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原发性肝癌伴胆管癌栓误诊分析

谭蔚锋^{1△}, 冉荣征^{1△}, 杨昊玉², 刘随意¹, 罗祥基¹, 刘辰¹, 易滨¹, 沈锋¹, 张柏和¹, 姜小清^{1*}, 吴孟超¹

1. 第二军医大学东方肝胆外科医院胆道一科, 上海 200438
2. 解放军理工大学校务部卫生处, 南京 210007

[摘要] **目的** 总结原发性肝癌伴胆管癌栓诊断和鉴别诊断的要点, 分析常见的误诊原因。**方法** 回顾 18 年内收治的 392 例原发性肝癌伴胆管癌栓患者的临床诊断过程, 归纳该病易误诊的疾病类型, 分析术前临床误诊的主要原因。按照不同时期进行分组: 前期(1993 至 2001 年)128 例, 后期(2002 至 2011 年)264 例, 比较不同时期误诊率的差异以及误诊疾病类型的变化, 总结原发性肝癌伴胆管癌栓诊断和鉴别诊断的要点。**结果** 总体术前临床误诊率为 16.6%(65/392), 后期术前临床误诊率(9.8%, 26/264)低于前期(30.5%, 39/128) ($P < 0.001$)。后期 ERCP/MRCP 的检查率(91.7%, 242/264)高于前期[67.9%(87/128), $P < 0.001$]。ERCP/MRCP 的误诊率为 5.5%(18/329), 低于肝脏 B 超[26.8%(105/392), $P < 0.001$]及肝脏 CT/MRI[25.0%(98/392), $P < 0.001$]。常易误诊的疾病包括: 肝癌伴肝门部胆管压迫(4.1%, 16/392), 肝门部胆管腺瘤/癌(4.3%, 17/392), 远端胆管腺瘤/癌(包括壶腹部腺瘤/癌)(2.3%, 9/392), 胆管内黏液状腺瘤/癌(1.0%, 4/392), 转移性肝癌伴胆管癌栓(1.0%, 4/392), 胆管结石(3.8%, 15/392)。前、后期误诊为肝癌伴肝门部胆管压迫分别为 9.4%(12/128)和 1.5%(4/264), 误诊为胆管结石分别为 7.8%(10/128)和 1.9%(5/264), 差异有统计学意义 ($P < 0.01$)。**结论** 提高原发性肝癌合并胆管癌栓临床特征的认识水平, 合理应用影像学检查手段, 加强与相似疾病的鉴别, 可有效降低误诊率。

[关键词] 原发性肝癌伴胆管癌栓; 误诊; 鉴别诊断

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Misdiagnosis analysis of hepatocellular carcinoma combined with bile duct tumor thrombi

TAN Wei-feng^{1△}, RAN Rong-zheng^{1△}, YANG Hao-yu², LIU Sui-yi¹, LUO Xiang-ji¹, LIU Chen¹, YI Bin¹, SHEN Feng¹, ZHANG Bai-he¹, JIANG Xiao-qing^{1*}, WU Meng-chao¹

1. The 1st Department of Biliary Surgery, Eastern Hepatobiliary Hospital, Second Military Medical University, Shanghai 200438, China
2. Health Office of Administrative Affairs Department, PLA University of Science & Technology, Nanjing 210007, Jiangsu, China

[Abstract] **Objective** To summarize the key points for diagnosis and differential diagnosis of hepatocellular carcinoma combined with bile duct tumor thrombi(HCCBDT), and analyze the common reasons for misdiagnosis. **Methods** A total of 392 patients with HCCBDT over a 18-year period were included in this study. The liable disease types of misdiagnoses were summarized and the main causes of preoperative misdiagnosis were analyzed. The patients were divided into two groups according to the time periods: Group A(from 1993 to 2001, 128 patients) and Group B(from 2002 to 2011, 264 patients). The misdiagnosis rates and types of misdiagnosed diseases were compared between the two groups. The key points of diagnosis and differential diagnosis of HCCBDT were summarized. **Results** The overall preoperative misdiagnosis rate was 16.6% (65/392) in our patients. The misdiagnosis rate of Group B (9.8%, 26/264) was significantly lower than that of Group A (30.5%, 39/128) ($P < 0.001$). And 91.7% (242/264) patients received ERCP/MRCP examination in Group B, which was significantly higher than that in the Group A(67.9%, 87/128) ($P < 0.001$). The misdiagnosis rate of ERCP/MRCP(5.5%, 18/329) was significantly lower than those of B-type ultrasound examination (26.8%, 105/392) ($P < 0.001$) and CT/MRI scan(25.0%, 98/392) ($P < 0.001$). The misdiagnosed diseases included hepatocellular carcinoma with hilar bile duct compression (4.1%, 16/392), hilar bile duct adenoma/carcinoma (4.3%, 17/392), distal bile duct adenoma/carcinoma (including ampullary

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[作者简介] 谭蔚锋, 博士, 讲师、主治医师。E-mail: twf1231@263.net; 冉荣征, 硕士, 住院医师。E-mail: keith440@163.com

△共同第一作者(Co-first authors)。

* 通信作者(Corresponding author)。Tel: 021-81875281, E-mail: jxq1225@sina.com

adenoma/carcinoma) (2.3%, 9/392), mucus-like bile duct adenoma/carcinoma (1.0%, 4/392), metastatic liver cancer with bile duct tumor thrombi (1.0%, 4/392), and bile duct stones (3.8%, 15/392). The proportions of misdiagnosis as liver cancer with hilar bile duct compression in the Group A and Group B were 9.4% (12/128) and 1.5% (4/264), respectively, and those as bile duct stone were 7.8% (10/128) and 1.9% (5/264), respectively ($P < 0.01$). **Conclusion** More knowledge on the HCCBDT clinical features, effective imaging examination methods, and more efforts on differential diagnosis with the similar diseases can reduce misdiagnosis of HCCBDT.

[Key words] hepatocellular carcinoma with bile duct tumor thrombi; diagnostic errors; differential diagnosis

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原发性肝癌伴胆管癌栓(hepatocellular carcinoma with bile duct tumor thrombi, HCCBDT)是原发性肝癌的一种亚型,临床表现与其他恶性胆管梗阻性疾病以及部分胆管内良性占位性疾病高度相似,误诊率高^[1]。我们于1993至2011年18年间收治HCCBDT患者392例,现将该392例患者临床特征及常易误诊的疾病类型作一回顾性分析,旨在探讨和总结HCCBDT的诊断与鉴别诊断要点,分析该病常易误诊的疾病类型,归纳误诊的主要原因。

1 资料和方法

1.1 一般资料 第二军医大学东方肝胆外科医院1993至2011年18年间收治HCCBDT患者392例,均经病理证实。患者年龄18~85岁,平均(49.7±12.6)岁,其中男性325例(82.9%),女性67例(17.1%)。主要的临床表现包括黄疸(65.6%, 257/392)、腹痛或者腹胀(47.7%, 187/392)、发热(12.2%, 48/392)、黑便(4.8%, 19/392)。甲胎蛋白(AFP) > 20 μg/L者282例(71.9%),乙型肝炎病毒感染患者355例(90.6%),丙型肝炎病毒感染患者4例(1.0%)。

1.2 研究方法 回顾患者的诊治过程,分析术前临床误诊(截至术前或者采取重大治疗措施前)的主要原因,归纳该病常易误诊的疾病类型。同时,按照不同时期术前进行分组:前期(1993年1月1日至2001年12月31日)128例(A组),后期(2002年1月1日至2011年12月31日)264例(B组),比较不同时期误诊率的差异以及误诊疾病类型的变化,总结HCCBDT诊断和鉴别诊断的要点。

1.3 统计学处理 应用SPSS 17.0软件进行统计学分析,采用 χ^2 检验(必要时采用Fisher确切概率法)或非参数检验比较误诊率以及误诊类型的差异。检验水平(α)为0.05。

2 结果

2.1 不同时期术前临床误诊率比较 总体术前临

床误诊率为16.6%(65/392),前期(A组)为30.5%(39/128),后期(B组)为9.8%(26/264),两组术前临床误诊率差异具有统计学意义($P < 0.001$,表1)。前期(A组)术前临床误诊的39例患者中,24例通过手术获得纠正,15例在采取ERCP支架置入术的过程中获得纠正;后期(B组)26例患者中,16例通过手术获得纠正,10例在采取ERCP支架置入术的过程中获得纠正。

表1 不同时期术前临床误诊率比较

Tab 1 Comparison of preoperative clinical misdiagnosis rates between two time-period groups

Group	N	n(%)		
		True	False	P value
A	128	89(69.5)	39(30.5)	<0.001
B	264	238(90.2)	26(9.8)	

Group A: Patients included from 1993 to 2001; Group B: Patients included from 2002 to 2011

2.2 不同时期检查类型比较 392例患者均行B超及CT/MRI检查。行ERCP/MRCP检查的患者前期(A组)为68.0%(87/128),后期(B组)为91.7%(242/264),差异有统计学意义($P < 0.001$,表2)。

表2 不同时期 ERCP/MRCP 检查率比较

Tab 2 Comparison of ERCP/MRCP examination rates between two time-period groups

Group	N	n(%)		P value
		Accepted	Not accepted	
A	128	87(68.0)	41(32.0)	<0.001
B	264	242(91.7)	22(8.3)	

ERCP: Endoscopic retrograde cholangiopancreatography; MRCP: Magnetic resonance cholangiopancreatography. Group A: Patients included from 1993 to 2001; Group B: Patients included from 2002 to 2011

2.3 不同检查方法误诊率比较 ERCP/MRCP的

误诊率在前期(A组)、后期(B组)及全程分别为8.0%、4.5%、5.5%,均低于B超误诊率(32.0%、24.2%、26.8%)及肝脏CT/MRI误诊率(43.0%、16.3%、25.0%),差异有统计学意义($P < 0.01$)。比较B超与肝脏CT/MRI误诊率,在前期(A组)及全程来看,均无统计学差异($P > 0.05$);而后期(B组)CT/MRI的误诊率低于B超误诊率,差异有统计学

意义($P < 0.05$)。比较前期(A组)和后期(B组)误诊率,B超前期(A组)和后期(B组)误诊率差异无统计学意义($P > 0.05$),ERCP/MRCP前期(A组)和后期(B组)误诊率差异无统计学意义($P > 0.05$),而肝脏CT/MRI前期(A组)误诊率高于后期(B组)误诊率,差异有统计学意义($P < 0.01$)。详见表3。

表3 不同检查方法误诊率比较

Tab 3 Comparison of misdiagnosis rates between different imaging examination methods

Group	n(%)					
	B-type ultrasound		CT/MRI		ERCP/MRCP	
	True	False	True	False	True	False
A	68.0(87/128)	32.0(41/128)**	57.0(73/128)	43.0(55/128)**	92.0(80/87)	8.0(7/87)
B	75.8(200/264)	24.2(64/264)**	83.7(221/264)	16.3(43/264)* ^{△▲▲}	95.5(231/242)	4.5(11/242)
Total	73.2(287/392)	26.8(105/392)**	75.0(294/392)	25.0(98/392)**	94.5(311/329)	5.5(18/329)

CT: Computed Tomography; MRI: Magnetic resonance imaging; ERCP: Endoscopic retrograde cholangiopancreatography; MRCP: Magnetic resonance cholangiopancreatography. Group A: Patients included from 1993 to 2001; Group B: Patients included from 2002 to 2011. * $P < 0.01$ vs ERCP/MRCP; [△] $P < 0.05$ vs B-type ultrasound; ^{▲▲} $P < 0.01$ vs Group A

2.4 常见的误诊疾病类型 常见的误诊疾病包括:肝癌伴肝门部胆管压迫(4.1%,16/392),肝门部胆管腺瘤/癌(4.3%,17/392),远端胆管腺瘤/癌(包括壶腹部腺瘤/癌)(2.3%,9/392),胆管内黏液状腺瘤/癌(1.0%,4/392),转移性肝癌伴胆管癌栓(2例患者既往有胃癌切除史,2例患者有结肠癌切除史)(1.0%,4/392),胆管结石(3.8%,15/392)。上述常

见误诊疾病前期(A组)及后期(B组)误诊率相比,肝癌伴肝门部胆管压迫分别为9.4%和1.5%,胆管结石为7.8%和1.9%,差异有统计学意义($P < 0.01$);而肝门部胆管腺瘤/癌、远端胆管腺瘤/癌(包括壶腹部腺瘤/癌)、胆管内黏液状腺瘤/癌、转移性肝癌伴胆管癌栓在前期(A组)和后期(B组)的误诊率相比差异无统计学意义($P > 0.05$)。详见表4。

表4 不同时期误诊疾病类型对比

Tab 4 Comparison of misdiagnosed disease types between two time-period groups

Name of misdiagnosed disease	n(%)		
	Group A (N=128)	Group B (N=264)	P value
Hepatocellular carcinoma with hilar bile duct compression	12(9.4)	4(1.5)	0.000 5
Hilar bile duct adenoma/carcinoma	8(6.2)	9(3.4)	0.197 6
Distal bile duct adenoma/carcinoma(including ampullary adenoma/carcinoma)	5(3.9)	4(1.5)	0.159 2
Mucus-like bile duct adenoma/carcinoma	2(1.6)	2(0.8)	0.599 5
Metastatic liver cancer with bile duct tumor thrombi(stomach/colon carcinoma)	2(1.6)	2(0.8)	0.599 5
Bile duct stones	10(7.8)	5(1.9)	0.008 6

Group A: Patients included from 1993 to 2001; Group B: Patients included from 2002 to 2011

3 讨论

原发性肝细胞癌不易侵犯胆管系统^[2],伴胆管癌栓者较少见^[3],该病与胆管原发性肿瘤或胆管炎症性疾病临床表现相似,易误诊为胆管癌、胆管结石、急性化脓性胆管炎等疾病。误诊可导致手术时机的延误,甚至导致治疗措施选择不当。例如:部

分误诊为胆管癌肝转移的病例,放弃了手术切除,转而采取姑息性的治疗方法^[4]。该病通过合适的治疗可以减轻症状、乃至达到治愈^[5-6],笔者前期研究亦提示:HCCBDT患者非手术治疗效果显著差于手术切除^[7]。因此,接诊该类患者时,需要进行仔细的鉴别诊断。近年来,随着影像学技术的发展及对该病的认识程度逐步提高,此病的误诊率有了一定的下

降^[8]。在本组资料中,后期比前期术前临床误诊率显著下降,前期(A组)误诊率为30.5%(39/128),后期(B组)误诊率为9.8%(26/264)($P < 0.01$),表明在HCCBDT的诊断上取得了明显进步。分析误诊率降低的原因发现,MRCP/ERCP的误诊率明显低于B超、肝脏CT/MRI或CT等检查手段,而后期MRCP/ERCP检查率较前期有明显提高,提示误诊率的降低与MRCP/ERCP等检查率提高有明显关系。ERCP诊断HCCBDT正确率高,但是其操作相关的并发症发生率高,可引发胆管癌栓断裂出血及胆道继发性感染^[9],并不适宜推广为HCCBDT术前的常规检查方法。MRCP具有无创的优势,并且其诊断正确率可以与ERCP媲美,所以近年来我们优先采用MRCP进行术前诊断,而ERCP更多应用于姑息性治疗,或者术前准备(鼻胆管置入胆道引流)。另一方面,本研究后期的肝脏CT/MRI的误诊率较前期明显降低,提示肝脏CT/MRI阅片水平的提高可能对于降低误诊率也起到了重要作用。

HCCBDT患者主要以皮肤、巩膜黄疸逐渐加深为首发症状,少量伴有腹痛、发热。CT及MRI等影像学检查表现为肝内占位性病变以及胆管内条索样软组织影^[10-11]。HCCBDT患者AFP可出现明显增高^[12],此时,误诊的可能性相对较小。但是,若AFP呈阴性,甚至同时伴有糖类抗原(CA)19-9升高,则较难与胆道系统的其他占位性疾病进行鉴别。本研究中误诊疾病具体类型主要包括肝癌伴肝门部胆管压迫、肝门部胆管腺瘤/癌、远端胆管腺瘤/癌(包括壶腹部腺瘤/癌)、胆管结石、胆管内黏液状腺瘤/癌、转移性肝癌伴胆管癌栓等几类疾病。要降低误诊率,必须对以上疾病特点有充分的认识。

对比本研究中前、后期误诊率差异,肝癌伴肝门部胆管压迫分别为9.4%和1.5%,胆管结石为7.8%和1.9%,差异有统计学意义($P < 0.01$)。表明后期对于肝癌伴肝门部胆管压迫、胆管结石等疾病的鉴别诊断水平提高。分析原因除MRCP/ERCP应用增多、CT/MRI阅片水平增高外,可能与临床上肝癌伴肝门部胆管压迫、胆管结石的特征性影像学表现有关。肝癌伴胆管压迫与HCCBDT都有肝癌原发病灶,同时都有胆管异常表现,若原发灶紧贴胆管,经验不足时容易混淆。区别在于肝癌伴胆管压迫时,远端胆管继发性扩张,而受压迫的胆管节段(多数为一侧受压),表现为偏心性充盈缺损影;而HCCBDT特点为梗阻平面的胆管以及远端胆管均显著扩张,胆管内癌栓形成的充盈缺损影较为对称。胆管癌栓B超下表现为絮状回声不伴声影,而胆管

结石表现为强回声伴声影,掌握以上特征,通常不易混淆癌栓和结石。但若肝内原发灶不明显或将肝内原发灶误认为胆源性肝脓肿,则易误诊为胆管内泥沙样结石(胆管内泥沙样结石在B超下可表现为絮状回声,后方声影不明显,与癌栓回声相似)。根据以下特征,有利于减少此类误诊:癌栓在MRI检查T₂加权或者水成像上,表现为略高信号(与周围正常肝组织相比),而胆管结石则表现为相对低信号。

对比肝门部胆管腺瘤/癌、远端胆管腺瘤/癌(包括壶腹部腺瘤/癌)、胆管内黏液状腺瘤/癌以及转移性肝癌伴胆管癌栓等疾病,后期误诊率虽较前期有所下降,但是差异无统计学意义($P > 0.05$)。其中肝门部胆管腺瘤/癌及远端胆管腺瘤/癌病例,临床上均表现为进行性无痛性黄疸,同时影像学检查可以提示肝门部胆管或者远端胆管内软组织影,可与HCCBDT混淆。但是,胆管腺瘤多数呈侵袭性生长,故其侵及的胆管壁表现出管壁增厚、形态僵硬的影像学特征。胆管腺瘤还具有另一个较为特征性的影像学表现,即其远端胆管扩张,而接近肝门部肿瘤的胆管,又具有向肿瘤内收缩、变窄的趋势。对比胆管癌栓可以发现,由于其在胆管内呈堆积性生长,极少蔓延性浸润胆管壁组织,所以表现为胆管癌栓所分布的胆管呈纺锤形膨大(膨胀性扩张),胆管壁无明显增厚,并且过渡平滑(图1)。根据以上特点,不易误诊。只有原发灶不明显、胆管内癌栓体积小并且AFP呈阴性时,才难以与胆管腺瘤或者非侵袭性生长的胆管腺瘤进行区别,此时往往只有通过手术探查以及病理检查才能明确诊断。

HCCBDT患者既往有胃癌、结肠癌等其他肿瘤切除病史,并且AFP呈阴性,则易误诊为转移性肝癌伴胆管癌栓,其鉴别重点在于肝内病灶增强后的影像学表现。原发性肝癌肝内病灶增强后造影剂多呈“快进快出”的典型表现,而转移性肝癌肝内病灶强化后往往表现为“牛眼征”。对于肝内病灶强化后影像学表现不典型者,只有通过病理诊断才能明确。

胆管内黏液状腺瘤/癌是胆管肿瘤中罕见的病理类型,来源于胆管腺上皮,以分泌大量黏液为特点。黏液可引起肝内外胆管的梗阻以及继发性的扩张。术前B超可以提示胆管内占位呈絮状回声,CT、MRI提示肝内外胆管呈囊状扩张,局部胆管壁稍增厚。MRCP水成像提示肝内外胆管囊状扩张,病变一侧胆管扩张更明显,其扩张的胆管内无明显充盈缺损影,原发灶不明且胆管内癌栓较小的HCCBDT患者与该病具有部分共同特点,临床上易混淆,需要加强鉴别。

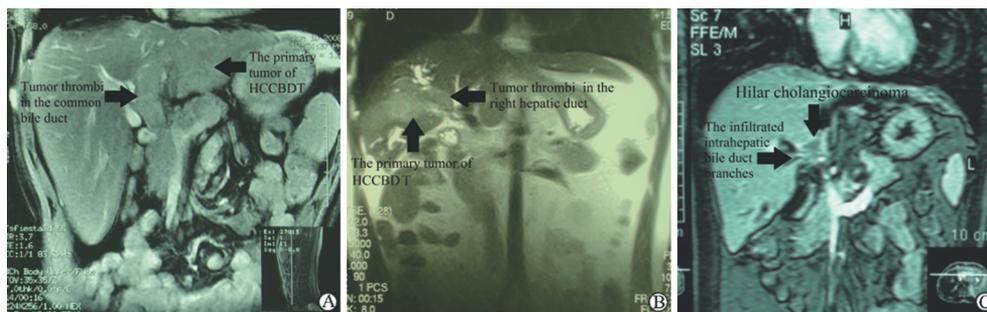


图1 HCCBDT与肝门部胆管癌 MRCP影像学对比

Fig 1 Comparison of MRCP imaging features between HCCBDT and hilar cholangiocarcinoma

HCCBDT: Hepatocellular carcinoma with bile duct tumor thrombi; MRCP: Magnetic resonance cholangiopancreatography. A: The primary tumor of HCCBDT located in the left lobe of the liver, and the bile duct tumor thrombi continued as the primary tumor extending from the left branch of the bile duct to the common bile duct. Tumor thrombi showed expansive growth in the bile duct, with the signal slightly higher than those of the surrounding normal liver tissues; the transition of the bile duct wall was smooth. B: The primary tumor of HCCBDT located in the right lobe; the bile duct tumor thrombi, which continued with the primary tumor, mainly located in the right hepatic duct and had an expansive growth, with the signal slightly higher than those of the surrounding normal liver tissues; the transition of bile duct wall was smooth. C: The hilar cholangiocarcinoma infiltrated the surrounding bile duct branches, and the transition of bile duct wall became stiff, with the distal bile duct dilated, but the nearby bile duct branches were narrowed toward the hilar bile duct tumor

综上所述,提高对 HCCBDT 临床特征的认识水平,合理应用影像学检查手段并掌握 HCCBDT 的影像特点,加强与相似疾病的鉴别诊断,有助于降低 HCCBDT 误诊率。

4 利益冲突

所有作者声明本文不涉及任何利益冲突。

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