

·论著·感染创面的修复·

本文亮点:

- (1) 分析并讨论了一种罕见但高危的坏死性筋膜炎——肠痿继发坏死性筋膜炎。
- (2) 通过对 94 例肠痿继发坏死性筋膜炎病例的临床资料进行回顾性分析,得出该种疾病死亡风险高。在综合治疗的基础上,行积极的肠道和创面处理或许是避免该类患者死亡的关键,其中 I 期造痿+后期重建和负压治疗是相对优选方案。

Highlights:

- (1) A kind of rare but high-risk of necrotizing fasciitis, necrotizing fasciitis secondary to intestinal fistulas (NFsIF) was analyzed and discussed.
- (2) Retrospective analysis of clinical data of 94 NFsIF cases showed that the disease had a high mortality risk. Based on comprehensive treatment, timely managements of intestines and wounds might be the key to avoid death in these patients, and first-stage colostomy+late-stage reconstruction and negative pressure therapy were relatively preferred options.



肠痿继发坏死性筋膜炎病例的临床资料分析及死亡危险因素筛查

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【摘要】 目的 分析肠痿继发坏死性筋膜炎(NF)病例的临床资料,并筛查这些病例的死亡危险因素。方法 该研究为回顾性观察性研究。检索 2000 年 1 月—2023 年 10 月入住山东第一医科大学附属省立医院(以下简称本单位)且符合入选标准的所有肠痿继发 NF 病例的资料,在 PubMed、Web of Science、Scopus、中国知网、中华医学期刊网数据库内检索建库至 2023 年 10 月符合入选标准的所有肠痿继发 NF 病例的资料并进行筛选。按照临床结局,将有效病例纳入存活组(男 47 例、女 24 例)和死亡组(男 16 例、女 7 例)并计算病死率。对比分析 2 组病例的临床资料,包括年龄、基础疾病(与 NF 最相关的病种)、就诊前症状持续时间、白细胞计数、NF 原因、腹膜炎体征、NF 累及范围、肠道处理措施和创面处理措施,筛选 94 例肠痿继发 NF 患者死亡的危险因素。结果 共纳入有效病例为 94 例,包括文献报告 90 例、本单位收治病例 4 例,病死率为 24.5%(23/94)。单因素分析结果显示,2 组患者年龄、基础疾病、就诊前症状持续时间、白细胞计数、NF 原因、腹膜炎体征和 NF 累及范围比较,差异均无统计学意义($P>0.05$);2 组患者肠道处理措施和创面处理措施比较,差异均有统计学意义(χ^2 值分别为 17.97、8.33, $P<0.05$)。多因素 logistic 回归分析显示,肠道处理措施和创面处理措施均是 94 例肠痿继发 NF 患者死亡的独立危险因素,其中 I 期造痿+后期重建和负压治疗均具有更高的保护效应(比值比分别为 0.05、0.27,95% 置信区间为 0.01~0.33、0.08~0.88, $P<0.05$)。结论 肠痿继发 NF 患者的死亡风险高,在综合治疗的基础上,行积极的肠道和创面处理或许是避免患者死亡的关键,其中 I 期造痿+后期重建和负压治疗具有更高的保护效应。

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【关键词】 筋膜炎,坏死性; Fournier 坏疽; 肠痿; 肠穿孔

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Analysis of clinical data of necrotizing fasciitis secondary to intestinal fistulas and screening the mortality risk factors

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【Abstract】 Objective To analyze the clinical data and to screen the mortality risk factors of necrotizing fasciitis (NF) secondary to intestinal fistulas (NFsIF). **Methods** This study was a retrospective observational study. The data of all NFsIF cases who met the inclusion criteria and were admitted into Shandong Provincial Hospital Affiliated to Shandong First Medical University (hereinafter referred to as our unit) from January 2000 to October 2023, and in PubMed, Web of Science, Scopus, China National Knowledge Infrastructure, and Chinese Medical Journal Network databases from its establishment to October 2023 were retrieved and screened. Based on clinical outcomes, the cases were divided into survival group (47 males and 24 females) and death group (16 males and 7 females), and the mortality rate was calculated. Clinical data of patients in the two groups including age, underlying diseases (most related to NF), symptom duration before presentation, white blood cell count, causes of NF, signs of peritonitis, scope of NF involvement, and intestinal management and wound management measures were compared and analyzed to screen the risk factors of death in 94 patients with NFsIF. **Results** A total of 94 valid cases were collected, including 90 patients reported in the literature and 4 patients admitted to our unit, with the mortality rate of patients being 24.5% (23/94). Univariate analysis showed that there were no statistically significant differences in age, underlying diseases, symptom duration before presentation, white blood cell count, causes of NF, signs of peritonitis, scope of NF involvement between patients in the two groups ($P>0.05$); there were statistically significant differences in intestinal treatment and wound treatment between the two groups (with χ^2 values of 17.97 and 8.33, respectively, $P<0.05$). Multivariate logistic regression analysis showed that both intestinal treatment measures and wound treatments measures were independent risk factors for death in 94 NFsIF patients, among which first-stage colostomy+late-stage reconstruction and negative pressure therapy had higher protective effects (with odds ratios of 0.05 and 0.27, respectively, 95% confidence intervals of 0.01–0.33 and 0.08–0.88, respectively, $P<0.05$). **Conclusions** The mortality risk of patients with NFsIF is high. Based on comprehensive treatments, active intestinal and wound treatment may be the key to avoid death, with first-stage colostomy+late-stage reconstruction and negative pressure therapy having higher protective effects.

【Key words】 Fasciitis, necrotizing; Fournier gangrene; Intestinal fistula; Intestinal perforation

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坏死性软组织感染(necrotizing soft tissue infections, NSTI)是指因感染诱发局部血液循环障碍,进而导致皮肤、皮下组织、筋膜和/或肌肉组织坏死的严重感染^[1]。NSTI可表现为坏死性蜂窝织炎、坏死性肌炎以及坏死性筋膜炎(necrotizing fasciitis, NF)。在NF患者中,感染因子可沿着筋膜平面迅速蔓延,病情进展极快,因此NF是临床中最主要的NSTI类型^[2]。1883年,Fournier首次描述了位于男性生殖器的NSTI症状,并将这种感染以其名字命名为福尼尔坏疽(Fournier's gangrene, FG)^[3]。目前的相关文献中,一般将局限于会阴区(包括生殖器、肛门、下尿道)的NSTI称为FG,将涉

及会阴区及以外区域的NSTI称为NF。

根据感染细菌包含的主要菌种类型及其来源,NF可分为3种类型^[2]。I型NF通常指肠道或泌尿系统来源的多种需氧菌和厌氧菌造成的混合感染;II型NF的致病菌通常为皮肤感染或血流感染的革兰阳性菌,细菌释放的LPS还可导致患者出现严重的全身性感染;III型NF通常指不属于I型或II型的NF,感染的细菌种类包括假单胞菌、克雷伯杆菌、梭状芽孢杆菌等。其中,I型NF的发病率高、病原菌复杂、感染扩散迅速,患者死亡风险较高。得到广泛认可的针对I型NF的核心治疗措施包括2个方面:广谱抗生素的使用、及时充分的对感染

区的清创引流^[1,4]。

肠痿继发 NF 属于罕见的 I 型 NF, 表现为肠道完整性受损, 肠道内容物及细菌直接外溢至皮下软组织造成腹壁、会阴区、腰背部或下肢发生 NF, 但通常没有急腹症表现。此类患者因缺乏腹部症状, 难以早期定位原发灶, 采用抗生素及感染区清创引流等治疗措施不足以控制病情进展, 导致该类患者病死率显著高于其他类型的 NF 患者。因此, 本研究拟对山东第一医科大学附属省立医院(以下简称本单位)20 余年来收治的以及目前可检索到的所有国内外已发表的肠痿继发 NF 病例进行回顾性分析, 期望归纳出此类疾病的临床特征, 并对其死亡危险因素进行筛查。

1 对象与方法

1.1 伦理学声明

本回顾性观察性研究通过本单位伦理委员会批准, 批号: 2023-214。本研究相关临床资料在对患者身份信息保密的前提下获准收集和分析使用。

1.2 有效病例筛选

1.2.1 本单位病例筛选 纳入标准: 年龄 ≥ 18 岁, 出院诊断包括“NF”或“FG”, 病历资料中有肠痿或肠(十二指肠至直肠)穿孔的明确证据。排除标准: 因非医疗原因中断治疗导致病例的临床资料不全, 肠道损伤位于肛管水平(肛痿或肛周脓肿)。通过本单位的电子病历数据库, 检索 2000 年 1 月—2023 年 10 月入住本单位烧伤整形外科且符合入选标准的所有病例。

1.2.2 已发表文献病例筛选 纳入标准: 病例报告(case report)或病例系列(case series)研究, 病例年龄 ≥ 18 岁, 病例的资料中有肠痿或肠(十二指肠至直肠)穿孔的明确证据以及与 NF 相关的描述。排除标准: 重复文献, 基础研究或内容不符的研究, 语言不是英文或中文的文献, 病例原始资料缺乏, 肠道疾患位于肛管水平。在 PubMed、Web of Science、Scopus、中国知网、中华医学期刊网数据库内检索以下主题词(Mesh)和关键词(Key words): [Mesh (necrotizing fasciitis) OR Mesh (Fournier gangrene)] And [Mesh (perforation, intestinal) OR Mesh (fistula, intestinal)], [(necrotizing fasciitis) OR (Fournier)] And [(perforation) OR (fistula)], [Mesh(坏死性筋膜炎)] And [Mesh(肠穿孔) OR Mesh(肠痿) OR Mesh(肛痿)], [(坏死性筋膜炎)

OR (Fournier) OR (福尼尔)] And [(穿孔) OR (肠痿) OR (肛痿)], 检索时间为建库至 2023 年 10 月。获得检索结果后进行双人平行筛选。

1.3 病例信息采集及分组

按照临床结局, 将有效病例纳入存活组(男 47 例、女 24 例)和死亡组(男 16 例、女 7 例), 计算病死率。对 2 组病例临床资料, 包括患者年龄、基础疾病(与 NF 最相关的病种)、就诊前症状持续时间(指入院主诉提供的症状持续时间)、白细胞计数、NF 累及范围、NF 原因、腹膜炎体征、肠道处理措施和创面处理措施等进行手动采集。

1.4 统计学处理

所有原始数据录入 Microsoft Excel 软件, 采用 SPSS 20.0 统计软件进行分析。计数资料数据用频数和/或百分率表示, 组间比较采用 χ^2 检验, 亚组病例数 < 5 时(频数为 1 时除外)采用 Fisher 确切概率法检验。符合正态分布的计量资料数据用 $\bar{x} \pm s$ 表示, 组间比较采用独立样本 t 检验; 不符合正态分布的计量资料数据以 $M(Q_1, Q_3)$ 表示, 组间比较采用 Mann-Whitney U 检验。对单因素分析中 2 组间比较, 差异有统计学意义的因子进行多因素 logistic 回归分析, 确定肠痿继发 NF 患者死亡的独立危险因素。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 有效病例筛选

共纳入有效病例 94 例, 包括文献报告 90 例^[5-94]、本单位收治病例 4 例。患者病死率为 24.5%(23/94)。

2.1.1 单因素分析 单因素分析结果显示: 2 组患者年龄、基础疾病、就诊前症状持续时间、白细胞计数、NF 原因、腹膜炎体征和 NF 累及范围比较, 差异均无统计学意义 ($P > 0.05$); 2 组患者肠道处理措施和创面处理措施比较, 差异均有统计学意义 ($P < 0.05$)。见表 1。

2.1.2 多因素 logistic 回归分析 以患者临床结局为因变量(临床死亡=1, 临床治愈=0), 以单因素分析中 2 组间比较差异具有统计学意义的 2 个变量(肠道处理措施: I 期造痿+后期重建=1, I 期肠道修复术=2, 无=3; 创面处理措施: 负压治疗=1, 仅清创换药=2)为自变量进行多因素 logistic 回归分析, 结果显示, 肠道处理措施和创面处理措施均是肠痿继发 NF 患者的独立危险因素, 其中 I 期造痿+后期

表 1 2 组肠痿继发 NF 患者临床资料比较

Table 1 Comparison of the clinical data of two groups of patients with necrotizing fasciitis secondary to intestinal fistulas

组别	例数	年龄(岁, $\bar{x} \pm s$)	基础疾病 ^a (例)						NF 原因(例)						
			无	肠道肿瘤	肠道溃疡或慢性炎症 ^b	肠道急性炎症或嵌顿 ^c	外伤或操作损伤 ^d	全身性疾病 ^e	直肠穿孔	结肠穿孔	盲肠穿孔	阑尾穿孔	回肠穿孔	十二指肠穿孔	胆囊穿孔
存活组	71	58±16	12	25	13	6	4	11	18	21	8	11	9	2	2
死亡组	23	62±17	1	11	0	4	3	4	6	4	2	5	3	3	0
统计量值	$t=-1.15$		—						—						
P 值	0.254		0.052						0.528						

组别	例数	就诊前症状持续时间[d, $M(Q_1, Q_3)$]	白细胞计数($\times 10^9/L, \bar{x} \pm s$)		腹膜炎体征(例)			NF 累及范围(例)			肠道处理措施(例)			创面处理措施(例)	
			阴性	阳性	仅会阴区	腹部 ^f	大腿或腰背部 ^g	小腿或胸部 ^h	I 期造瘘+后期重建	I 期肠道修复术 ⁱ	无	负压治疗 ^j	仅清创换药		
存活组	71	4.0(3.0, 8.0)	23±12	60	11	17	24	25	5	48	21	2	40	5	
死亡组	23	3.0(2.0, 7.0)	19±13	19	4	6	5	9	3	6	11	6	31	18	
统计量值	$Z=1.90$		$t=1.14$	$\chi^2=0.05$			$\chi^2=1.66$			$\chi^2=17.97$			$\chi^2=8.33$		
P 值	0.057		0.261	0.829			0.643			<0.001			0.004		

注: NF 为坏死性筋膜炎; ^a指与本次 NF 最相关的基础疾病, ^b包括克罗恩病、憩室炎、胃十二指肠溃疡和结核性肠炎, ^c包括阑尾炎和嵌顿疝, ^d包括骨盆骨折、腹部撞击、脊髓损伤以及抽脂术、结肠镜检查 and 顽固性便秘造成的损伤, ^e包括 2 型糖尿病、甲亢、心脏病和高血压等, ^f可包括会阴区; ^g可包括会阴区及腹部, ^h可包括会阴区、腹部、腰背部及大腿, ⁱ包括 I 期肠壁修补术和 I 期肠穿孔切除吻合术, ^j包括负压治疗后自行愈合、局部缝合、皮片或皮瓣修复; “—”表示无此统计量值

重建和负压治疗均具有更高的保护效应 ($P < 0.05$)。见表 2。

表 2 94 例肠痿继发坏死性筋膜炎患者死亡的多因素 logistic 回归分析结果

Table 2 Multivariate logistic regression analysis results of 94 patients with necrotizing fasciitis secondary to intestinal fistulas

变量	回归系数	标准误	Wald χ^2 值	比值比	95% 置信区间	P 值
肠道处理措施						
I 期造瘘+后期重建	-2.99	0.96	9.78	0.05	0.01~0.33	0.002
I 期肠道修复术 ^a	-1.73	0.93	3.42	0.18	0.03~1.11	0.065
创面处理措施						
负压治疗 ^b	-1.31	0.60	4.69	0.27	0.08~0.88	0.030
常量	1.50	0.88	2.94	—	—	0.087

注: 肠道处理措施以无处理为参照, 创面处理措施以仅清创换药为参照; ^a包括 I 期肠壁修补术和 I 期肠穿孔切除吻合术, ^b包括负压治疗后自行愈合、局部缝合、皮片或皮瓣修复; “—”表示无此统计量值

2.2 本单位收治的典型病例

例 1 男, 34 岁, 因右臀及右大腿红肿疼痛 4 d 至本单位急诊。患者入院 11 d 前曾行痔疮切除手

术, 9 d 前停止排气、排便伴发热, 4 d 前出现右侧臀部及右大腿红肿疼痛。体格检查显示, 血压 69~101 mmHg (1 mmHg=0.133 kPa), 心率 134 次/min, 茶色尿; 盆腹部压痛及反跳痛均为阴性; 直肠指诊阴性。实验室检查结果: 血红蛋白 105 g/L、白细胞计数 $6.18 \times 10^9/L$ 、血钾 6.42 mmol/L、中性粒细胞 0.907、降钙素原 8.44 ng/mL。CT 结果: 腹膜后、盆腔游离气体, 右侧髂部、股骨上段广泛积气且软组织肿胀。入院诊断: NF、肠梗阻、高钾血症。治疗方案: 对症支持治疗, 亚胺培南-西司他丁+奥硝唑抗感染治疗(后细菌培养结果为变形杆菌、肺炎克雷伯菌和大肠埃希菌阳性, 药物敏感试验结果显示细菌对亚胺培南敏感), 至急诊 3 h 后联合胃肠外科医师行腹腔镜下腹腔探查+结肠造瘘+右下肢清创负压治疗术, 术中明确腹腔内无异常, 盆腔直肠隐窝内可见脓性腹水 20 mL, 骶前筋膜下疑似血肿或脓肿, 遂行横结肠双腔造瘘术, 留置腹腔引流管; 右下肢可见筋膜坏死, 股四头肌深部可见粪便样物质伴明显臭味, 充分清创后填塞负压材料行负压治疗。术后患者恢复进食, 近端造瘘口排便通畅; 每日自远端造瘘口用 3 000 mL 生理盐水持续冲洗。入院 5 d, 肛门排出的冲洗液基本清洁, 肠镜检查见直肠下段腹侧巨大瘘口, 瘘口外见大量黏液及粪便样物质。入院 1 个月, 患者出现双侧腰部疼痛, 超

声示腹膜后及双侧肾周脓肿,遂行穿刺置管引流。入院 35 d,行引流管逆行碘造影 CT 扫描+三维重建,明确腹膜后脓肿与盆底脓腔贯通但与右下肢脓腔不通。联合肛肠科医师于肛门右侧盆底行引流术,见大量粪便样物质溢出。术后每日自腰部引流管用 1 000 mL 生理盐水逆行冲洗,臀部引流液日渐清洁。入院 65 d,患者一般情况良好,右下肢创面清洁后缝合且愈合良好,遵医嘱离院,建议后期至胃肠外科行直肠瘘口切除吻合+横结肠造瘘还纳术。见图 1。

例 2 男,51 岁,因右臀部、右大腿广泛红肿伴握雪感 1 周余入院。患者 5 年前确诊乙状结肠中分化腺癌,行姑息性左半结肠切除+横结肠造瘘术;2 年前确诊直肠中分化腺癌,行姑息性直肠部分切除+盆腔清扫+阑尾切除术。入院 15 d 前因心悸、大汗、胸闷、发热于急诊留观。体格检查显示,恶病质面容,右臀部、右下肢广泛红肿伴握雪感;盆腹部压痛及反跳痛均为阴性。实验室检查结果:血红蛋白 57 g/L、白细胞计数 $15.68 \times 10^9/L$ 、中性粒细胞 0.933、降钙素原 9.25 ng/mL。CT 结果:直肠术后,骶前软组织感染表现;右臀部、右大腿及膝部软组织感染且存在大量积气。入院诊断:臀部、右下肢 NF、盆腔骶前软组织感染、乙状结肠癌+直肠癌术后全身多处转移。治疗方案:禁饮食,给予肠外营养;对症支持治疗;亚胺培南西-司他丁联合奥硝唑抗感染治疗(后细菌培养结果为大肠埃希菌及铜绿假单胞菌阳性,药物敏感试验结果显示这 2 种菌均对亚胺培南敏感);入院当日行右下肢局部床旁姑息性清创引流术;联系胃肠外科医师行腹腔镜下探查,胃肠外科以没有明确肠瘘证据且腹腔情况复杂为由拒绝手术。入院 3 d 后行消化道碘水造影,明确回肠-盆腔-右大腿瘘。入院 1 周,由胃肠外科医师行回肠双腔造瘘术。术后患者恢复进食,近端造瘘口排便通畅。自远端造瘘口每日用 3 000 mL 生

理盐水持续冲洗,大量肠内容物从右大腿瘘口排出,日渐清洁。入院 25 d,患者一般情况良好,造瘘口良好,右大腿后侧创面每日少量分泌物被引出,患者家属可居家照护,遵医嘱离院。见图 2。

例 3 女,24 岁,因发热 8 d,便血 6 d,左下肢肿痛 2 d 入院。患者有系统性红斑狼疮病史 9 年,持续口服环磷酰胺、泼尼松及他克莫司;入院 8 d 前出现发热,后出现伴血块便血约 1 000 mL,入院 2 d 前左下肢后侧肿痛。体格检查显示,左大腿后侧至腘窝可见皮肤红肿、疼痛,伴握雪感,盆腹部压痛及反跳痛均阴性。实验室检查结果:血红蛋白 84 g/L、白细胞计数 $42.44 \times 10^9/L$ 、中性粒细胞 0.952、降钙素原 11.52 ng/mL。磁共振成像显示,盆腔、左侧盆壁、骶部、臀部及左大腿感染,且有积气表现。肠镜示直肠下段右侧巨大瘘口。入院诊断:NF、直肠穿孔、系统性红斑狼疮。治疗方案:对症支持治疗;美罗培南联合奥硝唑抗感染治疗;入院 6 h,行乙状结肠造瘘+下肢清创负压治疗+肛周盆底清创引流术。术后患者正常进食,近端造瘘口排便通畅;自远端造瘘口每日用 3 000 mL 生理盐水持续冲洗,臀部盆腔引流液日渐清洁。入院 42 d,患者一般情况良好,左下肢创面愈合良好,复查肠镜示直肠瘘口仍在。患者遵医嘱离院,建议后期至胃肠外科行直肠瘘口切除吻合术+乙状结肠造瘘还纳术。

例 4 男,58 岁,因吻合口瘘继发皮肤坏死 1 个月入院。患者 2 个月前确诊乙状结肠上皮内癌变,行乙状结肠癌根治性切除术,后出现吻合口瘘+胸腹背部大面积皮肤软组织坏死。体格检查显示,右腋下、右腰背部、下腹部大面积皮肤呈紫黑色,伴局灶性脓性渗液,有握雪感;腹软,无明显压痛及反跳痛。实验室检查结果:血红蛋白 109 g/L、白细胞计数 $23.36 \times 10^9/L$ 、降钙素原 8.26 ng/mL、中性粒细胞 0.912。CT 结果:乙状结肠术后,右前腹壁造瘘,右侧胸腹、臀腹及会阴区肿胀伴积气。入院诊断:

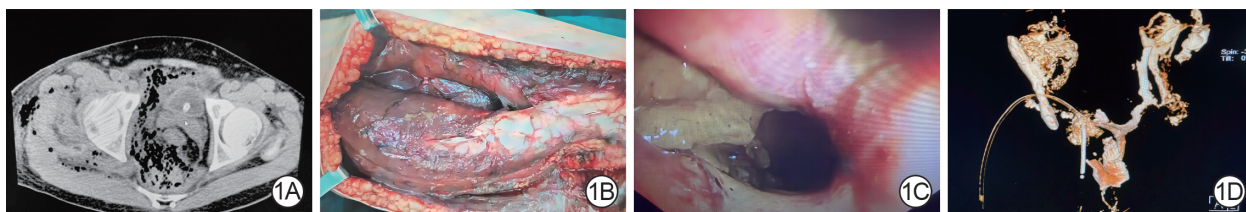


图 1 直肠瘘继发右下肢坏死性筋膜炎例 1 患者诊断过程。1A. 入院时 CT 示盆腔及右侧皮下多发游离气体;1B. 入院 3 h 急诊探查见右下肢后内侧切开皮下及肌间隙广泛筋膜坏死,大量脓性及粪便样物质积聚;1C. 入院 5 d 肠镜示直肠下段巨大瘘口;1D. 入院 35 d 引流管逆行碘造影 CT 扫描+三维重建示腹膜后脓腔与盆底脓腔贯通

Figure 1 Diagnosis process of necrotizing fasciitis of the right lower limb secondary to rectal fistula in case 1

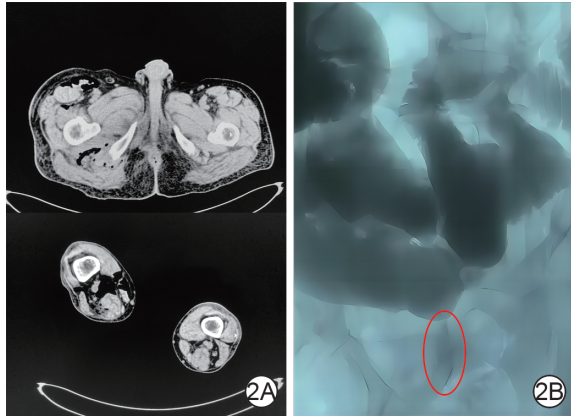


图2 回肠瘘继发右大腿坏死性筋膜炎例2患者的诊断过程。2A.入院时右侧臀部肌肉间隙内可见游离气体(上侧图),右大腿上段后侧可见肌肉深部巨大腔隙伴内侧软组织坏死液化缺损(下侧图);2B.入院3 d后,消化道碘水造影显示回肠-盆腔瘘(见红色椭圆标记)

Figure 2 Diagnosis process of necrotizing fasciitis of the right thigh secondary to ileal fistula in case 2

NF、结肠吻合口瘘伴腹腔感染、乙状结肠肿瘤。治疗方案:对症支持治疗;美罗培南联合奥硝唑抗感染治疗;入急诊8 h行皮肤软组织清创+负压治疗术,将坏死区域彻底清创后,继续负压治疗。入院62 d,患者一般情况良好,造瘘功能良好,所有创面经皮片移植后愈合。患者遵医嘱离院。

3 讨论

NF是一种引起皮下组织和筋膜坏死软组织感染的疾病,进展非常迅速,常导致患者出现高热、水电解质紊乱、意识障碍、贫血等症状,严重感染时可引发感染性休克与弥散性血管内凝血,致死风险极高^[95]。

3.1 NF的诊断

NF早期多表现为局灶性皮肤红肿热痛、伴发热等,与普通软组织感染具有相似性,难以引起接诊医师的警惕,待患者全身症状恶化或出现软组织坏死时,感染范围已大幅扩散,因此,NF的早期明确诊断对患者的预后意义重大。2004年,Wong等^[96]提出NF实验室风险指标评分,指出可通过对C反应蛋白、白细胞计数、血红蛋白、血钠、血肌酐和血糖6项指标进行评分(满分13分),得分 ≥ 6 分可怀疑NF, ≥ 8 分高度怀疑NF,该评分的应用显著提高了NF早期诊断率。除了以上血液指标,CT或磁共振成像可显示深部组织的炎性改变、液化坏死以及游离气体积聚,其中游离气体运动强烈提示I型NF。当高度怀疑NF时,行局部侵入性探查是

简便且必要的,切开皮肤,用手指向皮下深层探查,若可见洗肉水样渗液溢出,即“手指试验”阳性,即可确诊NF^[2]。

3.2 NF与FG的比较

FG的感染范围通常局限于会阴区,感染来源通常为肠道和泌尿系统的细菌,是临床中最为常见的I型NF。自1883年Fournier提出FG的概念以来,有关FG临床诊疗的研究已经非常丰富。2000年发表的一项回顾性分析显示,1 726例FG病例(病例收治时间为1950—1990年)的病死率为16%^[97];2020年发表的一篇FG系统综述共纳入了38项研究(研究发表时间2005—2018年)1 186例病例,这些病例的病死率为21%^[98];其他的小范围病例研究显示,FG病例的病死率为4%~36%^[3]。虽然NF感染累及区域较FG广泛得多,如继发于糖尿病足感染的下肢NF、继发于毛囊感染的项背部NF、继发于异物外伤的III型NF以及继发于肠瘘的腹膜后NF等^[99],但这些特殊类型的NF缺乏类似FG的大宗病例研究,难以获得高价值的信息。

3.3 肠瘘继发NF

肠瘘是指胃肠道与其他空腔脏器、体腔或体腔外有异常通道,肠内容物循此通道进入,并继发机体感染、内环境稳态失衡、器官功能受损等一系列问题^[100]。肠瘘的原因包括先天性发育缺损及后天性的炎症、肿瘤、外伤及手术并发症等。肠瘘是胃肠外科的严重疾病,通常有典型的腹腔感染表现(腹膜刺激征阳性)以及影像学表现。所以,肠瘘通常以诊断易、治疗难为特征。然而,当肠瘘发生在特殊部位(如盆腔、腹膜后、腹壁等)时,临床首表现为NF,而腹腔症状缺乏或轻微时,早期准确诊断就变得极为困难。诊断延迟必然导致处理延迟,进一步导致NF感染持续恶化及手术机会的丧失,最终导致患者病死率显著升高。本研究系统分析了目前已发表的肠瘘继发NF的病例报告,病死率为25.6%(23/90),然而,考虑个案报告的发表偏倚,临床中的实际病死率显然远高于此值。此外,很多迅速死亡的NF患者并没有机会被诊断为肠瘘继发NF,也造成诊断率和病死率的低估。

3.4 肠瘘继发NF的诊断与治疗策略

肠瘘继发NF的诊断与治疗需要同时考虑NF和肠瘘2个方面,目前并没有被广泛认可的诊断和治疗常规方案。根据本团队成功救治4例患者的临床经验,以及对文献90例患者诊疗过程的分析

讨论,本团队提出 9 个肠痿继发 NF 患者死亡相关的危险因素并对其进行单因素分析和多因素 logistic 回归分析。

首先,肠道处理措施是明确的肠痿继发 NF 患者死亡预测因子。以无处理作为参照,其他的肠道干预措施(包括 I 期造痿+后期重建和 I 期肠道修复术)的比值比均 <1 ,显示保护效应,且其中 I 期造痿+后期重建措施的比值比更低。因此,本团队认为 I 期造痿+后期重建应成为肠痿继发 NF 治疗的优选措施。I 期造痿的成功实施需要两方面准备,一是患者全身情况能够进行腹部手术(优选腹腔镜)及通常同时进行的皮肤软组织清创手术;二是明确造痿位置。常见的造痿位置是乙状结肠、横结肠、回肠等,应根据患者渗液性状、腹部体征、肿瘤位置、肠内容物淤积情况、皮肤感染区域、肠道粘连情况等因素进行综合考量和选择。此外,I 期造痿应尽量选择双腔造痿,痿口近端可通畅排便,辅助患者恢复进食和营养改善;痿口远端可进行持续冲洗,使后段肠道和 NF 感染腔隙逐渐清洁,对后续肠镜检查、肠道重建以及皮肤软组织感染控制均有积极作用。后期肠道重建应由胃肠外科医师选择合理的时机和方案。其次,创面处理措施也是明确的肠痿继发 NF 患者死亡预测因子。对于 NF 和 FG,早期及时的广谱抗生素和清创引流治疗是目前广泛公认的必要措施^[10]。本研究显示,与仅清创换药相比,负压治疗(比值比为 0.27)显示了明显的保护效应。此外,负压治疗可为后期皮片或皮瓣覆盖创面做准备,应作为创面处理的优选措施。

3.5 本研究的局限性

本研究基于本单位收治的 4 例患者和已发表病例报告中 90 例患者的临床资料数据进行分析,大部分原始数据不可追溯,数据偏倚显著。此外,根据 logistic 回归分析的经验准则,病例样本量应为阳性事件例数的 10~15 倍,本研究有效样本量为 94,理论上选择阳性因素 6~9 项。研究组成员充分考虑临床相关性、准确性、科学性、可及性以及缺失比例(所有亚组数据缺失应 $<5\%$)等,最终选择纳入 9 项肠痿继发 NF 患者死亡相关因素进行统计分析。其他(如病原菌类型、首次手术时间、手术次数等)也具有分析价值的因素未能入选,限制了本研究的临床意义。

3.6 小结

本研究聚焦于肠痿继发 NF 这一罕见却棘手的

NF 类型,汇报了本单位收治的 4 例病例,并检索了目前已发表的所有病例报告(90 例病例),较为全面地展示了该疾病的临床特征。本研究通过分析得出,肠痿继发 NF 患者的死亡风险高,在综合治疗的基础上,行积极的肠道和创面处理或许是避免患者死亡的关键,I 期造痿+后期重建和负压治疗是相对优选方案。

利益冲突 所有作者均声明不存在利益冲突

作者贡献声明 赵陈雨瑶、张玉坤:检索文献、双盲校对、分析数据;杨占杰、王明青、薛文君、霍然:病例诊治、研究设计及指导、论文审阅并修改;赵冉:数据处理、统计分析、论文撰写、经费支持

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