Fournier’s gangrene and intravenous drug abuse: an unusual case report and review of the literature

https://doi.org/10.1515/med-2019-0114
received February 9, 2019; accepted July 9, 2019

Abstract: Fournier’s gangrene is a potentially fatal emergency condition characterized by necrotizing fasciitis and supported by an infection of the external genital, perineal and perianal region, with a rapid and progressive spread from subcutaneous fat tissue to fascial planes.

In this case report, a 52-year-old man, with a history of hepatitis C-virus (HCV)-related chronic liver disease and cocaine use disorder for which he was receiving methadone maintenance therapy, was admitted to the Emergency Department with necrotic tissue involving the external genitalia. Fournier’s gangrene is usually due to compromised host immunity, without a precise cause of bacterial infection; here it is linked to a loco-regional intravenous injection of cocaine. A multimodal approach, including a wide surgical debridement and a postponed skin graft, was needed.

Here we report this case, with a narrative review of the literature.

Keywords: Fournier’s gangrene; Necrotizing Fasciitis; Surgery; Infection

1 Introduction

Fournier’s gangrene was described for the first time in 1764 by Baurienne as an idiopathic, necrotizing lethal process in a man affected by gangrene of the genitalia. However, the origin of this clinical condition must be linked to Jean Alfred Fournier who described a series of fatal cases of idiopathic gangrene of the genitalia with a sudden onset in 5 young men in 1883 [1]. Fournier’s gangrene is a potentially fatal condition; it is characterized by necrotizing fasciitis and supported by an infection of the external genital, perineal and perianal region, with a rapid and progressive spread from subcutaneous fat tissue to fascial planes [2]. This emergency condition always requires a multimodal approach: antibiotic therapy, surgery followed by intensive care, and oxygen hyperbaric therapy [3]. Because of its rarity, most of the limited knowledge about Fournier’s gangrene derives from case reports and retrospective studies with small sample size [4]. Here, in order to improve the knowledge concerning Fournier’s gangrene, we describe an unusual case due to injection of cocaine into the superficial dorsal vein of the penis, followed by a comprehensive literature review.

2 Material and methods

We performed a narrative review of the literature by searching “Fournier’s gangrene”, “necrotizing fasciitis” on PubMed and Scopus (Table). Case reports, case series, and reviews were chosen and used to extract data regarding gender, age, comorbidity, pathogens, number of surgical debridements performed, peri-operative outcomes, intra- and post-operative complications, length of hospital stay, and number of hospitalizations in intensive care units. Two authors (AB, AP) independently performed online bibliographic searches to identify titles and abstracts of interest. Full texts of relevant articles were further assessed for inclusion in this study.
Table 1: review of the Literature up-to-date to July 2019

| Reference          | Year | Gender | N. of cases | Mean age | Surgical debridement | Days of hospital stay | Sepsi / ICU | Hyperbaric oxygen therapy | Pathogen                                                                 | N. of deaths |
|--------------------|------|--------|-------------|----------|----------------------|-----------------------|-------------|---------------------------|--------------------------------------------------------------------------|--------------|
| Del Zingaro et al. [36] | 2019 | M      | 1           | 76       | 1                    | ND                    | 0           | 0                         | Pseudomonas putida, Stenotrophomonas maltophilia, Staphylococcus haemolyticus and Staphylococcus Warmeri | 0            |
| Arora et al. [37]   | 2019 | 50M    | 50          | 53       | 1                    | 12.6                  | ND          | ND                        | Escherichia coli, Staphylococci, Pseudomonas, Bacteroides, Streptococci    | 12           |
| Ali et al. [38]     | 2019 | M      | 1           | 45       | 1                    | ND                    | 1           | 0                         | ND                                                                      | 0            |
| Mostaghim et al. [39]| 2019 | M      | 1           | 38       | 1                    | ND                    | 0           | 0                         | Escherichia coli, Enterococcus faecalis, Bacteroides thetaiotaomicron, Streptococcus agalactiae, Clostridium clostridioforme | 0            |
| Zhou et al. [40]    | 2019 | M      | 1           | 58       | 1                    | ND                    | 1           | 0                         | ND                                                                      | 0            |
| Aslan et al. [41]   | 2019 | M      | 1           | 12       | 0                    | 8 h                   | 2           | 0                         | Pseudomonas aeruginosa                                                   | 1            |
| Heijkoop et al. [42] | 2019 | ND     | 14          | ND       | 6                    | 36                    | 9           | 0                         | ND                                                                      | 1            |
| Paone et al. [43]   | 2019 | M      | 1           | 72       | >1                   | ND                    | 2           | 0                         | ND                                                                      | 0            |
| Lin et al. [44]     | 2019 | 118M   | 118         | 58       | 1                    | ND                    | ND          | ND                        | Escherichia coli, Staphylococcus aureus, Streptococcus, Anaerobic bacteroides | 17           |
| Akella et al. [45]  | 2019 | M      | 1           | 37       | 1                    | ND                    | ND          | 0                         | Staphylococcus aureus, Streptococcus, Anaerobic bacteroides               | 0            |
| Klement et al. [46] | 2019 | M      | 1           | 53       | 1                    | ND                    | 1           | ND                        | ND                                                                      | 1            |
| Onder et al. [47]   | 2019 | M      | 1           | 64       | 2                    | ND                    | ND          | ND                        | ND                                                                      | 0            |
| Bersoff-Matcha et al. [48] | 2019 | 39M 16F | 55         | ND       | 1                    | ND                    | 9           | ND                        | Escherichia coli, MRSA, Streptococcus pyogenes, Enterococcus faecium, Enterococcus cloacae, Klebsiella pneumoniae, Streptococcus epidermidis, Bacteroides fragilis, Corynebacterium, Candida albicans, Aspergillus fumigatus | 3            |
| Louro et al. [49]   | 2019 | 14M 1F | 15          | 66.9     | 3.3                  | 46.8                  | ND          | ND                        | ND                                                                      | 0            |
| Reference                  | Year | Gender | N. of cases | Mean age | Surgical deb-ridement | Days of hospital stay | Sepsi / ICU | Hyperbaric oxygen therapy | Pathogen                                                                 | N. of deaths |
|----------------------------|------|--------|-------------|----------|------------------------|-----------------------|-------------|---------------------------|--------------------------------------------------------------------------|--------------|
| Ünverdi et al. [50]        | 2019 | 13M    | 13          | 54.3     | 1                      | 42                    | ND          | ND                        | Bacteroides Fragilis, Escherichia coli, Klebsiella spp, Pseudomonas aeruginosa | 0            |
| Hong-Cheng et al. [51]     | 2019 | 56M 4F | 60          | 53       | 1.17                   | ND                    | 1           | 0                         | Escherichia coli, Enterococcus faecalis, Proteus mirabilis, Klebsiella pneumoniae, Peptostreptococcus, Pseudomonas aeruginosa | 1            |
| Rachana et al. [52]        | 2019 | M      | 1           | 50       | 1                      | 18                    | 0           | 0                         | Fusobacterium varium, Escherichia coli, Bacteroides fragilis             | 0            |
| Joury et al. [53]          | 2019 | M      | 1           | 51       | 1                      | ND                    | ND          | 0                         | MRSA, Escherichia coli, Bacteroides fragilis                            | 0            |
| Selvi et al. [54]          | 2019 | 30M    | 30          | 62.9     | 6                      | 20                    | 9           | ND                        | Escherichia coli, Bacteroides                                        | 3            |
| Majdoub et al. [55]        | 2018 | F      | 1           | 70       | -                      | -                     | -           | -                         | Escherichia coli, Bacteroides, Polymicrobial flora (Escherichia coli, Enterococcus, Staphylococcus, Klebsiella) (7), Monomicrobial flora (Staphylococcus, Escherichia coli, Klebsiella, Enterococcus, Candida) (22) | 9            |
| Hahn et al. [56]           | 2018 | 33M 11F| 44          | 54.4     | 3.3                    | 47                    | 18          | ND                        | MRSA, Escherichia coli, Bacteroides, Enterococcus avium, Gemella morbillorum | 0            |
| Overholt et al. [57]       | 2018 | M      | 1           | 44       | 2                      | 13                    | 0           | 0                         | Escherichia coli, Enterococcus avium, Gemella morbillorum, Escherichia coli, Klebsiella, Staphylococci | 5            |
| Pehlivanli et al. [58]     | 2018 | 19M 4F | 23          | 65.9     | 6                      | 18                    | ND          | ND                        | Mixed flora (73), Streptococci (12), Staphylococci (10), Enterococci (10), Citrobacter (1), Pseudomonas (1), Candida (2) | 17           |
| Kranz et al. [4]           | 2018 | 154M   | 154         | 62.7     | 4.2                    | 26.6                  | 104         | 13                        | Mixed flora (73), Streptococci (12), Staphylococci (10), Enterococci (10), Citrobacter (1), Pseudomonas (1), Candida (2) | 17           |
| Kobayashi et al. [59]      | 2018 | M      | 1           | 68       | 1                      | 59                    | 1           | 0                         | Escherichia coli                                                       | 0            |
| Pandey et al. [60]         | 2018 | M      | 1           | 65       | 1                      | ND                    | ND          | ND                        | Escherichia coli                                                       | ND           |
| Matsuura et al. [61]       | 2018 | M      | 1           | 88       | ND                     | ND                    | ND          | 0                         | Rhizobium radiobacter                                                   | 1            |
| Sen et al. [62]            | 2018 | M      | 1           | 47       | 1                      | ND                    | ND          | 0                         | Staphylococcus aureus, Acinetobacter, Streptococcus pyogenes, Proteus mirabilis, | 1            |
| Elsaket et al. [63]        | 2018 | 43M 1F | 44          | 51       | 1.33                   | 26                    | 6           | ND                        | Staphylococcus aureus, Acinetobacter, Streptococcus pyogenes, Proteus mirabilis, | 5            |
| Heijkoop et al. [64]       | 2018 | ND     | 14          | ND       | 6                      | 36                    | 8           | 0                         | Streptococcus constellatus, Clostridium ramosum                           | 1            |
| Takano et al. [65]         | 2018 | F      | 1           | 44       | 1                      | ND                    | ND          | 0                         | Streptococcus constellatus, Clostridium ramosum                           | 1            |
| Reference           | Year | Gender | N. of cases | Mean age | Surgical debridement | Days of hospital stay | Sepsis / ICU | Hyperbaric oxygen therapy | Pathogen                                                                 | N. of deaths |
|---------------------|------|--------|-------------|----------|----------------------|-----------------------|--------------|---------------------------|---------------------------------------------------------------------------|-------------|
| Semenič et al. [66] | 2018 | M      | 1           | 30       | 2                    | 16                    | 1            | 0                         | Escherichia coli, Bacteroides fragilis, Prevotella oralis, Streptococcus anginosus | 0           |
| Abbas-Shereef et al. [67] | 2018 | M      | 1           | 71       | >1                   | 30                    | 1            | 0                         | Pseudomonas aeruginosa, Klebsiella pneumoniae, Candida albicans, Staphylococci, Group A Streptococcus | 0           |
| Wetterauer et al. [68] | 2018 | 20M    | 20          | 66       | 4                    | ND                    | 15           | 0                         | Escherichia coli, Klebsiella, Pseudomonas aeruginosa | 3           |
| Demir et al. [69]   | 2018 | 49M 25F | 74          | 57.6     | 1.87                 | 23.18                 | ND           | ND                        | Escherichia coli, Staphylococcus aureus, Streptococci, Enterobacter, Pseudomonas aeruginosa, Bacteroides, Proteus, Clostridium | 6           |
| Chen et al. [70]    | 2018 | M      | 1           | 29       | 2                    | 11                    | 1            | 0                         | Streptococcus Agalactiae, Staphylococcus haemolyticus, Escherichia coli, peptostreptococci, Prevotella corporis | 0           |
| Yuan et al. [71]    | 2018 | M      | 1           | 62       | 1                    | ND                    | 1            | ND                        | Enterococcus avium, Escherichia coli | ND           |
| Katsimantas et al. [72] | 2018 | M      | 1           | 68       | 2                    | 17                    | 0            | 0                         | Enterococcus faecalis, Streptococcus gordoni, Prevotella melaninogenica | 0           |
| Althunayyan et al. [73] | 2018 | F      | 1           | 36       | 2                    | 31                    | 1            | 0                         | Escherichia coli, Acinetobacter baumannii | 0           |
| Pittaka et al. [74] | 2018 | F      | 1           | 24       | >1                   | 14                    | ND           | ND                        | Bacteroides fragilis, Clostridium ramosum, Gram positive cocci | 1           |
| Taylor et al. [75]  | 2018 | F      | 1           | 58       | 1                    | ND                    | 1            | ND                        | ND                        | 9           |
| Dos Santos et al. [76] | 2018 | 29M 11F | 40          | 51.7     | 1.8                  | 19.6                  | 9            | ND                        | ND                        | 0           |
| Fukui et al. [77]   | 2018 | M      | 1           | 85       | 1                    | 104                   | 1            | 0                         | ND                        | 0           |
| Kuzaka et al. [78]  | 2018 | 13M    | 13          | 59.6     | >1                   | 31.9                  | 0            | ND                        | ND                        | 0           |
| Goel et al. [79]    | 2018 | M      | 1           | 60       | 1                    | 14                    | 0            | 0                         | ND                        | 0           |
| Ghodoussipour et al. [80] | 2018 | 54M    | 54          | 49.3     | 3.9                  | 37.5                  | 53           | ND                        | ND                        | 3           |
| Tenório et al. [81] | 2018 | 99M, 12F | 124         | 50.8     | ND                   | 21.7                  | ND           | 1                         | Escherichia coli, Proteus, Klebsiella, Pseudomonas, Staphylococci, Enterococcus, Clostridium | 32          |
| Weimer et al. [82]  | 2017 | M      | 1           | 55       | >1                   | 90                    | 1            | 0                         | Parabacteroides distasonis, Prevotella melaninogenica, Fusobacterium nucleatum, Bacteroides | 0           |
| Währmann et al. [83] | 2017 | F      | 1           | 46       | 3                    | ND                    | 1            | ND                        | Streptococci, Enterobacteria, gram+ | 0           |
| Wang et al. [84]    | 2017 | M      | 1           | 61       | 1                    | ND                    | ND           | ND                        | Klebsiella pneumoniae | 0           |
| Yücel et al. [85]   | 2017 | 11M, 14F | 25          | 54.3     | 2.4                  | 21.4                  | ND           | 0                         | ND                        | 1           |
| Reference          | Year  | Gender | N. of cases | Mean age | Surgical deb- | Days of hospital stay | Sepsi / ICU | Hyperbaric oxygen therapy | Pathogen                                                                 | N. of deaths |
|--------------------|-------|--------|-------------|----------|---------------|------------------------|-------------|----------------------------|--------------------------------------------------------------------------|--------------|
| Üreyen et al. [86] | 2017  | 18M, 11F | 29          | 51.5     | 1.8           | 11.5                   | 17          | ND                         | Escherichia coli, Acinetobacter, Streptococci, Staphylococcus aureus, Pseudomonas, Klebsiella, | 6            |
| Dell'Atti et al. [87] | 2017  | M      | 1           | 75       | 1             | 28                     | 1           | 0                          | ND                         | 0            |
| Yanaral et al. [88] | 2017  | 54M, 5F | 54          | 58.3     | 1.4           | 15.3                   | ND          | 0                          | Streptococci, Escherichia coli, Prevotella                        | 4            |
| Chia et al. [89]   | 2017  | 42M, 17F | 59          | 56       | >1            | 19                     | 11          | ND                         | ND                         | 9            |
| Kordahi et al. [90] | 2017  | M      | 1           | 57       | >1            | ND                     | ND          | ND                         | Escherichia coli, Streptococci, Proteus, Klebsiella pneumoniae, Enterococcus faecium, Pseudomonas aeruginosa, Staphylococcus aureus | 5            |
| Hong et al. [91]   | 2017  | 18M, 2F | 20          | 61.8     | 1.55          | 36.9                   | 15          | 0                          | Escherichia coli, P. mirabilis                                      | 0            |
| Sanders et al. [92] | 2017  | M      | 1           | 70       | 2             | ND                     | 1           | 0                          | Streptococcus anginosus, anaerobes, Gram -                           | 3            |
| Ferretti et al. [93] | 2017  | 19M, 1F | 20          | 56       | 4             | 31.7                   | 17          | 4                          | Escherichia coli (11), Klebsiella pneumoniae (3), Pseudomonas aeruginosa (3), Acinetobacter baumannii (2), Proteus mirabilis (2), Providencia stuartii (1) | 5            |
| Kumar et al. [94]  | 2017  | M      | 1           | 41       | 2             | 15                     | 1           | 0                          | Escherichia coli, Streptococcus pyogenes, Prevotella loeschei        | 0            |
| Ioannidis et al. [95] | 2017  | 20M, 4F | 24          | 58.9     | 1             | 16                     | 18          | 3                          | Escherichia coli, Streptococcus pyogenes, Prevotella loeschei        | 0            |
| Bocchiotti et al. [96] | 2017  | M      | 1           | 40       | 3             | ND                     | 0           | 0                          | Escherichia coli, Streptococcus pyogenes, Clostridium               | 0            |
| Choi et al. [97]   | 2017  | F      | 1           | 31       | 1             | 17                     | 0           | 0                          | Streptococcus anginosus, Pseudomonas, Clostridium                    | 0            |
| Sawayaama et al. [98] | 2017  | M      | 1           | 66       | 1             | ND                     | 0           | 0                          | ND                         | 0            |
| Laureman et al. [99] | 2017  | 125M, 43F | 168        | ND       | >1            | ND                     | 92          | 0                          | Enterococcus faecalis, Klebsiella pneumoniae, Escherichia coli, Clostridium difficile | 6            |
| Smith et al. [100] | 2017  | M      | 1           | 50       | >1            | ND                     | 1           | 0                          | ND                         | 0            |
| Baek et al. [101]  | 2017  | F      | 1           | 57       | 1             | ND                     | 1           | ND                         | ND                         | 0            |
| Huang [102]        | 2017  | M      | 1           | 46       | 1             | ND                     | 1           | ND                         | ND                         | 0            |
| Morais et al. [103] | 2017  | 12M, 3F | 15          | 70       | ND            | 32                     | ND          | 0                          | Escherichia coli, Proteus, Staphylococcus aureus, Enterococcus faecalis | 4            |
| Okumura et al. [104] | 2017  | M      | 1           | 70       | 1             | 39                     | 1           | 0                          | Klebsiella pneumoniae, Group G Streptococcus                      | 0            |
| Osbun et al. [105] | 2017  | ND     | 165         | 53.4     | 1.97          | 16.6                   | 43          | ND                         | ND                         | 11           |
| Kahn et al. [106]  | 2017  | M      | 147         | 52       | 2.5           | 19                     | 112         | ND                         | ND                         | 11           |
| Misiakos et al. [107] | 2017  | 47M, 15F | 62          | 63.7     | 4.8           | 19.7                   | 32          | 0                          | Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Proteus mirabilis | 0            |
| Obi [108]          | 2017  | 4M     | 4           | 34.3     | 1             | 17.3                   | 0           | 0                          | Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Proteus mirabilis | 0            |

Table 1 continued: review of the Literature up-to-date to July 2019
| Reference                      | Year | Gender | N. of cases | Mean age | Surgical deb-ridement | Days of hospital stay | Sepsi / ICU | Hyperbaric oxygen therapy | Pathogen                                                                 | N. of deaths |
|--------------------------------|------|--------|-------------|----------|------------------------|-----------------------|-------------|---------------------------|--------------------------------------------------------------------------|-------------|
| Pernetti et al. [109]          | 2016 | M      | 1           | 70       | 1                      | 21                    | 1           | ND                        | ND                                                      | 0           |
| Farías et al. [110]            | 2016 | M      | 1           | 46       | 1                      | 4                     | 1           | 0                         | ND                                                      | 0           |
| Ozkan et al. [111]             | 2016 | 7M, 5F | 12          | 62.4     | 5.7                    | 19.6                  | ND          | 0                         | Polymicrobial flora (6), monomicrobial (6) | 0           |
| Yoshino et al. [112]           | 2016 | M      | 1           | 64       | 1                      | 33                    | 1           | 0                         | Streptococcus. alpha-emolitico                                  | 0           |
| Crowell et al. [113]           | 2016 | M      | 1           | 54       | 3                      | 18                    | 1           | 0                         | Rhizopus (zygomycosis)                                              | 1           |
| Taken et al. [114]             | 2016 | 57M, 8F| 65          | 52.5     | 2.5                    | 9.2                   | 13          | 0                         | Escherichia coli, Streptococcus, Staphylococcus aureus, Enterobacter, Bacteroides, Pseudomonas aeruginosa, Proteus, Clostridium | 6           |
| Wanis et al. [115]             | 2016 | M      | 1           | 28       | 1                      | 14                    | 1           | 0                         | ND                                                      | 0           |
| Sheehy et al. [116]            | 2016 | M      | 1           | 48       | 2                      | ND                    | 1           | 0                         | Polymicrobial flora                                                | 0           |
| Sarkut et al. [117]            | 2016 | 32M, 32F | 64       | 57       | 3                      | 16.6                  | ND          | ND                        | ND                                                      | 18          |
| Sinha et al. [118]             | 2015 | F      | 1           | 30       | 1                      | ND                    | 1           | ND                        | ND                                                      | 0           |
| Marín et al. [119]             | 2015 | 53M, 6F | 59       | 68       | ND                     | 24.4                  | 50          | ND                        | ND                                                      | 15          |
| Chalya et al. [120]            | 2015 | 82M, 2F | 84       | 34       | ND                     | 28                    | ND          | ND                        | ND                                                      | 24          |
| Namkoong et al. [121]          | 2015 | M      | 1           | 61       | 1                      | ND                    | 1           | 0                         | ND                                                      | 0           |
| Schulz et al. [122]            | 2015 | M      | 1           | 59       | >1                     | ND                    | 1           | 0                         | ND                                                      | 0           |
| McCormack et al. [123]         | 2015 | 25M    | 25          | 56.6     | 1.4                    | ND                    | 3           | ND                        | Polymicrobial flora                                               | 5           |
| Tarchouli et al. [124]         | 2015 | 64M, 8F| 72          | 51       | 3.2                    | 28.7                  | 17          | 56                        | Polymicrobial flora (37), Monomicrobial flora (1) | 12          |
| Paonam et al. [125]            | 2015 | M      | 1           | 65       | 1                      | ND                    | 1           | 0                         | Escherichia coli, Enterococcus                                  | 0           |
| Oguz et al. [126]              | 2015 | 34M, 9F | 43       | 52       | >1                     | ND                    | 43          | 0                         | Polymicrobial flora (Escherichia coli 48%)                      | 6           |
| Asahata et al. [127]           | 2015 | M      | 1           | 70       | 1                      | ND                    | 0           | 0                         | Listeria monocytogenes, Escherichia coli                         | 0           |
| Ye et al. [128]                | 2015 | M      | 1           | 47       | 1                      | 21                    | 0           | 0                         | Pseudomonas aeruginosa                                           | 0           |
| Danesh et al. [129]            | 2015 | 8M     | 8           | 44       | >1                     | ND                    | ND          | 0                         | Enterococcus, Pseudomonas, Staphylococcus haemolyticus, Proteus, Clostridium | 3           |
| Ossibi et al. [130]            | 2015 | M      | 1           | 60       | 1                      | ND                    | 0           | 0                         | ND                                                      | 0           |
| Mahmoudi et al. [131]          | 2015 | M      | 1           | 44       | 1                      | ND                    | 1           | 0                         | ND                                                      | 0           |
| Cochetti et al. [22]           | 2015 | 2M     | 2           | 42.5     | 0.5                    | ND                    | 2           | 1                         | Staphylococcus warneri                                          | 1           |
| Samah et al. [132]             | 2015 | M      | 1           | 68       | 1                      | 1                     | 1           | 0                         | Bacteroides fragilis                                             | 1           |
| Papadimitriou et al. [133]     | 2015 | M      | 1           | 56       | 1                      | 90                    | 1           | 0                         | Polymicrobial flora                                               | 0           |
| Ozsaker et al. [134]           | 2015 | M      | 1           | 69       | 1                      | ND                    | 0           | 0                         | ND                                                      | 0           |
| García Marín et al. [135]      | 2015 | 53M, 6F | 59       | 68       | ND                     | ND                    | 18          | 0                         | ND                                                      | 15          |
| Toh et al. [136]               | 2014 | M      | 1           | 61       | 6                      | ND                    | 1           | 0                         | Polymicrobial flora                                               | 0           |
| Parry et al. [137]             | 2014 | M      | 1           | 48       | 1                      | ND                    | 0           | 0                         | ND                                                      | 0           |
| Tena et al. [138]              | 2014 | M      | 1           | 73       | 1                      | 55                    | 1           | 0                         | Actinomyces funkei, Clostridium hathewayi, Fusobacterium necrophorum | 0           |
| Matilsky et al. [139]          | 2014 | M      | 1           | 51       | 4                      | 30                    | 1           | 0                         | Polymicrobial flora                                               | 0           |
| Lee et al. [29]                | 2014 | 3M     | 3           | 50.7     | ND                     | ND                    | ND          | ND                        | ND                                                      | ND          |
| Reference          | Year | Gender | N. of cases | Mean age | Surgical debridement | Days of hospital stay | Sepr / ICU | Hyperbaric oxygen therapy | Pathogen                                                                 | N. of deaths |
|--------------------|------|--------|-------------|----------|----------------------|-----------------------|------------|---------------------------|---------------------------------------------------------------------------|--------------|
| Di Serafino et al. [140] | 2014 | M      | 1           | 63       | 1                    | ND                    | ND         | ND                        | ND                                                         | 0            |
| Galukande et al. [141] | 2014 | 2M     | 2           | 35.5     | 2.5                  | ND                    | 0          | 0                         | ND                                                         | 0            |
| Tattersall et al. [142] | 2014 | M      | 1           | 61       | 2                    | 47                    | 1          | ND                        | Escherichia coli                                                  | 0            |
| Omisanjo et al. [143]  | 2014 | 11M    | 11          | 51.9     | >1                   | 22.7                  | 7          | 0                         | Klebsiella (10), Escherichia coli, Pseudomonas aeruginosa, no microbes (1) | 0            |
| Rubegni et al. [144]  | 2014 | 2M     | 2           | 58.5     | 1                    | ND                    | 0.5        | 0                         | ND                                                         | 1            |
| Dinc et al. [145]     | 2014 | M      | 1           | 51       | >1                   | 16                    | 0          | 0                         | ND                                                         | 0            |
| Dayan et al. [146]    | 2014 | M      | 1           | 27       | >1                   | ND                    | 0          | 0                         | ND                                                         | 0            |
| Ludolph et al. [147]  | 2014 | 3M     | 3           | 48.7     | >1                   | ND                    | 0          | 0                         | ND                                                         | 0            |
| Omisanjo et al. [148] | 2014 | 7M, 5 F| 12          | 62.4     | 5.7                  | 19.6                  | ND         | 0                         | Pseudomonas, Acinetobacter, Escherichia coli, Enterococcus, Staphylococcus aureus, Proteus, Corynebacterium, Polymicrobial flora (6) | ND           |
| Shimizu et al. [149]  | 2014 | M      | 1           | 74       | 2                    | ND                    | 0          | 0                         | Proteus vulgaris, Prevotella denticola, Peptostreptococcus species     | 0            |
| Ho et al. [150]       | 2014 | F      | 1           | 78       | 1                    | 14                    | 0          | 0                         | ND                                                         | 0            |
| Aslanidis et al. [151]| 2014 | F      | 1           | 23       | >1                   | ND                    | 1          | 0                         | Candida albicans, Staphylococcus epidermidis, Klebsiella pneumoniae    | 0            |
| D’Arena et al. [152]  | 2014 | M      | 1           | 66       | 1                    | ND                    | 0          | 0                         | ND                                                         | 0            |
| Perkins et al. [153]  | 2014 | M      | 1           | 73       | 1                    | ND                    | 0          | 0                         | Candida albicans                                                      | 0            |
| Siwiński et al. [154]| 2014 | M      | 1           | 24       | >1                   | ND                    | 1          | 0                         | ND                                                         | 0            |
| Agostini et al. [155] | 2014 | M      | 1           | 64       | 2                    | 58                    | 1          | 1                         | Staphylococcus epidermidis, Proteus mirabilis, Enterococcus faecalis    | 0            |
| Oymaci et al. [156]   | 2014 | 10M, 6F| 16          | 61.2     | 4.44                 | 25.5                  | ND         | 0                         | Escherichia coli, Acinetobacter baumannii, Proteus mirabilis, Staphylococcus aureus, Enterococcus, Polymicrobial flora (14), Escherichia coli, Staphylococcus aureus, Enterococcus, Acinetobacter baumannii, Staphylococcus epidermidis, Proteus, etc. | 3            |
| Eskitascioglu et al. [157]| 2014 | 76M, 4F| 80          | 53.5     | 1.55                 | 34.78                 | ND         | 0                         | EScherichia coli, Staphylococci, Enterococci, Staphylococci, Klebsiella, Pseudomonas, Proteus, fungi | 3            |
| Yilmazlar et al. [158]| 2014 | 81M, 39F| 120        | 58       | 3                    | 14.5                  | 48         | 0                         | Escherichia coli, Streptococcus, Pseudomonas, Proteus, fungi           | 25           |
| Akbulut et al. [159]  | 2014 | M      | 1           | 77       | 1                    | 20                    | 0          | 0                         | Escherichia coli                                                      | 0            |
| Coyne et al. [160]    | 2014 | M      | 1           | 48       | 1                    | ND                    | 0          | 0                         | ND                                                         | 0            |
| Li et al. [161]       | 2014 | 48M, 3 F| 51          | 49.7     | >1                   | 17                    | ND         | 0                         | Escherichia coli, Streptococcus, Staphylococcus aureus, Pseudomonas, Proteus, Clostridium, Bacteroides | 6            |
| Reference                          | Year | Gender | N. of cases | Mean age | Surgical debridement | Days of hospital stay | Sepsis / ICU | Hyperbaric oxygen therapy | Pathogen                                                                 | N. of deaths |
|-----------------------------------|------|--------|-------------|----------|----------------------|-----------------------|--------------|---------------------------|---------------------------------------------------------------------------|--------------|
| Oyaert et al. [162]               | 2014 | M      | 1           | 43       | 1                    | 63                    | 1            | 0                         | Atopobium                                                               | 0            |
| Lee et al. [163]                  | 2013 | M      | 1           | 47       | >1                   | ND                    | 0            | 0                         | Enterococcus, Enterobacter                                              | 0            |
| Abate et al. [164]                | 2013 | M      | 1           | 63       | 1                    | 21                    | 0            | 0                         | Enterococcus faecalis, Citrobacter freundii, Pseudomonas aeruginosa, Escherichia coli, Bacteroides fragilis, Bacteroides ovatus | 0            |
| Anantha et al. [165]              | 2013 | M      | 1           | 59       | 1                    | 16                    | 1            | 0                         | Streptococcus anginosus                                                | 0            |
| Benjelloun et al. [166]           | 2013 | 44M, 6F | 50         | 48       | 2.5                  | 21                    | 11           | 0                         | Escherichia coli, Klebsiella                                            | 12           |
| Pastore et al. [167]              | 2013 | M      | 1           | 60       | >1                   | 34                    | 0            | 1                         | Streptococcus A                                                        | 0            |
| Eray et al. [168]                 | 2013 | 34M, 14F | 48         | 53.7     | ND                   | 25.3                  | ND           | 0                         | Escherichia coli, Bacteroides, Streptococci                              | 9            |
| Bjurlin et al. [169]              | 2013 | 40M, 1F | 41         | 49       | ND                   | ND                    | ND           | ND                        | Escherichia coli, Bacteroides, Streptococci, Staphylococcus aureus     | 2            |
| Park et al. [170]                 | 2013 | M      | 1           | 59       | >1                   | ND                    | 0            | 0                         | Escherichia coli, Anaerobes                                             | 0            |
| Subramanian et al. [171]          | 2013 | M      | 1           | 80       | 3                    | ND                    | 1            | 0                         | Escherichia coli, Bacteroides, Streptococci, Staphylococci, Pseudomonas, Klebsiella, Proteus | 0            |
| Sabzi Sarvestani et al. [172]     | 2013 | 28M    | 28          | 44.6     | 2.2                  | 17.22                 | ND           | 0                         | Escherichia coli, Bacteroides, Streptococci, Staphylococci, Pseudomonas, Klebsiella, Proteus | 10           |
| Katib et al. [173]                | 2013 | 20M    | 20          | 55.95    | 1.7                  | 22.3                  | 1            | 0                         | Acinetobacter spp. (most common)                                       | 0            |
| Czymek et al. [174]               | 2013 | 72M, 14F | 86         | 57.9     | 4                    | 52                    | 52           | ND                        | Poly microbial flora (71), Escherichia coli, Enterococci, Streptococci, Staphylococci, Pseudomonas, Staphylococci, etc. | 14           |
| Akilov et al. [175]               | 2013 | 28M    | 28          | 47.1     | 3.5                  | 24.4                  | 8            | 0                         | Monomicrobial flora (18), Staphylococci, Streptococci, Enterobacter, Pseudomonas | 0            |
| Bakari et al. [176]               | 2013 | 10M    | 10          | 50.5     | ND                   | ND                    | ND           | 0                         | Escherichia coli, Staphylococci, Pseudomonas aeruginosa, Klebsiella     | 0            |
| Avakoudjo et al. [177]            | 2013 | ND     | 72          | ND       | ND                   | 72                    | ND           | ND                        | Escherichia coli, Streptococci, Arcanobacterium                        | 7            |
| Chan et al. [178]                 | 2013 | M      | 1           | 78       | 1                    | ND                    | 1            | 0                         | Escherichia coli                                                        | 0            |
| Chan et al. [179]                 | 2013 | M      | 1           | 49       | 15                   | ND                    | 0            | 0                         | Escherichia coli, Streptococci, Arcanobacterium                        | 0            |
| Aliyu et al. [180]                | 2013 | 43M    | 43          | 37.82    | >1                   | 28                    | ND           | 0                         | Poly microbial flora (27)                                               | 6            |
| Ozkan et al. [181]                | 2013 | F      | 1           | 43       | 4                    | ND                    | 1            | 0                         | Escherichia coli                                                        | 0            |
| Khan et al. [33]                  | 2013 | M      | 1           | 47       | 3                    | ND                    | 1            | 0                         | Escherichia coli                                                        | 0            |
| Vyas et al. [182]                 | 2013 | 30M    | 30          | 39.6     | 2.2                  | 9.7                   | ND           | 0                         | Escherichia coli, Pseudomonas, Staphylococci                           | 6            |
3 Case report

A 52-year-old man with a history of a cocaine use disorder, who was in methadone maintenance therapy and affected by HCV-related chronic liver disease, was admitted to the Emergency Department of a high-volume hospital. At admission to our institution, he presented with fever, acute renal impairment, anuria, poor hygienic conditions, and necrotic tissue involving the external genitalia (Figure 1). The laboratory tests showed 29 x 10^9/L white blood cells with 95% neutrophils, haemoglobin 15.6 g/dl, glucose 103 mg/dl, aspartate transaminase 79 UI/L, alanine transaminase 68 UI/L, creatinine 2.58 mg/dl, C-reactive protein 56.2 mg/dl, procalcitonin >100 ng/ml. HIV testing was negative. The patient reported no other urological symptoms at hospital admission. He had a Charlson Comorbidity Index score of 2 and an Eastern Cooperative Oncology Group (ECOG) of 1, with no referring major comorbidities.

A scrotal ultrasound examination was performed. It showed the right testis augmented in volume with completely altered echogenicity, augmented vascular sign and hypoechoic areas. The left epididymis and involucres had irregular echogenicity. The left testis appeared to have irregular echogenicity and was hypervascularized with hypoechoic areas. A left hydrocele was present. Computed tomography (CT) was performed. It confirmed phlogosis and edema of the scrotum, with the right testis unrecognizable. Skin, subcutaneous planes, spermatic cord were thickened. Inguinal bilateral and right external iliac lymphadenopathy was described on CT.

The patient underwent resuscitation intravenous fluid support; antibiotic therapy was administered with tigecycline and meropenem. A single, prompt, extended surgical debridement of external genital, perineal, perianal and infrapubic regions to healthy tissue was performed. The patient also underwent at the same time right orchiectomy.

The microbiologic culture of the wound specimen revealed *Staphylococcus lugdunensis* with tigecycline susceptibility. Urine and blood samples cultures were negative. Tigecycline and meropenem were administered until discharge.

The anuric condition persisted for 24 hours; then polyuria developed, but with a renal impairment that required treatment with dialysis.

Five days after the surgical debridement the patient reported the injection of cocaine into the superficial dorsal vein of the penis.

The histologic report confirmed an inflammatory necrotizing process of subcutaneous tissue that expanded to skin, testicular and epididymis parenchyma, rete testis and peritesticular tissue.

![Figure 1: The physical examination was notable for necrotic-appearing tissue in the entire penis and scrotum, with areas of induration and crepitus](image-url)
No other wound treatments were performed for the wide extension of involved cutaneous area and the correct development of granulation tissue.

The patient was discharged 17 days after the surgical debridement and was admitted to the waiting list for a skin graft, which was successfully performed 1 month later.

**Ethical approval:** The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board of Perugia University.

Written informed consent was obtained from the patient.

4 Discussion

Fournier’s gangrene is a surgical emergency characterized by necrotizing fascitis of the genital, perineal and perianal soft tissue. It is a rare condition, representing 0.02% of hospitalizations, with an estimated incidence of 1.6 for 100,000 males/year [5]. This condition affects both males and females. Males are more affected than females with a ratio 10:1, and age of onset is becoming older (between 60s and 70s) [6].

The patient in our case of necrotizing fascitis was 52 years old. Fournier’s gangrene was initially described as an idiopathic process, which has been found to be true in only a few cases. Often the initial cause is an infection involving the ano-rectum (30-50%), uro-genitalia (20-40%) and genital skin (20%). [7-9]. Infection results in inflammation and edema, which leads to obliterating endarteritis of the subcutaneous vessels [10]. The resulting lower blood support leads to peripheral dissection, with consequent spread of infection between the subcutaneous tissue and the skin. The reduction of the blood supply therefore generates gangrena [11].

This necrotizing fascitis may be due to a condition of compromised host immunity, like diabetes, alcoholism, human immunodeficiency syndrome (HIV), lymphoproliferative diseases, arterial hypertension, renal and hepatic insufficiency, obesity, dementia, tobacco consumption, chronic steroid abuse, chemo- and radiotherapy, or cancer and surgical treatment [12-20]. In our case, a correlation between gangrene and a patient with a history of cocaine abuse undergoing methadone substitution treatment has been highlighted. The patient was also affected by HCV-related chronic liver disease.

The pathogen involved is both aerobic and anaerobic, gram-negative and gram-positive. Some authors suggest the use of three different antibiotic classes to start an empiric treatment to cover all types of pathogen. In most of the cases, a polymicrobial infection (54%) is demonstrated, and *Escherichia coli* is the most frequently isolated pathogen (46.6%). The pathogens with a lower incidence are the streptococcus, bacteroides, enterobacter, staphylococcus, enterococcus, pseudomonas, corynebacterium, and *Klebsiella pneumoniae* [21]. Our review confirms that *E. coli* is the most involved pathogen (53.1%) and a polymicrobial infection the most common cause (68%) of Fournier’s gangrene. However, many authors suggest the use of broad-spectrum penicillin or third-generation cephalosporins, an aminoglycoside (e.g. gentamicin) and metronidazole or clindamycin [11]. In our case tigecycline and meropenem were administered to cover aerobic gram-positive and gram-negative pathogens, as well as anaerobic gram-positive and gram-negative pathogens. The administration was related to renal-function impairment.

The risk of a fatal event makes this necrotizing fascitis an emergency clinical condition. Prompt management is mandatory; hemodynamic support with resuscitation with fluids, board-spectrum parental antibiotics and surgical debridement of the involved region are the main procedures [22, 23]. Thanks to these approaches, the mortality linked to Fournier’s gangrene has dropped from between 20% and 88% to lower than 10% [24, 25]. On the basis of the data we collected, the reported mortality was 14.1%. In our case, the patient survived the acute condition, and he is still alive.

The surgical debridement must be performed within a few hours of hospitalization, and the removal of necrotic tissue helps in stopping progression of necrotizing fascitis and in reducing the risk of death [26]. Nevertheless, Proud et al, in a retrospective study of 219 patients found no differences in mortality in patients treated within 24 hours and those not treated. The authors linked this result to the severity of the infection [27]. For some authors (Chowla et al), more than one surgical debridement is necessary to obtain adequate infection control [28]. From our review of literature, more than one surgical debridement was performed in more than 60% of cases. In our case, we performed one surgical debridement, with the goal of obtaining a partial resection of viable tissue adjacent to the necrotic one.

Negative pressure wound therapy (NPWT) may represent a solution to the risk of infection of the large open wound that usually remains after a surgical debridement, since the patient’s poor condition it may be difficult to create a skin flap with which to cover the wound [29]. In
The use of hyperbaric oxygen therapy (HBOT) is increasing in the management of Fournier’s gangrene, but evidence of efficacy is lacking [31]. In the HBOT treatment, the patient inhales 100% O2 in increased ambient pressure (2–3 atmospheres). HBOT has bactericide and bacteriostatic effects on anaerobic pathogens, in particular. It also improves bacterial lysis by leukocytes and stimulates collagen formation and superoxide dismutase with tissue survival [11,13]. Some authors have reported the range of mortality to be between 16% and 30%, whereas for the patients who undergo HBOT, the mortality is found to be approximately 17.6%.

In our case, our patient obtained a complete resolution of the necrotizing process without NPWT or HBOT, and a skin graft was then performed.

Cocaine, as described by Burnett [32], could be associated with priapism, and when administered into the corpora cavernosa, it could produce a prolonged erection [33]. In our knowledge, only two other cases of Fournier’s gangrene associated with penile injection of cocaine [33, 34] and three cases of penile necrosis [35] have been described. In both cases of Fournier’s gangrene, the necrosis was limited to the penis. The mechanism behind the necrotizing fasciitis after intra-corpora cavernosa injection of cocaine could be dual: cocaine has an intensive vasoconstrictive action that could lead to dermal necrosis that could be complicated by superinfection [33] or by inoculation of infective agents [34]. In our case, we believe that the inoculation of infective agents was the most plausible mechanism, since a skin commensal bacterium was involved.

5 Conclusion

Fournier’s gangrene is a potentially fatal condition that must be treated in a multimodal setting.

Here we report a rare case of genital and perineal necrotizing fasciitis after a loco-regional intravenous injection of cocaine.

To offer the patient the possibility of survival, a prompt application of a multimodal approach with intravenous fluid support, antibiotic therapy and aggressive surgical debridement is mandatory.
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