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Fournier's Gangrene: Paradigm Shifts in Literature

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Abstract

Background: Fournier's Gangrene, a swiftly progressing necrotizing infection, necessitates prompt and comprehensive intervention. In recent years, the landscape of its clinical management has undergone significant transformations, marked by notable shifts in risk factors, diagnostic approaches, and treatment strategies.

Methods: This comprehensive review delves into recent literature, scrutinizing changes in case presentations, diagnostic scoring systems, and the adoption of multidisciplinary approaches. Employing a systematic search, significant reports have been identified, providing valuable insights into the evolving dynamics of Fournier's Gangrene.

Results: The results of the literature analysis reveal emerging trends, including the identification of novel risk factors such as the influence of new medications. Additionally, novel diagnostic scoring systems have emerged, facilitating the early identification of patients at higher risk. The collaboration between specialists, combined with innovative diagnostics, has played a pivotal role in significantly enhancing patient care, fostering a more holistic approach to managing this challenging condition.

Conclusion: The evolving trends in Fournier's Gangrene underscore the paramount importance of rapid and precise diagnosis, as well as the implementation of multidisciplinary treatment strategies. This review accentuates the crucial role played by innovative diagnostic and therapeutic modalities, which have collectively contributed to improved patient outcomes. The dynamic nature of these trends emphasizes the ongoing need for adaptation in clinical practices, ensuring that healthcare professionals stay abreast of the latest advancements to optimize the management of Fournier's Gangrene and enhance overall patient prognosis.

Keywords: Fournier's Gangrene; Necrotizing Fasciitis; Sepsis; Surgical debridement; FDA

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Abbreviations

FG: Fournier Gangrene; NF: Necrotizing Fasciitis; FDA: US Food and Drug Administration; SGLT2i: Sodium Glucose co-transporter 2 inhibitors; VEGF: Vascular Endothelial Growth Factor

Background

Fournier's Gangrene (FG) is a rapidly progressing necrotizing fasciitis primarily affecting the perineal, perianal, and genital regions. Genital gangrene was first mentioned in the middle-ages medical works of famous Arab physician Avicenna. Bauriene in 1764 documented a case of scrotal gangrene resulting from a traumatic injury caused by an ox horn that involved multiple sessions of surgical debridement. However, the term "Fournier's gangrene" was later coined in 1883 by the French dermatologist Jean-Alfred Fournier. He described instances of fulminant gangrene affecting the genitals of otherwise *healthy young men* without apparent underlying causes. Overtime, this clinical condition has been denoted by various terms, including idiopathic gangrene of the scrotum, periurethral phlegmon, streptococcal scrotal gangrene, phagedena, and synergistic necrotizing cellulitis. Willison B. then introduced the term "necrotizing fasciitis" to describe the characteristic symptoms of FG [1-4].

The incidence of FG stands at 1.5 to 3 cases per 100,000 males annually, with a male-to-female ratio of approximately 10:1. The rare incidence of Fournier gangrene in women might be attributed to improved perineal drainage facilitated by vaginal secretions. Additionally, initial diagnostic challenges might arise due to the potential confusion with other genital infections, leading to underreporting in female cases [5].

In an observational study of 379 FG patients by Sugihara et al, they found a lower mortality rate

among those who underwent early surgical management in less than 48 h. Mok et al. found that the relative risk of death was 7.5 times greater in cases of necrotizing fasciitis that were not initially debrided adequately. Wong et al. reported a nine-fold increase in mortality if the procedure was delayed more than 24 h from the time of hospital admission [6].

Pathogenesis

Fournier's gangrene is classically defined as a type 1 necrotizing fasciitis, which typically has a poly-microbial origin, averaging 4 bacterial species per infection. In otherwise healthy males, minor trauma or may be surgical procedure *e.g.* circumcision, may be the trigger for the mono-microbial (type 2) FG caused by *Streptococcal* spp. or *Staphylococcus* spp. or even worse by MRSA [7].

As well, consumption of raw or undercooked seafood or injury by fish fins can lead to NF. In this group of infections, bacteria such as *Vibrio* spp., *Aeromonas* spp., and *Shewanella* spp. are commonly involved and are usually known as "marine bacteria" associated with freshwater and marine life (type 3) have been recently reported. Nevertheless, fungal etiologies (type 4) of necrotizing infections are rare but becoming increasingly recognized [7-9].

The pathogenesis involves a synergistic interplay of both aerobic and anaerobic microorganisms. Bacteria can infiltrate deeper tissues through open cuts or abrasions, subsequently infecting the subcutaneous tissue and causing its degradation. Bacteremia is believed to mark the initial stage in the progression towards fascia necrosis, inciting a cascade of cytokines that harm the endothelium, presumably initiating a coagulation cascade. This perpetuates the suppression of fibrinolysis and the formation of disseminated micro-thromboses in vessels that nourish the fascia *via* thromboplastin. Damage to the endothelium also induces fluid leakage, leading to tissue swelling and the infiltration of leukocytes, all of which collectively contribute to ischemia and necrosis of the fascia [9,10].

This symbiotic interaction significantly contributes to the rapid progression of the infection, which can advance at a rate as alarming as one inch per hour. The characteristic offensive smell and "dish water-like" discharge in FG is attributed to the role of anaerobes in this infection. Notably, the manifestations of this infection might not be readily discernible on the overlying skin, underscoring the urgency of early diagnosis and intervention to mitigate its potentially devastating consequences [9,10].

Risk factors

Over time, the recognized 'established' risk factors for FG development have gone some change, signaling a recent change in the game rules. Diabetes mellitus is the most commonly associated co-morbid condition (20%-70%). The other classic risk factors for Fournier's gangrene include elderly patients, obesity, immunosuppression (such as HIV), alcoholism, smoking, male sex, and the use of cytotoxic drugs [5].

The landscape of risk assessment for Fournier Gangrene (FG) is evolving, and traditional risk factors no longer adequately capture the diversity of presenting cases, as exemplified by a series of unusual scenarios. These cases encompass isolated penile gangrene, neonatal FG, and even FG occurrences following extensive masturbation or due to picquerism and those emerging post circumcision, challenging conventional expectations [11-15].

Moreover, the unexpected emergence of medication-induced FG has raised concerns and further contributes to the evolving landscape of risk factors. In August 2018, the US Food and Drug Administration (FDA) issued a black box warning that Sodium Glucose co-transporter 2 inhibitors (SGLT2i) may cause FG. The SGLT2i, known by the suffix –gliflozin, are a novel class of oral medications used to treat type 2 diabetes. They work by targeting a specific protein in the kidneys called SGLT2 which actively transports glucose from the renal tubules back into the bloodstream. By blocking SGLT2, these drugs hinder the kidneys' efficient reabsorption of glucose, causing more glucose to be excreted in urine. This process ultimately reduces blood glucose levels. Amongst the side effects of the SGLT2i is increased risk of urinary tract infections as well as genital fungal infections [16].

Elevated urinary glucose levels induced by SGLT2 inhibitors create a favorable environment for urinary and genital infections, serving as a precursor to the development of fasciitis gangrene [16].

Following the FDA's 2018 warning, there has been an elevated probability of reporting Fournier gangrene, particularly when individuals are exposed to factors associated with triggering the condition, as identified or suspected. This phenomenon can be attributed to a specific type of selection bias referred to as 'notoriety bias.' Consequently, the increased incidence of reported Fournier gangrene cases may be partially influenced by the heightened awareness generated by drug agencies' warnings [17].

However, a literature review focusing on cases of Fournier gangrene associated with SGLT2 inhibitors revealed a noteworthy observation. Among the total of 491 cases examined, 34% were females. This gender distribution cannot be solely explained by the notoriety bias, suggesting that factors beyond increased awareness may contribute to the reporting patterns in cases related to SGLT2 inhibitors [17].

Similarly, the emergence of antiangiogenic drugs, including monoclonal antibodies such as bevacizumab and tyrosine kinase inhibitors like sunitinib, has marked a significant advancement in the treatment of various cancer types. Nonetheless, these agents introduce side effects that were unobserved with traditional chemotherapy before. Within clinical practice, the most prevalent adverse events associated with antiangiogenic drugs include thromboembolic events and dermatological changes and delay to wound healing [18,19].

These agents exert inhibitory effects on Vascular Endothelial Growth Factors (VEGFs), resulting in a reduction in angiogenesis and a compromised tumor blood supply. This condition is probably a consequence of a disruption in the vascular endothelial cells of the skin, attributed to the suppression of VEGF signaling. This is primarily due to the fact that these drugs lack shared targets. It has been established that the inhibition of VEGF gives rise to disturbances in the coagulation cascade, thereby inducing a pro-thrombotic state. Thrombotic events within the small skin vessels can result in tissue ischemia and subsequent necrosis, which, in turn, facilitates bacterial colonization, culminating in the onset of infection. Notably, the occurrence of sunitinib-induced necrotizing fasciitis came to light during post-marketing surveillance, prompting a recent issuance of a black-box warning by the FDA [18,19].

In response, urologists need to adapt to these changing game rules, recognizing the need for a more flexible and comprehensive approach to risk assessment and diagnosis. In the ongoing effort to address the elevated mortality rates and rapid progression associated with Fournier Gangrene (FG), numerous algorithms and calculators

have been devised to improve disease identification and mitigate its severity. These tools rely on a combination of clinical observations and laboratory data to provide guidance to healthcare professionals regarding the imperative interventions necessary to avert swift patient deterioration.

Based on their series, Laor et al. proposed that an FGSI score of 9 or more indicated a 75% probability of mortality, whereas a score of 9 or less indicated a 78% survival probability. Uludag et al. added age and extension by anatomical regions to the FGSI, with a score ≥ 9 suggesting the patient is 13.64 times more likely to die [20-22].

Combined Urology and Plastics Index (CUPI) was developed to predict hospital Length of Stay (LOS); parameters include age at admission, hematocrit, serum bicarbonate, blood urea nitrogen, serum calcium, alkaline phosphatase, albumin, INR, lactate, and total bilirubin. Scores are 0 to 15, patients with a score ≤ 5 had an average LOS of 25 days, those with a score >5 had an average LOS of 71 days [23].

The diagnosis of FG is primarily based on clinical findings. FG has an insidious onset, with 40% of patients presenting with no symptoms, which makes early detection crucial. It usually begins with pain and itching of the perineum and scrotal skin. Examination of the genitalia and perineum and a digital rectal examination should be done. Fluctuance, crepitance, localized tenderness and wounds raises the possibility of FG. When a high suspicion of necrotizing fasciitis arises based on history and physical examination findings, immediate surgical debridement should never be postponed, regardless of the results yielded by any clinical scoring system [5].

Management

Given the extensive array of pathogenic microorganisms involved, urologists are often confronted with the challenge of making empirical antibiotic selections that encompass a broad spectrum of antibacterial coverage, spanning gram-positive, gram-negative, aerobic, and anaerobic bacteria. A typical choice of broad-spectrum antibiotics may entail the use of carbapenems or β-Lactamase inhibitors in conjunction with Clindamycin. In instances where there is suspicion of Methicillin-Resistant *Staphylococcus aureus* (MRSA) infection, the inclusion of vancomycin or linezolid becomes imperative. Patients with allergies to β-Lactamase inhibitor antibiotics may opt for aminoglycosides or fluoroquinolones along with metronidazole. In cases where there is a clear risk of fungal infection (particularly types I and IV), the addition of amphotericin B or fluconazole is warranted [24,25].

Emergency surgical debridement of the affected tissues is the primary management modality for NF. The extent of tissue extracted depends on the body region, which is infected. As a general rule, debridement will extend until healthy tissue is found. A second look is recommended within 48 h to ensure complete eradication of necrotic tissue and no further spread of hidden pockets of infection before planned closure [5,24,25].

Adjunctive treatment options

Hyperbaric Oxygen Therapy (HBOT) is a treatment method that involves breathing pure oxygen under increased atmospheric pressure within a sealed chamber. This therapeutic approach accelerates the healing process by augmenting tissue oxygen levels and effectively eliminating anaerobic bacteria. HBOT has demonstrated bactericidal effects against both aerobic and anaerobic infections. Recent research has highlighted the significant reduction in mortality rates among Fournier Gangrene patients undergoing HBOT. However, there remains a lack of consensus within the medical community regarding the adjunctive use of HBOT in FG management, leading to ongoing debates about its efficacy [26].

Vacuum-Assisted Closure (VAC) is a negative pressure wound therapy that transforms an open wound into a temporarily sealed and controlled environment. These devices promote angiogenesis and can enhance nourishment, facilitating tissue formation and creating an optimal setting for wound healing. Vacuum-assisted closure therapy streamlines the wound healing process. Evidence suggests that VAC therapy results in fewer dressing changes, reduced pain, fewer missed meals, increased mobility, and decreased hands-on treatment time for healthcare providers, and potentially shorter hospital stays compared to traditional methods. Importantly, these benefits are achieved without compromising patient safety or mortality rates in individuals with Fournier's gangrene [27].

Unprocessed honey has demonstrated antibacterial effects on various bacteria and fungi in laboratory settings, attributed to its low pH value, high permeability, and enzyme activity. It is cost-effective and readily available. However, its use is typically recommended for patients with minor skin lesions and no complications. Despite numerous studies showcasing the advantages of raw honey, its therapeutic efficacy remains a topic of debate [25,28].

Overall, European urological guidelines do not support any of the adjunctive therapy options (level 3 & 4) the due to lack of consistent evidence [6].

Defect closure

When dealing with small scrotal defects, it is recommended to attempt primary closure, as studies have indicated that this approach yields the most favorable functional and cosmetic outcomes. Ideally, a two-layer closure using absorbable sutures is performed. However, if there is noticeable excessive tension during closure, particularly if it distorts local anatomy, such as the anus, it is prudent to consider alternative reconstructive techniques. Closing wounds in layers is advised to minimize dead space. Primary closure can lead to complications such as infections, extended healing periods, and contractures that may result in deformities [6,29].

If primary closure is not feasible, the choice of treatment options varies based on the specific location of the defect, its size, and the intended functional outcome of the reconstruction. For instance, Karian et al. introduced a reconstructive plan for scrotal defects. According to their algorithm, defects covering less than 50% of the scrotum can either be left to heal naturally or be reconstructed using a scrotal advancement flap. In contrast, defects encompassing more than 50% of the scrotum or extending beyond it necessitate more extensive interventions such as flap reconstruction or a skin graft [6,29].

Conclusion

The evolving understanding of the evolving paradigm of FG marks a significant change in the once previously accepted as established risk factors, diagnosis and prognosis. Historically perceived as a straightforward condition, recent reports in literature have illuminated its complexity, challenging diagnostic and therapeutic approaches. This paradigm shift underscores the importance of continuous research and interdisciplinary collaboration in reshaping our comprehension of diseases. As we dive deeper into the underlying

mechanisms and risk factors, urologists are better equipped to diagnose FG promptly and tailor effective treatments. Moreover, these advancements emphasize the need for personalized, evidence-based interventions, moving away from generalized approaches in order to improve the quality of care for individuals afflicted with Fournier's Gangrene.

References

1. Zhang KF, Shi CX, Chen SY, Wei W. Progress in multidisciplinary treatment of Fournier's gangrene. Infect Drug Resist. 2022;15:6869-80.
2. Bauriene H. Sur une plaie qui s'est terminee par la sphacele de la scrotum. J Méd Chirurgie Pharm. 1764;20:251-6.
3. Fournier JA. Gangrene foudroyante de la verge. Semaine Médicale. 1883;4:589-97.
4. Wilson B. Necrotizing fasciitis. Am Surg. 1952;18(4):416-31.
5. Lewis GD, Majeed M, Olang CA, Patel A, Gorantla VR, Davis N, et al. Fournier's gangrene diagnosis and treatment: A systematic review. Cureus. 2021;13(10):e18948.
6. Uroweb. Urological Infections - The Guideline.
7. Misiakos EP, Bagias G, Patapis P, Sotiropoulos D, Kanavidis P, Machairas A. Current concepts in the management of necrotizing fasciitis. Front Surg. 2014;1:36.
8. Perkins TA, Bieniek JM, Sumfest JM. Solitary *Candida albicans* infection causing Fournier gangrene and review of fungal etiologies. Rev Urol. 2014;16(2):95-8.
9. Perkins TA, Bieniek JM, Sumfest JM. Solitary Candida albicans Infection Causing Fournier Gangrene and Review of Fungal Etiologies. Rev Urol. 2014;16(2):95-8. (Repeat 8)
10. Singh A, Ahmed K, Aydin A, Khan MS, Dasgupta P. Fournier's gangrene. A clinical review. Arch Ital Urol Androl. 2016;88:157-64.
11. Heiner JD, Eng KD, Bialowas TA, Devita D. Fournier's gangrene due to masturbation in an otherwise healthy male. Case Rep Emerg Med. 2012;2012:154025.
12. Galukande M, Sekavuga DB, Muganzi A, Coutinho A. Fournier's gangrene after adult male circumcision. Int J Emerg Med. 2014;7:37.
13. Moussa M, Abou Chakra M. Isolated penile Fournier's gangrene: A case report and literature review. Int J Surg Case Rep. 2019;62:65-8.
14. De La Torre M, Solé C, Fanjul M, Berenguer B, Arriaga-Redondo M, de Tomás E, et al. Neonatal Fournier's gangrene: Avoiding extensive debridement. Pediatr Infect Dis J. 2021;40(10):e384-7.
15. Akella P, Mishra AK, Grewal H. Fournier's Gangrene following piquerism. Am J Med Sci. 2019;358(3):e13.
16. Bersoff-Matcha SJ, Chamberlain C, Cao C, Kortepeter C, Chong WH. Fournier gangrene associated with sodium-glucose cotransporter-2 inhibitors: A review of spontaneous post marketing cases. Ann Intern Med. 2019;170(11):764-9.
17. Serrano Olave A, Bueno Moral AI, Martínez Bañón C, González Mesa E, Jiménez López JS. Fournier's gangrene under sodium-glucose cotransporter-2 inhibitors therapy in gynecological patients. Int J Environ Res Public Health. 2022;19(10):6261.
18. Piszczek J, Dalton B, Peters T, Ruether D, Urbanski S. Extensive necrotizing fasciitis associated with sunitinib therapy. Clin Genitourin Cancer. 2014;12(2):e47-9.
19. 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(6):588-91.
20. Laor E, Palmer LS, Tolia BM, Reid RE, Winter HI. Outcome prediction in patients with Fournier's gangrene. J Urol.1995;154:89-92.
21. Morais H, Neves J, Ribeiro HM, Ferreira M, Guimarães N, Azenha N, et al. Case series of Fournier's gangrene: Affected body surface area – the underestimated prognostic factor. Ann Med Surg (Lond). 2017;16:19-22.
22. Yılmazlar T, Işık Ö, Öztürk E, Özer A, Gülcü B, Ercan İ, et al. Fournier's gangrene: Review of 120 patients and predictors of mortality. Ulus Travma Acil Cerrahi Derg. 2014;32(7):333-7.
23. Ghodoussipour SB, Gould D, Lifton J, Badash I, Krug A, Miranda G, et al. Surviving Fournier's gangrene: Multivariable analysis and a novel scoring system to predict length of stay. J Plast Reconstr Aesthet Surg. 2018;71(5):712-8.
24. Yilmazlar T, Gulcu B, Isik O, Ozturk E. Microbiological aspects of Fournier's gangrene. Int J Surg. 2017;40:135-8.
25. Chernyadyev SA, Ufimtseva MA, Vishnevskaya IF, Bochkarev YM, Ushakov AA, Beresneva TA, et al. Fournier's Gangrene: Literature review and clinical cases. Urol Int. 2018;101(1):91-7.
26. Raizandha MA, Hidayatullah F, Kloping YP, Rahman IA, Djatisoesanto W, Rizaldi F. The role of hyperbaric oxygen therapy in Fournier's Gangrene: A systematic review and meta-analysis of observational studies. Int Braz J Urol. 2022;48(5):771-81.
27. Syllaios A, Davakis S, Karydakis L, Vailas M, Garmpis N, Mpaili E, et al. Treatment of Fournier's gangrene with vacuum-assisted closure therapy as enhanced recovery treatment modality. *In Vivo*. 2020;34(3):1499-502.
28. Sufya N, Matar N, Kaddura R, Zorgani A. Evaluation of bactericidal activity of Hannon honey on slowly growing bacteria in the chemostat. Drug Healthc Patient Saf. 2014;6:139-44.
29. Michael P, Peiris B, Ralph D, Johnson M, Lee WG. Genital reconstruction following Fournier's gangrene. Sex Med Rev. 2022;10(4):800-12.