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肺癌合并肺部感染患者病原菌分布、耐药性分析及血清炎性因子检测的临床意义 *

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摘要 目的：探讨肺癌合并肺部感染患者病原菌分布、耐药性分析及血清炎性因子检测的临床意义。**方法：**选取我院于 2018 年 6 月 ~2020 年 3 月期间收治的肺癌合并肺部感染患者 90 例为感染组，选取同期我院收治的肺癌未合并肺部感染患者 100 例为肺癌组，选取同期于我院进行体检的健康志愿者 60 例为对照组，对肺癌合并肺部感染患者的感染病原菌类型进行总结分析，分析常见病原菌药敏试验结果，统计病原菌耐药率。对比三组受试者的炎性因子水平。**结果：**90 例肺癌合并肺部感染患者的送检痰液标本共检出 100 株病原菌，100 株病原菌中以革兰阴性菌为主，其次为革兰阳性菌、真菌，分别占比 63.00%、22.00%、15.00%。肺炎克雷伯菌、鲍氏不动杆菌、铜绿假单胞菌对亚胺培南的耐药率较低，对氨苄西林、甲氨苄啶的耐药率均较高。凝固酶阴性葡萄球菌、金黄色葡萄球菌对万古霉素的耐药率较高，对左氧氟沙星的耐药率较低。白色念珠菌、热带念珠菌对两性霉素 B、氟康唑、酮康唑、伊曲康唑的耐药率均较低。感染组、肺癌组的血清白介素 -6（IL-6）、降钙素原（PCT）、肿瘤坏死因子 -α（TNF-α）水平均高于对照组，且感染组以上指标水平高于肺癌组（P<0.05）。**结论：**肺癌合并肺部感染患者体内病原菌种类繁多，对常见抗菌药物的耐药性存在差异，且患者体内存在较强的炎性反应，临床应根据药敏结果合理应用抗菌药物 。

关键词：肺癌；肺部感染；病原菌；耐药性；炎性因子

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Clinical Significance of Pathogen Distribution, drug Resistance Analysis and Serum Inflammatory Factor Detection in Patients with Lung Cancer Complicated with Pulmonary Infection*

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ABSTRACT Objective: To explore the clinical significance of the pathogen distribution, drug resistance analysis and serum inflammatory factor detection in patients with lung cancer complicated with pulmonary infection. **Methods:** From June 2018 to March 2020, 120 patients with lung cancer complicated with pulmonary infection in our hospital were selected as the infection group, 100 patients without lung cancer and pulmonary infection in our hospital as the lung cancer group, and 60 healthy volunteers who underwent physical examination in our hospital during the same period were selected as the control group. The types of infection pathogens of lung cancer complicated with pulmonary infection patients were summarized and analyzed, the drug susceptibility test results of common pathogenic bacteria were analyzed, and the drug resistance rate of pathogenic bacteria was calculated. Inflammatory factors were compared in the three groups. **Results:** A total of 100 strains of pathogenic bacteria were detected in the sputum samples of 90 patients with lung cancer complicated with pulmonary infection. Among the 100 strains of pathogenic bacteria, gram-negative bacteria dominated, followed by gram-positive bacteria and fungi, accounting for 63.00%, 22.00% and 15.00%, respectively. *Klebsiella pneumoniae*, *Acinetobacter baumannii* and *Pseudomonas aeruginosa* had lower drug resistance to imipenem, and higher drug resistance to ampicillin and trimethoprim. Coagulase-negative *Staphylococcus* and *Staphylococcus aureus* showed higher resistance to vancomycin and lower resistance to levofloxacin. The drug resistance rates of *Candida albicans* and *Tropical candida* to amphotericin B, fluconazole, ketoconazole and itraconazole were all low. The levels of interleukin-6(IL-6), calcitonin(PCT) and tumor necrosis factor-α (TNF-α) in the infection group and lung cancer group were all higher than those in the control group, and the levels of these indicators in the infection group were higher than those in the lung cancer group (P<0.05). **Conclusion:** There are many kinds of pathogenic bacteria in patients with lung cancer complicated with pulmonary infection, and there are differences in drug resistance to common antimicrobial agents, and there are strong inflammatory reactions in patients, so antimicrobial agents should be rationally applied in clinical practice according to drug sensitivity results.

Key words: Lung cancer; Pulmonary infection; Pathogen; Drug resistance; Inflammatory factors

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前言

肺癌为临床常见的呼吸系统恶性肿瘤，由于肺癌早期症状隐匿，症状无特异性，因此常被人们忽视，多数患者确诊时已发展至癌症晚期，治疗效果差，预后不良[1,2]。以往研究表明全世界每年有超过 100 万人死于肺癌[3]。随着人口老龄化的加重，工业化进程的加快，我国肺癌的发病率及病死率均逐年增加[4]。手术治疗是肺癌最重要和最有效的治疗手段，但由于肺癌患者多为中老年群体，且抵抗力低下，长时间住院并接受多种侵入性操作，加上出血、局部阻塞、化疗及全身免疫力低下等诸多原因，导致不少肺癌常伴发肺部感染[5-7]。而肺癌合并肺部感染患者由于病原菌耐药性的存在较一般的肺癌患者治疗难度明显增大，且患者生存期明显缩短[8]。此外，据以往研究显示[9]，肺癌合并肺部感染患者体内存在异常的炎性反应。鉴于此，本研究通过探讨肺癌合并肺部感染患者病原菌分布、耐药性分析及血清炎性因子检测的临床意义，为肺癌合并肺部感染患者临床用药方案的制定提供参考。

1 对象与方法

1.1 一般资料

选取我院于 2018 年 6 月 ~2020 年 3 月期间收治的肺癌合并肺部感染患者 90 例为感染组，男 52 例，女 38 例，年龄 36~62 岁，平均（51.28± 4.39）岁；体质量指数 21~26 kg/m^2，平均（23.58± 1.06）kg/m^2；肺癌类型：非小细胞肺癌 86 例，小细胞肺癌 4 例。选取同期我院收治的肺癌未合并肺部感染患者 100 例为肺癌组，男 52 例，女 48 例，年龄 35~63 岁，平均（51.09± 3.74）岁；体质量指数 22~26 kg/m^2，平均（23.36± 0.83）kg/m^2；肺癌类型：非小细胞肺癌 95 例，小细胞肺癌 5 例。本次研究已通过我院伦理学委员会批准进行。纳入标准：（1）肺癌参考《国际肺癌 TNM 分期标准》[10]，并经影像学及病理学确诊；（2）肺部感染参考《医院感染诊断标准》[11]，经 X 胸片及血清学证实存在感染病灶，均存在典型的呼吸道症状；（3）患者临床资料完整；（4）入院前一周内未接受过抗菌药物治疗。排除标准：（1）合并其他恶性肿瘤者；（2）合并心肝肾等脏器功能不全者；（3）合并其他血液疾病者；（4）合并心脑血管类疾病者；（5）有其他原发性的感染性疾病或免疫性疾病者；（6）合并精神障碍，无法正常沟通交流者。选取同期于我院进行体检的健康志愿者 60 例为对照组，男 35 例，女 25 例，年龄 34~64 岁，平均（50.84± 4.72）岁；体质量指数 20~26 kg/m^2，平均（23.25± 0.76）kg/m^2。感染组和肺癌组肺癌类型对比未见差异（P>0.05），三组性别、年龄、体质量指数对比未见差异（P>0.05）。

1.2 方法

1.2.1 细菌培养及药敏试验 于清晨使肺癌合并肺部感染患者以盐水漱口后，采集其深咳痰液于无菌容器中，采用生物梅里埃 VITEK2 Compact 型全自动细菌鉴定及药敏分析系统完成病原菌的鉴定，严格遵循临床检验规程操作。其中 ATCC 标准菌株由上海宝录生物科技有限公司提供。血琼脂平板由上海一研生物科技有限公司提供。

1.2.2 炎性因子检测 感染组、肺癌组患者均在入院后次日，对照组受试者于体检当天晨间抽取空腹静脉血 4 mL，经常规离心处理（3600 r/min 离心 13 min，离心半径 8 cm），分离上清液，置于 -30℃冰箱中待测。参考试剂盒（深圳晶美生物科技有限公司）说明书，采用酶联免疫吸附试验检测血清降钙素原（PCT）、白介素 -6（IL-6）及肿瘤坏死因子 -α（TNF-α）水平。

1.3 统计学处理

上述数据应用 SPSS 22.0 软件分析。计数资料以例（株）数或率表示，实施 x^2 检验。计量资料以（$\bar{x}$± s）表示，三组数据比较实施单因素方差分析 +LSD-t 检验。α=0.05 为检验水准。

2 结果

2.1 肺癌合并肺部感染患者的病原菌分布情况分析

90 例肺癌合并肺部感染患者的送检痰液标本共检出 100 株病原菌，100 株病原菌中以革兰阴性菌为主，其次为革兰阳性菌、真菌，分别占比 63.00%、22.00%、15.00%。详见表 1。

2.2 主要革兰阴性菌对抗菌药物的耐药率

肺炎克雷伯菌、鲍氏不动杆菌、铜绿假单胞菌对亚胺培南的耐药率比较低，对氨苄西林、甲氨苄啶的耐药率均较高，详见表 2。

2.3 主要革兰阳性菌对抗菌药物的耐药率

凝固酶阴性葡萄球菌、金黄色葡萄球菌对万古霉素的耐药率较高，对左氧氟沙星的耐药率较低，详见表 3。

2.4 主要真菌对抗菌药物的耐药率

白色念珠菌、热带念珠菌对两性霉素 B、氟康唑、酮康唑、伊曲康唑的耐药率均较低，详见表 4。

2.5 三组血清炎性因子水平比较

感染组、肺癌组的血清 PCT、IL-6、TNF-α 水平均高于对照组，且感染组以上指标水平高于肺癌组（P<0.05），详见表 5。

3 讨论

手术切除联合放化疗是治疗肺癌的有效手段，但由于中晚期肺癌患者常合并肺弹性回缩力下降、肺小动脉硬化等病理性改变，导致患者咳痰不畅，痰液凝聚肺部造成肺部感染[12-14]。此外，肺癌作为营养消耗类疾病，会大大降低患者体质，造成机体免疫力低下的情况，加之化疗药物在抑制肿瘤细胞增殖的同时还可降低细胞免疫力，较易诱发细菌感染[15]。肺癌患者治疗周期长，需长期住院，医院作为病原菌非常密集的场所，更易诱发肺部感染[16]。既往不少研究均证实[17,18]，肺部感染是肺癌患者极易发生的并发症之一，同时也是造成患者死亡的重要因素之一。肺部感染发生后将严重影响到肺癌患者本身的综合治疗，影响患者生活质量，降低患者生存期。随着广谱抗生素在临床的广泛应用，原本致病能力弱的细菌引起的感染越来越多，加之临床抗生素药物的滥用，致使耐药病原菌的生长空间更大，治疗更为艰难[19]。以往研究证实[20]，多周期的化疗使部分抗生素的敏感性下降，主要是因为化疗期间多次应用抗生素，引起药物敏感性下降及耐药菌株的产生。因此，及时了解肺癌合并肺部感染患者病原菌分布及耐药情况，可以指导临床合理用药，改善患者预后。

本次研究结果中，90 例肺癌合并肺部感染患者的送检痰液标本共检出 100 株病原菌，100 株病原菌中以革兰阴性菌为主，其次为革兰阳性菌、真菌。这与鲍秋红等人[21]研究结果基本

表 1 肺癌合并肺部感染患者的病原菌分布情况分析

Table 1 Analysis of the pathogen distribution in patients with lung cancer complicated with pulmonary infection strains

Pathogen	n	Constituent ratio(%)
Gram-negative bacteria	63	63.00
Klebsiella pneumoniae	17	17.00
Acinetobacter baumannii	15	15.00
Pseudomonas aeruginosa	15	15.00
Escherichia coli	8	8.00
Oligotrophic maltophilia	8	8.00
Gram positive bacteria	22	22.00
Coagulase-negative Staphylococcus	7	7.00
Staphylococcus aureus	7	7.00
Enterococcus faecium	4	4.00
Streptococcus pneumoniae	4	4.00
Fungus	15	15.00
Candida albicans	8	8.00
Candida tropicalis	7	7.00
Total	10	100.00

表 2 主要革兰阴性菌对抗菌药物的耐药率

Table 2 Resistance rate of main gram negative bacteria to antibacterial drugs strains

Antibacterial drugs	*Klebsiella pneumoniae*(n=17)		*Acinetobacter baumannii*(n=15)		*Pseudomonas aeruginosa*(n=15)	
	n	Resistance rate(%)	n	Resistance rate(%)	n	Resistance rate(%)
Ampicillin	15	88.24	9	60.00	14	93.33
Cefazolin	7	41.18	8	53.33	12	80.00
Gentamicin	5	29.41	6	40.00	7	46.67
Amikacin	3	17.65	4	26.67	4	26.67
Cefatriaxone	4	23.53	7	46.67	12	80.00
Imipenem	2	11.76	1	6.67	1	6.67
Trimethoprim	13	76.47	10	66.67	14	93.33
Cefuroxime	5	29.41	7	46.67	11	73.33
Ciprofloxacin	4	11.76	3	20.00	5	33.33

表 3 主要革兰阳性菌对抗菌药物的耐药率

Table 3 Resistance rate of main Gram-positive bacteria to antibacterial drugs strains

Antibacterial drugs	Coagulase-negative *staphylococcus*(n=7)		*Staphylococcus aureus*(n=7)	
	n	Resistance rate(%)	n	Resistance rate(%)
Levofloxacin	1	14.29	1	14.29
Gentamicin	6	85.71	2	28.57
Vancomycin	6	85.71	4	57.14
Linezolid	4	57.14	3	42.86
Trimethoprim	4	57.14	1	14.29
Teicoplanin	5	71.43	2	28.57
Ciprofloxacin	7	10.00	4	57.14

表 4 主要真菌对抗菌药物的耐药率

Table 4 Resistance rate of main fungi to antibacterial drugs strains

Antibacterial drugs	*Candida albicans*(n=8)		*Candida tropicalis*(n=7)	
	n	Resistance rate(%)	n	Resistance rate(%)
Amphotericin B	0	0.00	0	0.00
Fluconazol	0	0.00	0	0.00
Ketoconazole	1	12.50	0	0.00
Itraconazole	0	0.00	0	0.00

表 5 三组血清炎性因子水平比较($\bar{x}\pm s$)

Table 5 Comparison of serum inflammatory factors in three groups ($\bar{x}\pm s$)

Groups	PCT(ng/L)	IL-6(ng/L)	TNF-α(pg/mL)
Control group(n=60)	0.67± 0.25	11.28± 2.20	27.91± 2.35
Lung cancer group(n=100)	4.71± 1.32*	19.14± 3.25*	39.68± 2.79*
Infection group(n=90)	8.32± 1.27*#	32.31± 2.28*#	47.89± 2.36*#
F	18.946	16.729	13.481
P	0.000	0.000	0.000

Note: compared with the control group, *P<0.05; compared with the lung cancer group, #P<0.05.

一致。分析其原因,革兰阴性菌是人体上呼吸道和肠道的正常菌群,属于条件性感染菌株,当机体抵抗力降低或局部微生态平衡失调时可侵入下呼吸道引起感染[22]。临床在进行经验性治疗时可选择以针对革兰阴性菌为主的抗菌药物。此外,本研究中真菌感染的比例较小但不容忽视,真菌的感染形式复杂,难以控制,常成为患者死亡的终末事件,临床治疗需对此类感染引起一定重视。进一步的耐药分析结果显示,肺炎克雷伯菌、鲍氏不动杆菌、铜绿假单胞菌对亚胺培南的耐药率较低,凝固酶阴性葡萄球菌、金黄色葡萄球菌对左氧氟沙星的耐药率较低,白色念珠菌、热带念珠菌对两性霉素 B、氟康唑、酮康唑、伊曲康唑的耐药率均较低。病原菌的耐药性主要由质粒介导的β-内酰胺酶产生,临床可根据培养的结果、药敏及参考既往临床治疗效果选择药物,有目的地使用抗生素,最大程度地避免耐药菌的出现,进而控制感染以降低病死率[23,24]。本次研究结果还显示,感染组、肺癌组的血清 IL-6、PCT、TNF-α 水平均高于对照组,且感染组以上指标水平高于肺癌组,表明肺癌合并肺部感染患者处于炎性应激中,炎性反应影响了患者的免疫功能,同时还可损伤其肺血管内皮功能,进一步激活机体的免疫系统,增加肺部感染风险[25-27]。可见在临床中针对肺癌合并肺部感染患者给予合理的抗生素、抗菌治疗的同时,还应给予抗炎药物进行感染的预防,有利于患者病情改善[28-30]。

综上所述,肺癌合并肺部感染患者体内病原菌种类繁多,对常见抗菌药物的耐药性存在差异,且患者体内存在较强的炎性反应,临床应根据药敏结果合理应用抗菌药物。

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