Eur J Clin Microbiol Infect Dis (2001) 20:910–913
DOI 10.1007/s100960100620

BRIEF REPORT

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Fournier's Gangrene in HIV-Infected Patients

Published online: 12 December 2001

Fournier's gangrene (FG) is a form of necrotizing fasciitis occurring around the genitals. It usually affects patients with underlying systemic conditions like chronic alcoholism (25–50%) or diabetes mellitus (40–60%) [1]. Increased risk has also been reported after immunosuppressive treatment, such as chemotherapy for malignant disease and adrenal steroids, or in transplant recipients. It can affect patients of widely varying ages, from neonates to the very old. The highest incidence has been reported among patients around 50 years of age [2]. The pathogens most commonly found are *Escherichia coli*, *Bacteroides* spp., streptococci, staphylococci, peptostreptococci and clostridia, all of which belong to the normal flora of the lower gastrointestinal tract and perineum [3]. Localised cellulitis at the site of entry progresses to a diffuse inflammatory reaction involving deep fascial spaces. An obliterating endarteritis causes cutaneous and subcutaneous vascular thrombosis with necrosis of the tissue, which allows commensal flora to enter previously sterile areas. Tissue destruction then results from a combination of ischemia and the action of different bacteria.

Although the importance of bacterial infections in patients infected with the human immunodeficiency virus (HIV) was recognised early [4], necrotising fasciitis is unusual in these patients and FG is exceptional. Since the first description of a patient with AIDS and FG appeared in 1991 [5], only nine other cases have been reported in the Western literature [6, 7, 8, 9, 10, 11]. Reported here are two additional cases of FG that occurred in HIV-infected patients and a review of previously published cases.

In June 1998, a 39-year-old man was admitted to hospital for pain, swelling of the scrotum and fever of 5 days' duration. One year previously, oral lichen planus had been diagnosed, which was being treated with steroids. On admission he was febrile (temperature, 38.5°C) and hypotense (110/60 mmHg). Oropharyngeal candidiasis was evident. A necrotic area was found over the scrotum with a malodorous yellow-brown discharge, erythema and swelling of the perineum. The perirectal area and abdominal wall were not affected. No general predisposing factors could be identified.

Surgical debridement of the necrotic tissue was performed, and imipenem and gentamicin were administered for 15 days. Culture of the necrotic tissue grew *Escherichia coli* and a *Peptostreptococcus* sp. *Citrobacter freundii* was isolated from blood cultures. Urine culture was sterile. Although the patient denied any risk behaviour for HIV infection, HIV serology was positive: his CD4+ cell count was 6/mm^3 and the HIV viral load was 1,879,000 RNA copies/ml. Triple antiretroviral treatment was initiated, but 1 month later the patient developed bilateral pneumococcal pneumonia and died as a result of nosocomial *Pseudomonas aeruginosa* sepsis.

In October 1998, a 67-year-old man was admitted to hospital with fever and pain affecting the scrotum. He had been diagnosed with HIV infection 5 years previously during a preoperative study for a transurethral resection of a bladder carcinoma (stage I). His only infectious complication had been a perianal abscess that needed surgical debridement 2 years prior to presentation. The patient was being treated with triple antiretroviral therapy; 2 months prior to admission his viral load had been undetectable and his CD4+ cell count was 386/mm^3. Seven days before consultation he developed a high temperature and discharge through a perianal fistula. Oral ofloxacin treatment was started, but the patient remained febrile and developed a tender swelling of the right hemiscrotum.

A general examination showed a toxic febrile patient (temperature, 39°C) who had evident cyanosis and bronzin of the scrotum with induration, crepitus and areas of cutaneous necrosis and a perianal fistula without discharge or anal abscess. FG was diagnosed and an ur-

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Table 1 Epidemiology, clinical features, etiology, treatment and outcome of Fournier's gangrene in 12 HIV-infected patients

Characteristic	Patient [reference no.]								
	Patient 1 [PR]	Patient 2 [PR]	Patient 3 [5]	Patient 4 [6]	Patient 5 [7]	Patient 6 [8]	Patient 7 [9]	Patient 8 [10]	Patient 9, 10, 11, 12 [11]
Age (years)	39	58	33	29	49	47	48	21	34–41
CDC stage	A3	A2	C3	C3	A2	A3	ND	ND	ND
CD4/mm^3	6	386	120	6	475	178	ND	ND	<200
Viral load (copies/ml)	1,879,000	0	ND	ND	ND	ND	ND	ND	ND
Onset (days)	5	6	ND	7	3	2	3	3	ND
Localisation	scrotum	right hemi-scrotum	right hemi-scrotum	left hemi-scrotum, left axilla, right eye	scrotum/ penis	scrotum/ penis	anal sphincter, distal rectum	scrotum, perineum	scrotum/penis, rectum
Entry portal	ND	perianal fistula	ischiorectal abscess (IV drugs in femoral veins)	hyfrecation	elective circumcision	balanitis	perianal fissure	proctitis	perianal fistula
Blood cultures	*Citrobacter freundii*	sterile	sterile	*Pseudomonas aeruginosa*	sterile	sterile	ND	ND	ND
Necrotic tissue cultures	*Escherichia coli*, *Pepto-strepto-coccus* sp.	*Streptococcus viridans*, *Peptostrepto--coccus* sp., *Bacteroides* sp.	*Streptococcus* sp., *Escherichia coli*, *Peptostrepto-coccus* sp., *Proteus mirabilis*	*Streptococcus* sp.	*Strepto-coccus* sp., *Staphylo-coccus* sp.	*Escherichia coli*, *Pepto--streptococcus* sp.	*Enterococcus* sp., gram-negative anaerobes	ND	*Klebsiella pneumoniae*, *Streptococcus* sp., *Proteus mirabilis*
Antibiotics	imipenem + gentamicin	imipenem + gentamicin	cefotaxime + metronidazole + penicillin	penicillin + gentamicin + metronidazole	penicillin + clindamycin + aztreonam	cefotaxime + metronidazole + tobramycin	gentamicin + metronidazole + penicillin	ND	broad spectrum
Surgical reconstruction	yes	yes	no	no	yes	yes	yes	yes	yes
Outcome	cured, died 1 month later (*Pseudomonas aeruginosa* sepsis)	cured	died (dissemi-nated candidiasis)	cured	renal failure (HD), cured	cured	cured	cured, died 3 months later (bacterial pneumonia)	cured (n=4)

PR, present report; ND, no data; HD, hemodialysis; IV, intravenous

gent radical debridement of the subcutaneous necrotic area was performed; debridement of deep fascia or muscle was not required. Imipenem and gentamicin were administered. Blood cultures were negative. Cultures of the necrotic tissue grew *Streptococcus viridans*, a *Peptostreptococcus* sp. and a *Bacteroides* sp. Reconstructive surgery with a skin graft was performed 10 days following debridement, and a fistulotomy was performed 4 weeks later. At 2-year follow-up the patient remained well.

A computerised search of the Medline database was conducted to reveal all cases of FG in HIV-infected patients reported in the English-language literature from 1980 to 2000. The key words used were "immunodeficiency virus infection", "AIDS", "Fournier's gangrene" and "gangrene of scrotum". A total of 10 cases were found, and all of the cited publications could be located and analysed [5, 6, 7, 8, 9, 10, 11] (Table 1). Those publications were examined for case details and references to other published cases. Only cases reported from Western countries were analysed.

All 12 patients (10 published previously and 2 reported here) were male. The mean age was 40.8 years (range, 29–58 years), and risk factors for HIV infection were as follows: homosexual intercourse (n=8), intravenous drug use (n=1), heterosexual intercourse (n=1) and not reported (n=2). The CD4+ lymphocyte count was available for 10 patients; all were below 500/mm^3 and eight were below 200/mm^3. Only four of the patients were receiving antiretroviral therapy. The clinical stage of HIV infection was reported for seven patients; five were in stage C, and two in stage A. FG led to the diagnosis of HIV infection in three patients.

Three of the 12 patients had some other underlying disorders, in addition to HIV infection, that could have compromised their immunity. One patient developed perineal gangrene during week 3 of treatment with etoposide for a severe widespread Kaposi's sarcoma. Another patient was a chronic alcoholic, and the third had been receiving steroids for a long time. Neutropenia, another identified risk factor for the development of FG, was recorded in only one patient.

The source of infection was recognised in 11 patients: anorectal foci in 8 (perianal fistula in 6, recurrent proctitis in 1 and drainage of bilateral ischiorectal abscesses in 1), urogenital in 3 (1 balanitis, 1 hyfrecation and 1 elective circumcision because of phimosis and recurrent balanitis). Fever and pain were the cardinal complaints, and erythema and swelling of the scrotum with induration and crepitus of the perineal area were the usual signs. Obvious cutaneous necrosis was evident in 11 patients. Extension beyond the genitalia was observed in five patients. The condition progressed for 2–6 days (average, 3.7) after the onset of clinical manifestations, a pace which is a bit slower than in the general population.

Blood cultures were positive (*Citrobacter freundii* and *Pseudomonas aeruginosa*) in two of seven patients tested. Necrotic tissue cultures showed polymicrobial infection in all 11 patients tested. Group A *Streptococcus* was the most commonly isolated organism, followed by *Peptostreptococcus* spp., *Escherichia coli*, *Clostridium* spp., *Proteus* spp., *Pseudomonas aeruginosa* and coagulase-negative staphylococci.

All patients underwent urgent surgical debridement and received parenteral broad-spectrum antimicrobial agents in double or triple combinations to cover gram-negative aerobes, streptococcal species and anaerobic organisms. Rapid improvement was observed in nine patients. Although only one patient died during the first admission, two other patients died in the following months. Patient 3 developed acute renal failure, fever and disseminated intravascular coagulation and died 16 days following admission; necropsy revealed a disseminated *Candida* infection. Patient 5 needed short-term hemodialysis for acute renal failure, resulting in complete recovery in a few weeks. Patient 8 had a slow-healing wound, but he refused a second surgical treatment and died 3 months later of bacterial pneumonia. Seven patients needed multiple debridements. Reconstructive surgery was necessary in eight patients. The nine surviving patients were asymptomatic at the end of follow-up.

Although FG is not common, it is by no means a rarity, with more than 400 cases being reported in the literature [12]. In HIV-infected patients, however, only 12 cases have been communicated from Western countries. Although the incidence of perianal or genital infections is high among homosexual HIV-infected males, the incidence of FG remains very low. In a retrospective analysis of a cohort of more than 1,300 HIV-infected patients followed for 10 years, Consten et al. [11] reported an incidence of perineal sepsis of 3.7% (50 cases) with only four cases of FG (incidence, 0.3%). According to those data, HIV infection would not appear to be a significant risk factor for FG. However, in 9 of the 12 cases we examined, AIDS had developed before FG, and 9 patients had a CD4+ cell count <200/mm^3. Three of the patients had at least one other known risk factor for FG, and 11 patients had a local focus of infection that could have been the portal for FG. It can be hypothesised that the HIV-induced immunosuppression of these patients contributed to the progression from minor perianal infections to FG.

In assessing the relationship between HIV and FG, it is also possible that HIV infection may have been overlooked in other cases of FG affecting patients with a good immunologic status. However, the fact that FG mainly affected those HIV-infected patients who were at an advanced stage of the disease suggests that severe immunosuppression can increase the risk of FG, but the role of CD4+ cell depletion seems to be minor.

In 1993, Stephens et al. [2] compared the rate of mortality due to FG in the preantibiotic era (series published before 1945) with that of the postantibiotic era (cases reported from 1945 to 1988) and found no differences, with a death rate of around 20–22%. Probably any survival benefit coming from improved treatment is masked by a trend towards increased mortality caused by the advanced age of patients and comorbidity. We found that

mortality rates due to FG reported within the last decade (1986–1996) range from 7% to 33%, with no difference being noted between HIV-positive and HIV-negative patients. Moreover, the data presented here show that FG is uncommon in patients with HIV infection in Western countries. In some aspects it behaves like a low-incidence opportunistic infection, similar to bacilar angiomatosis or *Rhodococcus equi* pneumonia.

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