

DOI:10.13350/j.cjpb.240113

• 临床研究 •

肺癌放疗后继发肺部感染病原菌特点及呼吸指标、血清炎性因子水平变化分析

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【摘要】 目的 分析肺癌放疗后继发肺部感染患者的病原菌分布特点,了解呼吸指标、血清炎性因子水平变化情况。

方法 选取本院治疗的65例肺癌放疗后继发肺部感染者为研究对象,同时选取同期65例未发生感染的患者为对照组。采集肺部感染患者痰液或支气管肺泡灌洗液标本进行病原菌鉴定及药敏试验。检测所有患者呼吸指标(包括肺动态顺应性、气道阻力、气道平均压、响应频率)及血清炎性因子(包括降钙素原、超敏C-反应蛋白、肿瘤坏死因子- α)水平。对比肺部感染组与对照组、不同肺部感染严重程度患者的呼吸指标与血清炎性因子水平。结果 共分离出65株病原菌,其中92.31%分离自呼吸道痰液标本,7.69%分离自支气管肺泡灌洗液标本。49.23%为革兰阴性菌,主要为铜绿假单胞菌、肺炎克雷伯菌、流感嗜血杆菌。27.69%为革兰阳性菌18株,主要为肺炎链球菌、金黄色葡萄球菌。23.08%为真菌,主要为白色假丝酵母菌。革兰阴性菌对环丙沙星、诺氟沙星、庆大霉素的耐药率高于50%,对哌拉西林/他唑巴坦、头孢哌酮、亚胺培南、美罗培南、阿米卡星的耐药率低于30%。革兰阳性菌对青霉素、阿莫西林、氯霉素、阿奇霉素、环丙沙星、左氧氟沙星的耐药率高于50%,未产生对万古霉素、利奈唑胺的耐药株。真菌对氟康唑、氟胞嘧啶的耐药率为13.33%,对伊曲康唑的耐药率为6.67%,未产生对两性霉素B、伏立康唑的耐药株。肺部感染组患者肺动态顺应性低于对照组,气道阻力、气道平均压、响应频率高于对照组,差异有统计学意义($P<0.05$)。重度肺部感染患者肺动态顺应性低于轻度、中度感染组,气道阻力、气道平均压、响应频率高于轻度、中度感染组,差异有统计学意义($P<0.05$)。肺部感染组患者血清降钙素原(PCT)、肿瘤坏死因子- α (TNF- α)、超敏C-反应蛋白(hs-CRP)水平显著高于对照组,重度肺部感染组患者血清降钙素原(PCT)、肿瘤坏死因子- α (TNF- α)、超敏C-反应蛋白(hs-CRP)水平显著高于轻度、中度感染组,差异均有统计学意义($P<0.05$)。结论 肺癌放疗后继发肺部感染患者病原菌以革兰阴性菌为主,对临床常见抗菌药物的耐药率较高。肺癌放疗后继发肺部感染患者的呼吸指标变差,PCT、TNF- α 、hs-CRP炎性因子水平升高,并随肺部感染严重程度加重而加大变化,临幊上应做好检测与防控。

【关键词】 肺癌;肺部感染;呼吸指标;血清炎性因子

【文献标识码】 A

【文章编号】 1673-5234(2024)01-0065-05

[Journal of Pathogen Biology. 2024 Jan;19(1):65-69.]

Analysis of the distribution characteristics of pathogenic bacteria and changes in respiratory indicators and serum inflammatory factor levels in secondary pulmonary infections in lung cancer patients after radiotherapy

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【Abstract】 **Objective** To analyze the distribution characteristics of pathogenic bacteria and changes in respiratory indicators and serum inflammatory factor levels in patients with secondary lung infection after radiotherapy for lung cancer. **Methods** 65 patients with secondary lung infection after radiotherapy for lung cancer who were treated in our hospital were selected as the study subjects, while 65 patients who did not develop infection after radiotherapy for lung cancer during the same period were selected as the control group. The sputum or bronchoalveolar lavage fluid samples were collected from patients with pulmonary infection for pathogen identification and drug sensitivity testing. The respiratory indicators (including lung dynamic compliance, airway resistance, mean airway pressure, response frequency) and serum inflammatory factors (including procalcitonin, hypersensitive C-reactive protein, and tumor necrosis factor- α) were detected in all patients. The respiratory indicators and serum inflammatory factor levels between the pulmonary infection group and the control group were compared, as well as patients with different levels of pulmonary infection severity. **Results** A total of 65 pathogenic bacteria were isolated, of which 92.31% were isolated from respiratory sputum samples and 7.69% were isolated from bronchoalveolar lavage fluid samples. 49.23% were Gram negative

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bacteria, mainly *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Haemophilus influenzae*. 27.69% were 18 strains of Gram positive bacteria, mainly *Streptococcus pneumoniae* and *Staphylococcus aureus*. 23.08% were fungi, mainly *Candida albicans*. The resistance rate of Gram negative bacteria to ciprofloxacin, norfloxacin, and gentamicin is higher than 50%, while the resistance rate to piperacillin/tazobactam, cefepime, imipenem, meropenem, and amikacin was lower than 30%. The resistance rate of Gram positive bacteria to penicillin, amoxicillin, chloramphenicol, azithromycin, ciprofloxacin, and levofloxacin was higher than 50%, and no resistant strains to vancomycin or linezolid had been developed. The resistance rate of fungi to fluconazole and flucytosine was 13.33%, and the resistance rate to itraconazole was 6.67%. No resistant strains to amphotericin B and voriconazole had been developed. Comparing the respiratory indicators between the pulmonary infection group and the control group, the Cydn of the pulmonary infection group was lower than the control group level, while the Raw, Pmean, and Fres were higher than the control group level. The difference was statistically significant ($P < 0.05$). The Cydn of patients with severe pulmonary infection was lower than that of patients with mild and moderate infection, while Raw, Pmean, and Fres were higher than those of patients with mild and moderate infection. The difference was statistically significant ($P < 0.05$). The levels of Serum procalcitonin (PCT), tumor necrosis factor- α (TNF- α), and hypersensitive C-reactive protein (hs CRP) in patients with pulmonary infection were significantly higher than those of the control group, and the levels of serum procalcitonin (PCT), tumor necrosis factor- α (TNF- α) and hypersensitive C-reactive protein (hs CRP) in patients with severe pulmonary infection, were significantly higher than those of patients with mild to moderate infection, and the differences between the groups were statistically significant ($P < 0.05$). **Conclusion** The pathogenic bacteria in patients with secondary lung infection after radiotherapy for lung cancer were mainly Gram negative bacteria, with a high resistance rate to common clinical antibiotics. The respiratory indicators of patients with secondary lung infection after radiotherapy for lung cancer deteriorate, and the PCT, TNF- α , and hs-CRP of inflammatory factors increases and changes with the severity of pulmonary infection, so it was necessary to conduct detection and prevention and control in clinical practice.

【Key words】 lung cancer; pulmonary infection; respiratory indicators; serum inflammatory factors

原发性肺癌是我国发病率最高的肿瘤类型,已成为当今世界范围内第一大恶性肿瘤,近年来,发病率和死亡率显著上升,有关研究发现,死亡位居前十位的恶性肿瘤构成中,肺癌占比高于20%,是癌症患者死亡的主要原因之一,为患者、家庭、社会带来沉重负担^[1-2]。目前,肺癌的治疗方式主要以外科手术切除、放疗、化疗和免疫治疗等为主。由于早期症状不明显,容易错过手术时机,因此放化疗成为主要治疗手段^[3]。肺癌患者进行放疗期间,在杀伤癌细胞的同时也会造成粒细胞减少,损害机体免疫功能,容易合并诸多并发症。肺癌放疗的主要并发症之一是肺部感染,发生率约为10%,是肺癌患者高病死率的主要原因之一,对患者生命健康造成严重威胁^[4]。因此,对肺癌放疗后继发肺部感染患者及早进行诊断、干预,对于改善患者治疗效果、延长生存期具有重要意义。目前针对肺癌放疗后肺部感染者呼吸指标、血清炎性因子的研究较少,本研究通过分析于本院进行治疗的65例肺癌放疗后继发肺部感染患者的临床资料,探析肺癌放疗后继发肺部感染患者病原菌分布特点及呼吸指标、血清炎性因子水平变化特点,现报道如下。

材料与方法

1 研究对象

选取于本院进行治疗的65例肺癌放疗后继发肺

部感染患者为本次研究对象。年龄58~79(65.78±8.62)岁。男性45例,女性20例。28例放疗周期≤2周,37例放疗周期>2周。根据第八版国际肺癌原发灶-淋巴结-远处转移(tumor-node-metastasis, TNM)分期,2例为I期,6例为II期,35例为III期,22例为IV期。按照《2015 WHO 肺癌病理分类》进行分类,20例为非小细胞癌,23例为鳞癌,22例为小细胞癌。同时选取同期65例肺癌放疗后未发生感染的患者为对照组。纳入标准:①临幊上通过影像学检查、病幊学及细胞学,符合《原发性肺癌诊疗指南(2015)》相关标准,确诊为原发性肺癌,均进行1个疗程以上的放疗治疗;②全程积极配合进行放疗治疗及相关检查;③肺部感染患者均自愿参与本次研究,已获得患者或其家属的知情同意并签署知情同意书;④放疗前未合并其他组织感染者。排除标准:①伴重要器官损伤或血液系统疾病者;②合并其他恶性肿瘤疾病;③入院前已合并感染者;④肺癌术后辅助放化疗治疗者;⑤出现严重并发症;⑥无法完成整个放疗过程者。

2 诊断标准

2.1 肺部感染 肺部感染者参照《医院感染诊断标准》^[5]关于肺部感染的相关标准,具备至少2项或2项以上表现:①出现发热、咳嗽、呼吸困难等肺部感染症状及体征,体温超过38.5℃;②血常规检查提示提高($>10 \times 10^9/L$);③影像学示肺部片状、斑片状炎性浸

润性阴影或间质性改变,部分伴胸腔积液;④采集标本培养提示细菌阳性。

2.2 肺部感染程度 应用肺炎严重指数(Pneumonia Severity Index, PSI)分级评分标准^[6],对肺部感染患者进行严重程度评估,包括一般资料、体格检查、基础疾病、护理情况及实验室和X线检查等结果进行评分,PSI<91分为轻度感染,PSI为91~130分为中度感染,PSI>130分为重度感染。

3 病原菌鉴定及药敏试验

患者清晨空腹状态下,用生理盐水漱口2次后,刺激患者咳嗽。咳出喉咙深部痰液,弃去第一口痰液,留取第二口痰液作为采集标本。针对无法自行咳痰患者,收集其支气管肺泡灌洗液。将采集到合格标本进行肉汤培养基培养,用全自动细菌鉴定分析仪(VITEK-60,法国梅里埃)鉴定病原菌。K-B纸片扩散法进行药敏试验,试纸条法(ATB Fungus-3,法国梅里埃)进行真菌药敏试验,药敏试验结果依美国临床和实验室标准化协会标准判读。质控菌株:铜绿假单胞菌ATCC27853、肺炎克雷伯菌ATCC700603、金黄色葡萄球菌ATCC25923,由本地区临床检验中心提供。

4 呼吸指标检测

由专业检验人员采用呼吸参数检测仪检测患者呼吸指标,包括肺动态顺应性(dynamic compliance,Cdyn)、气道阻力(airway resistance,Raw)、气道平均压(mean airway pressure,Pman)、响应频率(response frequency,Fres)。检测结果依据仪器说明书进行判读。

5 血清炎性因子水平检测

患者于空腹状态下抽取静脉血3~5mL,静置20min后,离心30min(r=10.5cm,3000r/min),提取血清。采用电化学发光法,检测血清降钙素原(Procalcitonin,PCT)水平,采用免疫比浊法检测血清超敏C-反应蛋白(hypersensitivity C-reactive protein,hs-CRP)水平,采用酶联免疫吸附剂检测血清肿瘤坏死因子-α(tumor necrosis factor-α,TNF-α)水平。

6 统计学分析

采用SPSS 26.0对研究数据进行统计分析,组间比较采用t或F检验,P<0.05差异有统计学意义。

结 果

1 肺部感染患者病原菌分布特点

共分离出65株病原菌,其中60株(92.31%,60/65)分离自呼吸道痰液标本,5株(7.69%,5/65)分离自支气管肺泡灌洗液标本。革兰阴性菌32株(49.23%,32/65),主要为铜绿假单胞菌(15.38%,10/65)、肺炎克雷伯菌(10.77%,7/65)、流感嗜血杆菌

(9.23%,6/65)。革兰阳性菌18株(27.69%,18/65),主要为肺炎链球菌(10.77%,7/65)、金黄色葡萄球菌(9.23%,6/65)。真菌15株(23.08%,15/65),主要为白色假丝酵母菌(15.38%,10/65)。见表1。

表1 肺癌放疗后继发肺部感染病原菌分布特点
Table 1 Distribution characteristics of pathogenic bacteria in secondary lung infections after radiotherapy for lung cancer

病原菌 Pathogenic bacteria	菌株数 No. of strain	构成比(%) Constituent ratio
革兰阴性菌	32	49.23
铜绿假单胞菌	10	15.38
肺炎克雷伯菌	7	10.77
流感嗜血杆菌	6	9.23
大肠埃希菌	4	6.15
鲍曼不动杆菌	3	4.62
嗜麦芽窄食单胞菌	1	1.54
产气肠杆菌	1	1.54
革兰阳性菌	18	27.69
肺炎链球菌	7	10.77
金黄色葡萄球菌	6	9.23
表皮葡萄球菌	3	4.62
屎肠球菌	2	3.08
真菌	15	23.08
白色假丝酵母菌	10	15.38
光滑假丝酵母菌	3	4.62
热带假丝酵母菌	2	3.08

2 耐药性分析

2.1 革兰阴性菌耐药性分析 对32株革兰阴性菌进行药敏试验,结果显示:对环丙沙星、诺氟沙星、庆大霉素的耐药率高于50%,分别为53.16%(17/32)、56.25%(18/32)、62.50%(20/32),对头孢他啶的耐药率为31.25%(10/32),对哌拉西林/他唑巴坦、头孢吡肟、亚胺培南、美罗培南和阿米卡星的耐药率低于30%,分别为28.13%(9/32)、18.75%(6/32)、9.38%(3/32)、15.63%(5/32)和3.13%(1/32)。

2.2 革兰阳性菌耐药性分析 对18株革兰阳性菌进行药敏试验,结果显示:对青霉素、阿莫西林、氯霉素、阿奇霉素、环丙沙星、左氧氟沙星的耐药率高于50%,分别为94.44%(17/18)、72.22%(13/18)、55.56%(10/18)、66.67%(12/18)、55.56%(10/18)、55.56%(10/18),对庆大霉素的耐药率为22.22%(4/18),未产生对万古霉素、利奈唑胺的耐药株。

2.3 真菌耐药性分析 对15株真菌进行药敏试验,结果显示,对氟康唑、氟胞嘧啶的耐药率为13.33%(2/15),对伊曲康唑的耐药率为6.67%(1/15),未产生对两性霉素B、伏立康唑的耐药株。

3 不同分组患者呼吸指标对比

3.1 感染组与对照组患者呼吸指标对比 对比肺部感染组患者与对照组患者的呼吸指标,结果显示:肺部感染组患者Cdyn为(27.42±6.16)mL/cm H₂O低于

对照组患者,Raw 为(20.98±4.40)cmH₂O/(L·s),Pmean 为(7.87±1.35)cmH₂O,Fres 为(21.86±3.50)Hz 高于对照组患者,差异有统计学意义($P<0.05$)。见表 2。

表 2 不同肺部感染严重程度患者呼吸指标对比(±s)

Table 2 Comparison of respiratory indicators in patients with different levels of pulmonary infection severity

分组 Group	Cdyn (mL/cm H ₂ O)	Raw [cmH ₂ O/(L·s)]	Pmean (cmH ₂ O)	Fres (Hz)
对照组(n=65)	27.42±6.16	20.98±4.40	7.87±1.35	21.86±3.50
感染组(n=65)	39.41±7.29	15.65±4.07	6.59±1.25	18.51±2.23
T	-10.125	7.172	5.617	6.511
P	0.000	0.000	0.000	0.000
轻度感染(n=17)	33.68±4.59	17.32±2.95	6.99±1.16	18.84±2.67
中度感染(n=33)	27.34±3.69	20.75±3.44	7.81±1.02	21.70±2.29
重度感染(n=15)	20.49±4.39	25.62±3.45	9.01±1.44	25.65±3.08
F	41.230	25.015	12.108	27.853
P	0.000	0.000	0.000	0.000

3.2 不同感染程度患者呼吸指标对比 对比三组不同肺部感染程度患者呼吸指标,结果显示:重度感染组患者 Cydn 为(20.49±4.39)mL/cm H₂O 低于轻度、中度感染组患者,Raw 为(25.62±3.45)cmH₂O/(L·s),Pmean 为(9.01±1.44)cmH₂O,Fres 为(25.65±3.08)Hz 高于轻度、中度感染组患者,组间差异有统计学意义($P<0.05$)。见表 2。

4 不同分组患者血清炎性因子水平变化

4.1 感染组与对照组患者血清炎性因子水平对比

对比肺部感染组患者与对照组患者的血清炎性因子水平,结果显示,肺部感染组患者 PCT、TNF- α 、hs-CRP 水平分别为(18.40±6.50)ng/mL、(4.08±1.83)ng/mL、(11.78±3.33)mg/mL,显著高于对照组水平,差异有统计学意义($P<0.05$)。见表 3。

表 3 不同肺部感染严重程度患者血清炎性因子水平对比(±s)

Table 3 Comparison of serum inflammatory factor levels in patients with different severity of pulmonary infection

分组 Grouping	PCT (ng/mL)	TNF- α (ng/mL)	hs-CRP (mg/mL)
对照组(n=65)	6.60±1.08	2.48±0.36	7.84±1.16
感染组(n=65)	18.40±6.50	4.08±1.83	11.78±3.33
T	14.430	6.924	9.007
P	0.000	0.000	0.000
轻度感染(n=17)	10.80±3.05	2.61±0.60	8.31±1.41
中度感染(n=33)	18.57±2.82	3.89±1.07	11.70±2.38
重度感染(n=15)	26.65±4.62	6.17±2.23	15.89±1.65
F	88.650	28.646	56.646
P	0.000	0.000	0.000

4.2 不同肺部感染严重程度患者血清炎性因子水平对比 对比三组不同肺部感染程度患者,血清炎性因子水平,结果显示,重度感染组患者 PCT、TNF- α 、hs-

CRP 水平分别为(26.65±4.62)ng/mL、(6.17±2.23)ng/mL、(15.89±1.65)mg/mL,显著高于轻度、中度感染组患者,差异有统计学意义($P<0.05$)。见表 3。

讨 论

肺癌是全球第一大恶性肿瘤,临床表现主要为咳嗽、咳血、胸痛等,由于临床症状不典型,早期难以被发现,是全球首要癌症致死死因,每年约有 200 万新发病例、约 180 万人死于肺癌^[7]。研究发现,虽然放疗可以延长患者生存期,但容易引发多种并发症和患者免疫力降低^[8]。

本次研究共分离病原菌 65 株,主要来自痰液标本,其中 49.23% 为革兰阴性菌,以铜绿假单胞菌、肺炎克雷伯菌为主,真菌构成比较其他感染类疾病占比高。与苏端玉等^[9]研究结果一致。肺癌患者经过放疗后,自身机体平衡被破坏、免疫力降低,加之长期使用抗菌药物会导致菌群失调,同时放疗引起患者免疫功能抑制等因素会导致真菌感染数量显著提高^[10]。

本研究病原菌药敏结果显示,革兰阴性菌对环丙沙星、诺氟沙星、庆大霉素的耐药程度较高,对哌拉西林、头孢吡肟、亚胺培南、美罗培南、阿米卡星的耐药较低。革兰阳性菌对青霉素、阿莫西林、氯霉素、阿奇霉素、环丙沙星、左氧氟沙星的耐药率较高,未产生对万古霉素、利奈唑胺的耐药株。真菌对氟康唑、氟胞嘧啶、伊曲康唑的耐药率较低,未产生对两性霉素 B、伏立康唑的耐药株。与刘治辉等^[11]研究结果相近。不同研究报道的细菌耐药性不同,其原因与不同地区的流行菌株和受试药物不同有关。相关研究显示,在放疗后多数病原菌对大部分抗菌药物的耐药率均有所提高,因此,在患者进行放疗前,临床可对患者进行药敏试验,参考试验结果进行针对用药,可有助于降低耐药率^[12]。

肺癌放疗患者继发肺部感染后,可能会出现继发性败血症、感染性休克等并发症,炎性因子表达水平、呼吸指标的变化可反应出患者肺部功能、机体免疫状态及肺部感染的程度^[13-15]。本次研究发现,肺部感染组患者 Cydn 低于对照组水平,Raw、Pmean、Pmean 显著高于对照组。重度肺部感染者 Cydn 低于轻度、中度感染者的水平,Raw、Pmean、Pmean 高于轻度、中度感染者。肺部感染组患者血清 PCT、TNF- α 、hs-CRP 水平显著高于对照组水平,重度肺部感染组患者血清 PCT、TNF- α 、hs-CRP 水平显著高于轻度、中度感染者。与张定富等^[16]研究结果一致。PCT 主要由甲状腺 C 细胞合成和分泌,可有效反映机体器官损伤程度,hs-CRP 是机体应激状态下产生的一种蛋白,在

感染性疾病诊断及炎症发生方面有较高的预测价值。

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【收稿日期】 2023-09-22 【修回日期】 2023-11-19

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【收稿日期】 2023-10-07 【修回日期】 2023-11-28