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· 专题研究 ·

肝门部胆管癌行全胰腺十二指肠联合肝脏切除、 异体肝移植术1例报告并文献复习（附视频）

郭宇¹, 窦剑², 刘军桂¹, 曹经琳², 刘翔¹, 金奎¹, 雷磊¹, 赵文利¹, 段伟宏¹

(1. 中国人民解放军火箭军特色医学中心 肝胆外科, 北京 100088; 2. 河北医科大学第三附属医院 肝胆外科, 河北 石家庄 050051)

摘要

背景与目的: 肝门部胆管癌是指发生在左右肝管、汇合部以及肝总管上段, 起源于胆管上皮细胞的一种恶性肿瘤。由于肝门区结构复杂, 肿瘤与门静脉、肝动脉等紧邻, 故肝门部胆管癌容易出现血管、神经侵犯以及淋巴结转移; 加之位置隐匿, 早期缺乏特异性症状, 患者往往因出现黄疸等晚期症状才会就诊。目前手术切除仍是改善预后的主要有效治疗方式, 但对肝胆外科医生而言, 肝门部胆管癌的外科治疗仍然是最为困难的挑战之一。笔者报告1例肝门部胆管癌侵犯胃、十二指肠、胰腺的患者施行全胰腺十二指肠联合全肝脏切除、异体肝移植术的治疗经过, 以为该病的诊疗提供更多的参考依据。

方法: 回顾分析中国人民解放军火箭军特色医学中心与河北医科大学第三附属医院共同完成治疗的1例肝门部胆管癌病例的临床资料, 并复习相关文献, 总结相关的经验教训。

结果: 患者为51岁男性, 有乙型肝炎病史, 因腹腔积液就诊。剖腹探查(肿块为涉及肝脏、胰头、肝十二指肠韧带的一个完整无法分离的区域)与PET/CT检查(肝右叶稍低密度伴FDG代谢增高, 伴门静脉主干及右支累及可能, 未见明显远处转移)均考虑恶性肿瘤, 但术前穿刺活检未能诊断。经讨论后对患者实施了全胰腺十二指肠联合肝脏切除与异体肝移植术(术前CT提示门静脉、肝动脉已闭塞或肿瘤侵犯, 因此, 术中采用肠系膜上静脉与供体门静脉吻合, 用脾动脉翻转后与供体的肝固有动脉吻合)。患者术后恢复顺利, 术后病理示: 肝门部中-高分化胆管癌, 侵犯十二指肠及胃组织, 侵犯胰腺, 多处神经侵犯, 未见明确脉管癌栓, 切缘未见癌累及。术后8个月因消化道出血、感染死亡。

结论: 针对肝门部胆管癌的治疗, 手术切除仍是其主要治疗方式, 对于不能行根治性切除的肝门部胆管癌患者, 肝移植是一个可以实现R₀切除, 提供潜在治愈机会的选择。然而, 目前联合全胰腺十二指肠切除的病例报道仍然较少, 该病例的分析与总结将有助于今后更多的探索与实践。

关键词

Klatskin 肿瘤; 胰十二指肠切除术; 肝切除术; 肝移植

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作者简介: 郭宇, 中国人民解放军火箭军特色医学中心主治医师, 主要从事肝胆胰疾病外科治疗方面的研究(窦剑为共同第一作者)。

通信作者: 段伟宏, Email: changxinzhong@163.com

Simultaneous total pancreaticoduodenectomy and total hepatectomy with orthotopic liver transplantation for hilar cholangiocarcinoma: a case report and literature review(with video)

GUO Yu¹, DOU Jian², LIU Jungui¹, CAO Jinglin², LIU Xiang¹, JIN Kui¹, LEI Lei¹, ZHAO Wenli¹, DUAN Weihong¹

(1. Department of Hepatobiliary Surgery, PLA Rocket Force Characteristic Medical Center, Beijing 100088, China; 2. Department of Hepatobiliary Surgery, Hebei Medical University Third Hospital, Shijiazhuang 050051, China)

Abstract

Background and Aims: Hilar cholangiocarcinoma refer to a malignant tumor originating from the epithelial cells involving the left, right hepatic ducts, biliary confluence or the upper segment of the common hepatic duct. Due to the complex anatomy of the hilar region and its proximity to major vessels such as the portal vein and hepatic artery, this tumor is prone to vascular or neural invasion, and lymph node metastasis. Additionally, its inconspicuous location and lack of early specific symptoms often result in patients seeking medical treatment only when advanced symptoms like jaundice appear. Currently, surgical resection remains the primary effective treatment for improving prognosis. However, surgical management of hilar cholangiocarcinoma remains one of the most challenging tasks for hepatobiliary surgeons. Here, the authors report a case of hilar cholangiocarcinoma invading the stomach, duodenum, and pancreas, treated with total pancreatectomy and duodenectomy combined with total hepatectomy and orthotopic liver transplantation, aiming to provide further reference for the diagnosis and treatment of this disease.

Methods: The clinical data of a case of hilar cholangiocarcinoma, collaboratively treated by the PLA Rocket Force Characteristic Medical Center and Hebei Medical University Third Hospital were retrospectively analyzed. Relevant literature was reviewed and pertinent experiences and lessons learned from this case were summarized.

Results: The patient, a 51-year-old male with a history of hepatitis B, sought medical attention due to abdominal ascites. Abdominal exploration (revealing a tumor involving an inseparable region of the liver, pancreatic head, and hepatoduodenal ligament) and PET-CT scan (indicating a slightly low-density lesion with increased FDG metabolism in the right lobe of the liver, possibly involving the main portal vein and right branch, with no apparent distant metastasis) suggested a malignant tumor, but preoperative biopsy failed to provide a definitive diagnosis. After discussion, the patient underwent total pancreatectomy and duodenectomy combined with total hepatectomy and orthotopic liver transplantation (anastomosing the superior mesenteric vein with the donor portal vein and anastomosing the inverted splenic artery with the proper hepatic artery of the donor, due to preoperative CT indicating occlusion or tumor invasion of the portal vein and hepatic artery). The postoperative recovery was uneventful, and the pathology revealed moderately to well-differentiated cholangiocarcinoma of the hepatic hilar region involving the duodenum, stomach, and pancreas, with multiple neural invasions, no clear vascular tumor thrombus, and margins free of cancer. The patient died of gastrointestinal bleeding and infection 8 months after surgery.

Conclusion: Surgical resection remains the primary treatment for hilar cholangiocarcinoma. For patients ineligible for radical resection, liver transplantation is an option that can achieve R₀ resection, providing a potential opportunity for cure. However, there are currently still relatively few reported cases of

combined total pancreaticoduodenectomy. The analysis and summary of this case will contribute to further exploration and practice in the future.

Key words Klatskin Tumor; Pancreaticoduodenectomy; Hepatectomy; Liver Transplantation

CLC number: R735.7

胆管癌是胆道最常见的原发性肿瘤，占所有胃肠道恶性肿瘤3%^[1]，其起病隐匿，后期进展迅速，通常向上侵犯肝门部及肝内胆管，向下侵犯肝十二指肠韧带及远端胆管，造成梗阻性黄疸等多种临床表现。1965年美国医生Gerald Klatskin最开始在《美国医学杂志》上对胆管分叉部腺癌的病例及临床特点进行阐述，故肝门部胆管癌又叫Klatskin瘤^[2]。在胆管癌中，肝门部胆管癌是较多见且治疗相对困难的，占比高达58%~75%，好发于60岁以上老年人群，其男性患者略多于女性患者^[3]。由于肝门区结构复杂，肿瘤与门静脉、肝动脉等紧邻，故肝门部胆管癌容易出现血管、神经侵犯以及淋巴结转移；加之位置隐匿，早期缺乏特异性症状，患者往往因出现黄疸等晚期症状才会就诊，因此，肝门部胆管癌患者的根治性手术切除率较低，手术风险较高，预后较差^[4-5]。但手术切除仍是唯一可能带来治愈的治疗方式^[6]。近期，笔者为1例肝门部胆管癌侵犯胃、十二指肠、胰腺的患者施行了全胰腺十二指肠联合全肝脏切除、异体肝移植术，现报告如下。

1 临床资料

1.1 病史情况

患者 男，51岁，既往乙型肝炎病史20年，未系统治疗。2020年6月因发现腹腔积液先后就诊于多家医院，影像学检查提示肝硬化。因无法最终明确诊断，后于当地医院以“肝炎、肝硬化”保守治疗，效果不佳。2020年7月，患者由于腹胀加重，于当地医院就诊，为进一步明确诊断行剖腹探查术，术中见右肝萎缩、肝十二指肠韧带挛缩，质地硬，与周围组织无明显分界，腹腔内可见淡黄色腹腔积液，因无法明确是否为恶性肿瘤，也难以获取组织活检（病变位置深在），遂关腹。当时考虑“恶性可能性大”，无法进一步明确，单纯切除肝脏或不可行，因为胰头、肝十二指肠韧带与肝脏成为一体，此时手术处理为“全或无”

方式，即：要么行肝脏、胰腺整体切除，要么手术终止。

1.2 术前情况

患者2020年9月为求进一步诊治就诊于中国人民解放军火箭军特色医学中心肝胆外科，行PET/CT检查提示：肝右叶稍低密度伴FDG代谢增高，考虑恶性肿瘤，伴门静脉主干及右支累及可能，余未见明显转移。腹部CT示（图1）：肝门部胆管、肝右叶胆管、胆总管壁增厚且强化，门静脉海绵样变，肝右叶异常密度，腹腔及腹膜后多发肿大淋巴结。为进一步明确诊断，2020年9月9日于CT引导下对肝脏可疑区域行细针穿刺活检（10针），病理回报为肝脏坏死组织，未见肿瘤细胞。此时患者一般状况逐渐恶化，腹水增多，黄疸逐渐加重（总胆红素最高391.45 μmol/L），后行经皮经肝胆道穿刺减黄，效果不佳，同时出现进食困难。鉴于PET/CT未发现远处转移，患者较年轻且手术意愿强烈，经科室讨论后尝试为患者施行“全胰腺十二指肠联合全肝脏切除、异体肝移植术”。手术难度主要在以下几点：（1）如果为恶性肿瘤，则其侵犯范围很广，包括肝脏、肝十二指肠韧带、胰腺直至周围血管；（2）门静脉CT上未显示，考虑闭塞，导致腹腔大量积液，同时大量侧支循环建立，术中易出血；（3）肝总动脉、肝固有动脉在CT上并不清楚，考虑与肿瘤侵犯有关。鉴于此，如果施行全肝联合全胰腺切除、异体肝移植，那么对应的手术方式为：（1）全胰腺十二指肠、肝脏、远端胃、脾脏整体切除，肝十二指肠韧带内结构整体随肿瘤切除；（2）术中预先保留脾动脉，避免损伤，移植肝脏时将其翻转至右侧，远端与供体肝脏的肝动脉吻合；（3）在门静脉、脾静脉、肠系膜上静脉汇合处下方将门静脉、脾静脉整体随肿瘤切除，保留肠系膜上静脉与供体的门静脉吻合（注意此时在供体获取时特别多留取较长门静脉以备吻合）。后与家属充分沟通、交流，充分完善术前准备后于2020年10月8日在河北医科大学第三附属医院为患者施行“全胰腺十二指肠联合全肝

脏切除、异体肝移植术”。供者为50岁男性, ABO血型O型(Rh阳性), BMI 25.95 kg/m², 死因为脑出血。捐献患者家属在红十字会见证下签署相关

知情同意书, 经河北医科大学第三医院医学伦理委员会审批通过, 资料上报中国人体器官分配与共享计算机系统。

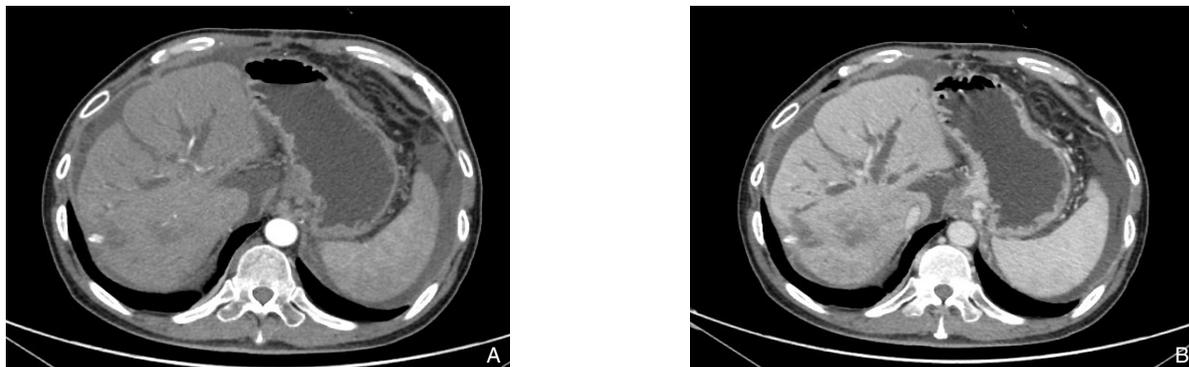


图1 术前腹部CT扫描图片 A: 动脉期图像见肝右叶见斑片状低密度, 边界欠清, 呈轻度强化; B: 静脉期图像见肝门部胆管显示不清, 右肝管强化, 门静脉受累, 肝内胆管扩张

Figure 1 Preoperative abdominal CT scan images A: Arterial phase image showing patchy low density in the right lobe of the liver with indistinct borders, with mild enhancement; B: Venous phase image showing unclear visualization of the hilar bile ducts, enhancement of the right hepatic duct, involvement of the portal vein, and dilation of intrahepatic bile ducts

1.3 手术过程

剖腹探查, 腹腔内大量腹水(3 000 mL), 无腹膜转移结节, 大网膜及周围有大量曲张的静脉, 肝脏、肝十二指肠韧带、胰头等触之质地硬, 无法分离。根据术前设计, 准备行全肝联合全胰腺整体的切除。从右侧开始, 游离肝脏右三角韧带、右镰状韧带、肝十二指肠韧带右侧, Kocher手法游离十二指肠直至显露肠系膜上静脉右侧。再从左侧开始, 游离肝脏左三角韧带、左镰状韧带、肝十二指肠左侧分离, 离断远端胃, 在腹腔干发出脾动脉处向左游离出脾动脉并注意保护。游离脾脏, 连同胰腺尾部一起翻起, 在脾门处将脾动脉离断, 保留全程脾动脉。在小肠系膜处游离肠系膜上动脉, 经动脉入路离断胰十二指肠下动脉及胰十二指肠下静脉, 使胰腺与肠系膜上动脉彻底分离。将肝脏上方下腔静脉彻底分离, 再将左、右肾静脉上方的肝下下腔静脉彻底分离后, 准备切除肝脏及周围脏器。切除手术: 在腹腔干发出

肝总动脉后将肝总动脉离断、缝扎; 在脾静脉汇入门静脉处下方1 cm处离断肠系膜上静脉, 远端以血管夹夹闭以待吻合; 分别夹闭肝上下腔静脉及肝下下腔静脉后离断, 游离下腔静脉后方的细小分支血管, 整体移除全肝脏、全胰腺十二指肠、远端胃、脾脏、肝十二指肠韧带、肝总动脉及门静脉(图2A-B)。在完成全肝联合全胰腺整体切除之后, 上腹部胆管癌周围的12b、12p、8a、8p等淋巴结均随同标本整体移出体外, 规范清扫腹腔干周围的第9组淋巴结。清扫范围比单纯肝门部胆管癌或胰腺癌的清扫范围略广一些。肝脏移植: 将灌注后的供肝放入腹腔, 首先完成肝上下腔静脉及肝下下腔静脉的吻合, 接着将供体门静脉与受体的肠系膜上静脉吻合(图2C), 开放血流通道, 肝脏颜色逐渐红润。将脾动脉翻转后与受体的肝固有动脉相吻合(图2D)。最后行胆肠、胃肠吻合。手术过程见视频1。

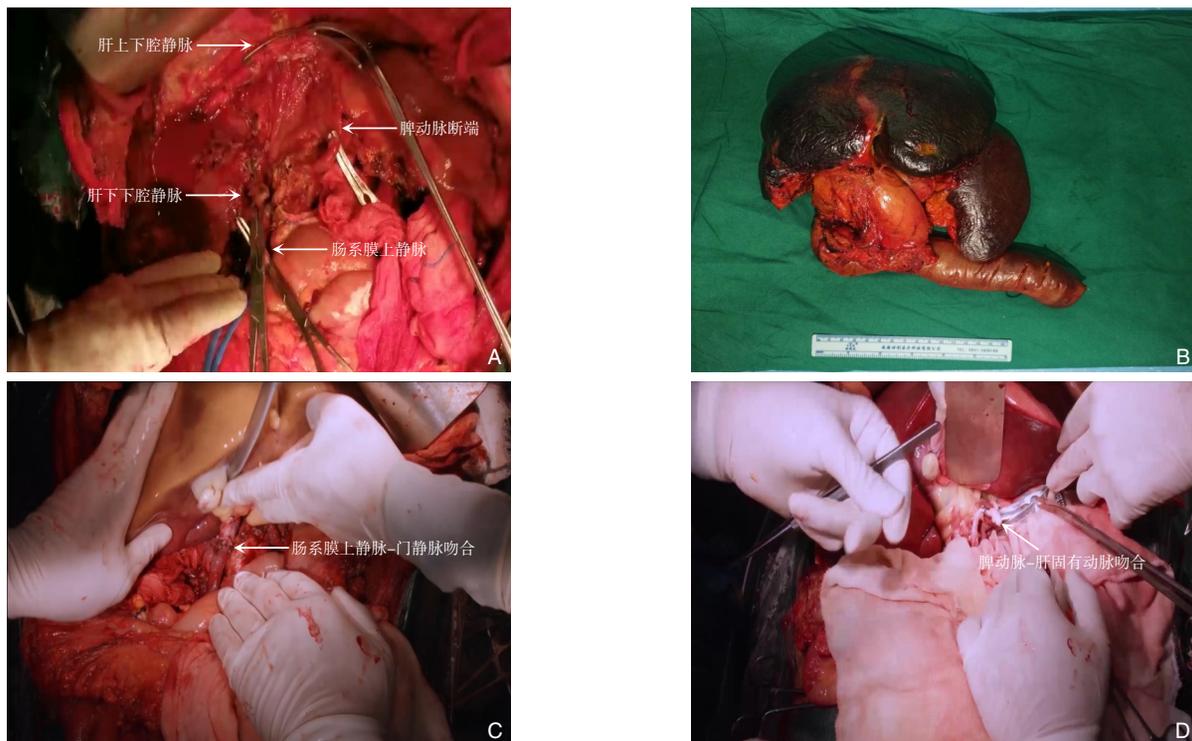


图2 术中图片 A: 全胰腺十二指肠、肝脏、脾、远端胃移除后; B: 切除的全胰腺十二指肠、肝脏、脾脏、远端胃标本; C: 肠系膜上静脉与门静脉吻合; D: 脾动脉与供肝固有动脉吻合

Figure 2 Intraoperative images A: After removal of the entire pancreas, duodenum, liver, spleen, and distal stomach; B: Resected specimen of the entire pancreas, duodenum, liver, spleen, and distal stomach; C: Anastomosis of the superior mesenteric vein with the portal vein; D: Anastomosis of the splenic artery with the proper hepatic artery of the graft



视频1 手术过程

Video 1 Operation procedure

扫描至移动设备观看手术视频:



<http://www.zpwz.net/zgptwkzz/article/html/pw230589>

行胃镜检查示胃肠吻合口有一小溃疡引起动脉出血, 镜下止血成功。在全胰腺切除之后, 根据以往的经验, 由于胰岛素和胰高血糖素均去除了, 激素系统的紊乱会导致胃泌素等引起胃酸产生的酸性物质分泌异常增加, 容易导致残余胃体吻合口附近顽固性溃疡发生, 而该患者又必须使用他克莫司及激素进行后续抗排斥治疗, 这也加重了吻合口溃疡发生的几率和出血的风险, 最后的出血应该也考虑是消化性溃疡引起的出血可能。术后病理: 肝门部中-高分化胆管癌, 侵犯十二指肠及胃组织, 侵犯胰腺, 见多处神经侵犯, 未见明确脉管癌栓, 切缘未见癌。术后因患者进食一般, 营养较差, 未行放化疗。术后8个月因消化道出血、感染死亡。

2 结果

患者术后常规采用他克莫司及激素进行抗排斥治疗。术后血糖波动在 2~27 mmol/L, 调整胰岛素用量后有所好转。患者术后出现上消化道出血,

3 讨论

目前, 手术切除仍然是肝门部胆管癌患者获得长期生存的首选治疗方式。而 R₀ 切除是影响肝门部胆管癌患者术后生存的重要因素之一, 同时

也决定了手术范围的大小^[7-8]。假如手术未能达到R₀切除,中位生存时间<10个月^[9],故手术切除是提高生存期最有效、最主要的治疗手段。鉴于R₀切除是影响肝门部胆管癌术后长期生存率的重要因素,而肝移植可以实现完全的R₀切除,提供潜在治愈机会的选择,因此,肝移植作为一种新的治疗措施逐渐被肝胆外科医师接受^[10-11]。在肝移植领域的早期,进行肝移植的肝门部胆管癌患者5年生存率为28%,肿瘤复发率高达51%,因此肝门部胆管癌之前被认为是肝移植的绝对禁忌^[12-14]。直到后续研究优化了肝门部胆管癌的肝移植适应证和手术方案,提出了严格的选择标准,肝门部胆管癌肝移植的预后和生存率才得到显著提高^[15]。德国汉诺威大学Pichlmayr等^[16]认为符合以下纳入标准的肝门部胆管癌患者行肝移植治疗是有效的:(1)剖腹探查证实无法切除,已确诊为国际抗癌联合会(Union for International Cancer Control, UICC) II期;(2)因肿瘤浸润等原因只能行R₁或R₂切除;(3)切除后肝内局部复发者。后来Klempnauer等^[17]统计了32例肝门部胆管癌患者,施行肝移植治疗的患者肿瘤切除率已达50%,表明该标准是有效的,但是仍然需要多中心、大样本量的研究。后来美国梅奥诊所提出新辅助治疗后再进行肝移植的治疗方案^[18]。在严格的肝移植标准下5年生存

率达到82%,明显优于根治性手术切除组。国内专家就肝门部胆管癌的肝移植治疗也提出了《肝门部胆管癌诊断和治疗指南(2013版)》^[19-20]:(1)肿瘤局限于肝内而采用常规手术方法不能将之切除,或患者合并硬化性胆管炎或肝功能失代偿;(2)无淋巴结转移、神经浸润或肝外远处转移。在满足上述两条标准的情况下才可以行肝移植术。中山大学一项纳入676例肝门部胆管癌病例的荟萃分析^[21]显示,肝移植与根治性切除对于肝门部胆管癌的术后1、3、5年的生存率影响无明显差异,但肝移植的病例复发率更低,远期生存要优于根治性切除组;尤其对于不可切除的肝门部胆管癌,肝移植要明显优于根治性切除。

复习相关文献,首先以“肝移植”“胰头十二指肠切除术”“肝门部胆管癌”“全胰腺切除”等作为关键词在中国知网检索相关中文文献,未发现全胰腺十二指肠切除联合肝移植的相关文献,检索出的文献均为胰头十二指肠切除联合肝移植。继续在MEDLINE数据库检索相关英文文献,以“Hilar Cholangiocarcinoma”“Liver Transplantation”“Pancreatico-duodenectomy”“Total Pancreatico-duodenectomy”作为关键词检索,检索出2篇全胰腺十二指肠切除联合肝移植病例文献(表1)。

表1 胰十二指肠切除联合肝移植相关文献统计

Table 1 Literature on pancreaticoduodenectomy combined with liver transplantation

文献作者	病例数	疾病	手术方式	生存时间(截至发稿)
黄建钊,等 ^[22]	1	肝门部胆管癌	胰头十二指肠切除联合原位肝移植	12个月
周天保,等 ^[23]	1	肝门部胆管癌	胰头十二指肠切除联合原位肝移植	12个月
何晓顺,等 ^[24]	1	肝门部胆管癌伴肝转移、胰头局部侵犯	胰头十二指肠切除联合原位肝移植	11个月
彭承宏,等 ^[25]	1	十二指肠乳头癌伴肝转移	胰头十二指肠切除联合背驮式肝移植	8个月
	1	胰头癌伴肝转移	胰头十二指肠切除联合原位肝移植	15个月
	1	胰腺癌伴肝转移	胰头十二指肠切除联合原位肝移植	4个月
Namgoong,等 ^[26]	1	胰母细胞瘤	全胰腺切除联合活体肝移植	7年
Dhupar,等 ^[27]	1	胰腺神经内分泌肿瘤	全胰腺十二指肠切除联合原位肝移植	2年
	1	胰腺神经内分泌肿瘤	全胰腺切除联合原位肝移植	8年
	1	胰腺神经内分泌肿瘤	全胰腺切除联合原位肝移植	16年
	1	壶腹周围癌	全胰腺十二指肠切除联合原位肝移植	9年

通过对该病例的分析和总结及文献复习,笔者认为有许多值得进一步思考的问题。首先,对于该病例,在选择手术方式时有以下几点考虑:(1)虽然术前高度怀疑恶性肿瘤,但是不能明确,PET/CT提示局部有高代谢,但多次活检均为阴性;

(2)当时也怀疑是自身免疫相关疾病,并做了相关检测,但结果均为阴性;(3)该病例曾行剖腹探查术,术中证实肿块为一个完整的、无法分离的区域,手术要么行彻底的根治,要么什么也不能做,类似“全或无”的手术;(4)在使用了所有的检查

及常规的治疗方式后, 针对患者后期3 000~3 500 mL/d的腹水引流, 总胆红素最高391.45 $\mu\text{mol/L}$ 的情况, 在详细告知患者及其家属各种手术风险的前提下, 提出这样的手术方式及设计是一种迫不得已、相对积极的处理方案; (5) 针对术前讨论提出的门静脉、肝动脉均已闭塞, 很难进行供体-受体血管吻合的问题, 笔者结合以往胰腺癌侵犯门静脉-肠系膜上静脉、肝总动脉的经验, 提出可以用肠系膜上静脉同供体门静脉吻合, 以脾动脉翻转后与供体的肝固有动脉吻合, 解决肝脏的血供问题^[28-31]。术中及术后证实是可行的。其次, 该病例的成功经验在于: 只有采用全肝联合全胰腺切除的方法才可以完整地切除肿瘤, 利用供体门静脉与受体肠系膜上静脉吻合, 供体肝固有动脉与受体脾动脉吻合, 避开受侵犯的门静脉、肝总动脉, 可以最大程度达到R₀切除效果, 而且也能充分保障肝脏的供血。在患者术前一般状况差、生命进入倒计时的情况下接受这种手术, 其恢复的风险较大, 但术后相当一段时间内, 患者没有出现吻合口瘘, 供肝存活良好, 精神状态比较理想。但患者术后仅存活8个月, 在没有肿瘤复发的证据下, 消化道出血及营养不良没有及时处理, 使患者在贫血、消耗情况下, 逐渐衰竭, 最终死亡。患者术后先后在3家医院就诊, 治疗不连贯、不成体系化, 使得预后存活时间未达到令人满意的效果。

总之, 肝门部胆管癌患者常常伴有区域或远处淋巴结的转移, 虽然也有专家通过联合肝移植和胰十二指肠切除术治疗肝门部胆管癌, 但是效果并不理想, 风险较大, 尚需谨慎^[32-34]。该病例由于手术方式的选择相对激进, 肝脏移植过程中血管吻合方式比较少见, 创伤比较大, 术后生存时间仅8个月, 必然会带来学术上的争议, 笔者也对此进行了回顾与反思, 并希望同行给予更多的建议。

利益冲突: 所有作者均声明不存在利益冲突。

作者贡献声明: 郭宇、窦剑、刘军桂是文章的主要撰写人, 完成相关文献资料的收集和分析及文章初稿的写作; 段伟宏、窦剑、刘军桂、曹经琳、刘翔、金奎、雷磊、赵文利参与手术及文献资料的分析、整理; 段伟宏指导论文写作和修改。全体作者都阅读并同意最终的文本。

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