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Perineal soft tissue infections

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ABSTRACT

Fournier's gangrene (FG) is an aggressive necrotizing soft tissue infection of the perineum. FG takes hold as a mixture of pathogenic organisms enter the host via injured gastrointestinal or genitourinary mucosa. After soft tissue insult, a synergistic, polymicrobial infection destroys tissue through an obliterative endarteritis. FG particularly affects older, obese men with type 2 diabetes mellitus, but can affect everyone. Special populations at risk include patients who have undergone gender reassignment surgery. Early, aggressive debridement and fluid resuscitation are mandatory. Careful decisions must be made regarding the fecal stream, antibiosis, topical coverings and the use of adjunctive therapy. While untreated FG is certainly fatal, with effective diagnosis and treatment survival rates approach 95%.

Introduction

Perineal soft tissue infection, also called Fournier's Gangrene (FG), was initially described in 1764 by Baurienne but takes the name of the Parisian venereologist, Jean Alfred Fournier.[1,2] FG is a type of necrotizing soft tissue infection that afflicts the perineum, involving anogenital and urogenital regions tracking along Colles', Buck's (Fig. 1a) and Dartos (Fig. 1b) fascia. The infection is bound by the pubic symphysis anteriorly, rami laterally, and urogenital diaphragm posteriorly. However, FG has been reported to spread beyond these structures superiorly into Scarpa's fascia and in advanced cases more deeply into muscle.[3,4] The infection leads to an immune mediated, obliterative endarteritis of the fascia and soft tissues.[5,6] As testicular circulation originates from the abdominal aorta, separate from that of the fascia, the gonads themselves are typically spared.[3]

Epidemiology

Patients with FG are sparsely encountered with an incidence of 1.6:100,000 males per year in the United States. While FG can affect everyone, patients tend to be 10:1 male, greater than 40 years old, white, with 2–3 comorbidities, making $1–38,999 annually, on Medicare, presenting to urban hospitals with a tendency toward the southern states.[7,8] The incidence of women with FG has been estimated at 8.2% to 23%.[9,10] Unfortunately, ICD9 codes do not exist for FG in women and work-arounds have to be employed for epidemiologic reports. Of the females who have been identified, they are on average sicker than men and have increased risks for mechanical ventilation and dialysis. Women also have longer hospitalizations, and higher mortality rates.[7] Furthermore, women experience significantly higher rates of peritonitis (58.3 vs 7.7%) and retroperitoneal involvement (58.3 vs 15.4%).[11] Comorbidies commonly associated with FG among men and women include hypertension (31–50.2%), diabetes (37–40.2%), and obesity (11–22.4%).[7,8] Inpatient mortality has been reported from 4% to 43%.[8,12,13]

Special populations

Patients with diabetes

Patients in any immunocompromised state, but specifically type 2 diabetes mellitus (T2DM) are at higher risk for developing FG.[5,7,8] Sodium-glucose cotransporter-2 (SGLT2) inhibitors function to induce glucosuria and improve glycemic management.[14] SGLT2 inhibitors are well known to cause genital and urinary tract infection, however, the use of this class of antidiabetic medication may be associated with an increased risk of developing FG. Fifty-five cases of FG were identified among diabetic patients who received SGLT2 inhibitors since the product was released by the Food and Drug Administration (FDA) in 2013. This was compared against 19 cases of FG collected over 35 years preceding 2013. These 19 cases specifically included those diabetic patients those who used other forms of glycemic control.[15] Due to lack of power and need for a more specific control group, the correlation has been drawn into question.[16,17] However, these data reinforce the high risk of FG development in this population. In August 2018 the FDA responded by issuing a warning about the role of this class in developing peritoneal infection.[18]

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Patients who have undergone gender reassignment surgery

Patients who have undergone gender reassignment surgery represent a special, at risk population.[19] The terms for this surgery vary from gender dysphoria to reassignment to affirmation surgery. The surgeries are further classified as male-to-female (MTF) or female-to-male (FTM). A large retrospective study conducted at a tertiary care university hospital in Detroit found 82 patients who underwent a total of 1,383 operations as part of the affirmation process. There was an even split of MTF and FTM. Surgical site infections (SSI) were studied as the primary outcome measure. Forty-three (52.4%) patients developed an SSI at least once during their genital reconstruction process, of whom 34 (87%) were in the FTM group and nine (21%) in the MTF group ($p < 0.001$).[20]

The MTF gender affirmation patient post-operative population includes those who prefer only an esthetic outcome without a functional vagina (vulvoplasty without a vaginoplasty), and those who undergo vaginoplasties. There is a trend in gender affirmation surgeries towards use of an intestinal pedicle during creation of the neovagina, and this may shift the SSI rates and FG rates towards those who undergo MTF affirmation surgery.[21]

An expedient diagnosis of FG among post-operative gender affirmation surgery patients requires a high index of suspicion by a vigilant clinician. One reported case study describes a patient with a distant history of male-to-female transition who received a radical debridement four days after presenting with right labial abscess, far beyond current recommendations.[22]

Etiology

FG is a subtype of the broader infective category, necrotizing fasciitis (NF). NF can occur widely, unbound by fascial distribution and can be either polymicrobial, type I, or monomicrobial, type II. The type of fasciitis is correlated with mechanism of injury and location, as artfully illustrated by Stevens and Bryant.[6] Organism modality of entry into the fascial spaces are multifold and typically are associated with an inciting event such as urinary tract infection, genital piercing, prosthetic penile implant surgery, post coital trauma, or rectal foreign body perforation.[15] Bacteria cultured in FG are most commonly a mix of anaerobes and aerobes, gram positives and negatives, commensurate organisms and pathogens that include: E. Coli, Streptococcus sp., Enterococcus sp., Pseudomonas sp., and increasingly with type II infections, methicillin resistant Staphylococcus aureus.[6,13,23,24] Due to interrelationships between epidemiology, common injuries and microbial patterns, FG is usually a type I NF. The type of infection will help direct management and prognostics.[6]

Diagnosis

FG is extremely aggressive, spreading 2−3 cm/hour and requires quick diagnosis and matched intervention.[25] The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) and the Fournier's Gangrene Severity Index (FGSI) have been developed to aid in early recognition and academic pursuit.[13,26] Much effort has been spent exploring FG features via CT, MRI, ultrasound and X-ray. However,

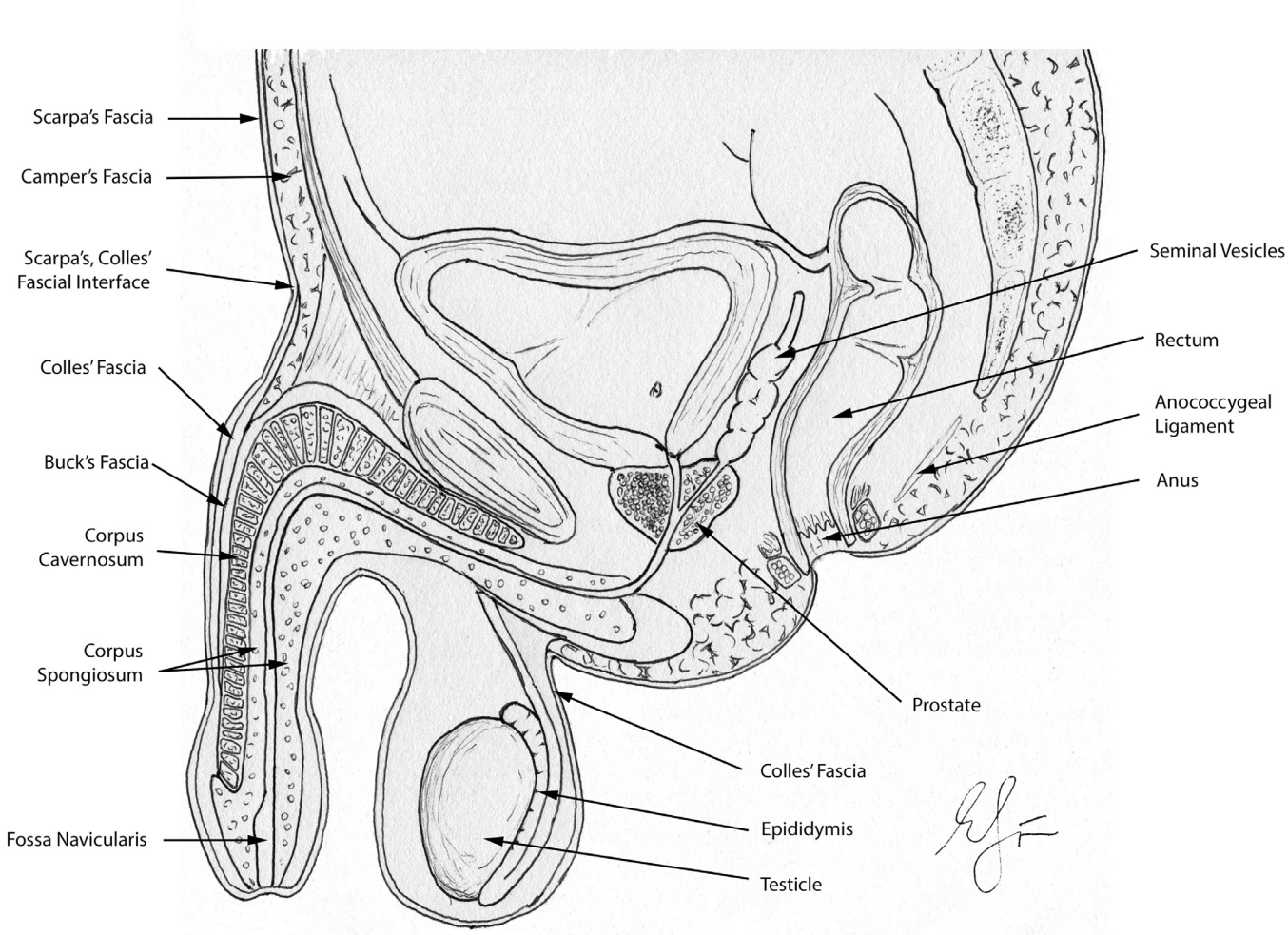

Fig. 1. Sagittal view 1b dorsal dissection revealing fascial planes.

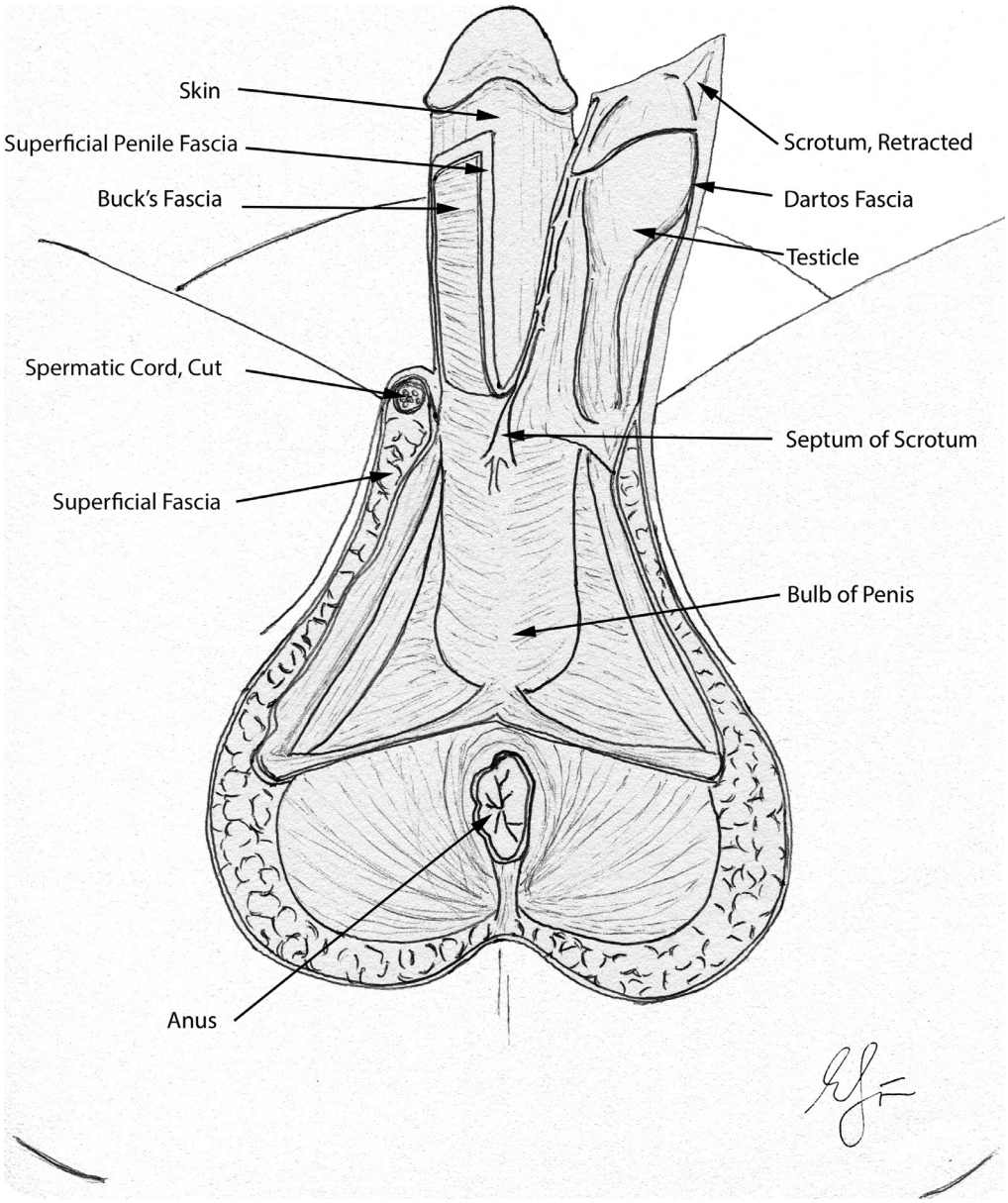

Fig. 1. Continued.

most will agree that the 'finger test' is the gold standard. The finger test can be performed at the bedside with an incision is made over the suspected infection and finger inserted, applying pressure laterally on the dermal and subcuticular tissue. The test is positive if tissue planes separate easily.[3]

Debridement

Speed of diagnosis and time to first debridement are correlated with a decreased morbidity and mortality.[3,12] FG is often managed by an interdisciplinary team consisting of urologic, general, plastic surgery, infectious disease and hospitalists. All necrotic, non-viable tissue must be removed with some recommending a more extensive debridement into healthy, bleeding tissue.[5] Findings associated with FG include thrombosis of vessels leading to a lack of bleeding, pus, gray soft tissue complexion, 'dirty-dishwater' fluid, and aforementioned positive finger test.[4] Due to the larger vessel caliber and varied source, it is rare that debridement of the deep fascia, muscles, or testicles is required.[3,23] Patients often require multiple operations ranging from a mean of 2.5 to 3.5 surgical debridements.[12,27] Although source control is mandatory to FG containment, each surgical debridement carries an increased mortality risk (OR 1.27 [95% CI 1.1−1.5], $p = 0.001$).[7] If infection has spread to the testicles, orchidectomy must be performed. However if anticipated, testicles can be relocated and protected in healthy subcuticular tissue of the medial thighs. With resolution they must be placed in a reconstructed scrotum for effective spermatogenesis.[28,29]

Recently, the status quo regarding mandatory reoperation has been challenged. Spence et al. in their retrospective of 158 patients with necrotizing soft tissue infection, including the extremity, trunk as well as FG patients, found that mortality did not differ between planned re-exploration and re-exploration based on clinical evaluation (9 vs. 15%, $p = 0.35$). Furthermore, they identified that the mandatory operation group had an increased length of stay (LOS) (21 vs. 14 days, $p = 0.35$) and required more debridements (2 [2−6] vs. 2 [1−2] $p =< 0.001$). Despite the mandatory re-operative group being older (52 vs. 49 years, $p < 0.02$), with an increased rate of diabetes (71 vs. 49%, $p = 0.02$) and longer duration of symptoms (7 vs. 4 days, $p < 0.01$), these data provide compelling evidence for further inquiry.[30]

Fecal diversion

Indications

Based on wound location and architecture, surgeons are often consulted for fecal diversion in patients with FG. FG can involve the fascial planes, but also perineal structures, including the external and internal sphincters of the anus. Further, during debridement, the anal sphincters and pudendal nerves are at risk of injury.[24,31] Fecal contamination of wounds leads to skin breakdown and inhibition of the healing process.[32] Therefore, diversion is indicated for any cause anal incontinence based on intraoperative assessment and or anal manometry.[3,31,33] Historically, open trephine colostomy has been performed, but this has given way to laparoscopic methods and, in certain reports, catheter-based diversion.[24,32,34–36] Two types of diversion, colostomy and balloon retained rectal catheter are presently debated in literature.

Alternatives and outcomes

The requirement for fecal diversion, both colostomy and fecal management system (FMS), at the time of debridement was found to be the strongest predictor for a prolonged hospital length of stay (LOS) (OR 11.10 [95% CI 6.20–19.70], $p =< 0.001$).[8] In the following, we will summarize several studies that have compared colostomy to fecal management systems (FMS).

Rosen et al. in their 2016 manuscript, compare thirty-five FG patients with colostomy to FMS based diversion in their single center, 2010–15 retrospective. Groups were not significantly older, male, sicker based on FGSI, LRINEC or the Acute Physiology, Age, Chronic Health Evaluation II (APACHE II) risk stratification scores.[13,26,37] Authors report that patients with FMS had a significantly lower number of surgical procedures (4.2 ± 0.6 vs. 9.0 ± 2.4, $p = 0.01$) despite equivocal hospital LOS, intensive care unit (ICU) LOS, or mortality. On subgroup analysis, in patients with and without an endorectal balloon, those without had a shorter hospital LOS (32.6 ± 4.7 vs. 16.3 ± 4.4; $p = 0.05$), shorter ICU LOS (8.0 ± 1.6 vs 2.8 ± 1.8; $p = 0.01$), more surgical procedures (3.0 ± 0.5 vs. 4.0 ± 0.8; $p = 0.01$) and a similar time to healing (4.2 ± 0.9 vs. 3.0 ± 0.5; $p = 0.6$).[36] A limitation to these observations, as with many retrospectives, include a lack of data on why patients were selected for colostomy or FMS, but these data do suggest FMS is associated with superior outcomes (Table 1).

These findings are supported by Eray et al. In their retrospective, 48 FG patients with preserved sphincters, without rectum injury, after debridement were compared between FMS and colostomy. It was found that the FMS group required fewer surgeries (1.9 ± 0.2 vs. 2.6 ± 1.1, $p = 0.015$) and had a shorter total LOS including stoma closure (24.1 ± 11.1, vs. 40.5 ± 23.4, $p = 0.008$). Unfortunately, FSGI, LRINEC, or APACHE II scores at presentation were not provided.[34]

Cost considerations

Financial cost and resource utilization must come into the decisional framework when considering an intervention. As these patients often require aggressive resuscitation, intravenous (IV) antibiotics, advanced wound therapy and monitoring, care is often expensive. Saffle et al. retrospectively observed in their single center study that their 30-patient cohort with FG had a mean LOS of 25.3 ± 15.6 days (range 3–62). Charges associated with their care averaged \$131,500 ± 108,300 (range: 3460–512,300).[38]

Patients who receive stomas on average have longer length of stays that include the initial encounter and the reversal readmission. Patients with colostomies experience more surgical procedures and surgical risk with placement of the stoma and the seemingly innocuous re-anastomosis. Eray et al. observed a significant increase in the cost of colostomy over FMS (\$10,950.5 ± 5574.1 vs. 6695.9 ± 2462.7, $p = 0.006$).[34] Ozturk et al. also observed a mean increase of \$6650 for colostomy.[33]

Table 1
Summary of outcomes in patients with Fournier's Gangrene (FG) with colostomy vs. Fecal Management System (FMS) or other.

Study	Number of patients			Total hospital LOS			Mean number of operations			Total cost (USD)			Mortality		
	Total patients	Col.	FMS/Other	Col.	FMS/Other	P-value	Col.	FMS/Other	P-value	Col.	FMS/Other	P-value	Col.	FMS/Other	P-value
Ozturk et al.,[33] 2011*	44	18	26	24	14.5	0.06	5	4	0.772	+6650‡	NR	NR	7	4	0.078
Eray et al.,[34] 2015†	48	32	16	40.5 ± 23.4	24.1 ± 11.1	0.008	2.6 ± 1.1	1.9 ± 0.2	0.015	10,950.5 ± 5571.4	6695.9 ± 2462.7	0.006	8	1	0.117
Rosen et al.,[36] 2016†	35	7	21	33.9 ± 4.7	27.9 ± 3.7	0.3	9.0 ± 2.4	4.2 ± 0.6	0.01	NR	NR	NR	1	1	0.5

Col. = Colostomy; FMS = Fecal Management System; LOS = Length of Stay; USD = United States Dollars, indexed to study publish date; NR = Not Reported.
* Compared colostomy patients with FG to all other FG patients.
† Compared colostomy patient with FG to FG patients with FMS.
‡ Cost differential of colostomy patients over all other patients with FG.

Special considerations

Despite the above cost benefits and associated outcomes demonstrating superiority of FMS over colostomy, there are relative and absolute contraindicationa for the method. An FMS is contraindicated with very deep wounds, extensive perianal involvement, rectal neoplasm, penetrating rectal injury and fistula.[3,35] A thorough rectal vault assessment is indicated before the use of a rectal catheter.

Management

FG patients should initially be managed in the ICU to monitor for sepsis, fluid resuscitation with wide-bore IV catheters, inotropic and hemodynamic support, antibiotic administration, frequent laboratory draws, wound care, and fecal management.[4,24]

Resuscitation

The goal of initial, rescue efforts is to restore end organ perfusion. Loflin and Winters describe in excellent detail the physiology and current recommendations regarding fluid resuscitation in sepsis.[39] They recommend balanced fluids such as Plasma-Lyte and lactated Ringer's as they have been shown to be superior to the supraphysiologic sodium and chloride containing normal saline in severe sepsis. The addition of albumin is recommended in patients with shock refractory to crystalloid. Although fluid resuscitation should be individualized, an initial 30 mL/kg bolus of crystalloid is recommended based on the Surviving Sepsis Guidelines.[39,40] If fluid responsiveness is in question, hemodynamic response should be assessed before and after a passive leg raise or 250−500 mL fluid bolus. A lack of response implies that the peak of Frank-Starling curve has been gained.[39]

Antibiosis

Polymicrobial organisms work in tandem toward tissue destruction and immune evasion in FG.[23] Due to the severe nature of FG and variety of microbes, after cultures are obtained, broad spectrum antibiotics should be initiated. Agents that can be considered include penicillin [Pfizerpen, Pfizer, New York, NY], metronidazole [Flagyl, Pfizer, New York, NY] and a third generation cephalosporine.[23,24] Anaerobic coverage should be started promptly and discontinued only with strong evidence as they can be difficult to culture.

Temporary tissue coverage

After the acuity of the situation has resolved, patients who have been widely debrided are left with challenging tissue defects. Insensible fluid losses can be a dire concern if not vigilantly accounted for. Topical substances which can be applied to the defects are reported to have mixed or unspecified results. These agents include honey, 0.025% sodium hypochlorite (Dakin solution), hydrogen peroxide, lyophilized collagenase, and fibrin glue for non-infected skin closure.[3] The use of vacuum assisted closure (VAC) devices have been reported with increasing frequency in the literature. Wound VAC pumps work by applying a vacuum to porous foam that is covered with a thick, occlusive dressing. They have been shown to reduce the hospital LOS and number of dressings applied in FG.[41] Patients with FG are at risk for serious sequelae due to immobility, therefore early ambulation in conjunction with resuscitation and treatment is always recommended. Wound VAC systems which rely on adhesive occlusive barrier films around the groin and legs prove to be a significant challenge in the context of physical therapy recommendations. Goh et al. published a case series of 15 patients with perianal sepsis, 5 of whom had FG. Two of the 5 had concurrent wound VAC dressings. Authors point out that the use of VAC and FMS requires specialized nursing staff, but in this series VAC was correlated with faster wound healing, especially in patients with exudative wounds.[32]

Adjunctive therapies

The use of hyperbaric oxygen (HBO) therapy in FG is debated. HBO involves placing the patient within a pressurized vessel, with 100% oxygen. Indications for HBO range from decompression sickness to arterial insufficiencies to necrotizing soft tissue infection. Potential benefits include increased PaO2, up to 2000 mmHg, leading to the generation of reactive oxygen and nitrogen species. These factors are postulated to increase fibroblast and vascular endothelial growth factors, the latter leading to neovascularization of the wound bed.[42] However, many facilities do not have access to HBO vessels, patients are frequently too sick to transport, and outcomes are mixed within FG literature.

Summary

Fournier's gangrene is an aggressive necrotizing soft tissue infection of the perineum.[1−5] After soft tissue insult, a synergistic, polymicrobial infection takes hold, destroying tissue through an obliterative endarteritis.[5] FG particularly affects older, obese men with type 2 diabetes mellitus, but can affect people of all demographics.[7,8] Early, aggressive debridement and fluid resuscitation are mandatory. Careful decisions must be made regarding the fecal stream, antibiosis, topical coverings and the use of adjunctive therapy. While untreated FG is certainly fatal, with effective diagnosis and treatment survival rates approach 95%.[7,8]

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