



## Oncology

## Delayed brain metastasis from renal cell carcinoma

Fatma Kolsi<sup>a,b,\*</sup>, Haifa Mechergui<sup>a,b</sup>, Brahim Kammoun<sup>a,b</sup>, Manel Mellouli<sup>b,c</sup>,  
Mansour Khrifech<sup>a,b</sup>, Med Zaher boudawara<sup>a,b</sup>

<sup>a</sup> Department of Neurosurgery, UHC Habib Bourguiba, Sfax, Tunisia

<sup>b</sup> Sfax University, Tunisia

<sup>c</sup> Anatomopathology Laboratory, UHC Habib Bourguiba, Sfax, Tunisia

## ARTICLE INFO

## Keywords:

Renal cell carcinoma

Brain metastasis

Surgery

Radiotherapy

## Introduction

Renal cell carcinoma (RCC) is the most common type of malignancy of the kidney. Approximately, it is accounted for 1% of all adult malignancies. Thus, it is difficult to know the exact percentage of patients with kidney cancer that is or will become metastatic.<sup>1</sup> The series are often incomplete with variable preoperative assessments. If it is conventional to quote the figure of 50%, the reality is more variable. In the Zisman series studying 814 patients, 43% of the patients were metastatic from the outset and 29% became. In other study, Kim YH reported that 25–40% of patients presents brain metastasis at the time of initial diagnosis of RCC<sup>2</sup> and 10% will develop within 5 years.<sup>2</sup> However, a few cases have been reported where brain metastasis occurred after a delay of more than 10 years. One of these patients died after the brain surgery.<sup>3</sup>

In the present study, we report a case of a double delayed cerebral metastasis of RCC. The first one occurred initially 8 years after nephrectomy and the second 5 years after surgery associated to whole brain radiotherapy and targeted therapy.

## Case report

We report the case of 47-years-old man with the history of renal cell carcinoma (T2 N0 M0) grade III Fuhrman treated by total nephrectomy in 2006. In 2013, he had undergone a pulmonary metastectomy and pulmonary radiotherapy follow-up. He was admitted in December 2014 with one-week history of left-sided weakness, headache and vomiting. Computed tomography imaging and magnetic resonance imaging

revealed an hemorrhagic space-occupying lesion of the right parietal lobe with an intense enhancement, surrounded by edema causing an important mass effect (Fig. 1a). The patient underwent craniotomy and a total resection of the hemorrhagic lesion was performed. The post-surgical imaging showed total resection (Fig. 1b).

Macroscopic lesion resection was performed, and the final histopathological finding was compatible with a metastatic brain tumor from the RCC (Fig. 2a and b). The patient was then addressed for radiation therapy then targeted therapy with sorafenib.

On post-operative, the patient recovered without any neurological deficits. He survived 4 years with no complains. He was re-admitted in 2018 with the same neurological signs. Brain computed tomography revealed a parietal tumor recurrence of the right median with wide meningeal contact with the craniotomy flap. The tumor is in the form of discretely heterogeneous iso-dense tissue with intense enhancement. We note an important *peri-lesional* edema in glove finger exerting a mass effect on the right lateral ventricle which is pushed forward and partially collapsed. Magnetic resonance imaging (MRI) showed a voluminous intra-axial mass, right parietal, para-sagittal, with large meningeal contact with the craniotomy flap, iso signal T1 hypersignal T2, strongly enhanced after injection of GADOLINIUM containing hemorrhagic plaques (Fig. 3a). The whole body computed tomography revealed pulmonary metastasis with nodules affecting the dorsal segments of the right and left sup-lobes with bone metastasis at the 6th rib. The patient underwent craniotomy and a total resection of the hemorrhagic lesion was performed. The post-surgical imaging showed total resection (Fig. 3b).

\* Corresponding author. Department of Neurosurgery, UHC Habib Bourguiba, Sfax, Tunisia.

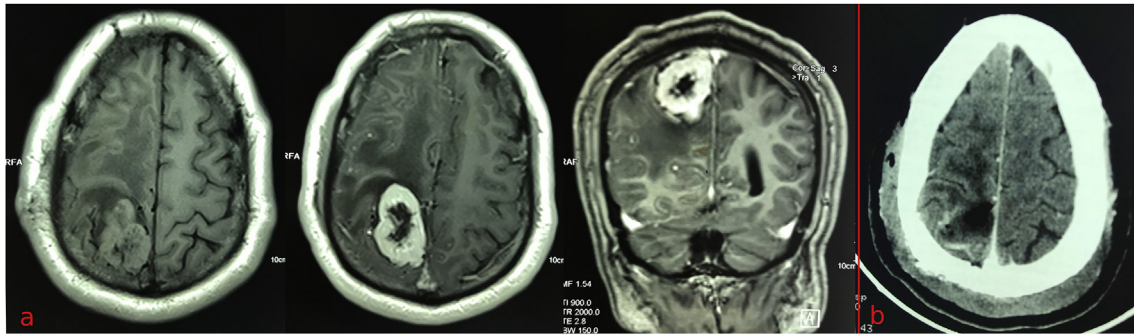
E-mail address: [kolsineifar.fatma@gmail.com](mailto:kolsineifar.fatma@gmail.com) (F. Kolsi).

<https://doi.org/10.1016/j.eucr.2018.10.020>

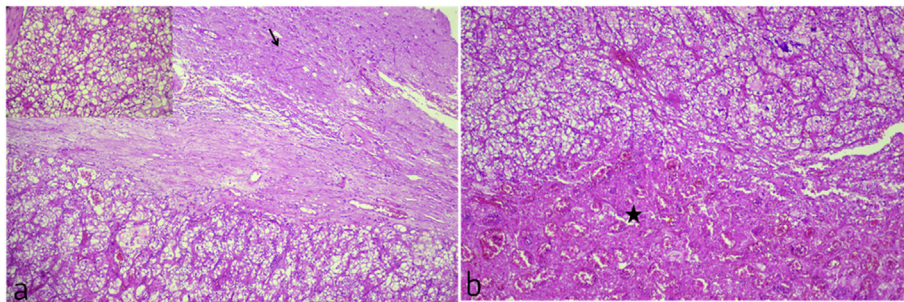
Received 25 September 2018; Accepted 31 October 2018

Available online 05 November 2018

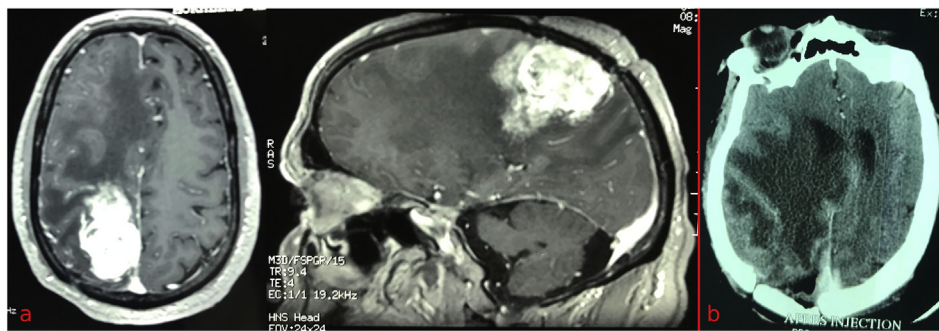
2214-4420/ © 2018 Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



**Fig. 1.** aMagnetic resonance imaging (Dec 2014): Right parietal intra-axial mass with enhancement in cockade + important right hemispherical peri-lesional edema. Figure 1b: post operative imaging: total resection.



**Fig. 2.** A: Infiltration of cerebral tissue (→) with tumor epithelial cells with clear cytoplasm arranged in a compact-alveolar growth pattern separated by a delicate branching network of vascular tissue (hematoxylin and eosin stain, original magnification x 20). (In cart): the cells have a small and round nucleus (hematoxylin and eosin stain, original magnification). B: Presence of area with necrosis (\*) (hematoxylin and eosin stain, original magnification x20).



**Fig. 3.** a Magnetic resonance imaging: voluminous parietal tumor recurrence. Fig. 3b Post operative Ct scan: total resection.

**Discussion**

Renal cell carcinoma is the most common kidney cancer which tends to metastasize to the brain in about 4–11% of cases with an average interval from nephrectomy to brain metastasis of 1–5 years.<sup>1,4</sup> The rarity of this disease makes the prognosis unknown, and in most cases, poor because of the lack of an effective treatment for this chemo and radio-resistant malignancy. Treatment options include brain surgery as much as possible, a whole brain radiotherapy and a targeted therapy seems to improve the overall survivor.<sup>1,2,4</sup> Physicians know that late recurrence is one of the specific behaviours of RCC; unfortunately, little is known about the phenomenon.

Two hypotheses were posed<sup>5</sup>:

- It is possible that growth of a microscopic brain metastasis that occurs in the early stage is so slow that a considerable amount of time elapses before the tumor is diagnosed. This can be correlated with the slow growing nature of RCC, as indicated by its low mitotic index.
- The second hypothesis is based on the role of immunodeficiency in the accelerated growth of a microscopic metastases.

A surgery resection is widely indicated. It is a capital step in the

treatment of cerebral metastasis. Generally, we propose to the patient a surgery resection, a whole brain radiotherapy and a stereotactic radiosurgery. Historically, most patients with brain metastases from renal cell carcinoma were considered unsuitable for systemic therapy. Recent clinical trials involving targeted therapy showed an impact on the evolution and an improved prognosis of the patients included in the study.<sup>5</sup>

Considering the potential risk of hemorrhage of RCC metastasis and the acceptable survival after surgery, surgical resection has a certain role in the treatment of brain metastasis of RCC, especially if the lesion is large, symptomatic, accessible, and surrounded by cerebral edema. However, it should be kept in mind that the morbidity and mortality associated with the operation was not negligible due to poor general condition of the patients with metastatic tumor in general. Pathologic confirmation and aggressive treatment must be considered in the delayed brain metastases, since the patients usually have good prognosis after them.<sup>4</sup>

The prognosis depend on many factors in particular: the possibility of surgery resection, location of the cerebral metastasis especially if it infiltrates a functional area, presence of extra cranial metastases. Multivariate analysis showed that supratentorial metastasis, lack of neurologic deficit, and lack or resection of pulmonary metastasis were favorable prognostic factors. Regarding whole brain radiotherapy in

metastase of RCC, it is limited compared with those from other primary tumors such as lung or breast. It remains an option treatment for patients with non resectable brain metastasis lesions. Thus, the surgery resection or radiosurgery is more efficacious.<sup>1,2,4</sup>

In our case, the patient had been diagnosed with RCC and had undergone nephrectomy at the age of 47. He lived for 8 years without any evidence of recurrence before the brain metastasis was diagnosed. We choose the surgery resection after all investigation as well as histopathological confirmation which revealed the tumor to be a metastatic carcinoma that had originated from the RCC. To be radical and more efficient, we have completed with targeted therapy and radiotherapy despite the radio resistant of this kind of tumor.

## Conclusion

Surgical removal of brain metastasis from renal cell carcinoma seems to be benefit for patient survival. However, local recidive and resistance of the traditional radiation therapy, make the management of brain metastasis from renal cell carcinoma difficult. Recent studies showed excellent outcomes with the stereotactic radiosurgery and targeted therapy.

## Conflicts of interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

## References

1. Treatment of brain metastases from renal cell cancer Carsten Nieder, M.D.a,b,\* , Oddvar Spanne, Ph.D.c, Tone Nordøy, M.D.c, Astrid Dalhaug, M.D.a a Department of Internal Medicine, Division of Oncology, Nordland Hospital, Bodø, Norway Faculty of Medicine, Institute of Clinical Medicine, University of Tromsø, Tromsø, Norway Department of Oncology, University Hospital of North Norway, Tromsø, Norway Received 15 May 2009; received in revised form 7 July 2009; accepted 7 July 2009.
2. Kim YH, Kim JW, Chung HT, Paek SH, Kim DG, Jung HW. Brain metastasis from renal cell carcinoma. *ProgNeuroSurg.* 2012;25:163–175.
3. Leo J. Schouten M.D., Ph.D. Joost Rutten M.Sc. Hans A. M. Huveneers M.Sc. Albert Twijnstra M.D., Ph.D. Incidence of brain metastases in a cohort of patients with carcinoma of the breast, colon, kidney, and lung and melanoma.
4. Choi1 Won Ho, Koh1 Young-Cho, Song1 Sang Woo, Roh2 Hong Gee, Lim3 So-Dug. Departments of 1Neurosurgery, 2Radiology, 3Pathology, konkuk university medical center, seoul, korea extremely delayed brain metastasis from renal cell carcinoma brain tumor. *Res Treat.* 2013;1:99–102.
5. ChuanOu Yen, Ho Hao-Chung, Cheng Chen-Li. Treatment of metastatic renal cell carcinoma to the brain: a report of long-term survival following multimodal treatment and sequential use of targeted agents Chih-Chin Yu Jian-Ri Li\* Division of Urology, Department of Surgery, Taichung Veterans General Hospital, Taichung, Taiwan. *ROC Urological Science.* April 2014;25(4).