

## . 个案报道 .

## 以颅骨转移为首发表现的肝癌 1 例

刘援援 周志华 胡 帅 王豪升 袁 俊 周劲旭

**【摘要】** 肝癌是最常见的实体恶性肿瘤之一,病死率较高,发生肝外转移的时间窗短,通常发生在肿瘤的晚期,预后不佳。原发性肝癌颅骨转移是一种罕见的转移性肿瘤,以孤立性头部包块为首发症状者更为罕见。本文报道 1 例 65 岁女性病人,因右顶部肿物进行性增大就诊,头颅 CT、MRI 显示右顶骨占位,大小约 6.4×5.6 cm,骨质破坏严重。完善术前检查后,在全麻下行右顶部占位切除术。术中见肿瘤位于硬脑膜外,侵犯上矢状窦。完整切除肿瘤,术后病理结果为转移性肝癌。术后腹部 CT 检查发现肝脏占位。但术后肝脏肿瘤标记物(甲胎蛋白、癌胚抗原、糖类抗原 199 及 125)在正常范围。术后随访 4 个月,颅骨转移未见复发。这提示头部肿物短期内迅速增大时,应考虑到颅骨转移的可能。

**【关键词】** 颅骨转移瘤;原发性肝癌;显微手术

**【文章编号】** 1009-153X(2024)10-0638-03 **【文献标志码】** B **【中国图书资料分类号】** R 739.91; R 651.1<sup>†</sup>

**A case of hepatocellular carcinoma with skull metastasis as the first manifestation**

LIU Yuan-yuan<sup>1,2</sup>, ZHOU Zhi-hua<sup>3</sup>, HU Shuai<sup>2</sup>, WANG Hao-sheng<sup>2</sup>, YUAN Jun<sup>2</sup>, ZHOU Jin-xu<sup>2</sup>. 1. Department of Neurosurgery, The Lu'an Hospital Affiliated to Anhui Medical University, The Lu'an People's Hospital, Lu'an 237000, China; 2. Department of Neurosurgery, The 904th Hospital of Joint Logistic Support Force of PLA, Wuxi 214040, China; 3. Department of Pathology, The 904th Hospital of Joint Logistic Support Force of PLA, Wuxi 214040, China

**【Abstract】** Hepatocellular carcinoma is one of the common solid malignant neoplasms, associated with a high mortality rate. Extrahepatic metastasis typically occurs in the advanced stage of the tumor, featuring a narrow time window and an unfavorable prognosis. Skull metastasis of primary hepatocellular carcinoma represents a rare metastatic lesion, and the manifestation of an isolated skull mass as the initial symptom is even more infrequent. This paper presents a case of a 65-year-old female patient who sought medical attention due to the progressive enlargement of a mass on the right parietal region. Cranial CT and MRI examinations disclosed a space-occupying lesion in the right parietal bone, approximately 6.4 × 5.6 cm in size, accompanied by severe bone destruction. After the completion of preoperative assessment, a resection of the right parietal space-occupying lesion was conducted under general anesthesia. Intraoperatively, it was identified that the tumor was located outside the dura mater and invaded the superior sagittal sinus. The tumor was successfully and completely excised, and the postoperative pathological diagnosis confirmed it as metastatic hepatocellular carcinoma. Postoperative abdominal CT scan revealed a liver space-occupying lesion; however, postoperative liver cancer-related tumor markers (alpha-fetoprotein, carcinoembryonic antigen, carbohydrate antigen 199, and 125) were all within the normal range. The patient was followed up for 4 months postoperatively, and no recurrence of skull metastasis was noted. This case implies that when a head mass undergoes rapid growth within a short period, the possibility of skull metastasis should be contemplated.

**【Key words】** Skull metastases; Primary hepatocellular carcinoma; Microsurgery

**1 病例资料**

65 岁女性,因右顶部肿物进行性增大于 2020 年 7 月 22 日入院。入院体格检查:右顶部肿物明显突出皮面,呈半球形,大小约 6.4 cm×5.6 cm,表面皮肤未见异常,触之质软,无压痛,局部皮肤粗糙,皮温正常,有波动感,活动度差。血清丙氨酸氨基转移酶(alanine aminotransferase, ALT)83 U/L(正常值 0~50 U/L),使用保肝药物治疗 2 d 后恢复至 47 U/L。头颅 CT 显示右顶骨骨质破坏明显,一团块状软组织肿块占位影,大小约 6.4 cm×5.6 cm(图 1A);颅骨三维重建可见右顶骨

骨质破坏严重(图 1B)。头部 B 超显示皮下软组织内范围约 67 mm×25 mm 的低回声,边界尚清,局部颅骨骨质连续性中断,内部见 53 mm×26 mm 的低回声,与外部低回声相连续,考虑血肿可能。头颅 MRI 显示右顶骨骨质破坏伴周围软组织肿块,大小约 6.4 cm×5.6 cm,呈不均匀强化(图 1C~G)。完善术前准备后,2020 年 8 月 4 日在全身麻醉下行右顶部占位切除术。术中见肿瘤位于硬脑膜外,侵犯上矢状窦,完整切除肿瘤,可见肿瘤包膜完整,呈灰黄暗红色,实性,质中等;术中快速病理检查显示肉瘤样肿物。术后免疫组化结果:转移性肝癌,癌细胞增殖活性中等。术后病理结果:肉眼见凸形扁圆形肿块一枚,大小 6.7 cm×6.7 cm×2 cm,切面灰黄暗红色,实性,一侧似有包膜(图 1H~J);镜下见切片示瘤组织,成片密集排列,形成实性癌巢或腺样结构,瘤细胞圆形,大小较一致,间质内见大量血窦,示右顶骨转移性癌。术后行腹部 CT 平扫+增强检查发现原发肝脏占位(图 1K)。值得注意的

doi:10.13798/j.issn.1009-153X.2024.10.016

作者单位:237000 安徽六安,安徽医科大学附属六安医院神经外科(刘援援);214044 江苏无锡,联勤保障部队第 904 医院神经外科(刘援援、胡 帅、王豪升、袁 俊、周劲旭),病理科(周志华)

通信作者:周劲旭,Email:zxh071109@sina.cn

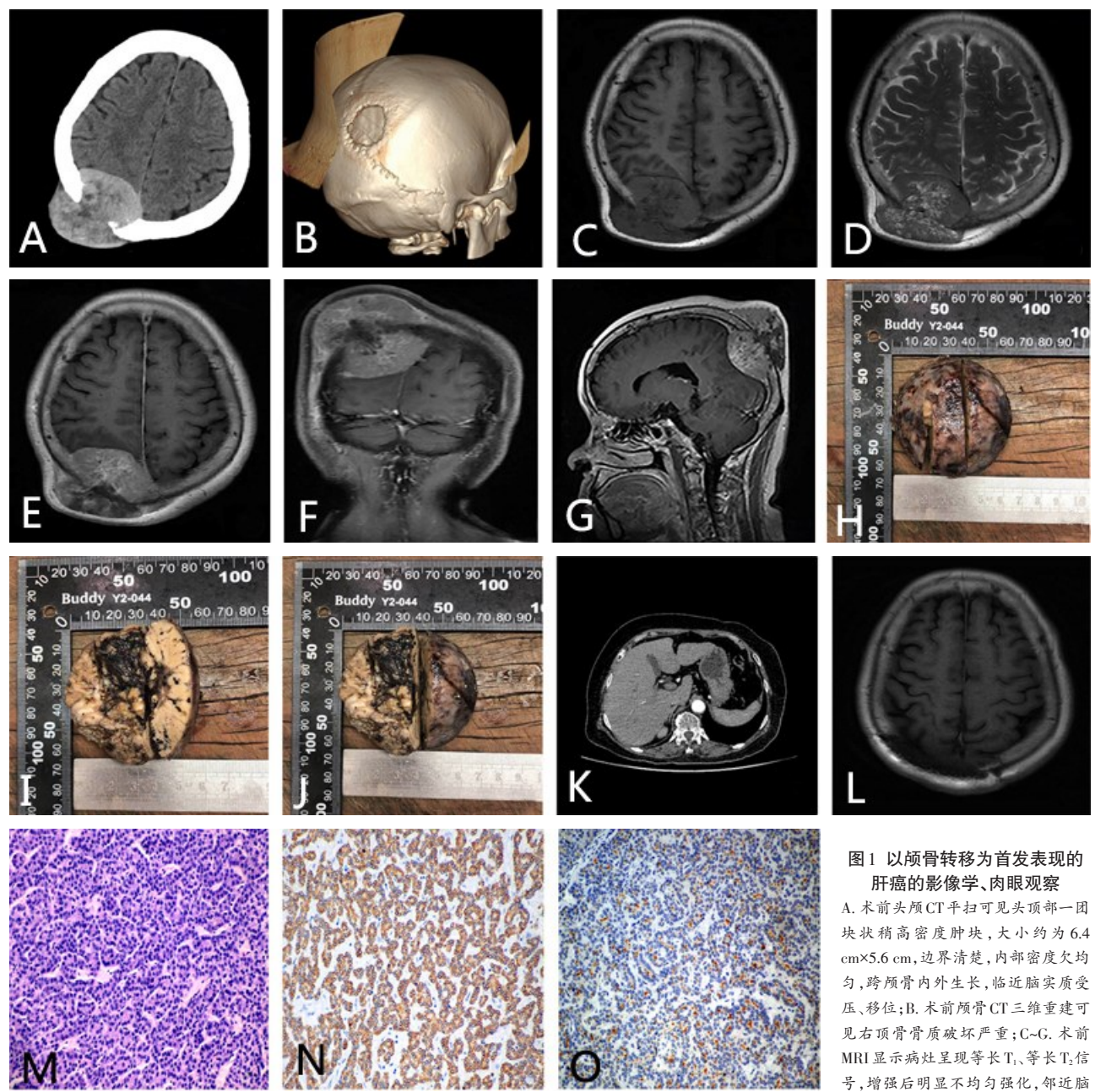


图1 以颅骨转移为首发表现的肝癌的影像学、肉眼观察

A. 术前头颅CT平扫可见头顶部一团块状稍高密度肿块,大小约为6.4 cm×5.6 cm,边界清楚,内部密度欠均匀,跨颅骨内外生长,临近脑实质受压、移位;B. 术前颅骨CT三维重建可见右顶骨骨质破坏严重;C-G. 术前MRI显示病灶呈现等长T<sub>1</sub>、等长T<sub>2</sub>信号,增强后明显不均匀强化,邻近脑

膜强化;H-J. 术中肉眼观察肿瘤组织,大小约6.7 cm×6.7 cm×2 cm,呈扁圆形肿块,切面呈灰黄暗红色,包膜完整;K. 术后腹部增强CT发现肝左叶一直径约3.8 cm大小的结节影,增强后动脉期强化,门脉期及静脉期呈相对低密度,考虑肝癌;L. 术后随访4个月,复查头部MRI未见颅骨转移复发;M-O. 术后病理(HE, ×100)和免疫组织化学染色(×100)显示,Heppar-1(+),GPC3(+)表达阳性

Figure 1 Images and intraoperative findings of a patient with hepatocellular carcinoma presented with skull metastasis as the initial presentation

A: The preoperative plain head CT scan reveals a mass-like slightly hyperdense lesion in the right parietal region, approximately 6.4 cm×5.6 cm in size, with a distinct boundary, heterogeneous internal density, and growth across the inner and outer surfaces of the skull, resulting in compression and displacement of the adjacent brain parenchyma. B: The preoperative three-dimensional reconstruction of the skull CT indicates severe destruction of the right parietal bone. C-G: The preoperative MRI shows the lesion presenting with isointense T<sub>1</sub> and T<sub>2</sub> signals, and manifesting significant heterogeneous enhancement after contrast administration, with adjacent meninges also demonstrating enhancement. H-J: Intraoperative gross examination of the tumor tissue discloses a flat-round mass approximately 6.7 cm×6.7 cm×2 cm in size, with a grayish-yellow and dark red cut surface and an intact capsule. K: The postoperative abdominal enhanced CT detects a nodule approximately 3.8 cm in diameter in the left lobe of the liver, showing significant enhancement in the arterial phase and relatively low density in the portal and venous phases, suggesting hepatocellular carcinoma. L: The four-month postoperative follow-up with head MRI reveals no recurrence of skull metastasis. M-O: The results of postoperative pathological examination (HE staining, ×100) and immunohistochemical staining (×100) indicated that the tumor cells showed positive expression of Heppar-1 and GPC3.

是,此时病人术后血清肝脏肿瘤标记物(甲胎蛋白、癌胚抗原、糖类抗原 199 及 125)仍均处于正常范围。术后随访 4 个月,颅骨转移未见复发(图 1L)。

2 讨 论

肝癌是最常见的实体恶性肿瘤之一,病死率较高<sup>[1]</sup>,发生肝外转移的时间窗短,通常发生在肿瘤的晚期,预后不佳<sup>[2]</sup>。目前,原发性肝癌颅骨转移的报道并不常见<sup>[3-4]</sup>。本文病例因进行性增大的头部肿物入院,颅骨骨质破坏严重及肿瘤对脑组织及静脉窦的压迫明显,手术指征明确;术后病理结果显示转移性肝癌。回顾性分析入院后各项检查结果,值得注意的是,病人入院时腹部 B 超显示轻度脂肪肝,实验室检查血清 ALT 轻度异常,并未出现明显的原发性肝癌的表现;术后肝脏肿瘤标记物包括甲胎蛋白、癌胚抗原、糖类抗原 199 及 125 仍均处于正常范围;仅术后腹部增强 CT 显示肝左叶占位。肝癌颅骨转移的常见临床表现为头部肿物、头痛、四肢无力、癫痫等。本文病例首发及唯一症状仅为右顶部无痛性肿物。肝癌颅骨转移病例有时并未出现原发肿瘤的表现,这可能与肿瘤的早期转移有关<sup>[5-6]</sup>。

针对肝癌颅骨转移的诊断与治疗,有以下建议:①针对头部肿物短期内迅速增大,头部 CT 显示颅骨呈溶骨性破坏,应进一步行 MRI 检查,同时高度怀疑恶性肿瘤颅骨转移者,积极寻找原发癌灶;②肝癌颅骨转移预后差,需要制定个体化诊疗方案,以期减少病人痛苦,改善生存质量,延长总生存期;③该类转移性肿瘤血供丰富,术中可能发生大量出血(本例病人从切开头皮后便开始大量出血),建议术前明确瘤体血供,同时应准备足量血制品。

综上所述,原发肝癌颅骨转移较为隐匿,早期的原发性肝癌颅骨转移者可能并未出现肝脏原发肿瘤的明显临床表现<sup>[7,8]</sup>。这提示头部肿物短期内迅速增大时,应将颅骨转移作为鉴别诊断之一。

【利益冲突声明】:本文不存在任何利益冲突。

【作者贡献声明】:刘媛媛负责撰写论文及修改论文;周劲旭参与修改论文及最后定稿;周志华、胡帅、王豪升、袁俊负责收集临床数据和影像学资料。

【参考文献】

[1] ANWANWAN D, SINGH SK, SINGH S, *et al*. Challenges in liver cancer and possible treatment approaches [J]. *Bba- Rev Cancer*, 2020, 1873(1): 188314.

[2] BROWN ZJ, TSILIMIGRAS DI, RUFF SM, *et al*. Management of hepatocellular carcinoma: a review [J]. *JAMA Surg*, 2023, 158(4): 410-420.

[3] HAN S, ZHANG XH, LV T, *et al*. Skull metastasis from the liver: case report and literature review [J]. *World Neurosurg*, 2017, 108: 989.e15-989.e18.

[4] UEI H, TOKUHASHI Y, MASEDA M, *et al*. Surgical management of coincidental metastases to upper cervical spine and skull from hepatocellular carcinoma: a case report [J]. *J Int Med Res*, 2018, 46 (11): 4852-4859.

[5] AZARPIRA N, DEHGHANIAN A, SAFARIAN A, *et al*. Case report of skull metastasis from hepatocellular carcinoma after a liver transplant [J]. *Exp Clin Transplant*, 2014, 12(3): 265-268.

[6] LEI Q, CHEN H, ZHENG H, *et al*. Zygomatic bone metastasis from hepatocellular carcinoma and the therapeutic efficacy of apatinib: a case report and literature review [J]. *Medicine (Baltimore)*, 2019, 98 (18): e14595.

[7] FERRAZ VR, VITORINO- ARAOJO JL, SEMENTILLI L, *et al*. Lesion in scalp and skull as the first manifestation of hepatocellular carcinoma [J]. *Case Rep Neurol Med*, 2016, 2016: 2897048.

[8] BERNSTEIN Z, ADAMSON DC. Solitary metastasis to the skull as the first sign of hepatocellular carcinoma in a patient in long-term remission [J]. *Surg Neurol Int*, 2023, 14: 252.

(2022-06-08 收稿, 2024-04-03 修回)