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综合性医院肿瘤相关感染病原菌分布及耐药性分析*

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摘要 目的:通过对某院住院肿瘤患者感染的病原菌分布情况及耐药性分析,为肿瘤相关感染患者的经验性抗感染治疗提供参考。**方法:**对2015年细菌培养结果阳性的157例肿瘤内科住院患者的感染情况进行统计分析。**结果:**肿瘤内科患者的感染率为22.62%,分离出病原菌436株,其中革兰阴性菌占比58.26%,检出的金黄色葡萄球菌中MRSA的检出率为50%,粪肠球菌对万古霉素的敏感率为80%,屎肠球菌对万古霉素的敏感率为97.22%。主要G-杆菌中大肠埃希菌对阿米卡星耐药率1.79%,对碳青霉烯类、哌拉西林他唑巴坦耐药率为6.25%、26.79%;肺炎克雷伯菌对碳青霉烯类的耐药率25.58%-38.10%,对头孢哌酮舒巴坦耐药率15%。白色念珠菌对唑类耐药率<10%。**结论:**医院必须加强对常见细菌的耐药率的动态监测,降低细菌耐药率和多重耐药菌的产生。**关键词:**肿瘤;感染;病原菌分布;药敏结果;经验性用药
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Distribution of Pathogenic Bacteria and Drug Resistance of Tumor related Infections in General Hospitals*

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ABSTRACT Objective: To analyze the distribution of pathogens and drug resistance of patients with tumors in hospitals, and to provide reference for empirical anti-infective treatment of patients with tumor-related infections. **Methods:** Statistical analysis was performed on the infection status of 157 inpatients with tumors who were positive in bacterial culture in 2015. **Results:** The infection rate of tumor patients was 22.62%, and 436 strains of pathogens were isolated, of which Gram-negative bacteria accounted for 58.26%, and the detection rate of MRSA in *Staphylococcus aureus* was 50%. The sensitivity of *Enterococcus faecalis* to vancomycin is 80%, and the sensitivity of *Enterococcus faecium* to vancomycin is 97.22%. The resistance rate of *Escherichia coli* to amikacin in the main G-bacilli was 1.79%, and the resistance rate to carbapenems and piperacillin tazobactam was 6.25% and 26.79%; *Klebsiella pneumoniae* The resistance rate of carbapenems was 25.58%-38.10%, and the resistance rate to cefoperazone sulbactam was 15%. *Candida albicans* resistance to azoles <10%. **Conclusion:** The hospital must strengthen the dynamic monitoring of the resistance rate of common bacteria, reduce the rate of bacterial resistance and the production of multi-drug resistant bacteria.

Key words: Tumor; Infection; Pathogen distribution; Drug sensitivity; Empirical clinical medication

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前言

感染是肿瘤患者最常见的并发症之一,也是患者死亡的主要原因^[1-4]。肿瘤患者常伴随疾病复杂且严重,需多次住院治疗。各种抗肿瘤治疗导致患者免疫抑制,常出现白细胞下降,甚至急性粒细胞缺乏,机体免疫力极度低下,使其更易发生感染,且多为混合及耐药菌的感染,并发败血症的机会也相应增加^[13]。

一旦感染不仅影响患者的康复,延长了住院时间、增加了经济负担,甚至危及患者的生命,还对医务工作者自身安全带来威胁^[6-12]。

近年来,随着抗菌药物的不断使用及细菌生物学特征的不断变化,综合性医院感染病原菌的菌群分布与特征正逐渐发生变化,对临床治疗带来了一定的困难。临床实践中,针对肿瘤患者的抗感染治疗,由于病原微生物结果常有滞后,所以多结合

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临床体征和实验室常用的细菌感染检测方法包括细菌培养、白细胞计数、C-反应蛋白、降钙素原(PCT)^[14-17]以及NLR^[18,19]等开启经验性治疗。超广谱抗菌药物在肿瘤患者中往往经验性使用,但出现了过度使用甚至滥用的情况^[20,21]。

我国国内目前尚无肿瘤相关感染指南,而国际上常用的NCCN肿瘤相关感染指南与我国的国情有较大差异。及时了解和掌握肿瘤患者感染相关病原菌的分布及耐药性特征,对抗感染治疗起始方案制定至关重要,同时对于指导临床合理用药、减少耐药菌株形成及降低综合性医院院内感染率都具有重要意义。本文通过对2015年1月-2015年12月我院细菌培养结果阳性的157例肿瘤相关感染患者的病原菌分布及耐药趋势进行分析,以期对肿瘤感染患者的经验性用药提供参考。

1 资料与方法

1.1 临床资料

从我院HIS系统中收集2015年1月-2015年12月157例细菌培养阳性的肿瘤患者病例作为研究对象。

入组标准:①所有患者均确诊为肿瘤;②所有患者均诊断为感染;③所有患者均留取合格标本且细菌培养阳性并有药敏结果。标本取自于患者血液、尿液、痰液等,使用全自动血培养仪,按照程序对血标本进行培养和鉴定,判断依据形态学特征,滤过性和抵抗力等方面^[22]。

1.2 调查方法与统计分析方法

通过回顾性分析157例患者病例,监测血常规、PCT、细菌培养结果等来评估感染情况,同时对其药敏结果进行评估,用Excel2007统计分析感染的病原菌分布情况、药物敏感性及相关抗菌药物的耐药趋势。

2 结果

2.1 感染率及疾病类型分布

肿瘤内科全年住院患者2555例,因感染住院578例,感染率达22.62%。其中微生物送检的阳性检出率为27.16%;年龄>65岁的患者感染的发病率较高,为56.61%。肺癌、消化道肿瘤患者较多,且男性患者多于女性患者。详见表1。

表1 肿瘤内科患者疾病类型(例)及构成比(%)

Table 1 Disease types in oncology patients (cases) and composition ratio /%

Disease type	Male	Female	Total	Ratio/%
Lung cancer	27	8	35	20.71%
Rectal cancer	10	3	13	7.69%
Colon cancer	8	3	11	6.51%
Gastric cancer	5	5	10	5.92%
Pca	9	-	9	5.33%
Lymphoma	5	2	7	4.14%
Cervical cancer	-	6	6	3.55%
Esophagus cancer	6	0	6	3.55%
Bladder cancer	4	1	5	2.96%
Fibroid	-	4	4	2.37%
Other	43	15	45	37.28%
Total	117	52	169	100%

注:同一患者存在1个或多个原发肿瘤,合计总例数大于总例数。

Note: There are 1 or more primary tumors in the same patient, the total number of cases is greater than the total number.

2.2 感染部位分布

肿瘤内一科发生肺部感染、血流感染、腹腔感染的病例数明显高于肿瘤内二科,而肿瘤内二科发生泌尿系感染及其他部位感染的病例数与内一科相当。详见表2。

2.3 病原菌标本来源

肿瘤内一科送检的痰、尿、血等标本数明显高于肿瘤内二科,结果详见表3。

2.4 病原菌分布

共分离出病原菌436株,革兰阴性菌254株占58.26%,革兰阳性菌革兰阳性菌118株,占27.06%,真菌64株,见表4。

2.5 病原菌对药物的敏感性

患者分离的革兰氏阴性菌对抗菌药物的敏感性见表5,

MRSA的检出率为50%,粪肠球菌对青霉素的敏感率为40%,对万古霉素的敏感率为80%,中介率20%,屎肠球菌对万古霉素的敏感率为97.22%,对替考拉宁和利奈唑胺的敏感率均为100%。白色念珠菌和光滑假丝酵母菌对伏立康唑、伊曲康唑敏感率分别为90.91%和75%、100%和50%;三者对5-氟胞嘧啶和两性霉素B敏感度高,均为100%;对氟康唑敏感率分别为90.91%、66.67%、100%。

3 讨论

3.1 感染部位及标本来源分析

本次调查结果中,感染率达22.62%,较文献报道的高^[23]。肿瘤内一科发生肺部感染、血流感染、腹腔感染的病例数明显高

表 2 肿瘤内科患者感染部位分布(例)及构成比/%

Table 2 Infection sites in oncology patients (cases) and composition ratio/%

Infection site	Medical oncology #1	Medical oncology #2	Total	Ratio/%
Lung infection	35	26	61	35.06%
Urinary infection	16	16	32	18.39%
Blood infection	20	8	28	16.09%
Abdominal infection	9	2	11	6.32%
Abscess	2	1	3	1.72%
Gastrointestinal infection	1	2	3	1.72%
Respiratory tract infection	2	0	2	1.15%
Other	18	16	34	19.54%
Total	103	71	174	100%

注:同一患者存在 1 处或多处感染,合计总例数大于总例数。

Note: there are 1 or more infections in the same patient. The total number of cases is larger than the total number.

表 3 病原菌标本来源

Table 3 Sources of pathogenic bacteria sample

Sample	Medical oncology #1		Medical oncology #2		Total		Ratio/%	
	Sample amount	Detected amount	Sample amount	Detected amount	Sample amount	Detected amount	Sample	Detected
Phlegm	322	91	223	58	545	149	48.10%	39.73%
Urine	126	77	74	35	200	112	17.65%	29.86%
Blood	112	44	48	9	160	53	14.12%	14.13%
Whole blood	61	10	27	3	88	13	7.77%	3.47%
Secreta	9	6	5	5	14	11	1.24%	2.93%
Hydrot-horax	21	6	4	1	25	7	2.21%	1.87%
Ascites	18	2	11	4	29	6	2.56%	1.60%
Fester	6	4	3	2	9	6	0.79%	1.60%
Drain	3	2	2	2	5	4	0.44%	1.07%
Feces	6	0	23	3	29	3	2.56%	0.80%
Throat swab	10	2	3	1	13	3	1.15%	0.80
Other	17	7	2	1	16	8	1.41%	2.13%
Total	708	251	425	124	1133	375	100%	100%

于肿瘤内二科,而肿瘤内二科发生泌尿系感染及其他部位感染的病例数与内一科相当。可能与肿瘤内一科晚期高龄肿瘤患者较多有关。并且内一科肺癌、消化系统肿瘤患者较多,分别占其住院患者的 20.71%,23.67%。肺部感染、血流感染、泌尿系感染和腹腔感染发生率高,与文献报道的肺部和消化系统感染发生率相对较高有差别^[24]。有文献报道^[25],综合医院不同科室感染率存在差异,内科感染率最高,而感染部位中肺部感染占 33.16%,与本研究肺部感染所占比例 35.6%相差不大。在送检的标本中,痰标本为数最多,占 48.1%,其次为尿液、血液,分别占 29.86%,14.13%。肿瘤内一科送检的痰、尿、血等标本数明显高于肿瘤内二科,可能与肿瘤内一科感染的患者相对较多以及临床药师经常对医护患的宣教有关。在以后的工作中,临床药师也要加强对肿瘤内二科医患的宣教,充分告知患者标本采集

注意事项,优先进行痰标本培养、血培养,有利于提高标本检出率。在感染的患者年龄分布方面,65 岁以上的老年患者达 56.61%,老年恶性肿瘤患者机体功能下降、病情严重及受反复化疗、放疗等治疗手段的影响,骨髓造血功能受抑制、粒细胞缺乏^[26,27]、贫血、低蛋白血症,黏膜屏障及免疫系统遭到极大的破坏,导致患者防御功能进一步低下,易受病原菌感染。

3.2 病原菌及药敏结果分析

本次调查结果中,58.26% 的病原菌为革兰阴性菌,与孙佩玉等人^[28]分离 8907 株病原菌得出革兰氏阴性菌占医院感染病原菌所占比例 53.3%基本一致。本研究发现主要为大肠埃希菌、肺炎克雷伯菌、铜绿假单胞菌和醋酸钙不动杆菌,该类菌株主要为条件致病菌,这与国内流行病学报道的结果一致^[28,29],常见病原菌药敏结果分析:

表 4 肿瘤内科住院患者感染的细菌分布情况

Table 4 Bacterium infected of the medical oncology inpatients

Bacteria	Total/Case	Ratio/%
<i>Escherichia coli</i>	62	14.22%
<i>Klebsiella pneumoniae</i>	50	11.47%
<i>Enterococcus faecium</i>	41	9.40%
<i>Staphylococcus aureus</i>	40	9.17%
<i>Pseudomonas aeruginosa</i>	32	7.34%
<i>Serratia marcescens</i>	30	6.88%
<i>Calcium acetate Bowman acinetobacter</i>	28	6.42%
Other staphylococcus	15	3.44%
<i>Stenotrophomonas maltophilia</i>	13	2.98%
<i>Streptococcus</i>	13	2.98%
Other enterococcus	9	2.06%
<i>Enterobacter</i>	7	1.61%
Other	32	7.34%
<i>Candida albicans</i>	27	6.19%
<i>Candida tropicalis</i>	14	3.21%
<i>Candida glabrata</i>	11	2.52%
<i>Candida Krusei</i>	10	2.29%
<i>Candida Californica</i>	2	0.46%
Total	436	100%

表 5 患者分离的革兰氏阴性菌对抗菌药物的敏感性(%)

Table 5 Sensibility of isolated Gram-negative bacterium to antibiotic(%)

Antibiotics	<i>Escherichia coli</i>		<i>Klebsiella pneumoniae</i>		<i>Pseudomonas aeruginosa</i>		<i>Acinetobacter baumannii</i>	
	(62 strains)		(50 strains)		(32 strains)		(28 strains)	
	Sensitive	Drug resistant	Sensitive	Drug resistant	Sensitive	Drug resistant	Sensitive	Drug resistant
Levofloxacin	25.00	75.00	53.49	44.19	43.63	46.88	35.71	64.29
CPFX	21.43	76.79	50.00	25.00	53.13	34.38	35.71	64.29
Gentamicin	35.71	64.29	54.76	45.24	84.38	9.38	0.00	0.00
Trimethoprim/Sul-famethoxazole	32.14	67.86	67.44	27.91	0.00	100.00	40.74	55.56
Amikacin	94.64	1.79	69.77	25.58	87.50	6.25	39.29	60.71
Imipenem	85.71	10.71	72.09	25.58	46.88	53.13	40.74	59.26
Meropenem	87.50	12.50	74.42	25.58	62.50	37.50	39.29	60.71
Piperacillin / Tazobactam	60.71	26.79	53.49	32.56	62.50	28.13	37.04	62.96
Ceftriaxone	26.79	67.86	46.51	51.16	0.00	75.00	0.00	67.86
Piperacillin	9.43	86.79	30.23	62.79	51.61	32.26	17.86	64.29
Cefepime	48.21	50.00	51.16	41.86	62.50	28.13	35.71	60.71
Ceftazidime	35.00	45.00	50.00	45.45	60.71	39.29	37.04	62.96
Cefuroxime	20.00	70.91	37.50	62.50	0.00	0.00	0.00	0.00
Cefoxitin	55.36	37.50	69.05	28.57	0.00	0.00	0.00	0.00
Cefoperazone/Sul-bactam	56.25	21.88	75.00	15.00	65.22	21.74	74.07	7.41

Tetracycline	31.25	68.75	66.67	33.33	0.00	100.00	0.00	100.00
Ampicillin	15.38	84.62	0.00	5.00	0.00	100.00	0.00	0.00
Ampicillin/Sulbactam	19.57	71.74	40.00	60.00	0.00	100.00	0.00	0.00
Aztreonam	31.25	68.75	42.86	57.14	34.38	34.38	0.00	100.00
Tobramycin	28.57	50.00	52.38	42.86	87.50	9.38	0.00	100.00
Cefazolin	31.25	68.75	42.86	57.14	0.00	0.00	0.00	0.00
Ticarcillin/Carat	43.75	18.75	42.86	52.38	25.00	50.00	0.00	100.00
Ceftazidime	37.50	62.50	47.62	52.38	75.00	25.00	0.00	100.00
Ertapenem	93.75	6.25	61.90	38.10	0.00	100.00	0.00	100.00
Cefotaxime	33.33	66.67	42.86	52.38	0.00	75.00	0.00	100.00
Amo/Carat	70.00	30.00	0.00	0.00	0.00	0.00	0.00	100.00
Minocycline	0.00	0.00	0.00	0.00	0.00	0.00	48.00	16.00
Bacillosporin	0.00	0.00	0.00	0.00	0.00	0.00	100.00	0.00

(1)大肠埃希菌:对阿米卡星、美罗培南、亚胺培南和厄他培南敏感率高,均大于 85%,对哌拉西林 / 他唑巴坦敏感率为 60.71%,可经验性使用,对头孢他啶、头孢吡肟、头孢西丁和头孢哌酮 / 舒巴坦的敏感率分别为 35%、48.21%、55.36%和 56.25%。有报道称^[20],大肠埃希菌对青霉素类、一、二代头孢菌素类耐药性较高,特别是对氨苄西林的耐药率高达 81.9%。可能与大肠埃希菌产生超广谱 β -内酰胺酶(ESBLs)、头孢菌素酶(AmpC)有关。针对大肠埃希菌的药敏结果,临床上应采用含有碳青霉烯类、含酶抑制剂等复方制剂进行治疗。(2)肺炎克雷伯菌:对亚胺培南、美罗培南和头孢哌酮 / 舒巴坦敏感率 >70%,阿米卡星 69.77%、头孢西丁 69.05%、复方新诺明 67.44%、厄他培南 61.9%,提示临床可选择该类抗菌药物对肺炎克雷伯菌经验性治疗。而肺炎克雷伯菌对哌拉西林他唑巴坦的敏感率为 53.49%,提示该药不宜作为肺炎克雷伯菌感染的经验性治疗。(3)醋酸钙鲍曼不动杆菌:仅对头孢哌酮 / 舒巴坦和多粘菌素敏感率较高,可经验性用药。(4)铜绿假单胞菌:对庆大霉素、阿米卡星、妥布霉素和头孢他啶敏感率 >70%,临床可根据药敏结果选择性用药,美罗培南、哌拉西林 / 他唑巴坦、头孢吡肟和头孢哌酮 / 舒巴坦 >60%,该结果显示头孢他啶的敏感率高于美罗培南,可能与我院美罗培南使用过多有关,对亚胺培南敏感率仅为 46.88%,提示亚胺培南西司他丁已不适宜作为铜绿假单胞菌感染的经验性用药。据报道,铜绿假单胞菌与鲍氏不动杆菌有多重耐药铜绿假单胞菌感染逐年增多的趋势^[21],主要与其产生多种 β 内酰胺酶、外排泵过度表达及外膜蛋白缺失等多种机制有关^[22]。

肿瘤患者是医院感染的高危人群,及时了解病原菌分布及耐药趋势,有助于经验性治疗时选择适宜的抗菌药物。卫生部办公厅在 2011 年全国抗菌药物临床专项整治中强调:二级以上医院应根据临床微生物标本检测结果选择合理的抗菌药物,而接受抗菌治疗的住院患者,标本送检率应不低于 30%,所以为了进一步开展细菌耐药监测工作,应提高标本送检率,建立医院感染长效预警机制,定期针对不同病原菌耐药措施。除此之

外,医务人员对医院感染、医院感染控制预防整体认识不足,对医院感染报告制度、预防控制基本措施掌握不够。所以临床医务工作者应加强抗菌药物合理使用培训以及对患者的用药教育,加强院内消毒隔离、注意手卫生,对规范抗菌药物的使用及减缓耐药菌株发挥着积极作用。

4 结论

我院肿瘤内科感染的病原菌排名第一的为大肠埃希菌,其次为肺炎克雷伯菌、屎肠球菌和金黄色葡萄球菌,且多为耐药菌。医院必须加强对常见细菌的耐药率的动态监测,根据药敏结果合理选择抗菌药物,同时加强医务人员手卫生的管理,降低细菌耐药率和多重耐药菌的产生。

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