

doi: 10.13241/j.cnki.pmb.2014.30.020

支气管扩张合并支气管哮喘患者支气管肺泡灌洗液病原菌培养及药敏状况研究*

郑丽新¹ 赵明¹ 王玉¹ 苏迪¹ 郭晓东²

(1 解放军总医院呼吸科 北京 100853; 2 解放军第302医院 北京 100039)

摘要 目的:对支气管扩张合并支气管哮喘患者支气管肺泡灌洗液病原菌培养及药敏状况展开分析,实现多药耐药医院感染的有效预防与控制。**方法:**随机选取2010年9月~2013年8月期间收治的50例支气管扩张症合并支气管哮喘患者,对50例患者支气管肺泡灌洗液标本进行病原学检测及药敏试验,并对临床感染资料及病原菌耐药性进行统计学分析。**结果:**50例支气管扩张症合并支气管哮喘患者支气管肺泡灌洗液培养阳性率为30例,60.0%,共分离出48株细菌。其中,革兰阳性球菌5株,占分离菌的10.4%;革兰阴性杆菌41株,占分离菌的85.4%;真菌2株,占分离菌的4.2%。41株革兰阴性杆菌对抗菌药物的耐药性分别为:复方新诺明73.1%,阿米卡星22.0%,环丙沙星14.6%,头孢曲松48.8%,头孢噻肟41.5%,头孢哌酮19.5%,头孢他啶20.7%,头孢他啶/舒巴坦12.1%,头孢吡肟22.0%,庆大霉素17.1%,阿莫西林/克拉维酸41.5%,哌拉西林/他唑巴坦19.5%。**结论:**铜绿假单胞菌是支气管扩张合并哮喘患者感染中的常见病原菌,医务人员要结合病原菌高耐药率、高分离阳性率的特征,合理运用抗菌药物控制传播。

关键词:支气管哮喘;支气管扩张;支气管肺泡灌洗液;病原菌;耐药性

中图分类号:R562.25 文献标识码:A 文章编号:1673-6273(2014)30-5877-03

Cultivation of Bronchoalveolar Ravage Fluid and Sensitivity of Bronchiectasis Combined with Bronchial Asthma*

ZHENG Li-xin¹, ZHAO Ming¹, WANG Yu¹, SU Di¹, GUO Xiao-dong²

(1 Department of Respiratory, General Hospital of PLA, Beijing, 100853, China;

2 302 Hospital of PLA, Beijing, 100039, China)

ABSTRACT Objective: To analyze the bronchoalveolar ravage fluid culture and drug susceptibility of patients with bronchiectasis and bronchial asthma in order to achieve the effective prevention and control of multidrug-resistant for hospital infections. **Methods:** A retrospective analysis was carried on by bacterial identification and susceptibility about the clinical data of 50 patients with bronchial asthma who were enrolled in our hospital from September 2010 to August 2013. The bronchoalveolar ravage fluid samples were detected, the susceptibility was tested, and the clinical information and pathogen infection resistance were analyzed statistically. **Results:** Among the 50 cases with the bronchial asthma who were treated by the bronchoalveolar ravage fluid, 60.0% were cultured positively with the isolated 48 bacteria, five were *Gram-positive coccid*(10.4%), 41 were *Gram-negative bacilli*(85.4%), two were *fungi*(4.2%). 41 *Gram-negative bacilli* that resistant to the antimicrobial drugs were as follows: cotrimoxazole (73.1%), alizarin (22.0%), ciprofloxacin (14.6%), ceftriaxone(48.8%), cefotaxime(41.5%), cephalosporin's risperidone(19.5%), ceftazidime(20.7%), ceftazidime/sulfate(12.1%), caffeine(22.0%), gentamicin(17.1%), amoxicillin/clavulanic acid(41.5%), piperacillin/tazobactam(19.5%). **Conclusions:** It is suggested that the common bacteria is the pseudomonas aerations for the patients with bronchiectasis and bronchial asthma that requires the medical staff take responsibility of controlling the drug-resistant and spread on the basis of acquiring the high resistance to the pathogen and the rate of separation.

Key words: Bronchial asthma; Bronchiectasis; Bronchoalveolar ravage fluid; Pathogens; Drug resistance

Chinese Library Classification(CLC): R562.25 **Document code:** A

Article ID: 1673-6273(2014)30-5877-03

前言

支气管扩张是呼吸系统常见的化脓性炎症,主要致病因素为支气管的感染阻塞和牵拉。支气管哮喘是呼吸系统的常见病,其发病的危险因素包括遗传因素和环境因素两方面。支气

管扩张与支气管哮喘两种疾病相互作用会产生复杂、多样的临床症状,甚至呼吸系统毁损等后果,为临床治疗带来了严峻的考验^[1-3]。因此,对上述两种疾病的病原菌进行分析,掌握其耐药性是提高临床治疗的重点。本研究随机选取2010年9月-2013年8月期间我院收治的50例支气管扩张症合并支气管哮喘患

* 基金项目:国家自然科学基金青年科学基金项目(81301239)

作者简介:郑丽新(1985-),女,护师,主要从事呼吸系统等相关研究,E-mail:laohushanshang@163.com

(收稿日期:2014-03-15 接受日期:2014-04-13)

者,通过对其临床资料进行综合分析,初步了解支气管扩张症合并支气管哮喘患者支气管肺泡灌洗液病原菌培养及药敏状况,旨在提高对支气管扩张症合并支气管哮喘的诊断能力,现作报告内容如下。

1 资料与方法

1.1 临床资料

随机抽取我院 2010 年 9 月~2013 年 8 月期间收治的支气管扩张症合并支气管哮喘患者 50 例,所有患者均接受临床诊断确定,满足筛选标准^[4]。其中男性 32 例,女性 18 例;年龄范围 26~79 岁,平均年龄 49.8±15.1 岁。支气管扩张症合并支气管哮喘疾病诊断标准参考《支气管哮喘防治指南》中诊断标准,排除有严重心、肝等重要器官和血液病变者,妊娠期妇女,临床治疗期间不遵医行为者^[5]。

1.2 方法

支气管扩张症合并支气管哮喘患者入院后,均给予心电图、血常规、胸部 CT、肺功能、血浆皮质醇等常规检查。对患者进行喉部麻醉,行仰卧位,确保患者氧饱和度超过 90%,由患者鼻腔进镜,行常规内镜窥视检测,对指定病变支气管肺段实施支气管肺泡灌洗。完毕后,对病变支气管肺段插入纤维支气管管,注入同患者体温的生理盐水,30 ml/次,3 次,负压吸出支气管肺泡灌洗液^[6]。

1.3 检验指标及方法

送检支气管肺泡灌洗液菌落计数革兰阳性球菌超过 10⁴

cfu/mL,革兰阴性杆菌超过 10⁵ cfu/mL 则判断为支气管肺泡灌洗液感染。将所有试验菌株进行微生物检验常规操作,将菌株通过无菌定值接种环接种于麦康凯平板以及血琼脂平板,在 34℃~36℃ 的温度下孵育 20 h~24 h,无菌条件下生长培育 2 d。药物敏感试验运用 K-B 纸片扩散法,肠杆菌科产 ESBLs 菌株敏感试验运用双纸片法。根据 NCCLS/CLSI 准则判定耐药性、敏感性。药敏试验抗生素药物选择包括:头孢曲松、头孢哌酮、氨苄西林、环丙沙星、利福平、百炎净、万古霉素、庆大霉素、磺胺甲恶唑/甲氧苄啶、氨苄西林/舒巴坦等。

1.4 统计学分析

研究中所得到的相关数据采用 SPSS 12.0 统计学数据处理软件进行处理分析,各项参数以均数±标准差($\bar{x} \pm s$)表示,采用 t 和 χ^2 检验,以 P<0.05 为差异具有统计学意义。

2 结果

2.1 菌株来源

50 例患者中,支气管肺泡灌洗液培养阳性率为 30 例(60.0%)。共分离出 48 株细菌,其中革兰阳性球菌 5 株,占分离菌的 10.4%;革兰阴性杆菌 41 株,占分离菌的 85.4%;真菌 2 株,占分离菌的 4.2%。5 株革兰阳性球菌分别包括:金黄色葡萄球菌 3 株,肺炎链球菌 1 株,溶血葡萄球菌 1 株。41 株革兰阴性杆菌包括:铜绿假单胞菌 21 株,肺炎克雷伯菌 9 株,鲍曼不动杆菌 6 株,大肠埃希菌 3 株,嗜麦芽黄单胞菌 2 株。见表 1。

表 1 95 株支气管肺泡灌洗液病原菌来源及构成比(%)

Table 1 Pathogenic bacteria and constituent ratio of bronchoalveolar lavage fluid source of 95 strains(%)

病原菌 Pathogenic bacteria	株数 Strains	构成比 Constituent ratio
革兰阳性球菌 <i>Gram positive coccus</i>	5	10.4
金黄色葡萄球菌 <i>Staphylococcus aureus</i>	3	6.3
肺炎链球菌 <i>Streptococcus pneumoniae</i>	1	2.1
溶血葡萄球菌 <i>Staphylococcus haemolyticus</i>	1	2.1
革兰阴性杆菌 <i>Gram negative bacilli</i>	41	85.4
铜绿假单胞菌 <i>Pseudomonas aeruginosa</i>	21	43.8
肺炎克雷伯菌 <i>Klebsiella pneumoniae</i>	9	18.8
鲍曼不动杆菌 <i>Baumannii</i>	6	12.5
大肠埃希菌 <i>Escherichia coli</i>	3	6.3
嗜麦芽窄食单胞菌 <i>Stenotrophomonas maltophilia</i>	2	4.2
真菌 <i>Fungus</i>	2	4.2

2.2 病原菌耐药性

41 株革兰阴性杆菌对抗菌药物的耐药性分别为:复方新诺明 73.1%,阿米卡星 22.0%,环丙沙星 14.6%,头孢曲松 48.8%,头孢噻肟 41.5%,头孢哌酮 19.5%,头孢他啶 20.7%,头孢他啶/舒巴坦 12.1%,头孢吡肟 22.0%,庆大霉素 17.1%,阿莫西林/克拉维酸 41.5%,哌拉西林/他唑巴坦 19.5%。见表 2。

3 讨论

支气管扩张症是通过慢性气道毁损诱发弹力支撑组织、支气管管壁肌肉损伤,从而引发的不定数量支气管不可逆行扩张^[11-14],是引起肺损伤的常见疾病,其临床表现为反复支气管化脓性感染、慢性肺等,该疾病的主要致病菌由革兰氏阴性菌、革兰氏阳性菌以及真菌组成^[7-10]。支气管哮喘是一类气道非特异

表 2 41 株革兰阴性杆菌对常用抗菌药的耐药率(%)

Table 2 Antimicrobial drug resistance of 41 strains commonly used *gram-negative bacilli*(%)

抗菌药物 Antibacterial agents	耐药株数 Strains	耐药率 Antimicrobial drug resistance rate
复方新诺明 Paediatric Compound Sulfamethoxazole Tablets	30	73.1
阿米卡星 Amikacin	9	22.0
环丙沙星 Ciprofloxacin	6	14.6
头孢曲松 Ceftriaxone Sodium	20	48.8
头孢噻肟 Cefotaxime Sodium	17	41.5
头孢他啶 Ceftazidime	8	19.5
舒巴坦 Sulbactam	5	12.1
头孢吡肟 Cefepime	9	22.0
庆大霉素 Gentamicin	7	17.1
阿莫西林 / 克拉维酸 Amoxicilline/Clavulanic Acid	17	41.5
哌拉西林 / 他唑巴坦 Piperacillin/Tazobactam	8	19.5

慢性炎症,哮喘炎症以嗜酸粒细胞提升为首要标志^[15-17]。目前,针对支气管扩张症合并支气管哮喘患者的临床病原诊断以痰液培养为主,但是该方法容易污染,痰液质量存在不定性,因此临床诊断价值不高。相关研究显示,肺泡灌洗液相比于痰液,对支气管扩张症合并支气管哮喘患者诊断具有更高特性性、敏感性,且病原菌药敏状况更有利于临床抗感染治疗^[18]。

本研究结果显示,50 例支气管扩张症合并支气管哮喘患者支气管肺泡灌洗液培养阳性率为 60.0%,共分离出 95 株细菌,分离菌主要是格兰阴性菌,与相关细菌耐药性报道相符。临床常用的抗菌药物以喹诺酮类为主,虽然治疗效果良好,但仍存在细菌耐药性^[19,20]。我们通过本研究发现,患者机体支气管肺泡内部脓液、痰栓等通过接受支气管肺泡灌洗可以得到稀释,达到迅速吸引排除,有效改善支气管阻塞情况,增进通气功能,积极促进患者喘息症状,抑制感染,实现检测、治疗的目的。

总之,受不同菌株对抗菌药物的耐药机制、药敏情况不同影响,针对支气管扩张症合并支气管哮喘患者,临床治疗要结合药敏结果,有效降低抗菌药物用药不当而导致引发多重耐药菌株。

参考文献(References)

- [1] 王桢,骆磊,杨均,等. 呼吸内科病原菌的分布及耐药情况 [J]. 现代生物医学进展, 2013, 13(02): 298-302
Wang Zhen, Luo Lei, Yang Jun, et al. Department of Respiratory Medicine Pathogens Distribution and Drug Resistance [J]. Progress in Modern Biomedicine, 2013, 13(02): 298-302
- [2] Elkins MR, Anderson SD, Perry CP, et al. Inspiratory Flows and Volumes in Subjects with Non-CF Bronchiectasis Using a New Dry Powder Inhaler Device[J]. Open Respir Med J, 2014, 24, 8:8-13
- [3] Hill AT, Flume PA. Lung clearance index. A potential quantitative tool to assess treatment response in bronchiectasis [J]. Am J Respir Crit Care Med, 2014, 1, 189(5): 510-511
- [4] Jeong BH, Kim SY, Jeon K, et al. The First Korean Case of Nontuberculous Mycobacterial Lung Disease Caused by Mycobacterium absces-

sus Subspecies bolletii in a Patient with Bronchiectasis [J]. Tuberc Respir Dis(Seoul), 2014, 76(1): 30-33

- [5] Hasatani K, Shibata N, Naitou Y, et al. A case of acute necrotizing esophagitis associated with AA amyloidosis secondary to bronchiectasis[J]. Nihon Shokakibyo Gakkai Zasshi, 2014, 111(2): 288-295
- [6] Quirke AM, Perry E, Kelly C, et al. Patients with bronchiectasis, with or without rheumatoid arthritis, have an elevated anti-citrullinated peptide antibodies (ACPA) response [J]. Ann Rheum Dis, 2014, 73 (Suppl)1: 71-72
- [7] Goeminne PC, Nawrot TS, Ruttens D, et al. Mortality in non-cystic fibrosis bronchiectasis: A prospective cohort analysis [J]. Respir Med, 2014, 108(2): 287-296
- [8] Chalmers JD, McHugh BJ, Doherty C, et al. Mannose-binding lectin deficiency and disease severity in non-cystic fibrosis bronchiectasis: a prospective study[J]. Lancet Respir Med, 2013, 1(3): 224-232
- [9] Rowan SA, Bradley JM, Bradbury I, et al. Lung clearance index is a repeatable and sensitive indicator of radiological changes in bronchiectasis[J]. Am J Respir Crit Care Med, 2014, 1, 189(5): 586-592
- [10] Wu Q, Shen W, Cheng H, et al. Long-term macrolides for non-cystic fibrosis bronchiectasis: A systematic review and meta-analysis [J]. Respirology, 2014, 19(3): 321-329
- [11] Javadmoosavi SA, Shahabi Shahmiri S, Mostafapour E, et al. Comparison of the serum concentration of zinc in patients with bronchiectasis and control group[J]. Iran Red Crescent Med J, 2013, 15(7): 587-589
- [12] Hsieh MH, Fang YF, Chen GY, et al. The role of the high-sensitivity C-reactive protein in patients with stable non-cystic fibrosis bronchiectasis[J]. Pulm Med, 2013, 2013: 795140
- [13] Chalmers JD, Finch S. Sputum colour in non-CF bronchiectasis: The original neutrophil biomarker [J]. Respirology, 2013 [Epub ahead of print]
- [14] Kollert F, Venhoff N, Goldacker S, et al. Bronchoalveolar lavage cytology resembles sarcoidosis in a subgroup of granulomatous CVID [J]. Eur Respir J, 2014, 43(3): 922-924

(下转第 5836 页)

关联。Karsten 和 Fricc 等人发现, Notch 家族成员 Jagged1 是 CD46 的重要配体, CD46 通过调节 Notch 受体及配体的表达, 抑制 IFN- γ 、诱导 IL-10 的分泌, 进而影响患者全身性 Th1 型免疫反应^[21,22]。由于 Notch 信号调控干细胞的自我更新, 我们及他人研究结果提示, CD46 可能通过 Jagged1 调控肿瘤干细胞的自我更新特性, 这一推测还需后续的实验结果验证。

参考文献(References)

- [1] Dunn GP, Old LJ, Schreiber RD. The three Es of cancer immunoediting [J]. *Annu Rev Immunol*, 2004, 22: 329-360
- [2] Tomita Y, Yang X, Ishida Y, et al. Spontaneous regression of lung metastasis in the absence of tumor necrosis factor receptor p55 [J]. *Int J Cancer*, 2004, 112(6): 927-933
- [3] Iiai T, Sato Y, Nabatame N, et al. Spontaneous complete regression of hepatocellular carcinoma with portal vein tumor thrombus [J]. *Hepatogastroenterology*, 2003, 50(53): 1628-1630
- [4] Morice P, Thoury A, Sabourin JC, et al. Case 2. Spontaneous regression of peritoneal implants in borderline ovarian tumor after salpingo-oophorectomy [J]. *J Clin Oncol*, 2003, 21(18): 3536-3538
- [5] Zahl PH, Maehlen J, Welch HG. The natural history of invasive breast cancers detected by screening mammography [J]. *Arch Intern Med*, 2008, 168(21): 2311-2316
- [6] Kaplan RM, Porzsolt F. The Natural History of Breast Cancer [J]. *Arch Intern Med*, 2008, 168(21): 2302-2303
- [7] Woods WG, Gao RN, Shuster JJ, et al. Screening of infants and mortality due to neuroblastoma [J]. *N Engl J Med*, 2002, 346(14): 1041-1046
- [8] Schilling FH, Spix C, Berthold F, et al. Neuroblastoma screening at one year of age[J]. *N Engl J Med*, 2002, 346(14): 1047-1053
- [9] Smyth MJ, Dunn GP, Schreiber RD. Cancer immunosurveillance and immunoediting: the roles of immunity in suppressing tumor development and shaping tumor immunogenicity [J]. *Adv Immunol*, 2006, 90: 1-50
- [10] Kolev M, Towner L, Donev R. Complement in cancer and cancer immunotherapy [J]. *Arch Immunol Ther Exp (Warsz)*, 2011, 59(6): 407-419
- [11] Rutkowski MJ, Sughrue ME, Kane AJ, et al. Parsa AT Cancer and the complement cascade[J]. *Mol Cancer Res*, 2010, 8(11): 1453-1465
- [12] Shuptrine CW, Surana R, Weiner LM. Monoclonal antibodies for the treatment of cancer[J]. *Semin Cancer Biol*, 2012, 22(1): 3-13
- [13] Markiewski MM, Lambris JD. Is complement good or bad for cancer patients? A new perspective on an old dilemma [J]. *Trends Immunol*, 2009, 30(6): 286-292
- [14] Lucas SD, Karlsson-Parra A, Nilsson B, et al. Tumor-specific deposition of immunoglobulin G and complement in papillary thyroid carcinoma[J]. *Hum Pathol*, 1996, 27: 1329-1335
- [15] Niculescu F, Rus HG, Retegan M, et al. Persistent complement activation on tumor cells in breast cancer[J]. *Am J Pathol*, 1992, 140: 1039-1043
- [16] Jurianz K, Ziegler S, Garcia-Schüler H, et al. Complement resistance of tumor cells: basal and induced mechanisms [J]. *Mol Immunol*, 1999, 36: 929-939
- [17] Ollert MW, David K, Schmitt C, et al. Normal human serum contains a natural IgM antibody cytotoxic for human neuroblastoma cells[J]. *Proc Natl Acad Sci U S A*, 1996, 93(9): 4498-4503
- [18] Brändlein S, Pohle T, Ruoff N, et al. Natural IgM antibodies and immunosurveillance mechanisms against epithelial cancer cells in humans[J]. *Cancer Res*, 2003, 63(22): 7995-8005
- [19] Markiewski MM, DeAngelis RA, Benencia F, et al. Modulation of the antitumor immune response by complement [J]. *Nat Immunol*, 2008, 9(11): 1225-1235
- [20] Fishelson Z, Donin N, Zell S, et al. Obstacles to cancer immunotherapy: expression of membrane complement regulatory proteins (mCRPs) in tumors [J]. *Mol Immunol*, 2003, 40(2-4): 109-123
- [21] Karsten CM, Köhl J. The complement receptor CD46 tips the scales in T(H)1 self-control [J]. *Nat Immunol*, 2010, 11(9): 775-777
- [22] Le Fricc G, Sheppard D, Whiteman P, et al. The CD46-Jagged1 interaction is critical for human TH1 immunity [J]. *Nat Immunol*, 2012, 13(12): 1213-1221
- [15] Naccache JM, Bouvry D, Valeyre D. Bronchoalveolar lavage cytology resembles sarcoidosis in a subgroup of granulomatous CVID [J]. *Eur Respir J*, 2014, 43(3): 924-925
- [16] Orlando A, Thoma G, Slone DS, et al. A rapid, real-time quantitative polymerase chain reaction test for the identification of pathogens in bronchoalveolar lavage samples[J]. *J Trauma Acute Care Surg*, 2014, 76(3): 651-660
- [17] Lozo Vukovac E, Lozo M, Mise K, et al. Bronchoalveolar pH and inflammatory biomarkers in newly diagnosed IPF and GERD patients: A case-control study[J]. *Med Sci Monit*, 2014, 15, 20: 255-261
- [18] Pacheco AP, Paradis MR, Hoffman AM, et al. Age Effects on Blood Gas, Spirometry, Airway Reactivity, and Bronchoalveolar Lavage Fluid Cytology in Clinically Healthy Horses [J]. *J Vet Intern Med*, 2014, 16
- [19] Chan VL, So LK, Lam JY, et al. Major haemoptysis in Hong Kong: aetiologies, angiographic findings and outcomes of bronchial artery embolisation[J]. *Int J Tuberc Lung Dis*, 2009, 13(9): 1167-1173
- [20] Hayama M, Inoue H, Wada H, et al. Massive haemoptysis following dabigatran administration in a patient with bronchiectasis [J]. *BMJ Case Rep*, 2014

(上接第 5879 页)