

肝恶性肿瘤合并肝脓肿51例报道并文献分析

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Malignant Liver Tumors Combined with Liver Abscesses: 51 Cases Report and Literature Review

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0 引言

据统计, 2020年全球肿瘤新发1 930万例, 近1 000万例癌症患者死亡。肝恶性肿瘤是全球第三大致死肿瘤, 在新发恶性肿瘤中位列第七^[1]。我国是乙肝大国, 同样也是肝癌大国。2015年全国新发肝癌约37万例, 近32.6万例肝癌患者死亡^[2]。由于肝脏富血供的特点, 因而是肿瘤最易发生转移的器官之一^[3], 其中以胃肠道肿瘤肝转移最为常见, 约占71%^[4], 同时由于肿瘤患者免疫调节失衡、营养状况差、机体抵抗力低下等原因, 肝脏也成为易发生感染的脏器之一。

肝脓肿是指致病菌通过各种途径引起的肝实质化脓性感染, 其中以细菌性肝脓肿最为常见, 约占80%^[5]。国内外多项研究证明, 其与肝胆管疾病、腹腔感染、恶性肿瘤等存在关联^[6-7]; 恶性肿瘤相关性肝脓肿是除糖尿病、胆源性肝脓肿外常见的肝脓

肿类型。近年来, 与恶性肿瘤相关的肝脓肿报道逐年增加, 我国对肝恶性肿瘤合并肝脓肿的相关研究较少, 为实现早诊断、早治疗、优化预后尚需进一步总结临床经验。本文回顾性分析了51例肝脏恶性肿瘤合并肝脓肿患者的临床特征、影像学表现、病原学结果和治疗方式等, 为肝恶性肿瘤合并肝脓肿的诊断及治疗提供数据参考。

1 临床资料

1.1 一般资料

收集2015年1月1日至2021年12月31日期间在浙江大学医学院附属邵逸夫医院治疗肝恶性肿瘤合并肝脓肿的51例患者资料, 见表1。男性患者占比略高于女性, 平均年龄 64.76 ± 10.20 岁, 其中三分之二为原发性肝恶性肿瘤; 患者多合并肝胆疾病史, 仅20%既往接受过经导管动脉化疗栓塞术或射频消融治疗; 发热为最常见的初始症状, 多高热, 少部分有腹痛腹泻等症状, 超70%的患者行穿刺引流治疗方式, 仅3例行肝叶切除手术, 最终死亡5例, 死亡率9.80%。

1.2 实验室指标变化

入院血常规提示大部分患者均出现白细胞及中性粒细胞升高、血红蛋白及白蛋白降低的情况, 超70%的患者有直接胆红素升高, 一半出现总胆红素升高; 近一半患者出现谷丙及谷草转氨酶升高, 几

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表 1 51例肝恶性肿瘤合并肝脓肿患者临床资料 (n(%))

Table 1 Demographics and clinical characteristics of 51 patients with malignant liver tumors combined with liver abscesses (n(%))

Characteristics	Number
Gender	
Male	30(58.82)
Female	21(41.18)
Diabetes	
No	41(80.39)
Yes	10(19.61)
Hypertension	
No	34(66.67)
Yes	17(33.33)
Hepatobiliary disease	
No	29(56.86)
Yes	22(43.14)
Transarterial chemoembolization	
No	40(78.43)
Yes	11(21.57)
Radiofrequency ablation	
No	41(80.39)
Yes	10(19.61)
Primary tumor site	
Primary hepatic malignant tumors	30(58.82)
Metastatic hepatic malignant tumors	21(41.18)
Primary symptoms	
Fever	39(76.47)
Nausea/vomiting	1(1.96)
Abdominal pain/diarrhea	10(19.61)
Fatigue/poor appetite	1(1.96)
Fever temperature	
≤38℃	4(10.25)
38.1℃–39.0℃	14(35.90)
39.1℃–41.0℃	20(51.28)
≥41.1℃	1(2.56)
Treatment	
Anti-infection+Puncture drainage	36(70.59)
Anti-infection+Liver lobectomy	3(5.88)
Anti-infection+Incision and drainage	2(3.92)
Anti-infection treatment	10(19.61)
Outcome	
Improved	46(90.20)
Dead	5(9.80)

平均有C反应蛋白水平升高的情况，近三分之二存在纤维蛋白原升高，见表2。

1.3 影像学检查

1例患者影像学为外院检查，余50例患者影像学检查结果提示肝脓肿，其中多普勒超声检查诊断肝脓肿46例（92.00%），计算机断层扫描检查诊断肝脓肿48例（96.00%）。患者肝脓肿多发于右叶，左右叶均有脓肿者约6.00%，脓肿多为多房多个及单房单个，超一半的脓肿直径达5~10 cm，见表3。

1.4 病原学结果

51例患者中有10例因脓肿较小或发现肝脓肿时已经过经验性治疗，症状得到控制，故未行细

表 2 51例肝恶性肿瘤合并肝脓肿患者实验室检查指标 (n(%))

Table 2 Laboratory results of 51 patients with malignant liver tumors combined with liver abscesses (n(%))

Characteristics	Number
WBC increased	39(76.47)
NEU increased	45(88.24)
HGB decreased	41(80.39)
ALB decreased	47(92.16)
DBIL increased	36(70.59)
TBIL increased	27(52.94)
ALT increased	23(45.10)
AST increased	32(62.75)
ALP increased	34(66.67)
γ-GTP increased	38(74.51)
CRP increased	48(94.12)
FIB increased	31(60.78)

Notes: WBC: white blood cell count; NEU: neutrophils; HGB: hemoglobin; ALB: albumin; DBIL: direct bilirubin; TBIL: total bilirubin; ALT: alanine transaminase; AST: aspartate transaminase; ALP: alkaline phosphatase; γ-GTP: gamma-glutamyl transpeptidase; CRP: C-reactive protein; FIB: fibrinogen.

表 3 50例肝恶性肿瘤合并肝脓肿患者影像学表现 (n(%))

Table 3 Imaging features of 50 patients with malignant liver tumors and liver abscesses (n(%))

Characteristics	Number
Location of liver abscess	
Left lobe	10(20.00)
Right lobe	37(74.00)
Both lobe	3(6.00)
Characteristics of abscess cavities	
Single and unilocular abscesses	19(38.00)
Multiple and unilocular abscesses	6(12.00)
Single and multilocular abscesses	13(26.00)
Multiple and multilocular abscesses	21(42.00)
Liver abscess size(cm)	
<5	13(26.00)
5–10	28(56.00)
≥10	9(18.00)

菌学培养。41例行血液培养，阳性24例（58.54%）；40例行脓液培养，33例（82.50%）阳性。病原菌以肺炎克雷伯杆菌最为常见，其次是屎肠球菌及大肠埃希菌，具体病原菌见表4。

血液培养或脓液培养有一阳性即视为病原学细菌阳性，共39例，其中3种主要细菌肺炎克雷伯菌15例（38.46%），大肠埃希菌10例（25.64%），屎肠球菌9例（23.08%）。感染肺炎克雷伯菌及屎肠球菌患者中女性占比略高于男性，大肠埃希菌则相反；肺炎克雷伯菌及大肠埃希菌患者中61~70岁占比略高，屎肠球菌≤60岁比例略高。发现3种主要细菌感染患者均未合并糖尿病，大多无高血压病史；感染肺炎克雷伯菌患者初始多发热，有恶心呕吐和腹痛症状，大肠埃希菌多为发热及腹

表 4 肝脓肿患者血液培养和脓液培养细菌检出结果
Table 4 Detection results of various bacteria in the blood and pus cultures of patients with liver abscesses

Blood culture ^a (n)		Pus culture ^b (n)	
<i>Klebsiella pneumoniae</i>	10	<i>Klebsiella pneumoniae</i>	13
<i>Escherichia coli</i>	4	<i>Escherichia coli</i>	9
<i>Enterococcus faecium</i>	5	<i>Enterococcus faecium</i>	8
<i>Aeromonas hydrophila</i>	2	<i>Aeromonas hydrophila</i>	1
<i>Klebsiella aerogenes</i>	1	<i>Klebsiella aerogenes</i>	1
<i>Enterococcus faecalis</i>	1	<i>Enterococcus faecalis</i>	1
<i>Enterobacter cloacae</i>	1	<i>Enterobacter cloacae</i>	1
<i>Citrobacter freundii</i>	1	<i>Citrobacter freundii</i>	1
<i>Enterococcus gallinarum</i>	1	<i>Streptococcus anginosus</i>	1
<i>Staphylococcus aureus</i>	1	<i>Candida glabrata</i>	2
<i>Bacteroides fragilis</i>	1	<i>Morganella morganii</i>	1
		<i>Stenotrophomonas maltophilia</i>	1
		β -hemolytic streptococcus	2
		<i>Providencia rettgeri</i>	1
		<i>Candida albicans</i>	1
		<i>Klebsiella oxytoca</i>	1
		<i>Staphylococcus aureus</i>	1

Notes: a: Blood culture: Four cases involved two or more pathogenic bacteria with positive detection in the patients; b: Pus culture: Twelve cases involved cases or more pathogenic bacteria with positive detection in the patients.

痛，屎肠球菌患者均出现发热的初始症状；大肠埃希菌和屎肠球菌阳性患者发热多为高热（39.1℃~41.0℃），肺炎克雷伯菌阳性患者多集中38.1℃~39.0℃，有超四分之三的患者行抗感染+穿刺引流治疗方式。脓肿多集中肝右叶，肺炎克雷伯菌患者脓腔多为单房单个脓肿及多房单个脓肿，大肠埃希菌多为单房单个脓肿，屎肠球菌患者脓腔多为多房单个脓肿，最大直径均集中于5~10 cm；实验室指标变化程度不同，但趋势一致，大肠埃希菌和屎肠球菌患者出现白细胞升高、中性粒细胞升高、血红蛋白降低及白蛋白低水平的比例略高于肺炎克雷伯菌患者，3种菌群均出现C反应蛋白升高。肺炎克雷伯菌及大肠埃希菌阳性患者治疗后好转的比例均超90%，屎肠球菌患者为88.89%，见表5。

2 讨论

肝脏不仅是肿瘤易发器官，亦是易转移器官，同时也是易感染器官。近年来有关恶性肿瘤相关性肝脓肿的报道越来越多，既往文献报道发病率约为9.9%^[8]。本研究恶性肿瘤合并肝脓肿的发病率为15.7%，原发性肝癌及继发性肝恶性肿瘤合并肝脓肿的发病率为7.0%。这可能与肿瘤治疗手段的多样化、肿瘤患者的生存时间得到延长、出现感染风险也随之增加有关。既往研究报道肝脏的介入治疗可

增加细菌性肝脓肿的风险，TACE术后肝脓肿发生率为1.4%^[9]，RAF后发生率为0.7%^[10]，尽管TACE及RAF术后肝脓肿发生率很低，但随着TACE及射频、微波消融等治疗手段在肝脏肿瘤局部治疗中的广泛应用，肝脓肿的发生率也随之不断升高。

肝脓肿常表现为发热及腹痛，症状及体征不典型，特别是合并肝脏肿瘤时，症状及体征易被掩盖，易出现误诊及漏诊^[11]。简便快速的诊断是提高肝脓肿预后、降低死亡率的第一步。既往研究显示B型超声及CT是诊断肝脓肿的有效手段，灵敏度分别达85%、97%^[12]，本研究B型超声和CT的肝脓肿检出率分别达92%、96%。

此外，实验室化验结果也不具备特异性。本研究中血常规多表现为白细胞、中性粒细胞比例及绝对值、C反应蛋白等升高，大多患者存在血红蛋白下降；肝功能中胆红素、谷丙转氨酶、谷草转氨酶、碱性磷酸酶及谷氨酰转肽酶的升高；凝血功能检查提示60.78%的患者存在纤维蛋白原升高；这与刘瑶等^[13]研究结果一致。

诊断肝脓肿后，明确致病菌是肝脓肿治疗的关键。血培养及脓液培养有助于致病菌的确定。脓液培养阳性率通常显著高于血培养^[13]，本研究中脓液培养阳性率82.5%，较血液培养阳性率高出近30%，同时培养阳性最常见的细菌为肺炎克雷伯菌、屎肠球菌、大肠埃希菌，这与既往肝脓肿研究报道一致^[14]。

对于直径<3~5 cm的小脓肿，单独的抗生素往往治疗有效^[15]。本研究中肝恶性肿瘤合并小脓肿13例中有10例仅用抗生素治疗后，脓肿得到有效控制。Bamberger等^[16]证实对于小脓肿，抗菌治疗成功率达81.2%。对肝脓肿的抗生素治疗通常选择针对革兰氏阴性杆菌、革兰氏阳性球菌及厌氧菌进行覆盖，选用第三代头孢菌素加用甲硝唑或哌拉西林/他唑巴坦^[17]。但需注意的是，由于抗菌药物的滥用，肝脓肿常见致病菌对氨苄青霉素和氟喹诺酮类药物均具有耐药性，特别是耐碳青霉烯类的肺炎克雷伯菌比例增加，往往导致治疗的失败^[18]，本研究13例肺炎克雷伯菌中有5例为耐碳青霉烯类，远高于既往研究结果^[13-14]。

超声或CT引导下经皮穿刺是肝脓肿治疗的首选，包括穿刺抽液和穿刺置管引流。本研究中大多数患者（70.59%）采用穿刺置管引流。与穿刺抽液相比，穿刺置管引流治疗成功率更高。相较于外科手术，研究报道对于>5 cm的大脓肿，穿刺引流治疗死亡率无差异^[19]。穿刺置管引流相较于外科手术

表5 主要细菌感染肝脓肿患者的特征比较 (n(%))

Table 5 Characteristics of patients with liver abscesses infected by three main bacteria (n(%))

Characteristics	<i>K. pneumoniae</i> (n = 15)	<i>E. coli</i> (n = 10)	<i>E. faecium</i> (n = 9)	Characteristics	<i>K. pneumoniae</i> (n = 15)	<i>E. coli</i> (n = 10)	<i>E. faecium</i> (n = 9)
Gender				Primary tumor site			
Female	9 (60.00)	3 (30.00)	5 (55.56)	Metastatic hepatic malignant tumors	8 (53.33)	4 (40.00)	7 (77.78)
Male	6 (40.00)	7 (70.00)	4 (44.44)	Primary hepatic malignant tumors	7 (46.67)	6 (60.00)	2 (22.22)
Age (years)				Treatment			
≤60	5 (33.33)	2 (20.00)	4 (44.44)	Anti-infection+ Puncture drainage	12 (80.00)	8 (80.00)	8 (88.89)
61–70	7 (46.67)	4 (40.00)	3 (33.33)	Anti-infection+ Liver lobectomy	1 (6.67)	0 (0)	1 (11.11)
≥71	3 (20.00)	4 (40.00)	2 (22.22)	Anti-infection+ Incision and drainage	1 (6.67)	1 (10.00)	0 (0)
Hepatobiliary disease				Anti-infection treatment	1 (6.67)	1 (10.00)	0 (0)
No	7 (46.67)	6 (60.00)	5 (55.56)	Outcome			
Yes	8 (53.33)	4 (40.00)	4 (44.44)	Improvement	14 (93.33)	9 (90.00)	8 (88.89)
Diabetes				Death	1 (6.67)	1 (10.00)	1 (11.11)
No	14 (93.33)	10 (100)	9 (100)	Location of liver abscesses			
Yes	1 (6.67)	0 (0)	0 (0)	Left lobe	2 (13.33)	3 (30.00)	1 (11.11)
Hypertension				Right lobe	11 (73.33)	6 (60.00)	6 (66.67)
No	11 (73.33)	8 (80.00)	9 (100)	Both lobes	2 (13.33)	1 (10.00)	2 (22.22)
Yes	4 (26.67)	2 (20.00)	0 (0)	Characteristics of abscess cavities			
Primary symptoms				Single and unilocular abscesses	6 (40.00)	4 (40.00)	2 (22.22)
Fever	13 (86.67)	8 (80.00)	9 (100)	Multiple and unilocular abscesses	1 (6.67)	1 (10.00)	0 (0)
Nausea/vomiting	1 (6.67)	0 (0)	0 (0)	Single and multilocular abscesses	6 (40.00)	3 (30.00)	5 (55.56)
Abdominal pain	1 (6.67)	2 (20.00)	0 (0)	Multiple and multilocular abscesses	2 (13.33)	2 (20.00)	2 (22.22)
Fatigue and poor appetite	0 (0)	0 (0)	0 (0)	Liver abscess size (cm)			
Fever temperature				<5	4 (26.67)	0 (0)	2 (22.22)
≤38 ℃	1 (6.67)	1 (10.00)	1 (11.11)	5–10	10 (66.67)	8 (80.00)	6 (66.67)
38.1 ℃–39.0 ℃	8 (53.33)	1 (10.00)	3 (33.33)	≥10	1 (6.67)	2 (20.00)	1 (11.11)
39.1 ℃–41.0 ℃	4 (26.67)	6 (60.00)	5 (55.56)	WBC increased	11 (73.33)	9 (90.00)	8 (88.89)
≥41.1 ℃	0 (0)	0 (0)	0 (0)	NEU increased	13 (86.67)	10 (100)	9 (100)
Normal	2 (13.33)	2 (20.00)	0 (0)	HGB decreased	9 (60.00)	9 (90.00)	8 (88.89)
Accompanying symptoms				ALB decreased	14 (93.33)	10 (100)	9 (100)
Asymptomatic	7 (46.67)	7 (70.00)	3 (33.33)	DBIL increased	11 (73.33)	8 (80.00)	7 (77.78)
Fever	0 (0)	1 (10.00)	0 (0)	TBIL increased	11 (73.33)	5 (50.00)	5 (55.56)
Nausea/vomiting	1 (6.67)	1 (10.00)	1 (11.11)	ALT increased	8 (53.33)	6 (60.00)	7 (77.78)
Abdominal pain	4 (26.67)	0 (0)	2 (22.22)	AST increased	10 (66.67)	8 (80.00)	8 (88.89)
Other	1 (6.67)	1 (10.00)	2 (22.22)	ALP increased	10 (66.67)	8 (80.00)	6 (66.67)
More than two of the above symptoms	2 (13.33)	0 (0)	1 (11.11)	γ-GTP increased	12 (80.00)	9 (90.00)	7 (77.78)
Transarterial chemoembolization				CRP increased	15 (100)	10 (100)	9 (100)
No	15 (100)	8 (80.00)	7 (77.78)	FIB increased	10 (66.67)	7 (70.00)	5 (55.56)
Yes	0 (0)	2 (20.00)	2 (22.22)				
Radiofrequency ablation							
No	13 (86.67)	6 (60.00)	7 (77.78)				
Yes	2 (13.33)	4 (40.00)	2 (22.22)				

具有无需麻醉、低粘连风险、成本更低等优势。但对于多房性或未完全液化的肝脓肿，则不宜进行穿刺置管引流。

对于穿刺置管引流联合抗生素治疗效果不佳、脓肿破裂、解剖位置不适宜进行穿刺置管引流的患

者，外科手术是可选方案，包括切开引流及肝叶切除。本研究中2例患者选择手术切开引流，3例进行肝叶切除（其中1例因穿刺引流效果不佳）。对于大的、多房性肝脓肿，外科手术更具优势。临床诊疗流程总结见图1。

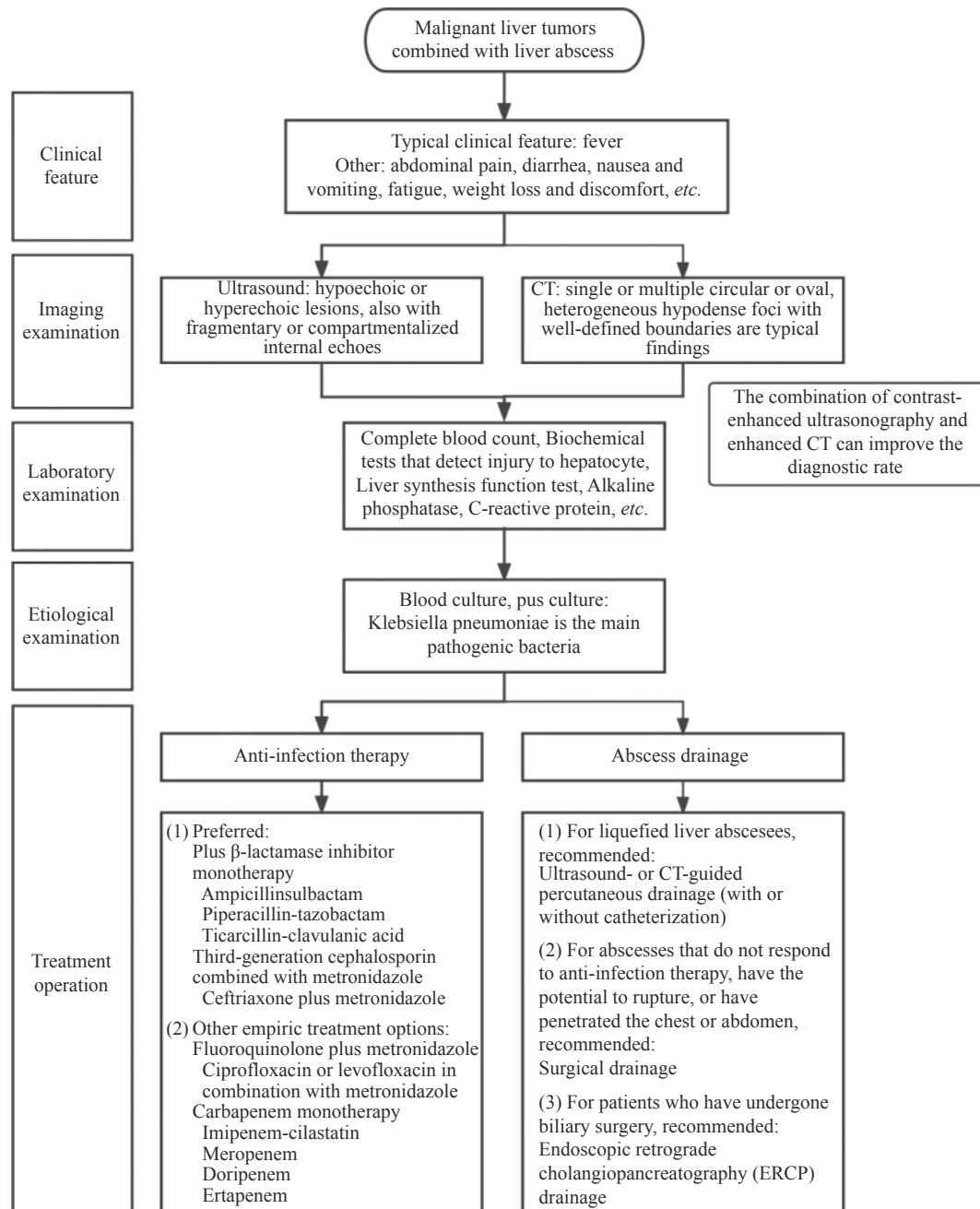


图1 肝脓肿临床诊疗流程图

Figure 1 Clinical diagnosis and treatment of liver abscesses

综上，细菌性肝脓肿发病率低，但致死率高，既往文献报道肝脓肿死亡率为6%~14%^[20]，本研究中死亡率达9.8%，5例死亡患者均为肝胆系统原发肿瘤（3例肝内胆管癌、1例原发性肝癌、1例胆囊癌）。随着肿瘤患者生存时间的延长，其发生肝脓肿的风险急剧升高。肺炎克雷

伯菌、屎肠球菌、大肠埃希菌仍是合并恶性肿瘤患者肝脓肿主要致病细菌。经皮穿刺置管引流联合抗生素治疗是其主要治疗手段，治疗效果不佳者，仍需手术干预。

利益冲突声明：

所有作者均声明不存在利益冲突。

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