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以转移灶为首发临床表现的肾癌患者临床特征分析

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摘要 目的 分析以转移灶为首发临床表现肾癌患者的临床特征。**方法** 回顾性分析了32例以转移灶为首发临床表现肾癌患者的临床资料,男性24例,女性8例,中位年龄56岁。**结果** 患者以骨转移灶(下肢痛4例、胸痛3例、背痛3例、枕部结节3例、胸壁肿物2例、肩疼1例、髂区痛1例、下肢麻木1例)、肺转移灶(咳嗽7例、咳血2例、体检发现肺占位2例)、脑转移灶(头痛1例、头晕1例)及淋巴结转移灶(颈部肿物1例)的症状和体征为首发临床表现。多发转移27例、单发转移5例。透明细胞癌31例、乳头状癌1例。肾肿瘤中位直径7.5cm。有肾原发灶病理资料的28例患者中,T₁期7例、T₂期12例、T_{3a}期9例,G₁2例、G₂11例、G₃12例、G₄3例,11例伴脉管瘤栓。全身治疗为干扰素-α+白细胞介素-II(24例)、索拉非尼(4例)及舒尼替尼(4例)。28例行减瘤肾切除术,11例行转移灶姑息放疗或切除。本组30例获随访,23例死亡,患者的中位生存期10个月(4个月~7年)。2例单发骨转移的患者,经全身治疗联合减瘤肾切除及转移灶切除或放疗,分别无瘤生存7年及19个月。**结论** 以转移灶为首发临床表现的肾癌患者,骨转移造成的临床表现最为常见。患者多为多发转移、伴不良病理预后因素,预后差、生存期短。对孤立骨转移的患者,全身治疗辅以原发灶及转移灶的姑息治疗,部分患者可能长期生存。

关键词 肾细胞癌 转移 临床表现

Clinical Analysis of Patients with Renal Cell Carcinoma Initially Manifestating Based on Metastatic Disease. Tian Jun, Li Changling, Ma Jianhui, et al. Department of Urology, Cancer Hospital of Chinese Academy of Medical Sciences/Peking Union Medical College, Beijing

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Abstract Objective To analyze the clinical features of patients with renal cell carcinoma (RCC) initially manifesting based on metastatic disease. **Methods** We retrospectively reviewed clinical data of 32 RCC patients with initial manifestations caused by metastatic disease. Twenty-four men and 8 women were identified with a median age of 56 years. **Results** The initial manifestations were caused by bone metastasis (4 cases of leg pain, 3 of chest pain, 3 of back pain, 3 of occipital mass, 2 of chest mass, 1 of shoulder pain, 1 of iliac region pain and 1 of acroesthesia of legs), lung metastasis (7 of cough, 2 of hemoptysis and 2 of detected lung mass in health examinations), brain metastasis (1 of headache and 1 of dizziness) and lymph node metastasis (1 of cervical mass). Twenty-seven cases had multiple and 5 had single metastasis. Thirty-one cases were clear cell carcinoma and 1 was papillary carcinoma. The median diameter of renal tumor was 7.5 cm. Of the 28 patients who had primary renal tumor pathological data, stages were 7 with T₁, 12 with T₂, 9 with T_{3a}. Grades were 2 with grade 1, 11 with grade 2, 12 with grade 3 and 3 with grade 4. Vessel tumor embolus were seen in 11 cases. Systemic treatment were interferon alfa combined with interleukin-II (24 cases) or sorafenib (4 cases) or sunitinib (4 cases). Twenty-eight patients had cytoreductive nephrectomy. Eleven had palliative radiation therapy or ablation for the metastatic diseases. **Conclusions** Manifestations caused by bone metastasis is the most common signs or symptoms in patients with RCC initially manifesting based on metastatic disease. The majority patients had multiple metastasis and usually with poor pathological prognostic factors. The prognosis of these patients was poor and life span was short. Systemic treatment combined with palliative therapy for primary and metastatic disease seems to be effective in achieving relatively long-term survival in some patients with single bone metastasis.

Key words Renal cell carcinoma; Metastasis; Manifestations

以转移灶的临床表现为首发的肾癌患者少见,国内外的相关研究也多为个案报道,缺乏成组病例的总结,临幊上对此类患者的临幊特征认识不足^[1]。笔者医院2001年1月~2009年12月期间共收治肾癌患者1590例,其中以转移灶的临床表现为首发的患者32例,仅占2.0%。本文结合文献,对以转移灶的症状和体征为首发的肾癌患者的临幊表现、病理特征及治疗特点进行分析,报道如下:

对象与方法

1. 一般情况:本组32例,男性24例,女性8例。中位年龄56岁(33~72岁)。病程14天~24个月,中位病程2个月。所有患者均经病理诊断证实。

2. 临幊表现与病理特征:以骨转移灶的临幊表现为首发的患者18例:骨痛12例(下肢疼痛4例、胸痛3例、背痛3例、肩部疼痛1例、髂区疼痛1例)、肿物5例(枕部结节3例、胸壁肿物2例)、下肢麻木1例;以肺转移灶的临幊表现为首发的患者11例:咳嗽7例、咳血2例、体检X线胸片发现肺部占位2例;以脑转移灶的临幊表现为首发的患者2例:头痛1例、头晕1例;以淋巴结转移灶的临幊表现为首发的患者1例:颈部肿物。本组有10例患者行转移灶切除(6例)或穿刺活检(4例)后,经病理检查提示才发现肾原发肿瘤。经影像学检查,32例患者中27例为多发转移,5例为单发转移(均为骨转移)。病理类型为透明细胞癌31例、乳头状癌1例;肾原发肿瘤中位直径为7.5cm(2.5~16.0cm)。依照2002年美国癌症联合会肾肿瘤分期标准及Fuhrman肾肿瘤分级标准,有我院肾原发灶病理资料的28例患者,病理分期为:T₁期7例、T₂期12例、T_{3a}期9例,病理分级为:G₁2例、G₂11例、G₃12例、G₄3例。这28例患者中11例伴脉管瘤栓、3例伴肉瘤样

分化。

3. 治疗与预后:32例患者均接受了全身治疗,其中细胞因子治疗24例:干扰素-α300万~600万U,肌内注射,3次/周,白细胞介素-2200万U,肌内注射,3次/周,6~8周为1个周期,可评估疗效者18例,部分反应(partial response, PR)1例、病灶稳定(stable disease, SD)2例、病灶进展(progression disease, PD)15例,反应率(response rate, RR)为5.6%。靶向治疗8例:索拉非尼治疗4例,400mg,每日2次,疗效为PR2例、SD2例;舒尼替尼治疗4例,50mg/d,疗效为PR2例、SD2例;靶向治疗RR为50%。原发灶的治疗:减瘤肾切除术28例、肾动脉导管栓塞2例。转移灶的姑息治疗:骨转移灶放疗7例,剂量20~60Gy,脑转移灶放疗2例,剂量30Gy,骨转移灶切除2例。

结 果

本组30例获得随访,失访2例。中位随访期12个月(4个月~7年)。23例患者死亡,中位生存时间10个月(4个月~7年)。无瘤生存2例,均为单发骨转移的患者,都接受了减瘤肾切除,1例行踝骨转移灶切除及细胞因子治疗,无瘤存活7年,另1例行肋骨转移灶放疗及舒尼替尼治疗,无瘤存活19个月。

讨 论

肾癌的首发临幊表现可以是血尿、腰痛、腹部肿块等“肾癌三联征”,也可以无明显临幊表现而由影像学检查发现肾肿瘤。由于肾癌易发生远处转移,而原发灶由于位置隐蔽可以无明显的症状或体征,因此一些肾癌患者可以以转移灶的临幊表现就诊。但由于此类患者较为少见(本组仅占同期收治肾癌患者的2.0%),临幊上肾原发灶的诊断易被延误。本组

有 45% (10 例) 的患者既是通过转移灶切除或活检经病理检查提示后才发现肾脏原发灶。

Wahner - Roedler 和 Sebo 等^[2]通过 Medline 检索了肾癌以转移灶为首发临床表现的报道,首先出现临床表现的转移灶部位多达 50 个,几乎涵盖身体各个器官,包括颅脑、脊髓、眼、鼻腔、口咽、牙龈、甲状腺、喉、乳腺、心脏、肺、软组织、皮肤、骨关节、阴道、阴茎、前列腺等,患者可以罕见的症状如鼻衄、咽痛、心肌梗死、阴道肿物等就诊。本组临床资料显示,以转移灶的临床表现为首发的肾癌患者中,骨转移造成的症状和体征最为常见,其次为肺转移形成的临床表现。肾癌最常见的转移部位为肺,其次为骨骼,但肺转移灶常无明显症状,文献报道在肺转移瘤患者中,有症状者仅占 26.8%,而骨转移瘤的患者超过 50% 会表现出相应的症状或体征,这可能是本组中以骨转移灶的临床表现为首发的患者最为多见的原因^[3~5]。本组以骨和肺转移灶的表现为首发的患者占全组的 90%,因而,临幊上对以骨转移或肺转移的表现就诊的患者,都应考虑原发肿瘤是否来源于肾脏。

本组的病理资料显示,以转移灶的临床表现为首发的肾癌患者中,肾原发肿瘤多有不良预后因素:肿瘤直径较大(中位直径达 7.5 cm)、T 分期较晚(32% 侵犯肾周脂肪)、分级较高(Fuhrman 分级 3 级及 4 级占 54%)或伴有脉管瘤栓(39%)。本组临床资料显示,以转移灶表现就诊的肾癌患者中,多数已伴有其他部位的多发转移,单发转移的患者仅占 15.6%。因此,临幊上对以转移灶临床表现为首发的肾癌患者,均应做胸、腹部 CT 及骨扫描等全面检查,以明确全身转移灶的情况。

本组患者以全身治疗为主,辅以减瘤性肾切除及转移灶的姑息手术或放疗。靶向治疗能明显延长晚期肾癌患者的无病生存期及总生存期,本研究中靶向治疗的反应率(50%)明显高于细胞因子(5.6%)。本组 87.5% 的患者接受了减瘤性肾切除,文献报道 IFN - α 或血管生成抑制剂联合减瘤肾切除,较单独使用 IFN - α 或靶向治疗可显著延长患者无进展生存期及生存期^[6,7]。以转移灶临床表现为首发的肾癌患者已属晚期,文献报道与根治性肾切除术后异时出现转移的肾癌患者相比,其预后更差,患者的平均

生存期不超过 1 年,本组患者中位生存期仅为 10 个月,考虑可能与此类患者多伴有不良预后因素有关^[1,8]。但有 2 例单发骨转移的患者,予细胞因子或靶向治疗,并行减瘤肾切除及转移灶的切除或放疗,分别无瘤生存 7 年及 19 个月。文献也有报道对肾癌伴孤立转移的患者,经全身治疗并切除原发灶及转移灶,部分患者可能获得长期生存^[3,9]。

以转移灶的临床表现为首发的肾癌患者较少见,肾原发灶的诊断常易延误。此类患者的临床表现以骨转移灶造成的症状和体征如骨痛和肿块等最为常见。因患者已为晚期,多伴不良病理预后因素,治疗效果差、生存期短。但对孤立骨转移的患者,全身治疗辅以积极的减瘤性肾切除及转移灶的姑息治疗,可能延长患者的生存期。

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