Cerebral metastasis in general is associated with a relatively short survival time. However, brain deposits may occur rather late during follow up. Nine cases of solitary brain metastasis of renal cell carcinoma with a latency period of more than 10 years after nephrectomy have been reported in the literature so far. This is the first report of a case describing a second solitary brain metastasis which occurred 16 years after a first metastatic brain lesion. Complete microsurgical resection alone led to an excellent outcome in this particular case as the patient refused any adjuvant therapy at the same time. Regular nuclear morphology, a low mitotic index, and the absence of chromosomal abnormalities in tumour cells may be indicative for a relative benign clinical course.

**CLINICAL PRESENTATION**

A 61 year old man with a history of a single generalised seizure presented to our department with facial palsy, gait instability, and intermittent dysphasia. He had previously had a left nephrectomy and splenectomy due to renal cell carcinoma 19 years ago. There was no renal vein involvement, lymphatic dissemination, or other evidence of systemic disease at the time of nephrectomy. In 1985, 3 years after diagnosis of primary renal cell carcinoma, the patient developed symptoms of psychomotor deterioration accompanied by apraxia. At that time, imaging studies showed a cystic, right parieto-occipital cerebral metastasis (fig 1). This lesion was completely excised. In 1999, the patient developed a moderate thyroid mass. Diagnostic ultrasound and suppression scintigram indicated a second metastatic lesion in the thyroid gland and a partial right and complete left thyroidectomy was performed 18 years after primary surgery for the renal cell carcinoma.

On admission in 2000, CT and MRI showed a solitary left dorsofrontal lesion composed of solid and cystic compartments (fig 1). The serum ferritene concentration was mildly increased, but other laboratory indices including CEA, AFP, PSA, CA 125, CA 19-9, and CA 15-3 were within normal limits. Chest radiography and abdominal sonography detected no evidence of systemic disease. There was no weight loss. The patient underwent a left frontal craniotomy with intraoperative ultrasound guidance. The highly vascularised tumour was microsurgically removed and the patient’s symptoms resolved entirely.

**PATHOLOGICAL EXAMINATION**

Because secondary brain metastasis of renal cell carcinoma as long as 19 years after excision of the primary tumour has never been reported, histological sections from all previously obtained specimens were thoroughly reviewed. The kidney tumour which was removed in 1981 showed the typical cellular pattern of a clear cell carcinoma. The first brain metastasis showed features of a clear cell adenopapillary carcinoma, with hyperchromatic nuclei and pseudopapillary structures. The thyroid tumour removed in 1999 showed a bimodal differentiation. Primary thyroid carcinoma could be excluded. The second cerebral metastasis in 2000 again displayed highly differentiated clear cells with trabecular and tubular growth and moderate necrosis. No vascular invasion into peritumoural brain was seen in histological sections of both metastasis. A panel of immunocytochemical stains showed strong expression of epithelial membrane antigen (EMA) and vimentin, but negative results for Lu5, thyroglobulin, and CD 30. The MiB-1
labelling index was below 1%. There were no chromosomal abnormalities in tumour cells. The tissue of both brain metastases did not contain any of the characteristic changes for the known VHL gene mutations, so that haemangioblastomas could be excluded from the differential diagnosis.

**POSTOPERATIVE COURSE**

The patient made an unremarkable recovery, with improvement of facial palsy and gait disturbances. The Aachen aphasia test (AAT) showed no signs of aphasia. No tumour remnants were seen on postoperative CT. As before, the patient refused radiation therapy. Fourteen months after surgery clinical evaluation showed no neurological deficit and a Karnofsky score of 100 was ascribed.

**DISCUSSION**

The clinical course of renal cell carcinoma may vary considerably. Whereas 25%–40% of the patients harbour metastatic lesions at the time of diagnosis already, the rate of solitary late recurrence (>10 years) ranges from 4.7% to 11%. Besides the most preferred sites of metastasis from renal cell carcinoma—lung and bones—the tumour metastasises to different brain regions with no predilection site in 4% to 10% of cases. Brain metastasis in most cases occurs at an advanced stage, usually with evidence of widespread disease. Single brain metastasis of renal cell carcinoma is exceedingly rare with only nine cases described in the literature (table 1). 39

Metastatic brain lesions in general are associated with a short life expectancy. Average reported survival periods after the diagnosis of brain metastasis range from 5 to 9.5 months; fewer than 10% live longer than 5 years after the diagnosis. 10 With brain metastasis from renal cell carcinoma only one patient has been reported to survive as long as 56 months so far. 10 There is no other report of a more than 16 year long asymptomatic survival after brain metastasis.

The histological appearance of all metastases in the described patient was nearly identical, with no progressive dedifferentiation or regression. The MIB-1 labelling index in the most recent metastasis was very low. The tumour shares various histological features with haemangioblastomas. In this respect it seems curious that renal carcinomas tend to occur in the presence of von Hippel-Lindau’s disease. In this particular case the location of the brain lesion favoured the diagnosis of metastasis, because haemangioblastomas often occur infratentorially. Moreover, immunohistochemical staining did not detect EMA and VHL-gene mutations were absent in DNA extractions from tumour cells. 11

The pathophysiology of late brain metastasis is still unclear. Apparently, our patient harboured a slow growing, low grade variant of renal cell carcinoma as indicated by a low mitotic index and non-invasive behaviour with respect to the surrounding brain tissue. The long latency may be attributed to the slow growing characteristic of renal cell carcinoma that was correlated with the low proliferation index, which did not increase over the course of disease. The MIB-1 index may be a prognostically valuable immunohistological marker in this form of metastatic disease. The relatively benign clinical course in our patient is probably related to a combination of several beneficial factors. Firstly, there was no gross vascular invasion of the tumour tissue. Secondly, nuclear morphology was unchanged in histological sections. Thirdly, there were no chromosomal abnormalities in tumour cells. Fourthly, the metastatic brain lesions have been carefully and microsurgically completely excised. Nevertheless, the reasons why some brain lesions dedifferentiate in short periods of time and others remain stable in their grade of malignancy are still to be determined.

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### REFERENCES


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### Table 1: Cases of renal cell carcinoma with brain metastasis occurring later than 10 years after the primary lesion

<table>
<thead>
<tr>
<th>Authors and year</th>
<th>Case No</th>
<th>Symptoms</th>
<th>Age (y), sex</th>
<th>Recurrence after primary (y)</th>
<th>Surgical treatment</th>
<th>Radiation dose</th>
<th>Survival (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Killebrew et al 1983</td>
<td>1</td>
<td>UN</td>
<td>55, F</td>
<td>13</td>
<td>Total removal</td>
<td>–</td>
<td>48</td>
</tr>
<tr>
<td>Ishikawa et al 1990</td>
<td>2</td>
<td>HA, aphasia, hemiparesis</td>
<td>46, F</td>
<td>14</td>
<td>Total removal</td>
<td>–</td>
<td>28</td>
</tr>
<tr>
<td>Cervoni et al 1993</td>
<td>3</td>
<td>HA, gait disturbance</td>
<td>61, M</td>
<td>13</td>
<td>en bloc resection</td>
<td>–</td>
<td>49</td>
</tr>
<tr>
<td>Jubelirer 1996</td>
<td>5</td>
<td>HA, vision ↓, hemiparesis</td>
<td>78, M</td>
<td>18</td>
<td>Total removal</td>
<td>–</td>
<td>12</td>
</tr>
<tr>
<td>Kuroki et al 1999</td>
<td>6</td>
<td>HA, aphasia, hemiparesis</td>
<td>60, F</td>
<td>15</td>
<td>Haematomy evacuation</td>
<td>41 Gy</td>
<td>UN</td>
</tr>
<tr>
<td>Present case</td>
<td>7</td>
<td>Confusion, aphasia</td>
<td>86, F</td>
<td>15</td>
<td>Debulking</td>
<td>–</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>61, M</td>
<td>12</td>
<td>Total removal</td>
<td>18 Gy</td>
<td>UN</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>Hemiparesis, aphasia, convulsion</td>
<td>62, F</td>
<td>16</td>
<td>Total removal</td>
<td>18 Gy</td>
<td>3</td>
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<tr>
<td></td>
<td></td>
<td>61, M</td>
<td>19</td>
<td>Total removal</td>
<td>–</td>
<td>Alive</td>
<td></td>
</tr>
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</table>
Single cerebral metastasis 3 and 19 years after primary renal cell carcinoma: case report and review of the literature
F Roser, S K Rosahl and M Samii

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