

坏死性筋膜炎研究现状

陈杰 夏军 王思群 魏亦兵

摘要 坏死性筋膜炎(NF)在全世界的发病率呈上升趋势,易误诊并易造成严重并发症和后遗症,致残率和死亡率较高。预防和控制NF发展,关键是提高临床认识,做到早期诊断、及时彻底引流,并配合有效的抗生素治疗及辅助治疗。该文就NF致病因素、危险因素、临床表现及诊断和治疗等研究现状作一综述。

关键词 坏死性筋膜炎;病因;诊断;治疗

DOI:10.3969/j.issn.1673-7083.2011.02.009

坏死性筋膜炎(NF)是一种罕见的潜在威胁生命的进行性感染性疾病,表现为感染沿深浅筋膜播散,在累及的血管内形成血栓,引起相应皮肤、皮下组织及筋膜组织坏死,多伴有毒血症。NF可继发于任何皮肤损伤或血源性传播,如皮肤活检术后、撕裂伤、昆虫咬伤、针刺伤、烧伤、外科伤口、皮肤脓肿、带状疱疹及静脉溃疡等^[1,2],之后快速扩散至整个肢体,因此早期清创和抗生素治疗是影响患者早期存活率的最重要因素。可是,此病与许多其他软组织疾病如蜂窝织炎很相似,早期诊断尤为困难。

NF在美国的年发病率为4.3/10万人^[3]。Andrews等^[4]报道,澳大利亚NF存活者平均住院36d,患者平均花费64517澳元,其中63%患者在重症监护病房(ICU)平均治疗11d。Argenta等^[5]也报道了相似的平均住院天数(34d)。目前这种快速恶化的感染性疾病的发病率在全世界均呈上升趋势,死亡率很高,且易误诊并造成严重并发症和后遗症,因此值得关注。

1 致病因素

按细菌菌种分类,NF可分为两型。I型为多种细菌,如厌氧菌与非A族溶血性链球菌混合感染;II型为单一细菌A族链球菌感染^[6]。目前尚无证据证明哪型感染更常见。有文献^[5,7]报道,20%~38%NF为I型,49%~68%NF为II型。Fitzmaurice等^[8]报道,NF患者25%为单一细菌(大多为A族溶血性链球菌)感染,71%~75%为厌氧菌与需氧菌混合感染。Taviloglu等^[9]研究显示,82%NF患者为多种细菌混合感染。

Park等^[10]报道海洋弧菌引起NF,该菌引起的病变症状较重。此外,克雷伯杆菌、埃希大肠杆菌、流感嗜血杆菌、肠炎沙门菌、副溶血性弧菌、黏质沙雷菌等也有致NF的报道^[11,15]。

有学者从NF致病基因方面展开研究。Morgan等^[16]报道1例金黄色葡萄球菌感染所致NF,检测出其肠毒素基因簇seg、sei、sem、sen和seo。其他一些学者^[17,19]也相继发表了此类研究成果。

2 危险因素

绝大多数NF患者存在危险因素,即为继发性,原因

不明或特发性者仅占15%~18.2%。糖尿病是NF最常见的危险因素,NF伴发糖尿病患者可达18%~60%^[20,21]。其他危险因素包括肥胖、外周血管疾病、静脉输液、吸烟、嗜酒、营养不良^[21,23]、慢性心脏疾病、长期皮质激素治疗、免疫抑制、肿瘤、年龄、慢性肾功能衰竭、先天性白细胞减少、吸毒、手术、介入操作(如经颈静脉肝内门腔分流)、透视、多普勒超声心动图检查、超声引导下经导管腹腔化疗或脓肿引流、泌尿生殖器械操作、注射、化疗、放疗、脑血管意外、急性感染性多神经炎、滥用药物、高血压、动脉硬化、痛风、艾滋病、梅毒、伤寒等^[24-27]。长期服用非类固醇类抗炎镇痛药可掩盖NF早期症状,延误诊断,也应作为NF危险因素^[28,30]。危险因素<3个者生存率为79%,死亡率为17%,而存在3个危险因素者预测死亡率为50%。尽管众多危险因素已被证实,但约50%NF患者发病时处于健康状态^[24]。

3 临床表现

NF临床表现呈现一渐进性皮肤变化过程。NF早期,只出现压痛、肿胀、红斑、皮温升高,捻发音、水泡等特殊体征比较罕见^[31,33]。Singh等^[34]报道显示,75例NF患者中91%出现局部压痛,99%出现水肿,72%出现红斑,73%出现溃疡,72%出现化脓或浆液性溢液。一些研究^[35,36]报道,除了常见症状外,83%NF患者有重度疼痛,86%出现发热,33%出现低血压(收缩压<12.27kPa)。Tang等^[37]报道,24例NF患者中有19例(79%)出现中毒性休克(均有重度疼痛),14例(58%)出现肢体肿胀,12例(50%)出现红斑,3例(13%)出现皮肤水肿。NF中期,可发生重度皮肤缺血,出现水泡或大疱,这在蜂窝织炎或丹毒是罕见的^[31,32]。由于营养血管遭破坏且血管栓塞,皮肤迅速出现苍白、青紫和坏死,皮肤表面常出现大小不一、散在的含血性液体的水泡或大疱。NF晚期,皮肤发黑,水泡破溃后露出黑色真皮层;皮下组织和浅筋膜、深筋膜呈进行性、广泛性坏死液化,皮肤漂浮其上。随着病灶部位感觉神经的破坏,剧烈疼痛可由麻木或麻痹所替代,这可能预示筋膜和皮下组织坏疽的开始,且坏疽多发生于36h内。若为产气荚膜杆菌、梭状芽胞杆菌等感染所致,则会出现捻发音。全身症状包括低血压、心动过速、反应迟钝或意识丧失、急性肾功能衰竭、酸中毒、白细

胞升高等休克症状^[32,38]。Angoules等^[39]回顾15年文献中458例肢体NF,其中下肢NF占68%,上肢NF为32%;304例中222例(73%)出现红斑,192例(63%)有疼痛,149例(49%)有肢体水肿,82例(27%)有化脓,55例(18%)有局部皮温增高。

4 诊断与鉴别诊断

伤口探查和清创时软组织活检是NF诊断的金标准,同时行需氧菌及厌氧菌培养、革兰染色,以排除少见菌如梭状杆菌、弧菌及真菌感染^[40]。

手指试验可帮助诊断。局麻下行2cm左右切口,手指探入皮肤与筋膜之间,如发现无出血,有恶臭味脓液,皮肤与筋膜易分离,则为手指试验阳性,应高度怀疑NF^[31,41]。对疑有NF者,CT检查有助于早期确立诊断及发现初步手术清创后进展性组织坏死所致并发症^[42]。B超可应用于NF早期诊断,其诱导脓肿抽吸培养,可识别致病菌,从而快速提供有价值的诊断信息。MRI具有较高的软组织对比分辨率,对于发现液体积聚很敏感,有助于确定最佳活检部位和实施治疗方案并监测治疗反应。MRI辅助检查较为费时,一旦病情危重、患者插管时,其作用受限^[43]。Fisher等^[44]提出NF诊断6项标准:①皮下筋膜广泛坏死,伴有广泛潜行灶,逆行向周围扩散;②全身性重度中毒症状伴神志改变;③未累及肌层;④伤口血培养未发现梭状杆菌;⑤有重要血管阻塞症状;⑥清创组织检查有广泛细胞浸润、筋膜邻近组织灶性坏死及微小血管栓塞。

NF应与下列疾病相鉴别^[45,46]:①丹毒:局部为片状红斑,无水肿,边界清楚,伴有淋巴管炎和淋巴结病变,轻度软组织肿胀或皮肤坏死,有发热,但全身症状较轻。②蜂窝织炎:早期两者临床鉴别诊断相当困难,蜂窝织炎只累及皮下组织,筋膜正常,影像显示皮下组织增厚,脂肪组织密度增高,伴有条索状不规则强化,伴或不伴皮下和浅筋膜积液,深部结构正常;常伴有淋巴侵犯,合适的抗生素治疗有效。③链球菌坏死:由 β -溶血性链球菌感染,以皮肤坏死为主,不累及筋膜。早期局部皮肤红肿,继而变成暗红,出现水疱,内含血性浆液和细菌。皮肤坏死后期呈干结、类似烧伤的焦痂。④气性坏疽:侵及深部或污染伤口,其特点为肌肉迅速坏死,早期出现“啞扎”音,局部疼痛严重,全身中毒征象伴中枢神经系统改变。⑤肌炎:特征为肌肉明显受累,临床特点为疼痛、感觉过敏、全身中毒征象。其诊断基于血中存在肌酸酐磷酸激酶,血尿中存在肌球蛋白,影像显示肌肉增厚,伴或不伴非均质强化。⑥其他疾病,如筋膜炎-脂膜炎综合征、糖尿病坏疽、坏疽性脓皮病等。

5 治疗

NF是外科危重急症,治疗原则是早期诊断,尽早清创,纠正休克及多器官损伤,应用大量有效抗生素和营养支持疗法。

Lille等^[47]报道,24h内清创者死亡率为6%,而延迟

清创者死亡率达到25%。这与Argenta等^[51]及Wong等^[48]报道的结论相一致。合理应用抗生素同样重要,初始治疗应采用针对革兰阳性球菌、革兰阴性杆菌和厌氧菌的广谱抗生素,常用的有青霉素、克林霉素^[49]。对于深部组织感染,加用蛋白合成抑制剂的疗效更好(83%对14%, $P=0.006$)^[50]。一些报道^[51,52]显示A族链球菌对红霉素的耐药率,在中国人中为92%,在美国人和加拿大人中为2.1%~4.6%,在中国香港人中为32%。高压氧治疗可提高组织氧分压,提高白细胞杀伤能力,减轻组织水肿,刺激成纤维细胞增生、胶原形成,促进早期伤口愈合。Fink等^[7]报道,NF患者首次清创后接受高压氧治疗的伤口愈合时间为28d,未接受高压氧治疗患者伤口愈合需48d。Wilkinson等^[53]研究提示,NF患者接受高压氧治疗的死亡率为6%,未接受高压氧治疗的死亡率为36%。Escobar等^[54]报道,42例NF患者接受与未接受高压氧治疗的死亡率分别为12%和34%,截肢率分别下降50%和0%。大量免疫球蛋白静脉给药可封闭抗体,阻断凋亡相关因子Fas及其配体结合,提高机体非特异性免疫功能,对于急性期NF治疗具有重要作用^[55]。研究^[56]表明,经静脉滴注免疫球蛋白治疗链球菌性中毒性休克患者的30d生存率达到67%,而未治疗者30d生存率为34%。

6 预后

NF发病急,进展快,临床少见,国外报道误诊率可高达75%,国内报道为50%。Angoules等^[39]回顾性分析411例四肢NF患者,多次清创术后仍不能控制感染者中86例(20.9%)行截肢术,6例(1.4%)行关节离断术。因此,早期诊断,及时彻底清创引流,结合高压氧、创面持续负压吸引等治疗,将大大提高NF预后满意度。

参考文献

- Kihiczak GG, Schwartz RA, Kapila R. Necrotizing fasciitis; a deadly infection. *J Eur Acad Dermatol Venereol*. 2006; 20(4):365-369
- Salcido RS. Necrotizing fasciitis: reviewing the causes and treatment strategies. *Adv Skin Wound Care*. 2007; 20(5):288-293
- Anaya DA, McMahon K, Nathens AB, et al. Predictors of mortality and limb loss in necrotizing soft tissue infections. *Arch Surg*. 2005; 140(2):151-157
- Andrews BT, Smith RB, Goldstein DP, et al. Management of complicated head and neck wounds with vacuum-assisted closure system. *Head Neck*. 2006; 28(11):974-981
- Argenta LC, Morykwas MJ. Vacuum-assisted closure: a new method for wound control and treatment; clinical experience. *Ann Plast Surg*. 1997; 38(6):563-576
- Elliott DC, Kufera JA, Myers RA. Necrotizing soft tissue infections. Risk factors for mortality and strategies for management. *Ann Surg*. 1996; 224(5):672-683
- Fink A, DeLuca G. Necrotizing fasciitis: pathophysiology and treatment. *MedSurg Nurs*. 2002; 11(1):33-36
- Fitzmaurice M, Lawson D, Friedman H. A novel approach for the application of the vacuum assisted closure device to the difficult anatomy. *J Plast Reconstr Aesthet Surg*. 2006; 59(11):1249-1250
- Taviloglu K, Cabioglu N, Çağatay A, et al. Idiopathic necrotizing fasciitis: risk factors and strategies for management. *Am Surg*. 2005; 71(4):315-320
- Park KH, Jung SI, Jung YS, et al. Marine bacteria as a leading cause of necrotizing fasciitis in coastal areas of South Korea. *Am J Trop Med Hyg*. 2009; 80(4):646-650

11 Robinson AB, DeWitt EM, Schanberg LE, et al. Necrotizing fasciitis caused by *Haemophilus influenzae* type E in a 17-year-old girl with systemic lupus erythematosus. *J Clin Rheumatol*, 2010; 16(1):49-50

12 Saito T, Matsunaga H, Matsumura Y, et al. Necrotizing fasciitis caused by *Haemophilus influenzae* type b in an elderly patient. *J Clin Microbiol*, 2009; 47(3):852-854

13 Rosser A, Swallow G, Swann RA, et al. *Salmonella enteritidis* necrotising fasciitis in a multiple myeloma patient receiving bortezomib. *Int J Hematol*, 2010; 91(1):149-151

14 Tena D, Arias M, Alvarez BT, et al. Fulminant necrotizing fasciitis due to *Vibrio parahaemolyticus*. *J Med Microbiol*, 2010; 59(Pt 2):235-238

15 Meisel M, Schultz-Coulon HJ. Life-threatening necrotizing fasciitis coli caused by *Serratia marcescens*. *HNO*, 2009; 57(10):1071-1074

16 Morgan WR, Caldwell MD, Brady JM, et al. Necrotizing fasciitis due to a methicillin-sensitive *Staphylococcus aureus* isolate harboring an enterotoxin gene cluster. *J Clin Microbiol*, 2007; 45(2):668-671

17 Humar D, Data V, Bast DJ, et al. Streptolysin S and necrotising infections produced by group G streptococcus. *Lancet*, 2002; 359(9301):124-129

18 Louie L, Simor AE, Louie M, et al. Diagnosis of group A streptococcal necrotizing fasciitis by using PCR to amplify the streptococcal pyrogenic exotoxin B gene. *J Clin Microbiol*, 1998; 36(6):1769-1771

19 Midrew KL, Simpson JF, Stratton CW, et al. Molecular diagnosis of necrotizing fasciitis by 16S rRNA gene sequencing and superantigen gene detection. *J Mol Diagn*, 2005; 7(5):641-645

20 Hung CC, Chang SC, Lin SF, et al. Clinical manifestations, microbiology and prognosis of 42 patients with necrotizing fasciitis. *J Formos Med Assoc*, 1996; 95(12):917-922

21 Dufel S, Martino M. Simple cellulitis or a more serious infection? *J Fam Pract*, 2006; 55(5):396-400

22 Li YH, Toh CL, Khoo C, et al. Necrotising fasciitis; an old enemy or a new foe. *Ann Acad Med Singapore*, 1997; 26(2):175-178

23 Lamagni TL, Neal S, Keshishian C, et al. Severe *Streptococcus pyogenes* infections, United Kingdom, 2003-2004. *Emerg Infect Dis*, 2008; 14(2):202-209

24 Raffoul T, Fournier B, Lecomte C. Necrotizing fasciitis after a blunt trauma. *Ann Chir Plast Esthet*, 2010; 55(1):78-81

25 Uzel AP, Steinmann G, Bertino R, et al. Necrotizing fasciitis and cellulitis of the upper limb resulting from centipede bite; two case reports. *Chir Main*, 2009; 28(5):322-325

26 Brodik G, van Bilsen SJ, Becker T, et al. Necrotizing fasciitis following laparoscopic left hemicolecotomy for diverticulitis. *J Laparoendosc Adv Surg Tech A*, 2010; 20(1):65-67

27 Ouazzani A, Dequanter D, Buttafucio F, et al. Cervical necrotizing fasciitis arising from dental abscess: a rare clinical observation. *Rev Med Brux*, 2009; 30(2):99-105

28 Souyni C, Olivier P, Grolleau S, et al. Severe necrotizing soft-tissue infections and nonsteroidal anti-inflammatory drugs. *Clin Exp Dermatol*, 2008; 33(3):249-255

29 Simonart T. Group a beta-haemolytic streptococcal necrotising fasciitis; early diagnosis and clinical features. *Dermatology*, 2004; 208(1):5-9

30 Aronoff DM, Bloch KC. Assessing the relationship between the use of nonsteroidal antiinflammatory drugs and necrotizing fasciitis caused by group A streptococcus. *Medicine(Baltimore)*, 2003; 82(4):225-235

31 Wong CH, Wang YS. The diagnosis of necrotizing fasciitis. *Curr Opin Infect Dis*, 2005; 18(2):101-106

32 Fustes-Morales A, Gutierrez-Castrellon P, Duran-Mckinster C, et al. Necrotizing fasciitis; report of 39 pediatric cases. *Arch Dermatol*, 2002; 138(7):893-899

33 Urschel JD. Necrotizing soft tissue infections. *Postgrad Med J*, 1999; 75(889):645-649

34 Singh G, Sinha SK, Adhikary S, et al. Necrotising infections of soft tissues: a clinical profile. *Eur J Surg*, 2002; 168(6):366-371

35 Sharma M, Khatib R, Fakh M. Clinical characteristics of necrotizing fasciitis caused by group G *Streptococcus*; case report and review of the literature. *Scand J Infect Dis*, 2002; 34(6):468-471

36 Brook I, Frazier EH. Clinical and microbiological features of necrotizing fasciitis. *J Clin Microbiol*, 1995; 33(9):2382-2387

37 Tang WM, Ho PL, Fung KK, et al. Necrotising fasciitis of a limb. *J Bone Joint Surg Br*, 2001; 83(5):709-714

38 Cunningham JD, Silver L, Rudikoff D. Necrotizing fasciitis; a plea for early diagnosis and treatment. *Mt Sinai J Med*, 2001; 68(4-5):253-261

39 Angoules AG, Kontakis G, Drakoulakis E, et al. Necrotising fasciitis of upper and lower limb: a systematic review. *Injury*, 2007; 38(Suppl 5):S19-S26

40 Headley AJ. Necrotizing soft tissue infections: a primary care review. *Am Fam Physician*, 2003; 68(2):323-328

41 Nazir Z. Necrotizing fasciitis in neonates. *Pediatr Surg Int*, 2005; 21(8):641-644

42 Becker M, Zbaren P, Hermans R, et al. Necrotizing fasciitis of the head and neck; role of CT in diagnosis and management. *Radiology*, 1997; 202(2):471-476

43 肖恩华, 李锦清. 坏死性筋膜炎临床和影像学表现. *临床放射学杂志*, 2002; 21(5):400-402

44 Fisher JR, Conway MJ, Takeshita RT, et al. Necrotizing fasciitis. Importance of roentgenographic studies for soft-tissue gas. *JAMA*, 1979; 241(8):803-806

45 Ayestary B, Dudrap E, Chartaux E, et al. Necrotizing pyoderma gangrenosum: an unusual differential diagnosis of necrotizing fasciitis. *J Plast Reconstr Aesthet Surg*, 2010; 63(8):e655-e658

46 Barr KL, Chhatwal HK, Wesson SK, et al. Pyoderma gangrenosum masquerading as necrotizing fasciitis. *Am J Otolaryngol*, 2009; 30(4):273-276

47 Lille ST, Sato TT, Engrav LH, et al. Necrotizing soft tissue infections; obstacles in diagnosis. *J Am Coll Surg*, 1996; 182(1):7-11

48 Wong CH, Chang HC, Pasupathy S, et al. Necrotizing fasciitis; clinical presentation, microbiology, and determinants of mortality. *J Bone Joint Surg Am*, 2003; 85(8):1454-1460

49 Seal DV. Necrotizing fasciitis. *Curr Opin Infect Dis*, 2001; 14(2):127-132

50 Zimbelman J, Palmer A, Todd J. Improved outcome of clindamycin compared with beta-lactam antibiotic treatment for invasive *Streptococcus pyogenes* infection. *Pediatr Infect Dis J*, 1999; 18(12):1096-1100

51 Jing HB, Ning BA, Hao HJ, et al. Epidemiological analysis of group A streptococci recovered from patients in China. *J Med Microbiol*, 2006; 55(Pt 8):1101-1107

52 Ho PL, Johnson DR, Yue AW, et al. Epidemiologic analysis of invasive and noninvasive group a streptococcal isolates in Hong Kong. *J Clin Microbiol*, 2003; 41(3):937-942

53 Wilkinson D, Doolette D. Hyperbaric oxygen treatment and survival from necrotizing soft tissue infection. *Arch Surg*, 2004; 139(12):1339-1345

54 Escobar SJ, Slade JB Jr, Hunt TK, et al. Adjuvant hyperbaric oxygen therapy (HBOT) for treatment of necrotizing fasciitis reduces mortality and amputation rate. *Undersea Hyperb Med*, 2005; 32(6):437-443

55 Li DM, Lun LD, Chen XR. Necrotising fasciitis with *Escherichia coli*. *Lancet Infect Dis*, 2006; 6(7):456

56 Kaul R, McGeer A, Norrby-Teglund A, et al. Intravenous immunoglobulin therapy for streptococcal toxic shock syndrome: a comparative observational study. The Canadian Streptococcal Study Group. *Clin Infect Dis*, 1999; 28(4):800-807

(收稿:2010-11-01; 修回:2010-12-17)
(本文编辑:翁洁敏)

广告目次

辉瑞制药有限公司(特耐) (封2)
史赛克(北京)医疗器械有限公司(人工关节) ... (插2)
上海锐尔医疗器械有限公司(VAC系统) ... (插3)

日本旭化成株式会社(益盖宁) (封3)
辉瑞制药有限公司(西乐葆) (封底)