case report

Pituitary metastasis of renal cell carcinoma: a case report

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Background. *Solitary metastasis of renal cell carcinoma in the pituitary gland is extremely rare and only in 7% of cases it is symptomatic.*

Case report. *We report the case of a 52 year old man presenting with visual disturbance and headache after three years of treatment due to the metastatic renal cell carcinoma. Magnetic resonance imaging (MRI) showed tumour mass in supraselar region compressing optic chiasm with no other brain metastatic lesions. The trans-sphenoidal reduction of the tumour was performed. Pathology and imunohistology revealed metastasis of clear cell renal carcinoma.*

Conclusions. *This is the 25th case of symptomatic pituitary metastases of renal cell carcinoma reported in literature.*

Key words: pituitary gland; renal cell carcinoma; metastasis

Introduction

Renal cell carcinoma is the most common primary tumour of the kidney accounting 1 - 3% of all adult malignancies.[1] Although brain is the fourth most common site of metastasis after lung, bone and liver with approximately 5%[1], solitary metastasis of renal cell carcinoma in the pituitary gland is extremely rare.[1-6] The frequency of pituitary metastases from systemic malignant tumours ranged from 1% to 25% at autopsy.[7] Only 7% of pituitary metastases are symptomatic.[2] Pituitary metastases occur usually in patients with highly disseminated disease. Breast and lung cancer are the most common diseases that metastasize to the pituitary gland.[2,6]

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Case report

We present the case of a patient diagnosed with a pituitary gland metastatic renal cell carcinoma after three years of treatment due

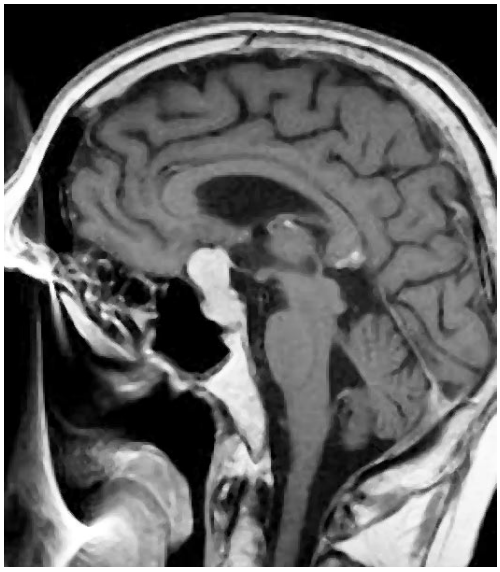

Figure 1a. Tumour mass in supraselar region presented by magnetic resonance imaging (MRI), sagittal image.

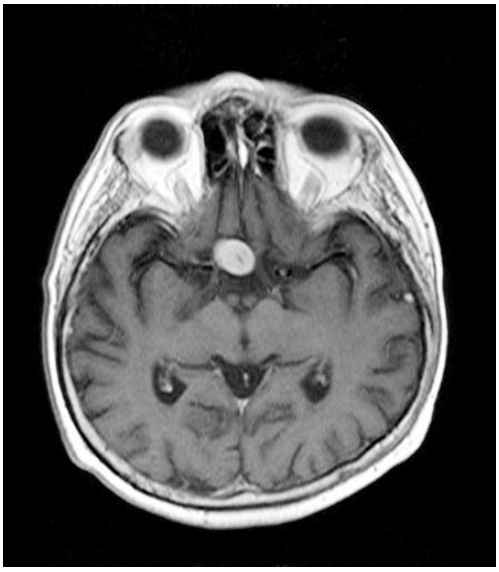

Figure 1b. Tumor mass in supraselar region presented by magnetic resonance imaging (MRI), axial image.

to the metastatic disease. In August 2003, a 49 year old man presented with tumour of the lower part of the left kidney. Left nephrectomy was performed. Pathology confirmed clear cell carcinoma, tumour stage T3bN0M0. During his first postoperative visit to the oncological department multiple bilateral lung metastases smaller than 1 cm in diameter were found along with osteolysis of the posterior part of the forth right rib. Patient ECOG score was 0. Since interferon and interleukin-2 were not registered for the treatment of metastatic renal cell carcinoma in Croatia, his treatment was started with chemotherapy – vinblastin 6 mg/m^2 every two weeks from December 2003 until June 2004.

Control examinations performed during the treatment revealed a stable disease. However, on control computed tomography (CT) in September 2004 the progression of the forth posterior rib lesion measuring now 3.5 x 6.8 cm in diameter with protrusion in intratoracic space was found. Lung metastatic disease was stable. There was no sign of other metastatic site. The palliative radiotherapy treatment to the progressed lesion of the forth posterior rib was performed; dose 30 Gy in 10 fractions. The second line chemotherapy was lomustin (CCNU) 160 mg every 5 weeks, 7 cycles, from October 2004 until May 2005.

CT scan done in May 2005 revealed the progression of lung metastases *i.e*. enlargement in size and number of lung lesions. On the contrary, the lesion of the forth rib was smaller than on the previous CT scan. Since June 2005 until September 2005 the patient was treated with 5-fluorouracil (5-FU) once a week and with an interferon A 2α 3 mil IU sc. three times a week (purchased by the patient). Due to the fatigue of the patient and enlargement of the fourth rib lesion, along with stable disease of other metastatic lung lesions, it was decided to perform reirradiation to enlarged lesion, total dose 30 Gy in 10 fractions. From December 2005 until April 2006, 5 - FU and interferon A 2α therapy was continued. Due to the progression of the lung lesions from April 2006 un-

Table 1. Reported cases of pituitary metastasis from renal cell carcinoma

Author	Age/Sex	Interval from primary diagnosis to pituitary metastasis	Endocrinological finding	Visual involvement	Treatment
Anniko *et al.* (1981)[8]	59/M	9 years	hypopituitarism	yes	surgery
Bounaguidi *et al.* (1983)[9]	53/M	0 year	hypopituitarism, diabetes insipidus	yes	surgery, RT to pituitary fossa
James *et al.* (1984)[3]	75/M	9 years	normal	yes	surgery
Eick *et el.* (1985)[10]	66/M	0 year	hypopituitarism	no	surgery, RT to pituitary fossa and whole brain
Horikoshi *et al.* (1988)[11]	51/M	0 year	hypopituitarism	yes	surgery, RT to pituitary fossa
McCormic *et al.* (1989)[5]	35/F	0 year	hypopituitarism	yes	surgery, RT to sella and parasellar region
Nishio *et al.* (1992)[12]	63/F	4 years	hypopituitarism	yes	surgery, RT to pituitary fossa
Koshiyama *et al.* (1992)[4]	57/M	0 year	hypopituitarism	yes	surgery, RT to pituitary fossa
Weiss *et al.* (1993)[13]	59/M	0 year	hypopituitarism	yes	surgery, RT to pituitary fossa
Uchino *et al.* (1996)[14]	63/F	4 year	NA	NA	surgery
Beckett *et al.* (1998)[15]	56/M	0 year	hypopituitarism	no	surgery, RT to pituitary fossa, interferon-α
Marar *et al.* – 2 cases (1998)[16]	54/M	3 years	hypopituitarism	yes	surgery
	73/M	8 years	hypopituitarism	no	surgery
Weber *et al.* (2003)[17]	62/M	4 years	diabetes insipidus	yes	surgery
Basaria *et al.* (2004)[18]	77/F	3 months	hypopituitarism	yes	surgery, stereotactic RT
Yokoyama *et al.* (2004)[1]	63/M	8 years	hypopituitarism, diabetes insipidus	yes	stereotactic RT
Pallud *et al.* (2005) [19]	70/M	6 years	NA	yes	surgery, RT to pituitary fossa
Liu et al. (2005)[7]	54/M	NA	hypopituitarism	yes	surgery, RT to pituitary fossa, interferon-α
Gopan *et al.* (2007) – five cases[20]	67/M	27 years	hypopituitarism, diabetes insipidus	yes	surgery, whole brain RT with boost to the pituitary fossa
	51/M	12 years	hypopituitarism	yes	surgery, whole brain RT , interferon-α, thalidomide, sunitinib
	53/M	0 year	hypopituitarism, diabetes insipidus	yes	surgery, RT to the sella
	67/F	11 years	hypopituitarism	no	stereotactic RT, sorafenib
	61/F	1 year	hypopituitarism	no	stereotactic RT, AG 013736*
Bisof *et al.* (2008) – this report	49/M	3 years	hypopituitarism	yes	surgery, whole brain RT

* phase II clinical trial with tyrosine kinase inhibitor AG-013736

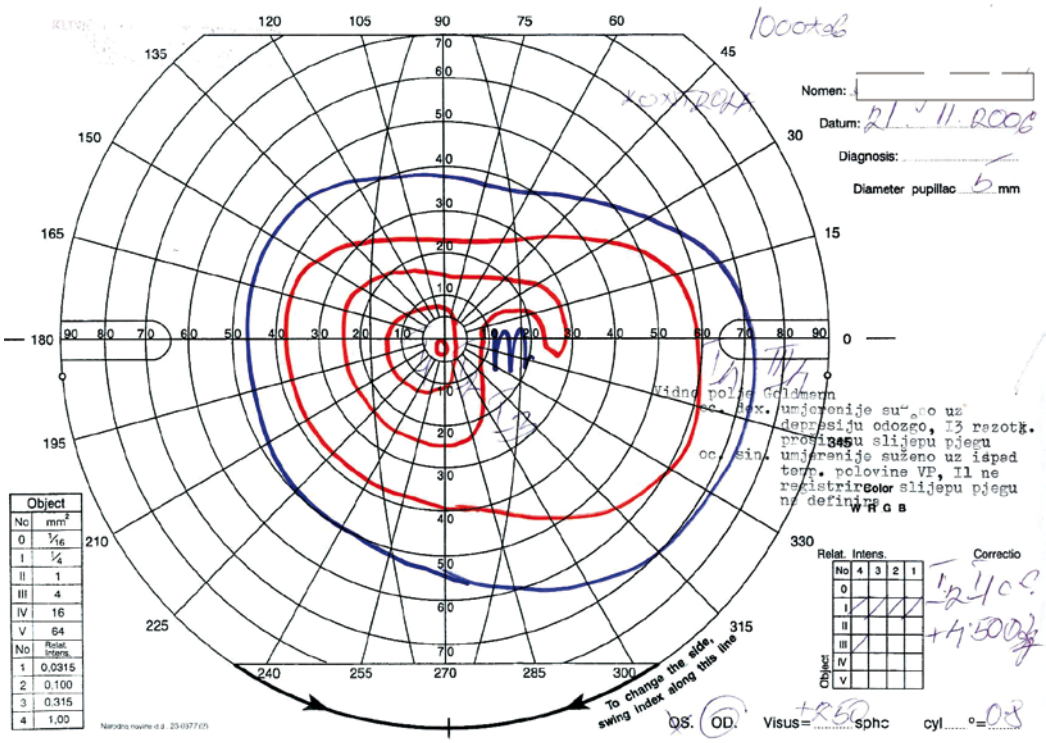

Figure 2a. Disturbances in visual function presented by Goldmann test, right eye.

til August 2006 the patient was treated with gemcitabin 600 mg/m^2, days 1 and 8, every 28 days (purchased by the patient).

In August 2006 vision disturbances and headache had been first reported. Magnetic resonance imaging (MRI) showed tumour mass in supraselar region 30 x 13 mm in diameter compressing optic chiasm. A radiological examination did not demonstrate other possible brain metastatic lesions. Based on the radiological imaging it was difficult to differentiate pituitary macroadenoma, meningeoma and metastasis of tumour (Figures 1a, 1b).

Since visual function deteriorated progressively, a trans-sphenoidal surgery was performed. Pathology and imunohistology revealed metastasis of clear cell renal carcinoma.

The visual function was quickly improved but Goldmann test (Figures 2a, 2b) showed still disturbances in the visual function. Endocrinological findings were almost consistent with panhypopituitarism: T4 = 80.8 nml/L (normal range 70 - 165), TSH < 0.05 mIJ/L (0.40 - 4.2), testosteron < 0.03 nmol/L (3 - 22, for > 50 yrs), SHBG 7 nmol/L (15 -100), cortisol = 13 nmol/L (138 - 690), aldosteron = 879 pmol/L (20 - 410). A replacement hormone therapy was introduced to the patient.

Postoperative control MRI after two months showed residual tumour 20x13x12 mm in diameter but now along with multiple brain metastases. The palliative brain photon beam radiotherapy was performed, total dose 30 Gy in 10 fractions. CT scan of thorax and abdomen revealed the progression of the lung metastases and the occur-

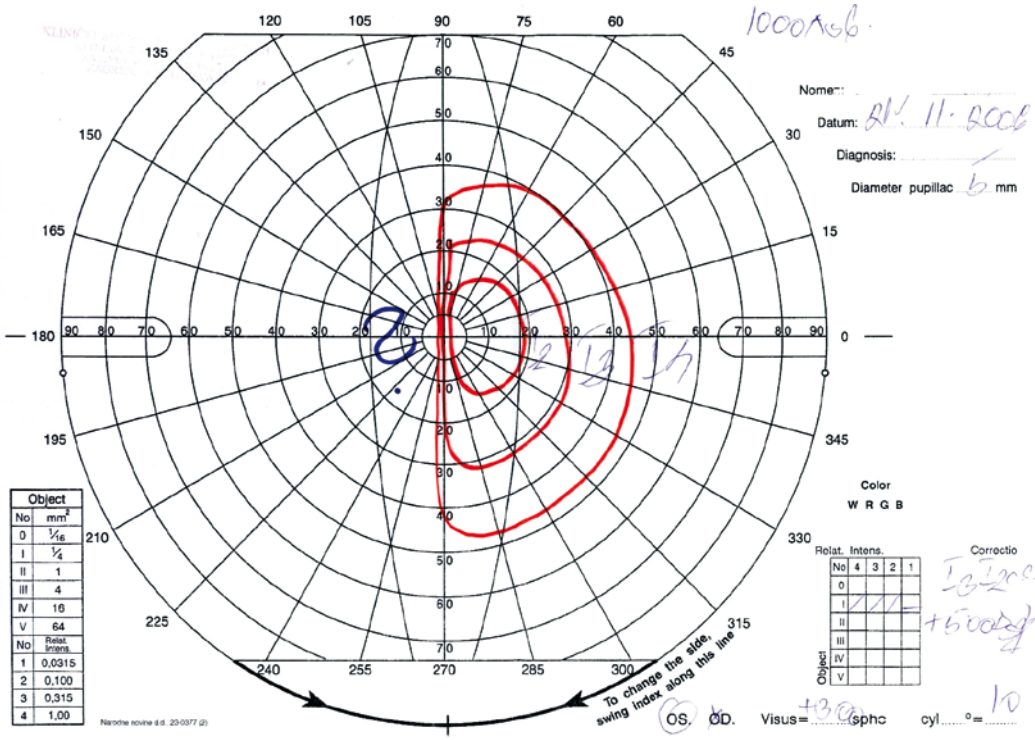

Figure 2b. Disturbances in visual function presented by Goldmann test, left eye.

rence of new bone metastases. Surprisingly, the patient was without respiratory disturbances but he reported fatigue. His general appearance was Cushingoidal. He died ten months after the operation of the pituitary gland.

Discussion

Up to our knowledge only 24 cases of symptomatic pituitary metastasis of renal cell carcinoma has been reported in the literature (Table 1). Only six of them were female, while 18 were men. The majority *i.e.* 19 patients presented with hypopituitarism, while 17 patients presented with visual field defect like our patient. Our patient has not experienced symptoms of *diabetes insipidus* which is reported to be more frequent in pituitary metastasis than in pituitary adenomas.[7,21] It is very difficult to differentiate pituitary metastasis from adenoma based on radiological and clinical findings.[2,3,10,12,22] But Liu *et al.*[7] found out that the strong enhancement of the tumour and the strong bone destruction without marked sellar enlargement are characteristic radiological features of pituitary metastasis. Fassett *et al.*[2] stated that thickening of the pituitary stalk, invasion of the cavernous sinus and sclerosis of the surrounding *sella turcica* could indicate pituitary metastasis. Tumour invasiveness usually makes the resection difficult. There was no significant survival benefit in surgical series.[2] The treatment of pituitary metastasis is multimodal, consisting of surgery, radiotherapy and chemotherapy. The long-term benefit of postoperative radiotherapy is not known

due to the rarity of such cases. The applied dose ranged in the literature from 9 to 60 Gy, with median dose 36 Gy.[6] Our patient was treated with 30 Gy in ten fractions due to the occurrence of brain metastases although first it was intended to apply a higher dose. Stereotactic radiotherapy can be beneficial in sparing the optic nerves. The primary aim of treating pituitary metastasis is to improve the quality of life through symptomatic relief and to prevent the neurological deterioration.

The overall median length of the patient's survival after the diagnosis of pituitary metastasis is only 180 days.[6] However, the paper recently published by Gopan *et al*.[20] reported the overall survival ranging from 6 to 46 months from the initial diagnosis of pituitary metastasis. This can be explained by the application of new chemotherapeutic agents like sorafenib and sunitinib. Stereotactic radiotherapy with or without whole brain radiotherapy was performed in all five reported patients.

In our case, whole brain radiotherapy was performed due to the brain dissemination. Sorafenib and sunitinib were not registered for the treatment of metastatic renal cell carcinoma in our country at the time.

Symptomatic pituitary metastasis of renal cell carcinoma is a rare case, occurring usually in highly disseminated renal cell carcinoma. Palliative surgery and radiotherapy treatment can contribute essentially to the improvement of the quality of life of such patients.

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