EUR REV MED PHARMACOL SCI
2026; 30: 46-50

FULMINANT FOURNIER GANGRENE IN BLADDER CANCER: CASE REPORT AND REVIEW OF THE LITERATURE

M. DE FELICE[1], M. TAMMARO[2], M. CATERINO[1], V. NACCA[1], R. CANGIANO[1]

[1]Department of Clinical Oncology, ASL Caserta, P.O. Piedimonte Matese, Caserta, Italy
[2]Department of Child, Women, General, and Specialized Surgery, Università degli Studi della Campania Luigi Vanvitelli, Naples, Italy

CORRESPONDING AUTHOR
De Felice Marco, MD; e-mail: marco.defelice1993@gmail.com

ABSTRACT – *Background:* The introduction of new target therapies and immunotherapy combinations has dramatically improved the prognosis of cancer patients. Surgery and radiotherapy currently represent the cornerstones of loco-regional management, both for palliative and curative purposes. It is no coincidence, therefore, that in recent years the frequency of complications once considered rare has increased.

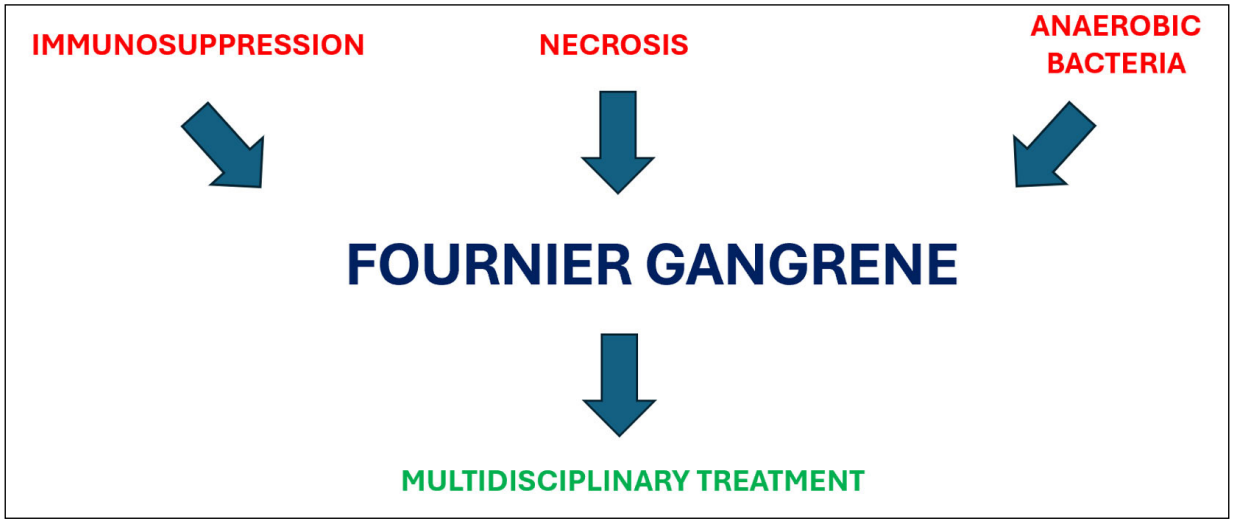
Case Report: Here we present the case of a patient affected by metastatic bladder cancer whose treatments (surgery, radiotherapy, and targeted therapy) favored a rapid and acute onset of Fournier syndrome. The fulminant course prevented the establishment of a potentially effective treatment.

Conclusions: Fournier gangrene is an acute perineal necrosis caused by anaerobic bacteria. Management is complex and requires a quick multidisciplinary approach, even though, among cancer patients, mortality is very high.

KEYWORDS: Fournier gangrene, Bladder cancer, Enfortumab vedotin, Fulminant onset, Anaerobes bacteria.

INTRODUCTION

Fournier gangrene (FG) is an acute and potentially fatal infective necrotizing fasciitis involving the perineal, genital, and perianal regions[1]. It was first described in 1883, representing a rare condition with an overall incidence of 1.6 cases per 100,000 nowadays, accounting for about 0.02% of hospital admissions[1]. The average age is 50.9 years with a ratio of men to women of 10:1[1]. Commonly, the disease is caused by a polymicrobial infection, which is why the clinical evolution is typically rapid and aggressive, involving the soft tissues of the perineum, perianal region, and external genitalia[1-3]. Predisposing factors include advanced age, recent perirectal or perineal surgery, diabetes mellitus, malignancies, perineal trauma or infection, immunocompromised status, and chronic alcoholism. Recently, the incidence of FG has increased, maybe related to the improvement in the treatment of oncological and hematological diseases[3]. It was suggested that the inability to carry out a rapid and effective immunological response may lead to altered clinical manifestations in cancer patients; however, in line with evidence from the general population of FG patients, fever, swelling, and pain represent the most frequent symptoms in cancer patients too, even though with a more aggressive course[4]. Here we describe an extremely interesting case of a 56-year-old male patient affected by high-grade metastatic bladder cancer with bone metastases, who developed rapidly fatal Fournier's syndrome during ongoing Enfortumab Vedotin treatment.



Graphical Abstract. A 56-year-old man affected by high-grade bladder cancer underwent radical cystectomy and lymphadenectomy. A large lytic lesion corresponding to the middle arch of the right ninth rib and the right iliac wing was reported after surgery. Both lesions underwent palliative radiotherapy for pain relief with 20 Gy in 5 fractions, then the patient started first-line treatment according to Cisplatin + Gemcitabine g1-g8 q21 for 4 cycles. At loco-regional disease progression, Enfortumab Vedotin, an antibody-drug conjugate, was infused. The combination of chemotherapy-induced immunosuppression, radiotherapy-induced bone necrosis of the right iliac wing, and resulting anaerobic conditions has favoured the development of uncontrolled anaerobic bacteria, resulting in a rare clinical complication known as Fournier syndrome, which is highly aggressive and rapidly fatal. Our experience highlights that chronicization of cancer diseases guaranteed by improvement of oncological treatments may provide fertile ground for the development of rare and fatal complications.

CASE PRESENTATION

A 56-year-old man affected by high-grade bladder cancer underwent radical cystectomy, lymphadenectomy, and Bricker urinary diversion in January 2024. Pathological stage pT4 pN0 was reported, with an infiltrated posterior surgical margin. Post-operative computed tomography (CT) performed in February 2024 revealed a large lytic lesion corresponding to the middle arch of the right ninth rib and right iliac wing, compatible with bone metastases, and a secondarism in the right corpus cavernosum. Both lesions underwent palliative radiotherapy for pain relief with 20 Gy in 5 fractions. He started first-line treatment with Cisplatin + Gemcitabine g1-g8 q21 for 4 cycles from March 2024 to June 2024, highlighting disease stability; he then started biweekly Avelumab maintenance. In October 2025, the patient needed a walker due to the recurrence of iliac and rib pain; therefore, a new radiological evaluation was performed, showing disease progression in both areas (Figure 1A). He immediately began second-line treatment with Enfortumab Vedotin regimen (day 1-day 8-day 15 q28), demonstrating partial pain control after the first administration. Suddenly, between day 8 and day 15 of the second cycle, the patient was admitted to our day hospital on a stretcher. Physical examination revealed the appearance of a large, severely painful perineal swelling with diffuse crepitus upon palpation (Figure 1B). Due to suspected FG, he was admitted to our Oncological Surgery Unit. An emergency CT scan was performed, revealing

Figure 1. CT scan showing progression of left iliac bone disease previously treated with radiotherapy, with a large lytic lesion extending towards the perirectal fat (**A**); perineal and scrotal swelling, with evident crepitus appreciable on palpation due to gas production by anaerobic bacteria (**B**); emergency CT revealing multiple air bubbles in the perineum bilaterally and in the scrotal sac (**C**).

multiple air bubbles in the perineum bilaterally, in the scrotal sac, and subcutaneously in the left hemithorax and abdomen (Figure 1C). Laboratory tests showed hemoglobin 8 g/dL, platelets 8,000 cells/mm^3, white blood cells 700 cells/mm^3, and procalcitonin within normal limits. The patient was afebrile. A combination of Piperacillin Tazobactam, Meropenem, and Metronidazole was started. However, due to the low platelet count, it was not possible to immediately perform an extensive surgical debridement; therefore, a local curettage with the positioning of percutaneous drains was preferred. Unfortunately, the patient died within a few days.

DISCUSSION

The relationship between FG and malignancies remains unclear, with potential mechanisms including tumor-related immunosuppression, local tissue invasion, and superimposed infections due to compromised tissue integrity. An inflammatory microenvironment promotes local thrombotic microangiopathy and obliterative endoarteritis[5,6]. Resulting hypoxia facilitates the growth of facultative and obligatory anaerobes, such as *E. coli*, *Bacteroides fragilis*, and *Clostridium perfringens*. The typical clinical features of FG include sudden pain and scrotal edema, crepitus, pain, infected purulent wounds, feeling of exhaustion, and pallor. The European Association of Urology Guidelines[3] strongly recommend immediately starting treatment with empiric parenteral broad-spectrum antibiotics that cover all probable causative organisms and may penetrate inflammatory tissue, preferably a combination with a third-generation cephalosporin or broad-spectrum penicillin, gentamicin, metronidazole, or clindamycin. A subsequent personalized antibiotic therapy should be started as quickly as possible according to cultural and clinical response[3].

In addition to the high mortality associated with Fournier gangrene, the morbidity related to the numerous surgical debridements is even higher[7,8]. Extensive debridements often result in severe disfigurement, which represents not only physical but also profound psychological barriers to recovery. The coexistence of an unresectable tumor further exacerbates this condition, creating an exceptionally challenging clinical scenario. This case is noteworthy, as bladder cancer rarely manifests with such extensive local invasion leading to destructive sequelae. Following diagnosis, prompt and aggressive surgical debridement is imperative to achieve infection control and to minimize the associated morbidity and mortality. In survivors, the hospitalization course typically progresses through two distinct phases[8]. The initial phase is centered on source control and generally necessitates multiple wide debridements, administration of broad-spectrum antibiotics, and urological assessment of the genitalia[8]. Fecal diversion may be required, as ongoing contamination may further deteriorate the clinical status[7]. The subsequent wound-healing phase involves coordinated management by wound care specialists, implementation of advanced dressing techniques – including negative-pressure wound therapy – and collaboration with plastic surgeons for definitive closure or skin grafting when indicated. Management of such complex presentations demands substantial institutional resources and should therefore be undertaken in tertiary care centers equipped to meet these multidisciplinary needs. A coordinated, team-based approach is essential, with the general surgeon assuming a central role in ensuring adequate source control and determining the optimal timing for wound closure[5-8].

Patients suffering from hematological malignancies are at increased risk of Fournier gangrene[9,10]. A systematic review conducted in June 2021 reported 44 patients primarily affected by acute myeloid leukemia and acute lymphocytic leukemia. In 10 patients, FG represented the first presentation of hematological malignancy. *Pseudomonas aeruginosa* (n = 21) and *Escherichia coli* (n = 6) were the most commonly isolated microorganisms. Surgery was performed in 39 patients, while vacuum-assisted closure and hyperbaric oxygen therapy were adopted in 4 and 3 patients, respectively[4].

Cancer-associated FG is not frequently reported in the literature (Table I). Most of the cases described are associated with anal or rectal cancer. These are almost exclusively very aggressive forms which, although successfully treated with a multidisciplinary approach resulting in complete resolution of the FG, present a poor prognosis, typically no longer than 12 months, highlighting a highly aggressive tumor[11-17]. Necrosis of the bladder or urethra may be reported[12].

The roles of chemotherapy, immunotherapy, and targeted therapy in bladder cancer management are well established, as they demonstrate efficacy in tumor downstaging for definitive treatment and in improving surgical outcomes. Radiotherapy may reduce the risk of cancer recurrence after surgery and is useful in treating painful metastases. In the EV-301 trial[18], grade ≥3 severity treatment-related adverse events occurring in ≥5% of patients treated with Enfortumab Vedotin included maculopapular rash (7.4%), fatigue (6.4%), and decreased neutrophil count (6.1%). However, no febrile neutropenia was reported[18].

Hematocrit and extension to the abdominal wall have been observed as independent risk factors for mortality in FG, as previously reported by

Table I. Reports about FG in cancer patients; as highlighted, no case of bladder carcinoma has been previously reported, while most cases concern rectal cancer.

Authors	Number of patients	Cancer
Del Zingaro et al[11]	1	Prostate
Yoshino et al[12]	18	Rectal
Rakusic et al[13]	1	Gastric
Barone et al[14]	1	Thyroid
Jdaini et al[15]	1	Penis
Komeda et al[16]	1	Hepatocarcinoma
Nonaka et al[17]	1	Testicular

You et al[19]. Also, the Neutrophil-to-Lymphocyte Ratio (NLR) has been established as a prognostic biomarker of FG severity, with a mortality risk more than twice as high for patients with an NLR ≥10[20]. However, these considerations should be interpreted with caution in the oncological population, due to extreme heterogeneity and difficulty in analysis.

The genesis of Fournier syndrome in our case is, in fact, undoubtedly multifactorial and complex: first, the disease progression extending to the sacroiliac region resulted in pelvic functional and anatomical alterations, with the development of necrotic areas particularly at risk of superinfection. Secondly, extensive radiation therapy fields led to the development of anaerobic conditions, particularly favorable for the growth of pathogenic bacteria, which, in turn, were facilitated by the immunosuppression induced by Enfortumab Vedotin. Finally, the patient's poor hygiene, with no caregiver, further contributed to the rapid development of Fournier's syndrome. The associated sepsis and severe thrombocytopenia contraindicated extensive surgical curettage, necessary to optimize local control. Neutropenia and the absence of fever both underlie a state of anergy, which further facilitates clinical progression. Therefore, the evolution was extremely rapid and led to the patient's death.

CONCLUSIONS

FG is a multibacterial infection with a multifactorial origin and an extremely poor prognosis. Although it is more common in hematological diseases, it should also be carefully considered as a complication in cancer patients. Cancer management, due to improved systemic and loco-regional pharmacological treatments, could lead to a progressive increase in incidence. Particular attention should be paid to patients with iliac bone metastases and pelvic tumors undergoing radiotherapy and surgery, which may create a microenvironment favorable to the growth of anaerobic bacteria, always considering the possibility of rapid clinical progression.

Conflict of Interest
The authors declare that they have no conflicts of interest.

Acknowledgements
We thank the patient and his family for providing informed consent for publication of this case.

Ethics Approval and Informed Consent
In accordance with the journal's policies, we confirm that written informed consent was obtained from the patient for the publication of this case report, including any images or clinical data. The patient was made fully aware of the purpose of the publication and agreed to the disclosure of anonymized information for scientific and educational purposes. Ethics Approval is not applicable due to the study's design.

Authors' Contribution
Conceptualization: MDF; methodology: RC and VN; Investigation: MDF and MC; supervision: RC; writing-original draft: MDF, MT, VN, RC and MC; writing, review and editing: MDF, MT and RC.

Funding
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

ORCID ID
De Felice Marco: 0000-0002-3798-9698

REFERENCES

1. Bowen D, Hughes T, Juliebø-Jones P, Somani B. Fournier's gangrene: a review of predictive scoring systems and practical guide for patient management. Ther Adv Infect Dis 2024; 11: 20499361241238521.
2. Singh A, Ahmed K, Aydin A, Khan MS, Dasgupta P. Fournier's gangrene. A clinical review. Arch Ital Urol Androl 2016; 88: 157-164.

3. EAU Guidelines. Edn. presented at the EAU Annual Congress Madrid, Spain 2025. Available at: https://uroweb.org/guidelines/urological-infections/chapter/introduction
4. Creta M, Sica A, Napolitano L, Celentano G, La Rocca R, Capece M, Calogero A, Califano G, Vanni L, Mangiapia F, Arcaniolo D, Spirito L, Fusco F, De Sio M, Imbimbo C, Mirone V, Sagnelli C, Longo N. Fournier's Gangrene in Patients with Onco-hematological Diseases: A Systematic Review of Published Cases. Healthcare (Basel) 2021; 9: 1123.
5. Koch GE, Abbasi B, Agoubi L, Breyer BN, Clark N, Dick BP, Friedrich JB, Hampson LA, Hernandez A, Maine R, Osterberg EC, Teal L, Woodle CT, Hagedorn JC. Multidisciplinary management in Fournier's gangrene. Curr Probl Surg 2024; 61: 101499.
6. Kopechek KJ, Patel HV, Koch GE. Modern Management of Fournier's Gangrene. Curr Urol Rep 2025
7. Huang S, Chen DC, Perera M, Lawrentschuk N. Role of diverting colostomy and reconstruction in managing Fournier's gangrene-a narrative review. BJU Int 2024; 134: 534-540.
8. Altomare M, Benuzzi L, Molteni M, Virdis F, Spota A, Cioffi SPB, Reitano E, Renzi F, Chiara O, Sesana G, Cimbanassi S. Negative Pressure Wound Therapy for the Treatment of Fournier's Gangrene: A Rare Case with Rectal Fistula and Systematic Review of the Literature. J Pers Med 2022; 12: 1695.
9. Simsek A. Perianal Infections in Patients With Hematologic Malignancy: The Risk of Fournier's Gangrene Leading to Mortality and Irreversible Organ Damage. Wounds 2022; 34: 31-35.
10. Kjellesvig S, Zaworski E, Saliba AN. Acute Myelomonocytic Leukemia Presenting as Fournier's Gangrene. WMJ 2024; 123: 131-134.
11. Del Zingaro M, Boni A, Paladini A, Rossi De Vermandois JA, Ciarletti S, Felici G, Ursi P, Cirocchi R, Mearini E. Fournier's gangrene secondary to locally advanced prostate cancer: case report and review of the Literature. G Chir 2019; 40: 481-496.
12. Yoshino Y, Funahashi K, Okada R, Miura Y, Suzuki T, Koda T, Yoshida K, Koike J, Shiokawa H, Ushigome M, Kaneko T, Nagashima Y, Goto M, Kurihara A, Kaneko H. Severe Fournier's gangrene in a patient with rectal cancer: case report and literature review. World J Surg Oncol 2016; 14: 234.
13. Rakusic Z, Krpan AM, Sjekavica I. Fulminant Fournier's gangrene in a patient with gastric cancer treated with ramucirumab and paclitaxel. Ther Adv Drug Saf 2020; 11: 2042098620946556.
14. Barone M, Grani G, Ramundo V, Garritano T, Durante C, Falcone R. Fournier's gangrene during lenvatinib treatment: A case report. Mol Clin Oncol 2020; 12: 588-591.
15. Jdaini A, El Moudane A, El Farhaoui H, Irzi M, Hemdellah DS, Barki A. Fournier's gangrene revealing an aggressive squamous cell carcinoma of the penis: An exceptional case report. Urol Case Rep 2023; 50: 102503.
16. Komeda Y, Nagamatsu S, Kaya D, Sueki A, Yamamoto C, Ohta K, Matsuo Y, Nishio Y, Kikukawa S, Matsuura K, Matsuo H, Uejima M, Moriya K. Fournier's Gangrene in the Course of Treatment of Advanced Hepatocellular Carcinoma with Molecular-targeted Therapy. Intern Med 2025; 64: 673-678.
17. Nonaka K, Kawase K, Takagi K, Takatsu Y, Maniwa K, Takao C, Komura M, Mushika Y, Takeuchi N, Kato T, Kusakabe M, Kondo M. Development of Fournier's gangrene after chemotherapy for the recurrence of testicular cancer despite the absence of anorectal lesions: A case report. Medicine (Baltimore) 2024; 103: e38688.
18. Powles T, Rosenberg JE, Sonpavde GP, Loriot Y, Durán I, Lee JL, Matsubara N, Vulsteke C, Castellano D, Wu C, Campbell M, Matsangou M, Petrylak DP. Enfortumab Vedotin in Previously Treated Advanced Urothelial Carcinoma. N Engl J Med 2021; 384: 1125-1135.
19. You Q, Guan J, Wu B, Du J, Miao Y, Bai X, Ma Y, Zhen S, He Z. Fournier's Gangrene: clinical case review and analysis of risk factors for mortality. BMC Surg 2024; 24: 251.
20. Seretis K, Bounas N, Sfaelos K, Gaitanis G, Bassukas I. The Neutrophil-to-Lymphocyte Ratio as a Prognostic Biomarker of Fournier's Gangrene Severity: A Meta-Analysis. Infect Dis Rep 2025; 17: 55.