

原发性肝透明细胞癌影像学及临床分析

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摘要 目的:探讨原发性肝细胞癌(PCCCL)的影像学及临床病理等特点,提高对肝透明细胞癌的认识,早期确诊、早期治疗、改善预后等,以避免临床误诊,并评价PCCCL的预后比例及疗效。方法:回顾性分析了2009年至2010年我院肿瘤科收治的3例肝透明细胞癌患者的临床资料、影像学资料,以及临床治疗和随访情况。结果:3例均为男性,2例行氩氦刀靶向消融治疗,1例行CT引导下射频消融治疗,术后随访半年2例过世,1例生存。结论:原发性肝细胞癌透明细胞型早期诊断尤为重要,及时手术切除及消融治疗是取得较好疗效的关键。

关键词 透明细胞癌;肝肿瘤;诊断;治疗;预后

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Primary Clear Cell Carcinoma of Liver: A Report of 3 Cases and A Review of Literature

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ABSTRACT Objective: To improve the awareness of the primary clear cell carcinoma of liver, to avoid misdiagnosis, early diagnosis, treatment and improve prognosis. **Methods:** Retrospective analysis of the 2009-2010 oncology in our hospital were treated three cases of clear cell carcinoma of liver in patients with clinical data, treatment and follow up the situation. **Results:** Three patients were males, two of them did argon-helium cryoablation, one did CT-guided radio-frequency ablation, Postoperative followed up for six months only one case is survival. **Conclusions:** Early diagnosis of the primary clear cell carcinoma of liver is particularly important. Timely, surgical resection and ablation therapy is the key to achieve better effect.

Key words: Clear cell carcinoma; Liver carcinoma; Diagnosis; Treatment; Prognosis

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原发性肝细胞癌透明型(Primary clear cell carcinoma of liver, PCCCL)是肝细胞癌的一种特殊病理类型,临床较少见,据统计其发病率约占肝细胞癌的10%^[1-3]。临床表现无特异性,术前诊断困难,明确诊断需病理学检查,手术切除可取得较好疗效。

1 临床资料

例1男,62岁,HBsAg阳性13年,2010年1月无诱因出现肝区疼痛,无纳差、腹胀、乏力、体重减轻等不适,化验血常规HGB 119g/L,余项正常,肾功、电解质正常,AFP阴性。心电图正常。CT考虑肝癌伴门脉癌栓。MRI示肝右叶巨块含脂质占位性病变,考虑肝癌伴瘤内出血,门脉右支癌栓形成(见图1-4)。于2010年1月22日行B超引导下穿刺活检,同时行氩氦刀靶向消融治疗。病理:肝脏透明细胞癌,低度分化。免疫组化:HBsAg(+),HBcAg(-),CD34(+),Ki67>30%,CK8(+),Hepa(+),CK7/CK19(-),a-SMA(+).术后15天出院。术后随访半年病人过世。

例2男,58岁,HBsAg阳性3年。2010年1月体检,腹部B超发现肝脏有约1cm低回声区,患者既往体健,无不适。入院

查血常规中白细胞、血小板较低,尿常规及便常规正常,乙肝五项HBsAg、HbeAb、抗HBc阳性,肿瘤标志物筛查均阴性,生化指标基本正常、肾功能、血糖、血脂、电解质均正常,AFP 8ng/ml。MRI示肝右叶后上段占位性病变(见图5-7)。于2010年3月15日行CT引导下穿刺活检,同时行射频消融治疗。病理:肝脏恶性肿瘤,考虑为肝脏透明细胞癌,中度分化。免疫组化:HBsAg(+),HBcAg(+),CD34(+),Hepa(+),Ki67 16%。术后12天出院,六个月后复查腹部MRI病灶凝固坏死完全,随访至今仍生存。

例3男,44岁,2009年2月出现肝区疼痛明显,纳差、肝区不适等消化道症状,入院查血常规正常,HBsAg阳性,肝功:ALT 57U/L、AST 57U/L,余正常,肾功、血糖、电解质均正常,AFP阴性,患者Child-Pugh分级为A级,CT示肝癌并肝内转移,动脉-门脉瘘,及门脉癌栓形成(见图8-9)。于2009年5月18日行B超引导下穿刺活检,同时行氩氦刀靶向消融治疗。病理:肝脏透明细胞癌。术后15天出院。术后随访半年病人过世。

2 讨论

2.1 原发性肝细胞癌的发生

原发性肝细胞癌是我国常见的恶性肿瘤之一,近年来世界各地肝癌发病率有上升趋势。肝细胞癌(HCC)为原发性肝癌中

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最常见的一种细胞类型。HCC 往往是在慢性肝病的背景下这些发展而来的,日本学者报道^[4]77.4%和 62.6%的肝癌病例分别与慢性肝炎和肝硬化有关,在病理组织学诊断中,只有 7.6%的肝癌病例为正常肝背景,此外,乙型肝炎病毒(HBV)或丙型肝炎病毒(HCV)抗原阳性所致的肝硬化占肝硬化病例的 80%,其他原因包括原发性胆汁性肝硬化(PBC)、自身免疫性肝炎、酒

精性肝硬化、纳什(NASH)和布加综合征(BCS)。近年来由于肝细胞特异性抗体 Hep Par 1 的面世,以及对 CD34 和细胞角蛋白(CK)19 等标志物组合使用水平的提高,使得许多少见形态的 HCC 得以明确诊断^[5-7]。本文对其中之一原发性肝脏透明细胞癌进行报道。

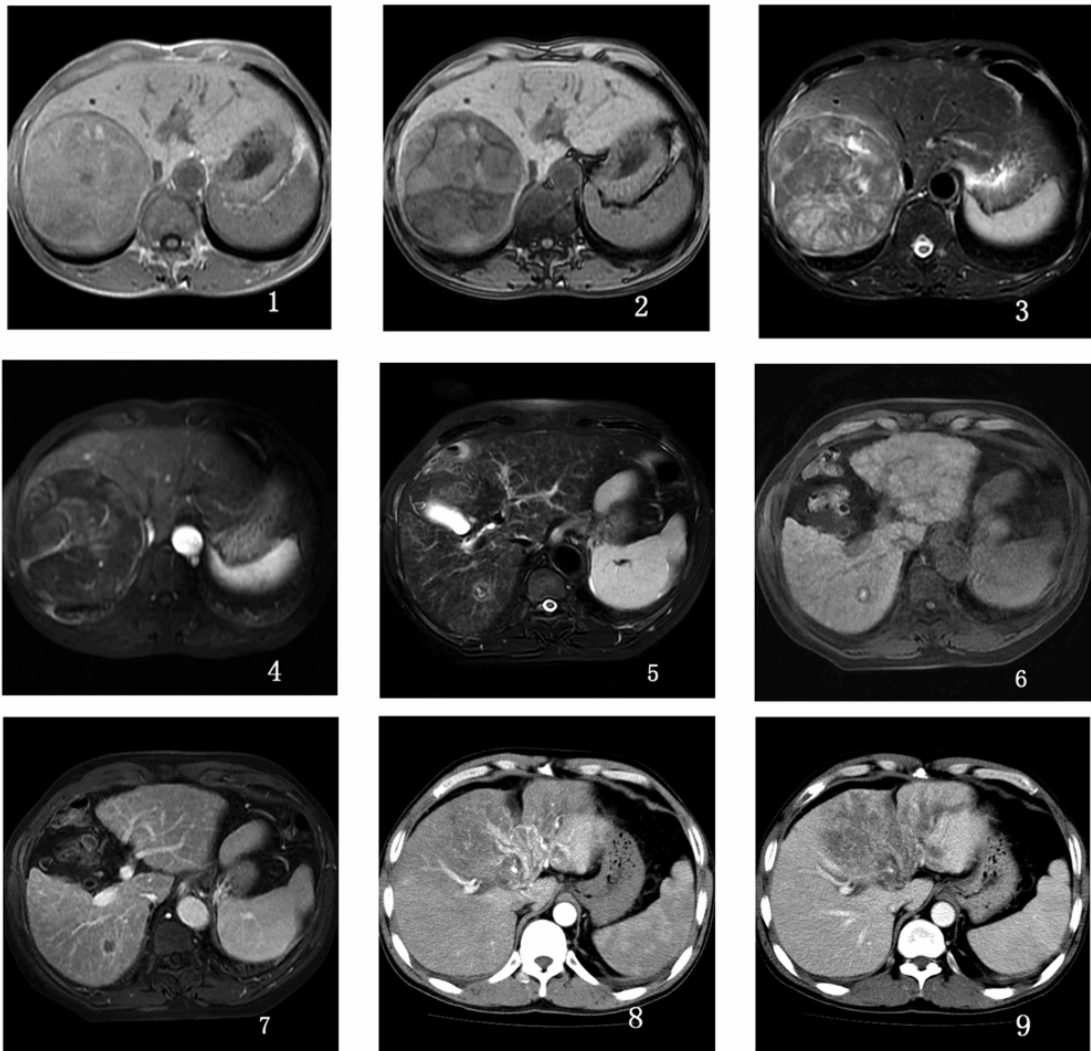


图 1-2 MR T1WI 双回波序列: 图 1 正相位病灶呈不均匀稍低信号, 其内见斑片状稍高信号, 图 2 反相位病灶信号明显减低, 说明病灶含大量脂质成分, 病灶内高信号不变, 说明合并瘤内出血

Fig. 1-2 MR T1WI double-echo sequences: Figure 1 Positive phase lesions were uneven lower signal, and there is the patchy slightly higher signal in the lesions. Figure 2 Anti - phase lesion signal is significantly reduced (suggesting the lesions contained a large number of lipid composition).The high signal in the lesions is constant (suggesting it combined intratumoral hemorrhage)

图 3 MR T2WI 病灶呈明显高信号(信号不均匀)

Fig. 3 MR T2WI The lesion showed high signal (Heterogeneous signal intensity)

图 4 注射 Dd-DTPA 后动脉期病灶不均匀轻度强化

Fig. 4 After Dd-DTPA injection, the arterial phase lesion was uneven slight enhancement

图 5 MR T2WI S6 病灶呈高信号, 边缘呈环形稍高信号

Fig. 5 MR T2WI S6 lesions showed high signal and the edge showed the ring slightly higher signal

图 6 LAVA Mask S6 类圆形稍高信号, 周边见低信号环

Fig. 6 LAVA Mask The S6 showed round slightly higher signal, and its edge was seen the low signal

图 7 MR 注射 Dd-DTPA 后延迟期肝 S6 病灶呈低信号影, 并见包膜明显环形强化

Fig. 7 MR After Dd-DTPA injection, S6 of the liver lesions in the delay phase showed low signal intensity, and the capsule was obvious ring enhancement

图 8 CT 增强扫描动脉期肝左叶不规则团块状病灶轻度强化, 伴动脉 - 门脉瘘

Fig. 8 CT Enhanced scan showed left hepatic lobe irregular massive lesion was slightly enhanced with artery - portal vein fistula in the arterial phase

图 9 CT 增强扫描延迟期病灶呈相对低密度, 伴门脉左支癌栓

Fig. 9 CT Enhanced scan showed the lesion was relatively low density in the delay phase, with portal left branch of the tumor thrombus

2.2 肝脏透明细胞癌的病理学检查

原发性肝脏透明细胞癌是肝细胞癌少见、特殊的类型,其临床特点类似于普通肝细胞癌,诊断通常是由相关的组织病理学、肿瘤标志物和免疫组织学,特别是 HepPar 1。

显微镜下,透明细胞的存在,以及脂肪变化是分化好的肝脏透明细胞癌的特征性表现,所有病例的肝脏透明细胞癌显示中度至明显的细胞质累积,透明细胞浆经 PAS 和 sudanIII 染色均呈现阳性反应,但以 PAS 染色阳性者占绝大多数,故胞浆内主要成分含有大量的糖原和脂质^[8,9],并把这种类型看成是低度恶性的肝细胞癌。国外报道^[10]在肝细胞免疫组织化学染色(DAKO)正常肝实质显示丰富, darkbrown 粗颗粒均匀染色,分散在几乎所有的肝细胞胞质。如果有足够的肿瘤组织可利用,阳性的肝细胞免疫组织化学染色(DAKO)能够诊断组织来源,这种免疫组织化学染色区分肝脏透明细胞癌与其他透明细胞肿瘤来源有 90%的敏感性和 100%的特异性^[11]。

2.3 肝脏透明细胞癌的影像学表现

肝脏透明细胞癌的影像学表现特点目前国内外均未见专门报道。根据以上 3 例所见,1 例行 CT 平扫显示病灶内含脂肪,2 例行 MRI 双回波序列示肿瘤病灶均含脂质成分,这与肿瘤细胞中含有较多糖原和脂质有关系,T2 加权及 DWI 序列呈高信号,这与肿瘤细胞质丰富,含有较多液体成分导致弥散受限有关,动态增强扫描,动脉期病灶轻度不均匀强化,以边缘强化为主,门脉期及延迟期强化仍不明显,其中 2 例均可见假包膜环形强化,这与组织学发现的纤维包膜相符。原发性肝细胞癌常见瘤内出血,占 HCC 病死率的 10%~15%^[12],肝脏透明细胞癌瘤内出血在以往文献中未见明确报道,本组其中有 1 例肿瘤较大(9cmx10cm),且伴有瘤内出血。1 例肿瘤恶性度较高,伴肝内多发转移灶,及门脉癌栓。由此可见,肝脏透明细胞癌与普通肝细胞癌在影像表现上有许多共同点,有时很难区分,但不难发现,肝脏透明细胞癌也有一些特征性表现:①肿瘤均含脂质成分,本组 1 例 CT 扫描 CT 值范围在(-15)Hu-(-48)Hu,2 例 MRI 扫描双回波序列病灶含脂质成分,②增强扫描病灶呈乏血供表现,以病灶边缘轻度强化为主。③T1 加权肿瘤边缘呈环形低信号,说明肿瘤有包膜,T2 加权及弥散加权成像均呈高信号,说明肿瘤细胞弥散受限。

2.4 肝脏透明细胞癌治疗与预后

通常认为肿瘤内含 >50%透明细胞时才能诊断肝脏透明细胞癌^[13]。含透明细胞介于 90%-100%的肝脏透明细胞癌是极其罕见的。有学者研究^[14]透明细胞 >70%的患者生存时间显著延长,这表明预后与透明细胞比例有关,透明细胞比例越大,预后越好。相比原发性肝细胞癌,透明细胞型肝癌进展缓慢,分化良好,恶性度低,并有包膜形成,包膜的形成可能限制肿瘤生长和扩散,有利于肿瘤的切除,因此外科手术切除是肝脏透明细胞癌的最有效的治疗方法,甚至达到长期存活。术前 Child-pugh 分级是影响肝脏透明细胞癌患者预后的独立危险因素,术前肝功能、肝硬化、HCV 感染、大血管侵犯和多肿瘤发生等是术后转移及术后复发的危险因素。本组病例中 2 例病人均有大血管侵犯,其中 1 例伴肝内多发转移,因此预后较差;另 1 例肿瘤较小,且为孤立病灶,有包膜形成,未侵及大血管,提示肿瘤预后较好,随访半年以上,复查 MRI 肿瘤凝固坏死完全,未见复发。

2.5 总结

通过对以上病例及目前国内的临床治疗研究,中街出肝脏透明细胞癌有以下提点:①肝脏透明细胞癌比例,男性明显高于女性,以上 3 例病例均为男性患者。②通过对以上 3 个病例研究,发现肝脏透明细胞癌有以下特点:①文献报道^[15]性别上男性居多(3 例均为男性);②临床表现缺少特征性,多以腹痛、腹胀、乏力等症状就诊,或体检发现;③病人多伴有肝炎病史(3 例均为 HBsAg 阳性);④肿瘤标记物(AFP)可为阴性。

肝脏透明细胞癌的治疗上主要采用手术切除的方式,对不能手术切除的患者,可行局部消融治疗(氩氦刀、射频、微波等),对于较小的肝脏透明细胞癌(直径 <5cm)行射频消融治疗,近期疗效与手术治疗效果相当,且具有对病人创伤小、恢复快等特点,本组病例其中 1 例患者行 CT 引导下射频消融治疗,术后随访半年复查 MRI 肿瘤坏死缩小,因此局部消融治疗效果较好,较易被病人接受。

参考文献(References)

- [1] 刘复生,刘彤华.肿瘤病理诊断学[M].北京医科大学中国协和医科大学联合出版社,1997:921
Liu Fu-sheng, Liu Tong-hua. Tumor pathology diagnostics [M]. Joint Press of Beijing Medical University and Peking Union Medical College, 1997:921
- [2] Liu QY, Li HG, Gao M, et al. Primary clear cell carcinoma in the liver: CT and MRI findings[J]. World J Gastroenterol, 2011, 17(7):946-952
- [3] Zhou H, Lv L, Ding X. Primary clear cell carcinoma of the liver with intracerebral hemorrhage as first presentation: case report[J]. Onkologie, 2011, 34(1-2):51-53
- [4] Atsushi Takahashi, Hironobu Saito, Yukiko Kanno, et al. Case of clear-cell hepatocellular carcinoma that developed in the normal liver of a middle-aged woman. Case of clear-cell hepatocellular carcinoma that developed in the normal liver of a middle-aged woman[J]. World J Gastroenterol, 2008, 1, 14(1): 129-131
- [5] Zimmerman RL, Burke MA, Young NA, et al. Diagnostic value of hepatocyte paraffin 1 antibody to discriminate hepatocellular carcinoma from metastatic carcinoma in fine-needle aspiration biopsies of the liver[J]. Cancer, 2001,93:288-291
- [6] Li T, Fan J, Qin LX, et al. Risk factors, prognosis, and management of early and late intrahepatic recurrence after resection of primary clear cell carcinoma of the liver [J]. Ann Surg Oncol, 2011, 18(7):1955-1963
- [7] Basile J, Caldwell S, Nolan N, et al. Clear cell hepatocellular carcinoma arising 25 years after the successful treatment of an infantile hepatoblastoma[J]. Ann Hepatol, 2010, 9(4):465-467
- [8] 丁一凡.原发性肝透明细胞癌-三例报道及文献复习[J].肿瘤防治研究,1987(14-2):101-102
Ding Yi-fan. Primary hepatic clear cell carcinoma- three cases report and literature review[J]. Cancer Research, 1987, (14-2):101-102
- [9] Ji SP, Li Q, Dong H. Therapy and prognostic features of primary clear cell carcinoma of the liver [J]. World J Gastroenterol, 2010, 16(6): 764-769
- [10] OliveiraAM, Erickson LA, Burgart LJ, et al. Differentiation of primary and metastatic clear cell tumors in the liver by in situ hybridization for albumin messenger RNA [J]. Am J Surg Pathol, 2000,24: 177-182

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- recurrent inguinal hernias in high-risk patients [J]. *Hernia*, 2004,8(4): 373-375
- [8] Van Nieuwenhove Y, Vansteenkiste F, Vierendeels T, Coenye K. Open, preperitoneal hernia repair with the Kugel patch: a prospective, multicentre study of 450 repairs[J]. *Hernia*, 2007,11(1):9-13
- [9] 谢晓峰, 闵志钧, 张箭平, 等. 腹股沟疝网塞修补术与前入路腹膜前修补术前瞻性对照研究(附 67 例报告) [J]. *中国现代手术学杂志*, 2008,12(2):124-126
- Xie Xiao-feng, Min Zhi-jun, Zhang Jian-ping. TycoMesh Plug and Preperitoneal Anterior Approach in Tension-free Repair for Inguinal Hernia: A Prospective Randomized Controlled Study (report of 67 cases)[J]. *China Modern Operative Surgery*, 2008,12(2): 124-126(In Chinese)
- [10] Nienhuijs S, Staal E, Keemers-Gels M, et al. Pain after open preperitoneal repair versus Lichtenstein repair: a randomized trial[J]. *World J Surg*, 2007,31(9):1751-1757
- [11] Kugel RD. Minimally invasive, nonlaparoscopic, preperitoneal, and sutureless, inguinal herniorrhaphy [J]. *Am J Surg*, 1999,178 (4): 298-302
- [12] Družijanić N, Sršen D, Pogorelić Z, et al. Preperitoneal approach for femoral hernia repair [J]. *Hepatogastroenterology*, 2011,58(110-111): 1450-1454
- [13] Li J, Zhang Y, Hu H, Tang W. Early experience of performing a modified Kugel hernia repair with local anesthesia [J]. *Surg Today*, 2008,38(7):603-608
- [14] Hoste W, Van Nieuwenhove Y, Vierendeels T. Early Belgian experience with the Kugel patch inguinal hernia repair [J]. *Acta Chir Belg*, 2006,106(1):44-46
- [15] Kurihara Y, Yamakawa T, Yoshino M, et al. Experience with direct Kugel patch method for repair of adult inguinal hernia [J]. *J Nihon Med Sch*, 2008,75(1):28-31
- [16] 李基业, 刘飞德, 姚胜, 等. 改良 Kugel 补片前入路腹膜前修补腹股沟疝(附 35 例报告)[J]. *中国微创外科杂志*, 2007,7(8):287-288
- Li Ji-ye, Liu Fei-de, Yao Sheng, et al. Modified Kugel patch in anterior preperitoneal inguinal hernia repair (35 cases)[J]. *Minimally Invasive Surgery*, 2007,7(8):287-288 (In Chinese)
- [17] Ceriani V, Faleschini E, Bignami P, et al. Kugel hernia repair: open "mini-invasive" technique, Personal experience on 620 patients [J]. *Hernia*, 2005,9(4):344-347
- [18] Kugel RD. The Kugel repair for groin hernias [J]. *Surg Clin North Am*, 2003,83(5):1119-1139
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- (上接第 3122 页)
- [11] 鞠新华, 张威, 王大山. 透明细胞型肝癌临床分析(附 3 例报告)[J]. *中国普外基础与临床杂志*, 2002(9-9-5): 355
- Ju Xin-hua, Zhang Wei, Wang Da-shan. Clinical analysis of clear cell carcinoma(three cases report) [J]. *General surgery bases and clinical magazine*, 2002(9-9-5):355
- [12] Miyamoto M, Sudo T, Kuyama T. Spontaneous rupture of hepatocellular carcinoma: a review of 172 Japanese cases[J]. *Am J Gastroenterol*, 1991, 86: 67-71
- [13] 张友会, 刘复生, 刘彤华, 等. 中国肿瘤病理学[M]. 北京科学技术文献出版社, 2001: 229
- Zhang You-hui, Liu Fu-sheng, Liu Tong-hua, et al. *Chinese Journal of Tumor Pathology* [M]. Beijing: Science and Technology Literature Publishing House, 2001:229
- [14] Sheng-Pu Ji, Qiang Li, Hui Dong. Therapy and prognostic features of primary clear cell carcinoma of the liver [J]. *World J Gastroenterol*, 2010,14,16(6): 764-769
- [15] 杨宏强, 彭心宇, 张士杰, 等. 原发性透明细胞型肝癌的病理临床分析[J]. *西部医学*, 2006 (3): 195-196
- Yang Hong-qiang, Peng Xin-yu, Zhang Shi-jie, et al. Primary clear cell type of liver cancer pathology clinical analysis [J]. *Western Medicine*, 2006, (3):195-196