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Chronic Headache as the First Symptom of an Undiagnosed Renal Cell Carcinoma

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Key Words

Brain metastasis · Renal cell carcinoma · Headache · Immunotherapy · Space-occupying lesion

Abstract

Renal cell carcinoma (RCC) is an uncommon tumor that rarely metastasizes primarily to the brain. Brain metastases are commonly observed in patients with metastatic RCC, with a reported incidence of 2–17%. The prognosis of brain metastatic RCC is poor. In this carcinoma type, the source is commonly evident. We report a case of a patient with undiagnosed incidental RCC, who presented chronic headache as the first manifestation.

Case Report

The patient was a 49-year-old Iranian male who suffered from chronic headache for 3 months. The headache was severe in intensity, general and not local. The patient did not report any history of such headache, and no family history of migraine headache existed. As a migraine headache case, he was treated by a psychiatrist in this period. On general physical examination, no abnormality was found. Neurological examination performed by a general neurologist was unremarkable, and no hemianopia was detected. Both visual field and acuity were normal. After a brain MRI without contrast, a space-occupying lesion in the left occipital lobe was detected (fig. 1, fig. 2, fig. 3). Before his admission to the urology ward, the patient was treated by a neurologist due to suspicion of a primary brain tumor. Due to the detection of a 5 × 4 cm right upper pole renal mass identified on incidental abdominopelvic sonography (fig. 4), urology consultation was requested.

General physical examination revealed no abnormality and neurologic examination was uneventful. His BMI was 28. Hematologic examination and biochemistry data including calcium, phosphor, lactate dehydrogenase, and alkaline phosphatase were normal. Urinalysis was normal with no microhematuria. Chest X-ray was negative for pulmonary metastasis, and whole-body bone scan was also negative. For prevention of intracerebral edema, intravenous administration of 0.5 mg dexamethasone every 6 h was started. Although the patient did not report any history of seizure, oral phenytoin tablets were prescribed for its prevention.

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He was admitted to our urology center for right radical nephrectomy, which was done uneventfully with flank incision. At the time of surgical excision, the right kidney with its intervening fascia, adrenal, and hilar lymph nodes was resected (**fig. 5**). Histopathologic evaluation revealed renal cell carcinoma (RCC), with clear cell type and nuclear Fuhrman grade 2, but without renal vein, adrenal, or hilar lymph node involvement. The pathologic staging was $T_2N_0M_2$. He refused first-line treatment with the tyrosine kinase inhibitor sunitinib due to financial constraints. He received 5 million units of daily alpha-interferon for 1 month without any side effects. A repeat brain CT scan revealed no change in the size of the primary brain tumor. Finally, the patient underwent left occipital craniotomy and total removal of the metastatic brain lesion. Histopathologic examination of the brain lesion revealed clear tumor cells with rather pleomorphic hyperchromatic nuclei separated by stroma containing prominent sinusoid-like vessels infiltrating the brain tissue, indicating a metastatic RCC. The patient received whole-brain radiotherapy for clearing the residual tumors. He was alive 1 year after the primary surgery and still on continuous oral prescription of phenytoin.

Discussion

RCC is the most lethal of all urological cancers. The incidence of RCC is increasing at 2–3% per year, and it accounts for 2.6% of all cancer cases in the United States [1, 2]. Patients with RCC develop metastatic spread in approximately 33% of cases. Common sites of metastases include the lung, liver, bone, brain, and adrenal glands [3–6]. It rarely metastasizes to the brain [7, 8]. The majority of these patients suffer from metastatic disease in multiple organs [9].

The median age of brain metastasis (BM) patients was found to be 66 years. BMs are mostly located in the cerebellum (33.3%) or the frontal lobe (33.3%) [6]. In 75% of BM patients, at least one lesion was larger than 2 cm. The majority of BM patients (83%) were symptomatic at diagnosis of BM, the most common symptoms being headache and ataxia [9]. Therefore, localizing and non-localizing central nervous system (CNS) symptoms are frequently observed. Symptoms such as headaches, confusion, altered behavior, and seizures have been reported in 80–98% of patients [7]. Clear cell carcinoma appears to be the predominant histology metastasizing to the brain and has been found in >90% of patients [7].

We reported a rare case of RCC, in whom headache was the first manifestation of the disease because of BM. Our patient did not have any other symptoms and only had a chronic headache. Walid et al. [8] reported a 47-year-old male with brain-metastasized RCC in whom the first presentation of his carcinoma was a 2-month history of numbness on his right side. An MRI of this patient revealed a lesion with probable metastatic disease, and an abdominopelvic CT scan showed a lesion in his left kidney. Noel et al. [10] conducted a retrospective review of patients who underwent stereotactic irradiation for BMs from RCC. In their study, metastasis appeared at the time of the primary tumor in 6 patients, and in 22 patients metastases appeared in the course of the disease, with a median interval of 40 months. Shuch et al. [7] believed all patients with metastatic RCC should receive initial CNS screening. In their study, patients with renal cell carcinoma with brain metastasis (RCC BM) were divided into 3 groups: 26.8% presented with RCC BM within 1 month of RCC diagnosis, 15.9% showed a disease-free interval after nephrectomy for localized disease and experienced a disease recurrence including RCC BM, and 57.2% had non-CNS metastatic disease that later progressed to brain involvement. In addition, 67.4% of the patients have CNS symptoms compared to 32.6% without CNS symptoms. There are many case reports of RCC BM where BM has occurred after nephrectomy, and the average interval from

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nephrectomy to BM was 1–3 years. Sadatomo et al. [11] have reported a case of brain-metastasized RCC 15 years after nephrectomy.

The choice for a specific type of local treatment depends on the size and number of BMs, their intracerebral location and the patient's condition. Patients are more at risk of rapidly progressing extracerebral metastases than of progressing BMs. Thus, more complex therapeutic concepts are urgently required for this patient population, and baseline and repeated CT scans of the brain should be provided in all patients in order to enable highly potent local treatment options [9].

Shuch et al. [7] studied several cases of RCC BM. In their large series of 1,855 cases, CNS involvement at the time of diagnosis of RCC was observed in 37 cases (2%). Isolated CNS involvement (like in our case) was rare and was found in only 7 patients (0.4%) of the Shuch series. A solitary site of BM was the most common type [7]. In large tumors (≥2 cm), craniotomy was performed and in smaller lesions stereotactic radiosurgery was used. Isolated BM from RCC is rare; thus, imaging of CNS should not be part of the routine surveillance after radical nephrectomy unless neurologic symptoms are present [7]. Based on the findings of Shuch et al. [7], patients with metastatic RCC should receive initial CNS screening only. CNS metastasis was asymptomatic in one third of the cases. The main determinant of CNS symptoms is the lesion size and not the total number of lesions. As part of the treatment of RCC BM, patients may require systemic steroids that can decrease the efficacy of immune-based treatments [7]. In their study, 1- and 2-year survival rates of RCC BM cases were 48 and 30%, respectively. Therefore, in selected patients with good performance status, an aggressive approach including cytoreductive nephrectomy, CNS treatment, and systemic therapy is warranted [7].

Another large series of patients with RCC BM was presented by Wronski et al. [12]. In their study, the mean survival time after metastatectomy was 12.6 months [12, 13]. They found that the median survival after craniotomy in patients with primary RCC in the left kidney was better than in patients with primary RCC in the right kidney (21.3 vs. 7.4 months). Vecil and Lang [14] reviewed the MD Anderson Cancer Center experience with a specific subset of patients with BMs who underwent metastatectomy [13]. Out of 35 patients, 16 cases (45.5%) had RCC BM. The surgical complication rate was 12%, and there was no operative mortality. The median survival time in patients with a single metastasis was 13.6 months.

Harada et al. [15] conducted a retrospective study on 325 RCC cases. They found a BM rate of 5.5%. Most BMs from RCC are well circumscribed, which makes them suitable for complete surgical resection [16].

Vogl et al. [9] studied 114 cases with RCC. They detected BM in 12 cases (10.5%). All BM patients had extracerebral metastasis at the most common site – the lung – at the time of diagnosis. The most common symptom was headache, seen in 41.7% of the cases. The authors concluded that extracerebral metastases rather than BMs determine the course of disease in patients with advanced RCC and brain lesions [9].

Although most patients with BM either did not benefit from cytokine treatment or were considered unsuitable for cytokine therapy [16, 17], we prescribed it to our patient without any side effects such as capillary leak syndrome or neurologic complications.

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BMs may dramatically endanger the patient by leading to local edema, increased intracranial pressure, and fatal bleeding [16]. We started daily intravenous injection of dexamethasone for the prevention of these conditions.

Interestingly, Fidler et al. [17] have shown that BMs occur late in the progression of metastatic RCC. However, our patient was an early RCC BM case. In addition, these patients are at risk of developing extracerebral metastases rather than at risk of extension of primary BMs [16]. Thus, proper surveillance of the brain and other organs is indicated.

Conclusion

For the treatment of unknown chronic neurologic symptoms such as headache, space-occupying brain lesions should be ruled out. Our patient was a very rare case of treatment-naïve metastatic RCC that presented with chronic headache as a sole symptom. Our patient exhibited an acceptable performance status and survival with aggressive therapy including cytoreductive surgery, brain metastatectomy, and whole-brain radiotherapy. To the best of our knowledge, this is the first report of this rare presentation published in the English literature. Finally, CNS screening should be part of routine surveillance of patients with metastatic RCC and unlocalized RCC.

Disclosure Statement

The authors have no conflict of interest to declare.

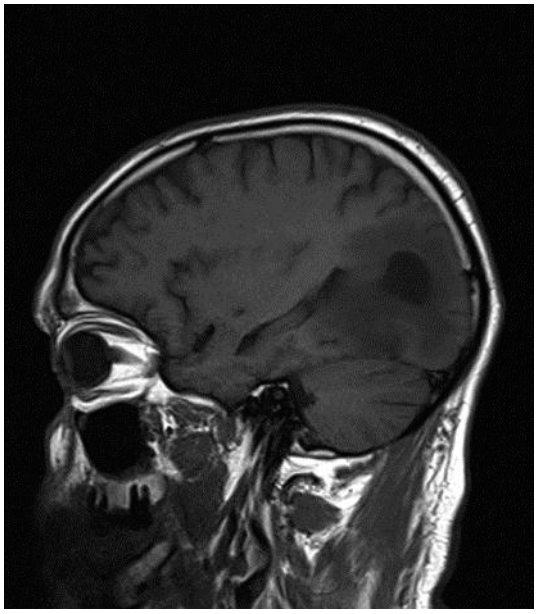

Fig. 1. On brain MRI (T1, T2), the space-occupying lesion is evident in the left occipital lobe.

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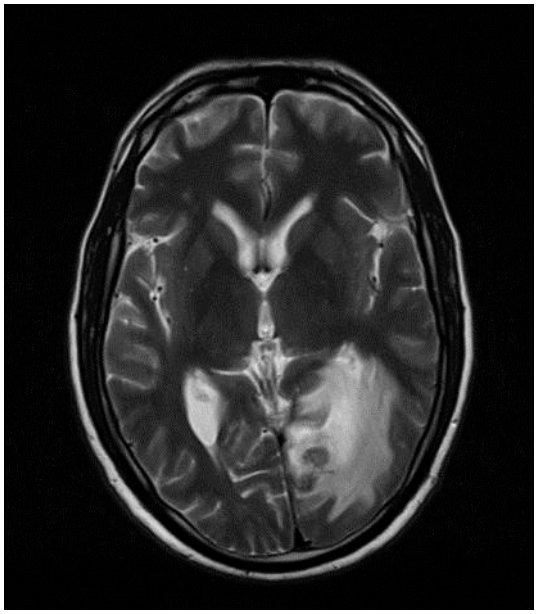

Fig. 2. On brain MRI (T1, T2), the space-occupying lesion is evident in the left occipital lobe.

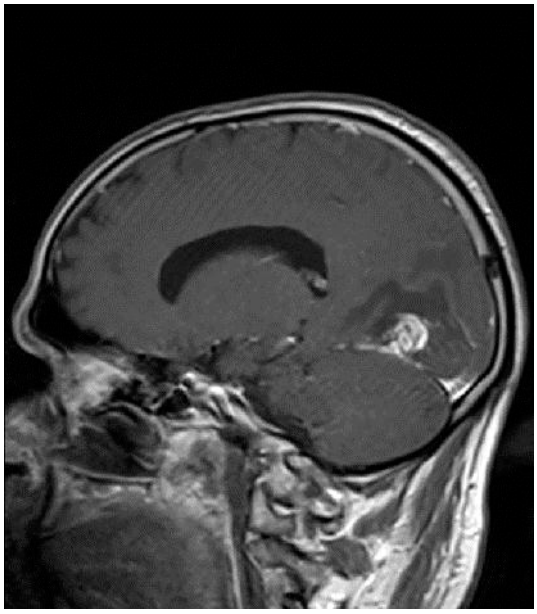

Fig. 3. On brain MRI (T1, T2), the space-occupying lesion is evident in the left occipital lobe.

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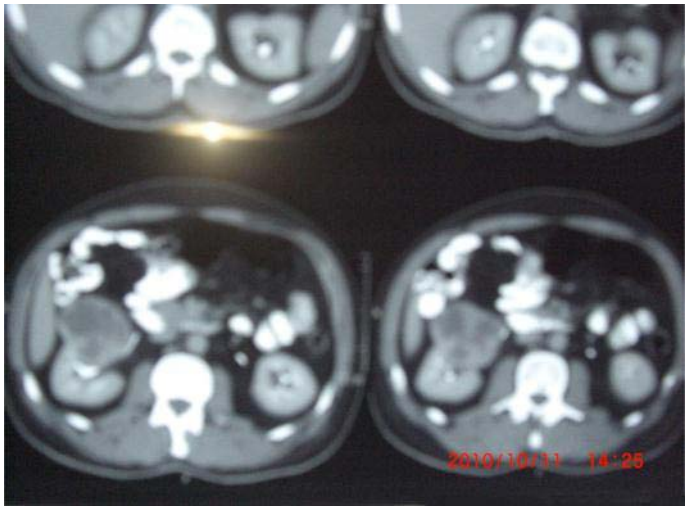

Fig. 4. Abdominopelvic contrast-enhanced CT scan, revealing the right renal upper pole heterogenous mass.

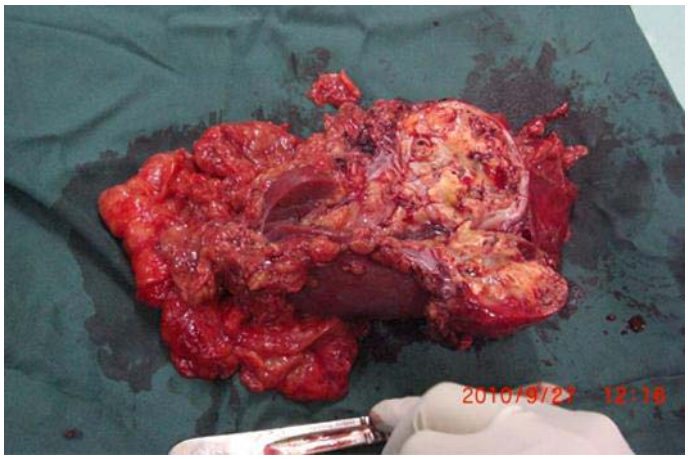

Fig. 5. Right radical nephrectomy specimen. A 5 × 6 cm, upper pole mass is evident. No adrenal, Gerota's fascia, and renal vein invasion was seen on histopathological examination.

References

1 Mason RJ, Abdolell M, Rendon RA: Tumour location as a predictor of benign disease in the management of renal masses. Can Urol Assoc J 2010;4:414–417.

2 Cohen HT, McGovern FJ: Renal cell carcinoma. N Engl J Med 2005;353:2477–2490.

3 Flanigan RC, Campbell SC, Clark JI, Picken MM: Metastatic renal cell carcinoma. Curr Treat Options Oncol 2003;4:385–390.

4 Moslemi MK, Al-Mousavi S, Dehghani Firoozabadi MH: Renal cell carcinoma mimicking adrenal tumor. J Oncol 2010;2010:987128.

5 Moslemi MK, Hosseini SJ, Joorabchin SM: Severe dyspnea due to pulmonary metastasis of renal cell carcinoma: is cytoreductive surgery of value? Case Rep Oncol 2010;3:339–343.

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6 Moslemi MK, Saghafi H, Firoozabadi MHD: Renal cell carcinoma with simultaneous bilateral adrenal metastasis: ipsilateral radical nephrectomy with contralateral adrenal preservation. Case Rep Oncol 2010;3:372–379.

7 Shuch B, La Rochelle JC, Klatte T, Riggs SB, Liu W, Kabbinavar FF, Pantuck AJ, Belldegrun AS: Brain metastasis from renal cell carcinoma: presentation, recurrence, and survival. Cancer 2008;113:1641–1648.

8 Walid MS, Johnston KE: Successful treatment of a brain-metastasized renal cell carcinoma. Ger Med Sci 2009;7:Doc28.

9 Vogl UM, Bojic M, Lamm W, Frischer JM, Pichelmayer O, Kramer G, Haitel A, Kitz K, Harmankaya K, Zielinski CC, Schmidinger M: Extracerebral metastases determine the outcome of patients with brain metastases from renal cell carcinoma. BMC Cancer 2010;10:480.

10 Noel G, Valery CA, Boisserie G, et al: LINAC radiosurgery for brain metastasis of renal cell carcinoma. Urol Oncol 2004;22:25–31.

11 Sadatomo T, Yuki K, Migita K, Taniguchi E, Kodama Y, Kurisu K: Solitary brain metastasis from renal cell carcinoma 15 years after nephrectomy: case report. Neurol Med Chir (Tokyo) 2005;45:423–427.

12 Wronski M, Arbit E, Russo P, Galicich JH: Surgery for brain metastases from renal cancer in 50 patients. Urology 1996;47:187–193.

13 Bhat S: Role of surgery in advanced/metastatic renal cell carcinoma. Indian J Urol 2010;26:167–176.

14 Vecil GG, Lang FF: Surgical resection of metastatic intraventricular tumors. Neurosurg Clin N Am 2003;14:593–596.

15 Harada Y, Nonumura N, Kondo M, Nishimura K, Takahara S, Miki T, Okuyama A: Clinical study of brain metastasis of renal cell carcinoma. Eur Urol 1999;36:230–235.

16 Bukowski RM, Young J, Goodman G, Meyers F, Isselle BF, Sergi JS, Mclain D, Fyfe G, Finke J: Polyethylene glycol conjugated interleukin-2: clinical and immunologic effects in patients with advanced renal cell carcinoma. Invest New Drugs 1993;11:211–217.

17 Fidler IJ, Yano S, Zhang RD, Fujimaki T, Bucana CD: The seed and soil hypothesis: vascularisation and brain metastases. Lancet Oncol 2002;3:53–57.