ORIGINAL ARTICLE

Our experience on Fournier's gangrene in a tertiary-stage care center and analysis of its relationship with blood count parameters

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ABSTRACT

BACKGROUND: Fournier's gangrene (FG) is rapidly progressing and life-threatening necrotizing fasciitis of genital and perineal regions. The aim of the study was to share our experience with FG and to analyze the relationship of clinical data with whole blood count parameters, inflammation cells, and systemic inflammation markers.

METHODS: The digital medical records of the adult patients followed-up and treated with diagnosis of FG between January 2016 to December 2020 were retrospectively analyzed. Data were as age, gender, total length of hospital stay, predisposing factors, etiological factors, total number of debridement's, surgical procedures, and antibiotherapy were collected. Serum glucose levels, complete blood count parameter levels, serum inflammation indicators and C-reactive protein (CRP) levels measured at the initial day of hospital admission, post-debridement 1st and 7th days were measured.

RESULTS: Thirty-six male patients were included, with a mean age of 56.42 (22–86) years. The most common predisposing factor was diabetes mellitus (n=13; 36.1%). The most frequently seen etiological cause was scrotal abscess (n=19; 52.8%). A statistically significant decrease was found in White blood cell count, neutrophil level, neutrophil-to-lymphocyte ratio (NLR) value and CRP level measured before debridement, post-debridement 1st and 7th days ($p<0.05$). There was a positive correlation between the number of debridement's and age, NLR, platelet-to-lymphocyte ratio, and CRP values at the initial admission time ($p<0.05$).

CONCLUSION: The infections of urogenital region are the essential etiological origin of FG. As a rare urological emergency, significant changes were observed in clinical data and blood count parameters during the course of FG.

Keywords: Debridement; Fournier's gangrene; inflammation cells; inflammation markers.

INTRODUCTION

Fournier's gangrene (FG) that has been first described by Jean-Alfred Fournier in 1883 is rapidly progressing and life-threatening necrotizing fasciitis of genital and perineal regions.[1] It involves an aerobic and anaerobic synergistic infection like other necrotizing infections.[2,3] FG is more frequently seen in males and those over 50 year of age, although seen in both genders and every age groups.[3,4] It should be beard in mind that it may present a progressive course despite some decreases in high mortality (20–30%) and morbidity rates parallelly with improving health-care services in the recent years.[5] The patients admit with soft tissue infections of scrotal, perineal, and perianal regions generally accompanied with edema, erythema, crepitation, or necrosis.[4] The predisposing factors may include diabetes, chronic alcoholism, AIDS, malnutrition, poor hygiene, low socio-economic status, cytotoxic drugs, and trauma.[6] Direct graph, ultrasonography, computed tomography or magnetic resonance imagine may be used to confirm the diagnosis of FG. The treatment of FG essentially requires complete and early large debridement, broad spectrum parenteral antibiotherapy, and hemody-

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namic stabilization since necrotizing fasciitis is progressive.[7] Multistage treatment approaches involve repetitive debridement's, protective colostomy, wound management, or skin reconstructions.[5–7] Vacuum-assisted closure (VAC) and hyperbaric oxygen therapy (HBOT) are experimental methods in the treatment of FG, and there is no clear evidence of benefit of their use.[8]

Various scoring systems such as FG Severity Index, Laboratory Indicator For Necrotizing Fasciitis Score, and Age-Adjusted Charlson Comorbidity Index are used to predict prognosis and mortality in FG.[9] Similarly with other branches, hematological inflammatory indicators that reflect the severity of systemic inflammation such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-eosinophil ratio (MER) have been subjected to studies for also urology practice.[10,11] Data on use of these indicators in predicting progression of FG are very limited. In our study, we have primarily aimed to share our clinical experience on FG and to analyze the relationship of these data with whole blood count parameters, inflammation cells, and systemic inflammation indicators.

MATERIALS AND METHODS

Study Design and Participants

The digital medical records of the adult patients (>18 years of age) followed-up and treated by the urology clinic with diagnosis of FG between January 2016 and December 2020 were retrospectively analyzed after receiving approval from the ethics committee of Gülhane Training and Research Hospital (Meeting No:2020/21, Project No: 2020–526). Data such as age, gender, total length of hospital stay, predisposing factors, etiological factors, total number of debridement's, surgical procedures, and type of antibiotherapy were recorded. In addition, serum glucose levels, complete blood count parameter levels (White blood cell [WBC] count, RBC count, hemoglobin, hematocrit, platelet count, neutrophils, lymphocytes, monocytes, and eosinophils), serum inflammation indicators derived as ratios between these parameters (NLR, PLR, and MER), and C-reactive protein (CRP) levels measured at the initial day of hospital admission, and post-debridement 1st and 7th days were evaluated.

Surgical Procedures

Fluid replacement and large surgical debridement of the necrotic tissue were performed rapidly (<3 h) in all the patients. A consultation was carried out by the department of infectious diseases before debridement procedure and broad spectrum antibiotherapy was administered pre-and post-operatively. Foley catheterization, suprapubic cystostomy, protective colostomy, or fasciotomy were implemented if needed depending on diffuseness status of the necrotic tissue. The tissues were washed using oxygenated water and cleansed by Povidone-iodine after debridement. The infected and necrotic tissues were resected by daily medical dressing, debridement was repeated under anesthesia if needed. VAC or HBOT was repeated according to size and healing status of the infected wound. Skin reconstructions such as grafting or flap surgery were performed in the non-suitable patients for primary closure after complete healing of the tissues was observed.

Statistical Analysis

With the statistical analysis of the obtained data, descriptive statistical data such as mean, standard deviation, standard error, variance, and median were calculated and recorded. As a result of the graphical and statistical determination of the conformity of the data to the normal distribution, the appropriate test was selected for the statistical analysis of the data. Spearman Rank Correlation and Paired Sample t-test were used for statistical evaluation of the data. The statistical significance of the obtained analysis results was evaluated with the p value and values <0.05 were considered statistically significant.

RESULTS

A total of 36 male patients admitted to our clinic because of FG according to available data. Mean age of the patients was 56.42±17.72 (range: 22–86) years. Median length of hospital stay was 12.5 (3–35) days and the mean number of debridement's was 2.94 (1–10). Ultrasonography was performed in all the patients; computed tomography was carried out in ten patients. The mortality rate for FG was 0% in our study.

Predisposing factors and etiological factors are summarized in Table 1. The most common predisposing factor was diabetes

Table 1. Summary of predisposing factors and etiological factors of the patients

	n	%
Predisposing factors		
Diabetes mellitus	13	36.1
Poor hygiene	5	13.9
History of pelvic surgery	4	11.1
Dementia	2	5.6
Paraplegia	2	5.6
History of pelvic tumor	1	2.8
None	9	25
Etiological factors		
Scrotal abscess	19	52.8
Epididymo-orchitis	10	27.8
Testicular abscess	4	11.1
Gunshot wounds	1	2.8
Perianal abscess	1	2.8
Priapism	1	2.8

Table 2. Summary of microbiological agents and antibiotics

	n	%
Detected in necrotic tissue		
Escherichia coli	7	19.4
Enterococcus faecalis	4	11.1
Klebsiella pneumoniae	3	8.3
Pseudomonas aeruginosa	2	5.5
Enterococcus faecium	2	5.5
Proteus mirabilis	2	5.5
Missing	16	44.4
Antibiotics		
Piperacillin + Tazobactam	16	44.4
Ciprofloxacin + Metronidazole	7	19.4
Ceftriaxone + Metronidazole	5	13.8
Meropenem	3	8.3
Ertapenem	3	8.3
Imipenem	2	5.5

Table 3. Summary of surgical procedures of the patients

	n	%
Surgical approaches		
Debridement	15	41.7
Debridement + Orchiectomy	7	19.4
Debridement + VAC	3	8.3
Debridement + Skin reconstruction	3	8.3
Debridement + Colostomy + VAC + Skin reconstruction	3	8.3
Debridement + VAC + Skin reconstruction	1	2.8
Debridement + Orchiectomy + VAC	1	2.8
Debridement + Orchiectomy + VAC + Fasciotomy	1	2.8
Debridement + Urethrectomy + Partial penectomy + HBOT	1	2.8
Debridement + Urethrectomy + Colostomy + VAC + Skin reconstruction	1	2.8

VAC: Vacuum-assisted closure; HBOT: Hyperbaric oxygen therapy.

mellitus (n=13; 36.1%). The most frequently seen etiological cause was scrotal abscess (n=19; 52.8%).

The microorganisms in tissue cultures and the types of antibiotics are shown in Table 2. *Escherichia coli* (19.4%) was the most common bacterium detected in necrotic tissue.

Summary of surgical procedures of the patients is summarized in Table 3. Orchiectomy was performed in 9 (25%) patients following debridement. VAC, protective colostomy, urethrectomy, partial penectomy, fasciotomy, and HBOT were implemented in totally 10 (27.7%), 4 (11.1%), 2 (5.6%), 1 (2.8%), 1 (2.8%), and 1 (2.8%) patients after debridement, respectively. A total of 5 (13.8%) patients underwent suprapubic cystostomy. Repeated debridement was performed in 24 (66.6%) of 36 patients. Skin reconstruction surgery (grafting or flap) was needed in totally 8 (22.2%) patients.

The changes in the blood parameters of the patients measured at the initial admission time, post-debridement 1st and 7th days are summarized in Table 4, respectively. A statistically significant decrease was found in WBC count, neutrophil level, NLR value, and CRP level measured before debridement, post-debridement 1st and 7th days (p^1=0.001, p^2<0.001, p^3<0.001 and p^1=0.002, p^2<0.001, P3 < 0.001 and p^1=0.012, p^2=0.002, p^3=0.013 and p^1=0.008, p^2<0.001, p^3<0.001, respectively, when p^1: Results at the initial admission time and post-debridement 1st day; p^2: Results at the initial admission time and post-debridement 7th day; and p^3: Results at debridement 1st and 7th days).

The results of the correlation analysis carried out for number of debridement's and surgical approaches are presented in Table 5. According to the results, there was a positive correlation between the number of debridement's and age, NLR, PLR, and CRP values at the initial admission time (p=0.01, p=0.01, p=0.001, and p=0.01, respectively). A positive correlation was encountered also between surgical approaches and predisposing factors (p=0.023).

In Figure 1, we can see that right scrotal absces s progressively advanced to FG within 2 h in a diabetic patient. Fasciotomy was needed following debridement, right orchiectomy, and VAC in this patient. Scrotum was closed primarily after left testicle was positioned in the scrotum.

DISCUSSION

FG is still an important disease of the urogenital region with a mortality rate approaching 40%.[5,6] The large size of the necrotic tissue, liver or kidney failure, necessity of protective colostomy, and advance age affect prognosis negatively.[7,12,13] A reduction reaching 16% has been found in mortality rate of FG thanks to aggressive and repetitive debridement.[14] The recurrence of necrosis in FG may be resulting from inadequate number of debridement, therefore, implementation of multiple debridement's (averagely 1.5, 3.3 or 3.5, respectively) is recommended, although recommended number varies between studies.[5,15,16] Mean number of debridement's was 2.94 in our study. Although the diagnosis of FG is mainly based on clinical findings, we routinely used ultrasonography in the presence or suspicion of FG. Thanks to ultrasonography, we got more detailed information about tissue edema, gas presence in soft tissue, and tissue contamination. Computed tomography has gained a progressively increasing importance in

Table 4. Analysis of patients' blood count parameters

Parameters	At first acceptance	The first postoperative day	The seventh postoperative day	p^1	p^2	p^3
Serum glucose (mg/dL)						
Mean±SD	175.94±106.85	154.58±74.45	134.67±47.53	0.023	0.006	0.063
Min-Max	66–465	89–376	69–270			
WBC count (x10^3/uL)						
Mean±SD	14.49±6.22	12.01±4.93	8.57±3.14	0.001	<0.001	<0.001
Min-Max	5.6–37.1	7–27	3.8–17.5			
RBC count (x10^6/µL)						
Mean±SD	4.64±0.65	4.3±0.62	4.2±0.72	<0.001	<0.001	0.235
Min-Max	3.27–6.65	3.1–5.81	3.19–5.95			
Hemoglobin (g/dL)						
Mean±SD	13.38±2.04	12.51±2.02	12±1.93	<0.001	<0.001	0.041
Min-Max	8.1–17.6	9–6.1	8.2–15.5			
Hematocrit (%)						
Mean±SD	39.73±5.57	37.16±5.69	35.85±5.75	<0.001	<0.001	0.094
Min-Max	27.7–52.1	26.3–47.2	24.5–46.5			
Platelet count (x10^3/uL)						
Mean±SD	284.44±82.34	292.42±120.36	295.92±130.77	0.564	0.537	0.822
Min-Max	106–430	127–729	73–658			
Neutrophils (x10^3/uL)						
Mean±SD	11.39±6.1	9.14±4.8	5.86±3.03	0.002	<0.001	<0.001
Min-Max	3.1–31.8	4.1–22.8	1.6–16.3			
Lymphocytes (x10^3/uL)						
Mean±SD	1.81±0.93	1.7±0.68	1.81±0.79	0.282	0.986	0.361
Min-Max	0.3–3.7	0.4–3.2	0.7–3.6			
Monocytes (x10^3/uL)						
Mean±SD	1.04±0.55	0.96±0.65	0.64±0.31	0.342	<0.001	0.003
Min-Max	0.2–3.1	0.3–4	0.2–1.9			
Eosinophils (x10^3/uL)						
Mean±SD	0.16±0.11	0.16±0.14	0.21±0.18	0.746	0.098	0.208
Min-Max	0–0.4	0–0.6	0–0.9			
NLR						
Mean±SD	10.19±13.62	6.81±8.14	3.81±4.28	0.012	0.002	0.013
Min-Max	1–63	1–46	1–23			
PLR						
Mean±SD	218.44±172.54	205.67±141.38	202.36±147.77	0.386	0.549	0.873
Min-Max	58–852	59–783	33–795			
MER						
Mean±SD	5.53±5.37	5.05±4.78	2.84±2.21	0.653	0.012	0.009
Min-Max	0.5–30	0.4–23	0–8			
CRP (mg/L)						
Mean±SD	123.78±95.63	94.66±71.89	45.9±39.23	0.008	<0.001	<0.001
Min-Max	6.07–417.8	4.8–341.6	3.5–198.4			

p^1: Results at the initial admission time and post-debridement first day; p^2: Results at the initial admission time and post-debridement seventh day; p^3: Results at debridement first and seventh days. WBC: White blood cell; RBC: Red blood cell; NLR: Neutrophil to lymphocyte ratio; PLR: Platelet to lymphocyte ratio; MER: Monocyte to eosinophil ratio; CRP: C-reactive protein.

Table 5. Correlation research for the number of debridements and surgical approaches

	p	Correlation factor
Correlation study applied for the number of debridements		
Age	0.01	+0.422
Predisposing factors	0.079	+0.297
Etiological factors	0.149	–0.245
Antibiotherapy	0.893	–0.023
At first acceptance		
NLR	0.01	+0.564
PLR	0.001	+0.524
MER	0.879	+0.026
CRP	0.01	+0.643
Correlation study applied for the surgical approaches		
Predisposing factors	0.023	+0.378
Etiological factors	0.563	–0.100
Antibiotherapy	0.602	–0.090

NLR: Neutrophil to lymphocyte ratio; PLR: Platelet to lymphocyte ratio; MER: Monocyte to eosinophil ratio; CRP: C-reactive protein.

diagnosis of FG in the recent years. This situation may be explained by providing data related with debridement margins, better identification of fascial planes, differential diagnostic support in obese patients, and more detailed visualization of emphysematous lesions.[17] Computed tomography was performed in ten patients in addition to ultrasonography taking urgency of the patients regarding debridement into consideration. As stated in the literature, we evaluated patients who could not be diagnosed clearly, who had mixed fascial planes or who had severe obesity, with computerized tomography as well as ultrasonography.

A predisposing factor plays a role in development of FG in at least half of the patients and diabetes is prominent (20–70%) among these factors.[5,18] The higher prevalence of FG in diabetic patients can be explained by diabetic neuropathy, immune system deficits and vascular system damages. Although, chronic alcohol abuse is blamed as a predisposing factor with a rate of 20–50%, it was detected in none of our patients.[3] Even though, the presence of a predisposing factor is usually detected in the studies, we have determined no predisposing factor in 25% (n=9) of the patients in our study. FG is frequently caused by the infections of urogenital region.[2] On the other side, compression wounds, trauma, surgeries and malignancies of urogenital region, self-catheterization, firearms injuries, priapism, urinary instrumentation, and shaving genital region are the other etiological factors.[2,5,12] The cases in whom FG developed following priapism secondary to cavernosal papaverine injection have been reported in the literature, although rare.[12,19] One of our cases admitted with complaint of priapism at the 5th day after papaverine injection and unfortunately partial penectomy was implemented. It is considered that testicular parenchyma is generally not affected in FG because of integrity and protective characteristic of tunica albuginea. Orchiectomy was performed in 25% (n=9) of the patients despite diffuse necrotic areas and large debridements.

Broad spectrum antibiotherapy should be absolutely administered because of polymicrobial (aerobic and anaerobic) flora. Third generation cephalosporin or triple regimen consisting of aminoglycoside, penicillin, and metronidazole can be prescribed.[3,5] More recent studies have stated that administration of carbapenem (imipenem, meropenem, and ertapenem) or piperacillin-tazobactam is more effective.[3,5,20] In our hospital, usually piperacillin-tazobactam (44.4%) was used as antibiotherapy for FG.

The changes in the blood cells of 74 patients with FG have been evaluated in a study and the decrease in the levels of infection cells (WBC, neutrophils, and lymphocytes) from the initial admission time until the discharge date was found statistically significant (p=0.01, p=0.01, and p=0.01, respectively).[21] Furthermore, our analysis results indicated a significant decrease in the levels of infection cells such as WBC and neutrophil similarly measured at the initial admission time, post-perative 1st and 7th days (p^1=0.001, p^2<0.001, p^3<0.001 and p^1=0.002, p^2< 0.001, p^3<0.001, respectively). NLR can be

Figure 1. Images of the patient who underwent debridement for Fournier's gangrene. **(a)** The image of the scrotum at first acceptance. **(b)** 2 h later image of scrotum. **(c)** Inflammation that has spread from the scrotum to the left inguinal and lumbar region. **(d)** Image of the scrotum after the first debridement. **(e)** Fasciotomy was performed 5 days after the first debridement.

used in septic diseases as an inflammatory indicator; furthermore, it is related with severity of disease. In the same manner, also NLR levels showed a statistically significant decline until the discharge date (p=0.01).[21] A NLR ≥10 value was attributed with more serious disease and bacteremia in FG.[22] It has been reported that length of hospital stay prolonged and mortality risk increased in the patients with higher NLR (≥10).[22] High NLR (>8) and high PLR (>140) levels have been accepted as the poor prognostic indicators in FG (p=0.022 and p=0.001, respectively).[23] In our study, NLR values calculated at the initial admission time, post-operative 1st and 7th days statistically significantly decreased (p^1=0.012, p^2=0.002, and p^3=0.013, respectively). The levels of CRP that is an acute phase reactant (such as below or over 150 mg/L) are used in several scoring systems for FG.[9,22] In our study, a significant decrease was detected in the CRP levels measured at the initial admission time, post-operative 1st and 7th days (p^1=0.008, p^2<0.001, and p^3<0.001, respectively). Serum glucose levels also significantly decreased at the initial admission time and following days (p^1=0.023 and p^2=0.006, respectively). We consider that this decline occurred thanks to glycemic regulation after hospitalization for FG. A statistically significant decrease was encountered also in the values of RBC count, hemoglobin, and hematocrit levels in the initial admission time and following days (p^1<0.001, p^2<0.001 and p^1<0.001, p^2<0.001 and p^1<0.001, p^2<0.001, respectively). We think that the decreases in these values are due to tissue loss caused by repeated and large debridements. In addition, intravenous fluids applied to these patients may explain the current situation.

It has been stated in a study which analyzed the correlation between mortality rate and blood count parameters that mortality rate was negatively correlated with platelet count at the initial admission and after the first debridement and positively correlated with NLR and mean platelet volume.[21] Whereas, we have carried out correlation analysis for the number of debridements and surgical approaches. We have found that the number of debridements was positively correlated with age, NLR, PLR, and CRP values at the initial admission time as well as a positive correlation between surgical approaches and predisposing factors. With this regard, the patients with advanced age and high levels of NLR, PLR, and CRP may need a higher number of debridements.

Our study had several limitations. The first limitation of our study carried out with a relatively lower number of patients was its retrospective design. The second limitation was inability to obtain tissue and aspirate cultures to determine the polymicrobial flora in a major part of the patients. The third limitation was the fact that surgical treatments and follow-up periods were not performed by an identical surgeon.

Conclusion

The mortality rates due to FG are not high as previously thanks to early aggressive debridement. Diabetes is still the most critical predisposing factor. The infections of urogenital region are the essential etiological origin of FG. Our study has presented precious information related with changes encountered in the clinical data and blood count parameters in the course of FG as a rarely seen urological emergency condition. WBC count, neutrophil, NLR, and CRP levels significantly decrease in the days following debridement. The number of debridement is positively correlated with age and NLR, PLR, and CRP values at the initial admission time. The available data can be supported by further multicenter, prospective, and randomized studies in the future.

Ethics Committee Approval: This study was approved by the Health Sciences University Gülhane Scientific Research Ethics Committee (Date: 29.12.2020, Decision No: 2020–526).

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ORİJİNAL ÇALIŞMA - *ÖZ*

Üçüncü basamak bir hastanede Fournier gangrenindeki deneyimlerimiz ve bunun kan sayımı parametreleri ile ilişkisinin analizi

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AMAÇ: Fournier gangreni, genital ve perineal bölgenin hızla ilerleyen ve yaşamı tehdit eden nekrotizan fasiitidir. Fournier gangreni ile ilgili deneyimlerimizi paylaşmak ve klinik verilerin tam kan sayımı parametreleri, enflamasyon hücreleri ve sistemik enflamasyon belirteçleri ile ilişkisini analiz etmek.
GEREÇ VE YÖNTEM: Fournier gangreni tanısı ile Ocak 2016–Aralık 2020 arasında takip edilen ve tedavi edilen yetişkin hastaların dijital tıbbi kayıtları geriye dönük olarak analiz edildi. Veriler yaş, cinsiyet, toplam hastanede kalış süresi, predispozan faktörler, etiyolojik faktörler, toplam debridman sayısı, cerrahi işlemler ve antibiyotik olarak belirlendi. Hastaneye yatışın ilk günü ile debridman sonrası birinci ve yedinci günlerde ölçülen serum glikoz düzeyleri, tam kan sayım parametresi düzeyleri, serum inflamasyon göstergeleri ve C-reaktif protein düzeyleri ölçüldü.
BULGULAR: Yaş ortalaması 56.42 (22–86) yıl olan 36 erkek hasta alındı. En yaygın predispozan faktör diabetes mellitusdu (n=13; %36.1). En sık görülen etiyolojik neden skrotal apseydi (n=19; %52.8). Debridman öncesi, debridman sonrası birinci ve yedinci günlerde WBC sayısında, nötrofil seviyesinde, NLR değerinde ve CRP seviyesinde istatistiksel olarak anlamlı azalma saptandı ($p<0.05$). İlk başvuru anındaki debridman sayısı ile yaş, NLO, PLO ve CRP değerleri arasında pozitif korelasyon vardı ($p<0.05$).
TARTIŞMA: Ürogenital bölge enfeksiyonları, Fournier gangreninin temel etiyolojik kökenidir. Nadir bir ürolojik acil durum olan Fournier gangrenin-de klinik verilerde ve kan sayımı parametrelerinde önemli değişiklikler gözlendi.
Anahtar sözcükler: Debridman; enflamasyon belirteçleri; enflamasyon hücreleri; Fournier gangreni.

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