Acta Neurochir (2003) 145: 793–797
DOI 10.1007/s00701-003-0061-y

Acta Neurochirurgica
Printed in Austria

*Case Report*

# Long-term management of bilateral metastases of renal cell carcinoma to the choroid plexus

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Published online July 25, 2003


## Summary

*Background.* Metastatic tumors to the brain presenting exclusively in the choroid plexus are exceedingly rare. These events are frequently associated with renal cell carcinoma (RCC), of which all reported cases have been solitary lesions.

*Method.* The authors present the unusual case of a patient with metastatic RCC who developed bilateral tumors of the choroid plexus. These tumors, one of which was confirmed to be metastatic RCC by histologic analysis, were treated over a 5-year period with a combination of interventions, including surgical resection, stereotactic radiosurgery, and chemotherapy, in conjunction with continual radiological monitoring.

*Findings.* Follow-up over a 5-year period demonstrated good control of the patient's intracranial disease and very little neurologic sequelae.

*Interpretation.* This strategy was successful in keeping the patient in good health with minimal neurological symptoms, despite the bilateral nature of the disease and its generally poor prognosis.

*Keywords:* Renal cell carcinoma; metastasis; choroid plexus; management.

## Introduction

Metastases from extracranial malignancies to the choroid plexus are rare, with estimates ranging from less than 1% to a few percent of all metastases to the brain [2, 11, 25]. Although a wide variety of solid cancers have been reported to metastasize to the choroid plexus, including carcinomas of the lung, breast, bladder, stomach, and colon, melanoma, and neuroblastoma, tumors originating from renal cell carcinomas (RCC) are the most common [1, 3, 6, 9, 10, 15, 18, 20, 28]. To date, only solitary metastases to the choroid plexus from the kidney have been reported [7, 11, 14, 16, 21, 26, 27]. We now report the case of a patient with bilateral metastases of RCC to the choroid plexus. Long-term, aggressive monitoring and treatment of the patient's metastatic brain disease kept her largely asymptomatic neurologically for 5 years.

## Case report

### *Clinical presentation*

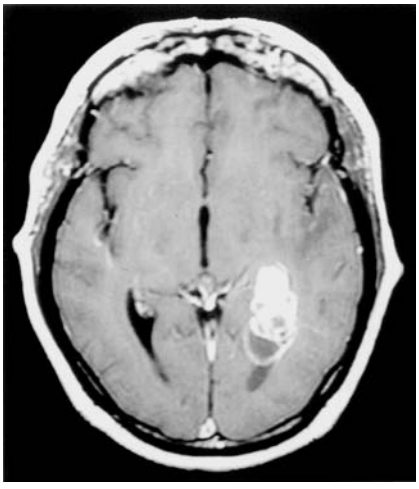
A 54-year-old right-handed Hispanic female presented to us with a 5-month history of progressively increasing headaches, which she reported to be much different in character from and more severe than her usual headaches. She had undergone a right-sided nephrectomy/adrenalectomy 4 years previously and a left-sided adrenalectomy 1 year previously for primary and metastatic RCC, respectively. At the time she had no other known metastases. The patient had no other neurological complaints. Her physical and neurological examinations were unremarkable except for mild papilledema on funduscopic examination. Magnetic resonance imaging (MRI) of the brain revealed a $4 \times 2.5 \times 2.5$ cm enhancing mass in the trigone of the left lateral ventricle (Fig. 1a). The anterior portion of the mass enhanced homogeneously, whereas the posterior portion was cystic in appearance. T2-weighted MRI revealed surrounding vasogenic edema. A preoperative cerebral angiogram revealed the vascular nature of the tumor (Fig. 1b).

### *Surgery*

The patient underwent a posterior temporal craniotomy to remove the mass, and she recovered without complications. Histopathological analysis of the tumor showed it to be metastatic RCC.

### *Postoperative course*

After the craniotomy, the patient reported that her headaches had ceased. Follow-up MRI scans at roughly 2-month intervals for the next year showed some residual dilatation of the left temporal horn but no



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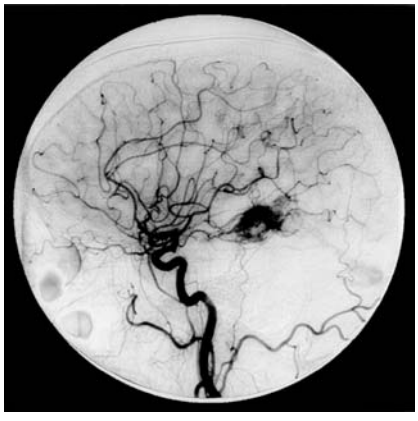

b

Fig. 1. (a) Preoperative MRI with gadolinium contrast demonstrating a homogeneously enhancing mass ($4 \times 2.5 \times 2.5$ cm) in the trigone of the left lateral ventricle. (b) Preoperative cerebral angiogram revealing tumor blush in region of left trigone

evidence of recurrent tumor in the left lateral ventricle (Fig. 2). During this period, new tumors were detected on one of her ovaries and in her liver, thyroid gland, and left kidney. The ovarian tumor proved to be benign, but the other lesions were RCC metastases. The patient was treated with adjunctive chemotherapy.

*Stereotactic radiosurgery (SRS)*

Two years after the craniotomy, despite the patient reporting no neurological symptoms except intermittent headaches, a follow-up MRI revealed two new choroidal masses in the temporal horn and trigone of the right lateral ventricle (Fig. 3). These masses were presumed to be metastases and were treated by stereotactic radiosurgery, with a dose of 1500 cGy at the 90% isodose line administered to the borders of the tumors. During the next few months, the patient underwent surgery to remove another thyroid metastasis, and a deep lobe parotid gland tumor became evident. After the radiosurgical treatment, follow-up MRI scans at 6, 9, and 15 months showed that the right-sided choroid plexus tumors were stable and that there was no recurrence of the left-sided tumor. The patient was feeling well and had gained weight.

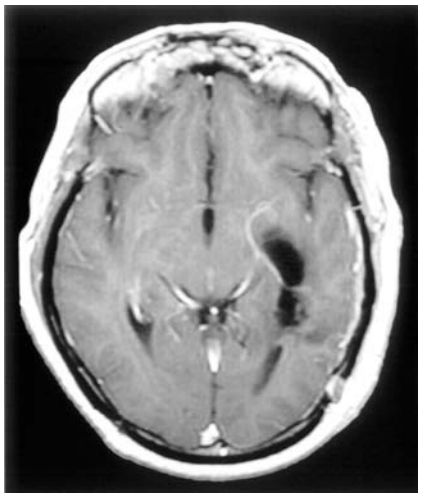

Fig. 2. Two-month postoperative MRI scan with gadolinium contrast demonstrating some residual dilatation of the left temporal horn but no evidence of tumor in the left lateral ventricle

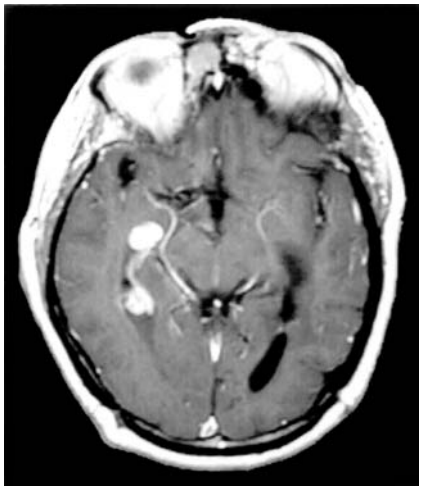

Fig. 3. Two-year follow-up MRI scan indicating new tumors in the right choroid plexus and no evidence of recurrent tumor in left lateral ventricle

*Post-SRS course*

Follow-up MRI scans 5 years after the craniotomy and 3 years after the radiosurgical treatment suggested slow growth of the right choroid plexus masses with attendant vasogenic edema in the right periventricular region. The patient's overall health and neurological condition were stable, except for progressive short-term memory loss.

## Discussion

The differential diagnosis of tumors presenting exclusively in the choroid plexus is narrow. The most common intraventricular tumor in adults is meningioma, whereas choroid plexus papillomas, carcinomas, and

Table 1. *Reports in the literature of solid tumor metastasis to the choroid plexus*

| First author/ref. no. | Age/sex | Primary lesion | Ventricular location of metastasis | Time from diagnosis of primary tumor to brain metastases (months) | Surgery/WBRT | Postoperative (or post-diagnosis) survival |
|---|---|---|---|---|---|---|
| *Iwatsuki [7]* | *75F* | *RCC* | *L. trigone* | *0*** | *yes/no* | – |
| *Matsumura [14]* | *68M* | *RCC* | *R. body* | *84* | *yes/no* | *30 months* |
| *Mizuno [16]* | *59M* | *RCC* | *L. body* | *48* | *yes/no* | *29 months* |
| *Raila [21]* | *48M* | *RCC* | *R. trigone* | *120* | *yes/no* | *3 weeks* |
| *Shigemori [26]* | *58M* | *RCC* | *R. body* | *32* | *yes/no* | *2 days* |
| *Suetake [27]* | *78M* | *RCC* | *R. trigone* | *4* | *yes/no* | *1 months* |
| *Kohno [11]* | *66M* | *RCC* | *R. trigone* | *84* | *yes/yes* | – |
| Kohno [11] | 66M | lung | R. inf. horn | 0** | yes/yes | – |
| Healy [6] | 73F | lung | B/l trigones | 11 | no/no | (1 day) autopsy |
| Kart [9] | 61M | lung | L. trigone | 0** | biopsy/no | 3 months |
| Tanimoto [28] | 64M | lung | R. trigone | 0** | yes/no | Several weeks |
| Kohno [11] | 45M | colon | L. trigone | 26 | yes/yes | – |
| Al-Anazi [1] | 81M | colon | diffuse ventricular | 96 | biopsy/no | – |
| Kendall [10] | – | adenocarcinoma* | 4th ventricle | – | – | – |
| Nakabayashi [18] | 64M | stomach | L. body | 0** | yes/no | 2 months |
| Kendall [10] | – | breast | R. trigone | 36 | – | – |
| Qasho [20] | 40M | bladder | R. ventricle | – | – | – |
| Kendall [10] | – | skin | 4th ventricle | – | – | – |
| Mertens [15] | 0M | neuroblastoma | R. trigone | – | – | – |
| Faber [3] | 29M | – | R. ventricle | 0** | no/no | (10 days) autopsy |
| *Our case* | *54F* | *RCC* | *B/l trigone* | *48* | *yes/SRS* | *60 months* |

*WBRT* Whole brain radiation therapy; *L* left; *R* right; *B/l* bilateral; – not reported.
* Adenocarcinoma of unknown origin.
** First presented as metastasis.

ependymomas tend to appear in children and young adults. Our patient's age and history of metastatic RCC to multiple organs, as well as the appearance of the lesions on radiographic imaging, and the histologic confirmation of the left-sided mass as metastatic RCC, favored a diagnosis of bilateral metastases to the choroid plexus.

Our review of the literature identified 20 other reported cases of metastatic tumors to the choroid plexus. Of the various solid tumors that were reported to metastasize to the choroid plexus, 7 of 20 were from RCC (Table 1). RCC metastasizes widely, most frequently seeding the lungs, bone, liver, and brain, in that order [22]. Both kidneys or the adrenal glands are involved in only a small proportion of cases [22, 23]. Metastases to the brain occurred in less than 15% of cases [2, 11, 25], and metastases to the choroid plexus tended to be a relatively late complication of the disease (mean time interval to initial metastasis after primary tumor diagnosis, 47 months; range, 0–84 months). The most common clinical presentation was generalized headache and change in mental status. Metastatic RCC showed a predilection for the right lateral ventricle; the present case is the first in which both lateral ventricles were involved. CT and MR imaging always revealed homogeneous enhancement of the lesion. All the reported patients underwent surgical intervention. Only 1 reported patient received postoperative whole brain radiation therapy [11]. Postoperative survival ranged from 2 days to more than 30 months. Our patient survived more than 60 months.

Patients with RCC metastases generally have an extremely poor outcome, with a 5-year survival rate of less than 10% after diagnosis, even with removal of the primary tumor [12]. Systemic therapy with chemotherapeutic or hormonal agents is largely ineffective, as is radiation therapy [19, 30]. Thus, it has been recommended that asymptomatic patients undergo close surveillance, with treatment withheld until tumors are observed to be growing or the patient becomes symptomatic. Thereafter, aggressive treatment, including surgical resection of tumors, systemic chemotherapy, and radiotherapy, is indicated [17]. For our patient, in whom multiple metastases emerged during our 5-year

management period, we adopted this strategy with an encouraging degree of success.

Given our patient's extensive history of tumors in numerous locations, only one of which was unrelated to RCC, the possibility exists that she harbored a genetic susceptibility to tumor formation involving an alteration of p53 or another tumor-suppressor gene. For example, choroid plexus tumors occur in individuals from families with Li-Fraumeni syndrome, in which the p53 tumor suppressor gene contains a germline mutation; the coincidence of primary choroid plexus tumors with renal cell and adrenocortical carcinomas has been observed in such patients [5, 13, 29, 31]. Involvement of both the choroid plexus and the kidneys is also seen in a transgenic mouse model of cancer susceptibility [4].

If it is assumed that all of the choroid plexus tumors in this patient represent metastases from the primary RCC, it remains to be explained why neoplastic cells originating in the kidney preferentially target the choroid plexus. Published reports of RCC metastases to the choroid plexus invariably involved solitary lesions that could be interpreted as happenstance occurrences. That there were two independent metastatic events in a single patient, on opposite sides of the brain and separated in time by several years, implies a selective affinity of RCC cells for the choroid plexus in this individual. There may exist some sort of complementarity between transformed cells of the kidney and normal cells in the choroid plexus, perhaps mediated by extracellular membrane proteins specific to the two cell types.

Despite its rich vasculature and lack of a blood brain barrier, the choroid plexus is less frequently affected by metastases than are other areas of the brain [2, 11, 25]. Evidence suggests that viral epitopes such as TAG (large tumor antigen), E16 (from simian virus 40), and human papilloma virus might play a role in the development of primary choroid plexus tumors [8, 13, 24]. These oncoproteins can form a complex with the tumor suppressor apparatus of the cell, specifically with the retinoblastoma (pRb) and p53 genes [32]. It may be that the inactivation of p53 and pRb through epigenic disruption [13] owing to the formation of Tag-p53 and Tag-pRb complexes may also be an important factor in allowing the metastasis of RCC to the choroid plexus.

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