciitis that is insidious, rapidly spreading and life-threatening. FGs due to rectal cancer occur rarely and there is a lack of clinical reference. In the present study, a severe FG due to rectal cancer perforation was described and the features of this rare disease were summarized with a literature review. A 57-year-old man was admitted because of rectal cancer-induced FG. The patient was misdiagnosed with extensive perianal abscess until the intraoperative biopsy confirmed that rectal cancer was the culprit. Incision, debridement and drainage were carried out to reduce infectious burdens. After that, the patient was transferred to Peking University People's Hospital for the subsequent therapy. Empirical broad-spectrum antibiotic therapy was used at the initial stage. Diversional transverse loop colostomy was performed to control infection and resume oral feeding. After four rounds of vacuum-assisted closure (VAC) therapy, radical resection and wound closure were accomplished. The scrotal defect was repaired by a skin flap. Pathological results indicated a moderately differentiated adenocarcinoma with perforation. The patient was discharged from the hospital on postoperative day 15 without any post-operative complications. No signs of recurrence were observed during a 22-month follow-up. In the setting of rectal cancer-induced FGs, the liquid resuscitation, broad-spectrum antibiotic therapy, and prompt debridement are the cornerstones of the initial management. Diversional colostomy and VAC therapy were effective in the management of severe infection and large wounds. The present case report also provided a clinical reference for the implementation of staged surgeries and the perioperative multidisciplinary management of FGs.

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Introduction

Fournier's gangrene (FG) is defined as necrotizing fasciitis of the perineal, genital, and/or perianal regions (1,2). FG is an extremely rare emergency, and the incidence is only 1.6/100,000 (3). The average age of patients is 50-60 years (4). Sepsis and shock may occur if FG is not promptly diagnosed and surgically debrided, with a mortality rate between 5-65% and the incidence rate exhibits a male-to-female ratio of 10:1 (4,5). The cause of the disease can be identified in 90% of cases. The common risk factors include diabetes mellitus, morbid obesity, alcoholism and immunosuppression. The presence of comorbidities, such as heart disease, renal failure, was described as related to an increased risk of mortality (4). Despite the advancements made in etiology and pathophysiology, the high mortality associated with FG has remained unchanged over the past decades (6). The common identifiable sources of infection include the skin, genitourinary tract and lower gastrointestinal tract (7). Among these sources, FG originating from anorectal disease carries the worst prognosis (1). The majority of anorectal sources are benign, such as perianal abscesses and fistula. FG due to rectal cancer is very rare, with only a few cases having been reported. In the setting of rectal cancer, the therapeutic options are more complex than for other forms of FG. The causative rectal tumor should be removed, but the timing of this is a complex clinical decision (8,9).

In the present study, the case of a rectal cancer patient with severe FG was reported and the features of this rare disease were summarized with an overview of the literature. This case highlights the rare presentations including severe FG associated with rectal cancer. Comprehensive examination should be carried out to reduce the occurrence of misdiagnosis. The present report also provided a clinical reference to facilitate perioperative management of rectal cancer-induced FGs. The case is presented in accordance with the CARE reporting checklist (2016) (10).

Case report

Main complaints. A 57-year-old man had intermittent hematochezia for two years and sudden perianal pain for 12 days.

History of present illness. Two years prior, the patient started having intermittent hematochezia without obvious causes. At that time, he had no abdominal pain, altered bowel habits or weight loss. The patient considered it was hemorrhoids, and

symptomatic treatment was administered. In the following years, hematochezia appeared at irregular intervals. A total of 12 days prior to diagnosis, the patient felt sharp perianal pain with a high fever that resulted in an emergency department visit. His body temperature was 38.8˚C, and his heart rate was 96 beats per minute (bpm). On physical exam, his perianal region, perineum and scrotum were reddening, and swelling with skin temperature arose. The patient was misdiagnosed with extensive perianal abscess without further imaging examinations. A combination of prolonged antibiotics and emergent surgery were applied immediately. An abscess was observed reaching from the left lower back and inguinal area into Scarpa's fascia and descending into the scrotum. During surgical exploration, an unexpected rectal mass was found. The diagnosis of well-differentiated rectal adenocarcinoma was established after frozen biopsy (Fig. S1). Incision, debridement and drainage were carried out systematically. A total of seven incisions, 2-3 cm each, were made on the abscess. The abscess was probed, and pus was drained as much as possible. After repeated irrigations, several loop drains were retained. An absorbent dressing was applied over the loop and changed regularly. After three days, the patient's vital signs returned to normal limits, and he was transferred to Peking University People's Hospital for further treatment. Since the onset, his food intake decreased by 50% in the past week and lost 2 kg of weight.

History of past illness. The patient reported no remarkable history of past illness.

Personal and family history. The patient smoked 10 cigarettes per day for 20 years and quit smoking 7 years prior. He drank a glass of wine per day (~15 g of ethanol per day). No significant personal or family history was noted.

Physical examination. The patient's vital signs were within normal limits. Physical examination revealed a body temperature of 36.5˚C, heart rate of 78 bpm, blood pressure of 138/89 mm Hg, and respiration of 18 breaths per minute. He looked pale, and the nutrition risk score was 3 points. Detailed scoring criteria were as follows: Malignant tumor (1 point); Food intake decreased by 1/2-3/4 in the past week (2 points); Age ≤70 (0 point). The incision and loop drainage of the first surgery were observed. Skin defects in the left scrotum and perineum were observed, and the external anal sphincter was exposed. A suspected cancer of the lower position was palpated by digital rectal examination under anesthesia.

Laboratory examinations. The patient's infectious indicators were elevated. The white blood cell count was $11.30x10^9$/l (reference values: 4.0-10.0$x10^9$/l), C-reactive protein was 15.2 mg/l (reference values: 0-10 mg/l), and erythrocyte sedimentation rate was 36 mm/H (reference values: 0-15 mm/l). The carcinoma embryonic antigen level was 37.4 ng/ml (reference values: 0~5.0 ng/ml). Other laboratory findings were unremarkable.

Imaging examinations. Magnetic resonance imaging (MRI) revealed that the full layers of the rectum were infiltrated. Mesorectal fascia and extramural vascular invasion were possibly positive. The right levator ani was invaded. Enhanced computed tomography showed circumferential thickening of the bowel from the lower rectum to the upper anal canal. The left inguinal and scrotal defects were also observed (Fig. 1).

Final diagnosis. Rectal cancer-induced FG was diagnosed.

Treatment. Considering the patient's malnutrition and high risk of infection, immediate radical resection was denied after a multidisciplinary meeting. Broad-spectrum empirical antibiotic treatment was initiated with imipenem (500 mg q12h), linezolid (600 mg q12h) and metronidazole (the initial dose was 1,000 mg and maintenance doses were 500 mg q6h) via an intravenous drip. Blood and tissue were collected for bacterial culture and drug sensitivity tests. *Escherichia coli* was positive in the bacterial cultivation and no anaerobic bacteria were detected. According to the drug susceptibility test, the patient was sensitive to imipenem and linezolid, thus these two antibiotics were maintained. With the infection indicators improving, antibiotics were gradually degraded. A total of four days after admission, a transverse loop colostomy was performed after a thorough examination. Benefiting from fecal diversion, the source of infection was under control. Enteral nutrition and parenteral nutrition were combined to improve his nutritional status. At the same time, a vacuum-assisted closure (VAC) device was applied to accelerate wound healing. The negative pressure was 100 mm Hg, with 5 min of suction followed by 2 min of rest. The prescribed dressing change period for VAC was three days. Each time, wounds were serially debrided under local anesthesia until healthy and viable tissue was visible (Fig. 2). A total of 12 days later, laparoscopic extra levator abdominoperineal excision (ELAPE) was performed. The distal sigmoid was closed without transverse colostomy reversal. The pelvic floor was reconstructed with biological mesh. The skin flap was transplanted by the plastic surgeon to repair scrotal defects. Pathological results indicated a moderately differentiated adenocarcinoma with perforation. No positive lymph nodes were identified. The proximal and distal margins were negative, but the circumferential resection margin was positive. The pathological TNM stage was T4N0M0. The paraffin-embedded sections from the primary tumor were cut at 4 μm thickness and attached onto slides. The sections were incubated with the specific primary antibody (1:100 dilution) at 37˚C for 2 h. Then the anti-rabbit IgG (1:500) was applied onto the sections and then observed by light microscopy. IHC indicated MLH1(+), PMS2(+), MSH2(+), MSH6(+), P53(-) and CerB-2(-) (Fig. 3). Next-generation sequencing indicated mutations in APC, ASXL1, FAT4, FBXW7, KRAS, SMAD3 and SOX9. The patient was discharged from the hospital on day 15 without any complications. Post-operative chemoradiotherapy was administered. Radiotherapy of 5,000 cGy was delivered in 25 fractions of 200 cGy five times per week for a total of 5 weeks. A total of six cycles of the XELOX regimen (130 mg/m^2 oxaliplatin on day 1 and 1,000 mg/m^2 capecitabine bid from day 1 to day 14) were applied.

Outcome and follow-up. The wound healed well, and no sign of recurrence was observed during follow-up for 22 months. The patient was satisfied with his recovery.

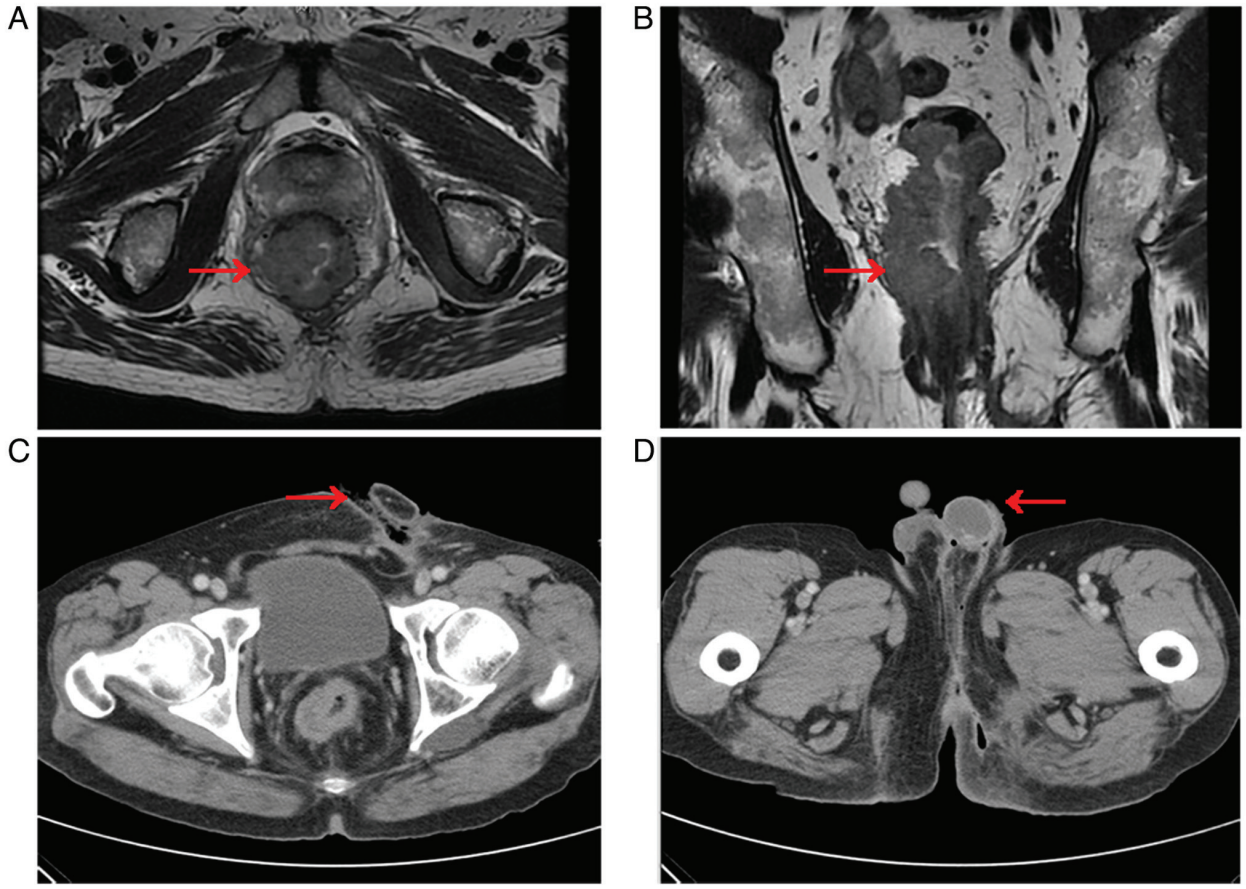

Figure 1. Preoperative imaging examinations of the patient. (A) Pelvic contrast-enhanced MRI revealed a rectal mass and it was almost circumferential. (B) The right musculus levator ani was invaded in MRI. (C) Abdominal CT indicated the left inguinal wound. (D) Left scrotal defect was found in pelvic CT. MRI, magnetic resonance imaging; CT, computed tomography.

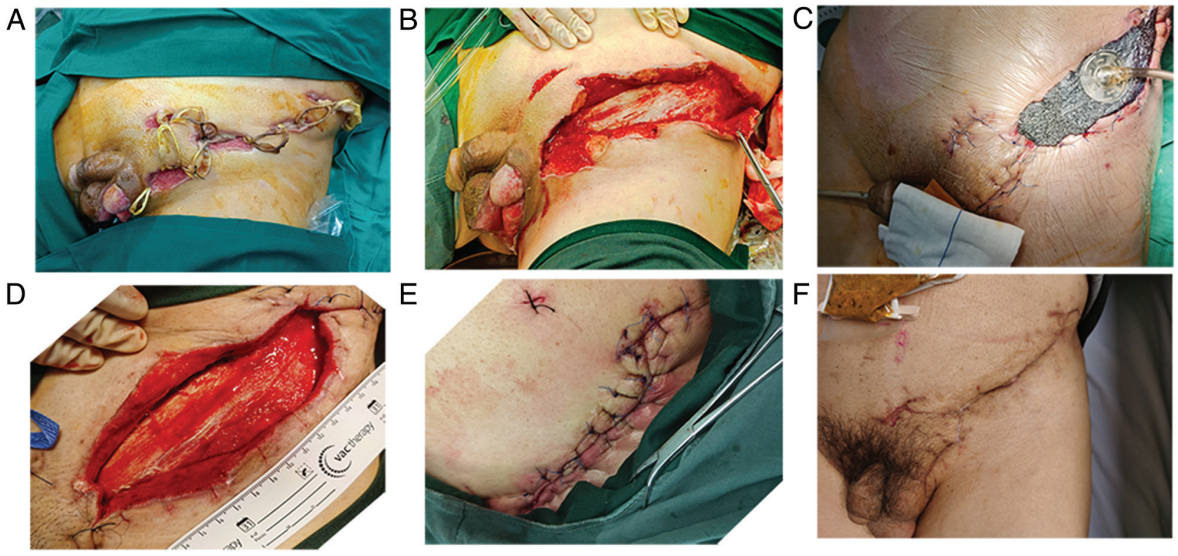

Figure 2. Wound changes of the patient. (A) Incision, debridement and loop drainage. (B) Exposure before VAC placement. (C) VAC implantation. (D) Granulation tissue formed and the wound partially healed. (E) The wound was sutured. (F) The wound healed completely. VAC, vacuum-assisted closure.

Discussion

There is a lack of successful clinical references for rectal cancer-induced FG. Rectal cancer-induced FG has several specific challenges. First, radical resection may not be possible because of severe infection. Second, the large area of open wounds increases the risk of tumor dissemination. Third, radical surgery is complicated because anaplasty is commonly

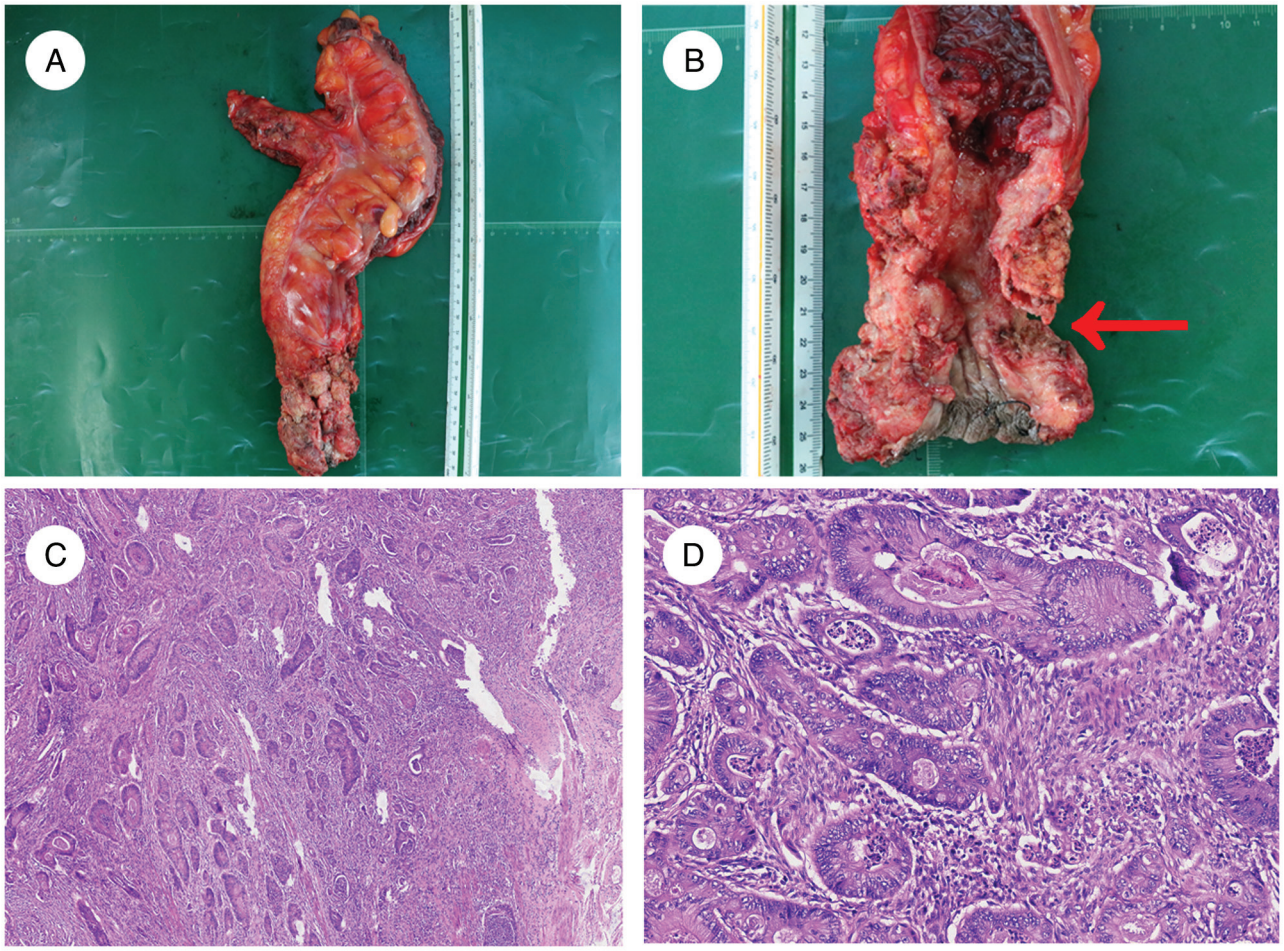

Figure 3. Surgical specimen and H&E staining of the case. (A) Holistic view of resected specimen. (B) Local view of resected specimen, and the perforation was indicated with red arrow. (C) Low-power field of H&E staining (magnification, x40). (D) High-power field of H&E staining (magnification, x100); atypical cancer cells arranged as an irregular glandular tubular (red arrow).

needed for the reconstruction of perineal and scrotal defects. Finally, post-operative adjuvant chemoradiotherapy is usually needed, which may increase the incidence of post-operative complications (1).

FG is a very insidious disease, with 40% of patients being asymptomatic. Due to its rarity without typical signs, early diagnosis of rectal cancer-induced FG is difficult, and misdiagnosis is common. The initial symptoms include but are not limited to perianal pain along with tenderness, usually with edema of the overlying skin, pruritus, crepitus and fever (11). Manifestations of rectal cancer-induced FG do not differ from the other FGs. Once the symptoms appear, accompanied by hematochezia or changes in bowel habits, rectal cancer-induced FG should be considered. Digital rectal examination is recommended for all FGs originating from anorectal disease. Diagnosis is usually made clinically, but radiological diagnostics, such as ultrasound, CT, or MRI, can determine the extent of the disease.

Sufficient multidisciplinary specialists are associated with the downward mortality trend of FG (12). In the current case, doctors from colorectal surgery, infectious disease departments, urinary surgery, plastic surgery, radiology departments, anesthesiology departments, intensive care units and radiotherapy departments participated in the multidisciplinary meeting. These experts' collaboration contributed to the optimal treatment plan.

Expedited treatment with liquid resuscitation, broad-spectrum antibiotic therapy and prompt debridement are the cornerstones of the initial management. Empiric antimicrobial therapy should start when the diagnosis is suspected. Antibiotic de-escalation should be based on the results of cultured pathogens and drug sensitivity tests (13). Wound care after debridement is essential and lays a foundation for wound closure. Different strategies have been proposed for wound care of FG, but their efficacy has not been fully elucidated. VAC promotes blood supply, inflammatory cell migration and granulation tissue formation. Current evidence supports that VAC therapy is effective in the management of large wounds with less pain, lower discomfort and greater mobility (14). For patients with disseminated FG, VAC offers an advantage in wound healing and survival (15). The authors' experience confirmed the safety and efficacy of VAC in the management of rectal cancer-induced FG.

Diversional stomas in FG did not reduce the risk of mortality; by contrast, this is a risk factor for poor outcomes (16). However, in the current case, rectal cancer invaded the external sphincter, anus-preserving surgery was unsuitable, and colostomy was inevitable. Loop colostomy

can avoid persistent stool infection and provide conditions for oral feeding. Perineal defects following transitional abdominoperineal resection (APR) are a challenge for anaplasty (17). ELAPE was based on precise anatomy and conformed to the principle of radical resection of low rectal cancer. ELAPE could reduce the occurrence of post-operative complications and chronic perianal pain when compared with traditional APR. In addition, it may further decrease the local recurrence rate and improve survival (18). Biological mesh was applied to reduce perineal hernia, perineal wound complications and post-operative radiation pelvic disease (19).

FG Severity Index is a numeric score developed in 1995 to stratify risk for FG patients (20). Since then, several modified scales have been proposed to optimize the accuracy of prognostic prediction. Recent studies have reported that age, diabetes, alcoholic liver disease, bedridden status, delayed hospital presentation, delta neutrophil index and hyperbaric oxygen therapy are prognostic factors of FG (21-23). However, their effects on rectal cancer-induced FGs require further investigation.

Several limitations exist in the present case report. First, the pictures before incision and drainage were unavailable. Second, the follow-up period was only 22 months, and the long-term outcome still needs further evaluation. Third, large-sample cohort studies are needed to summarize the regularity of rectal cancer-induced FGs.

In conclusion, the present case highlights the occurrence of FG as an extremely rare but life-threatening complication as a result of rectal cancer. In the setting of rectal cancer, the therapeutic options are more complex than for other forms of FG. The causative rectal tumor should be removed, but the timing of this is a complex clinical decision. The results of this case indicated that multidisciplinary evaluation, early intervention, staged management and close follow-up lead to successful treatment for rectal cancer-induced FG.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

All authors have contributed significantly to the content of the study. SH and YY confirm the authenticity of all the raw data. SH and BC collected and organized the patient's clinical data. SH wrote the first draft. KS designed the study. ZG and FL contributed to conceptualization and supervision. YY reviewed the manuscript. All authors were responsible for ensuring that the descriptions are accurate, and read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the ethics committee of Peking University People's Hospital. Approval number: 2022PHB053-001.

Patient consent for publication

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

Competing interests

The authors declare that they have no competing interests.

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