

TH Aung 歐天通
 YC Po 保延聰
 WK Wong 黃偉基

Hepatocellular carcinoma with metastasis to the skull base, pituitary gland, sphenoid sinus, and cavernous sinus

肝細胞癌顱底、垂體、蝶竇和海綿竇的轉移

Two cases of hepatocellular carcinoma, with metastases to the skull base, pituitary gland, sphenoid sinus, and cavernous sinus are reported. Patients presented with diplopia, retro-orbital headache, and multiple cranial nerve palsies. Pituitary metastases may require surgery as palliative treatment, and for the confirmation of histology. One of the current cases was diagnosed with hepatocellular carcinoma prior to transphenoidal resection of the pituitary metastasis. The second patient was found to have hepatocellular carcinoma after review of histology, and the development of signs and symptoms relating to the primary tumour.

本文報告了兩個轉移到顱底、垂體、蝶竇和海綿竇的肝細胞癌病例。患者有複視、眼球疼痛和數條顱神經癱瘓。垂體轉移的病例可能需要手術作為緩解性治療及組織學的確診。其中一名有垂體轉移的患者，在接受經蝶腫瘤切除前已確認患有肝細胞癌。另一名患者則是在術後的組織學檢查以及病人開始患現有關於症狀體徵，才被發現患有肝細胞癌。

Introduction

The diagnosis and treatment of metastasis to the pituitary gland can be difficult. The most common primary tumour sites are breast and lungs, while other primary visceral malignancies such as colon, prostate, renal, and pancreas have been described. Only one case of metastasis to the pituitary gland and skull base from a hepatocellular carcinoma (HCC) has been reported.¹ Patients with pituitary metastasis usually present with diabetes insipidus, anterior pituitary insufficiency, and retro-orbital pain.¹ Other presenting symptoms may include headache, or visual symptoms such as bitemporal hemianopsia or infrequently, chiasmal syndrome.^{2,3}

We report two cases of HCC with metastasis to the pituitary gland, sphenoid sinus, and cavernous sinus. Surgery involved a transphenoidal approach and partial resection of the tumour in both cases.

Case reports

Case 1

A 40-year-old previously healthy Chinese male was referred to the Department of Neurosurgery at the Princess Margaret Hospital in August 1997 with a 2-month history of sudden onset of diplopia, retro-orbital headache, and occasional vomiting. The patient also stated that he had lost 3 kg in weight over a 1-month period. Neurological examination identified a right sixth cranial nerve palsy. No other neurological deficits were noted. The patient's blood pressure was 120/70 mm Hg. Laboratory investigations were unremarkable.

A computed tomography (CT) brain scan with contrast undertaken the following month showed no abnormality. The patient later developed a partial right third cranial nerve palsy, which progressed to a complete right third cranial nerve palsy. Subsequent magnetic resonance imaging (MRI) of the brain depicted

Key words:

Carcinoma, hepatocellular;
Cavernous sinus;
Pituitary gland;
Sphenoid sinus

關鍵詞：

肝細胞癌；
 海綿竇；
 垂體；
 蝶竇

HKMJ 2002;8:48-51

Department of Neurosurgery, Princess Margaret Hospital, 2-10 Princess Margaret Hospital Road, Kowloon, Hong Kong
 TH Aung, FRCS, FRACS
 YC Po, FRCS
 WK Wong, MRCS

Correspondence to: Dr TH Aung

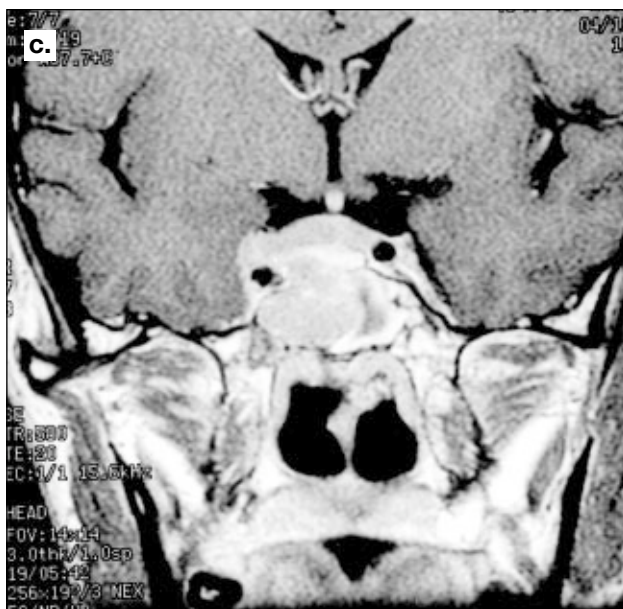
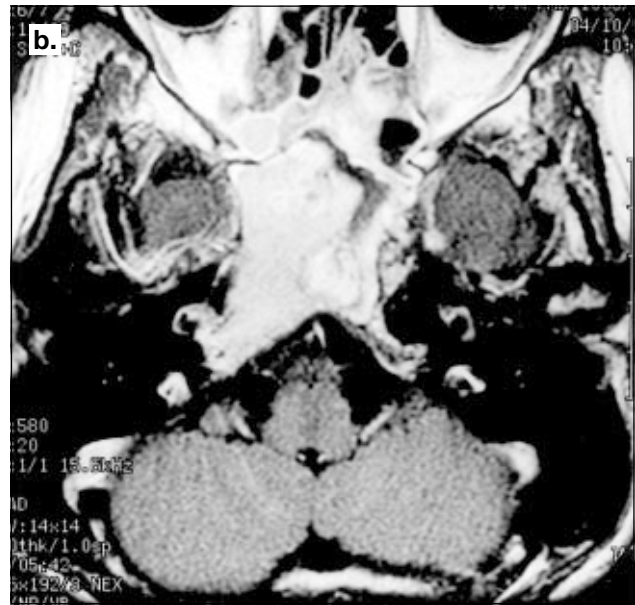


Fig 1. Sagittal (a), axial (b), and coronal (c) T1 weighted magnetic resonance images with gadolinium showing a pituitary mass and invasion of the sphenoid sinus and cavernous sinus

12-34 mIU/L). A clinical diagnosis of HCC and a pituitary tumour was made, and the patient was offered decompressive surgery of the pituitary region in view of his increasing neurological deficits, and for confirmation of the pathology.

The patient was given dexamethasone 2 mg four times daily, together with pepcidine 20 mg twice daily, to reduce cerebral oedema. Partial resection of the tumour was performed using a sublabial transphenoidal approach. The tumour was found to be vascular, greyish in colour, and soft in texture. It had eroded the right side of the floor of the sella, and invaded the pituitary fossa. Histopathology confirmed the tumour as metastatic HCC.

Postoperatively, the patient's headache subsided and his vision improved but there was a residual right third cranial nerve palsy. An MRI brain scan 12 days postsurgery depicted a right sphenoid sinus tumour with right cavernous sinus invasion. A CT scan of the abdomen 3 days later also revealed multiple nodules in both lobes of the liver, with invasion of the inferior vena cava. The patient declined palliative radiotherapy treatment for the sphenoid sinus and cavernous sinus lesion. He was discharged and subsequently died 3 months after initial presentation with liver failure. An autopsy was not performed.

Case 2

A 71-year-old Chinese man was referred to the Department of Neurosurgery in July 1996 with a 1-month history of headache, diplopia for 2 weeks, ptosis of the right eye for 1 week, and weight loss of 3 kg in 1 month. On examination, the patient was conscious with normal vision, but had right third and sixth cranial nerve palsies. Abdominal examination was normal. Complete blood count, clotting profile, blood glucose, and liver and renal function tests were normal.

an extra-axial mass in the pituitary fossa, clivus, sphenoid sinus, and right petrous apex, measuring approximately 2.38 x 2.5 x 3.04 cm in size (Fig 1). Abdominal examination revealed tenderness over the right subcostal region, with no palpable mass. Ultrasound examination of the abdomen was subsequently performed and demonstrated extensive multiple hepatic masses. Results of the complete blood count and liver function tests were normal. Hepatitis B virus surface antigen testing was positive. Serum alpha fetoprotein levels indicated a diagnosis of HCC (9793 mg/L [normal level, <10 mg/L]). Endocrine tests revealed a spot cortisol level of 618 nmol/L (normal range, 119-618 nmol/L), luteinising hormone level of 3.5 IU/L (normal level, <15 IU/L), follicle-stimulating hormone level of 12.9 IU/L (normal level, <12 IU/L), prolactin level of 599 mIU/L (normal range, 0-480 mIU/L), testosterone level of 2.96 nmol/L (normal range, 14-28 nmol/L), thyroxine level of 94 nmol/L (normal range, 62-148 nmol/L), and a thyroid-stimulating hormone level of 0.6 mIU/L (normal range,

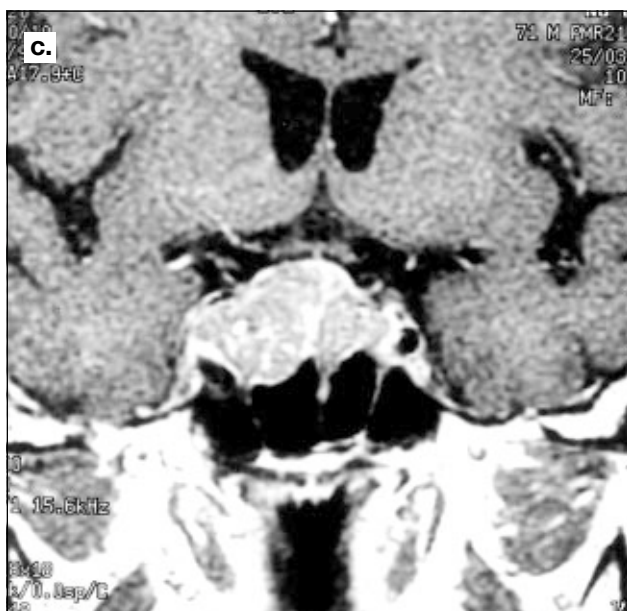
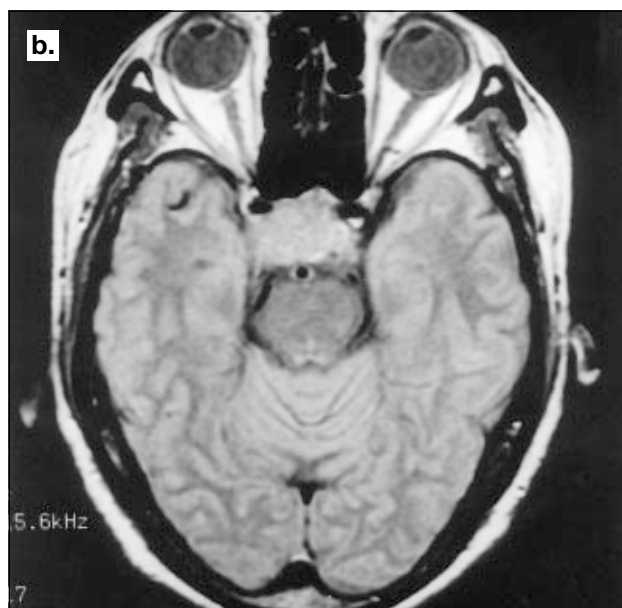
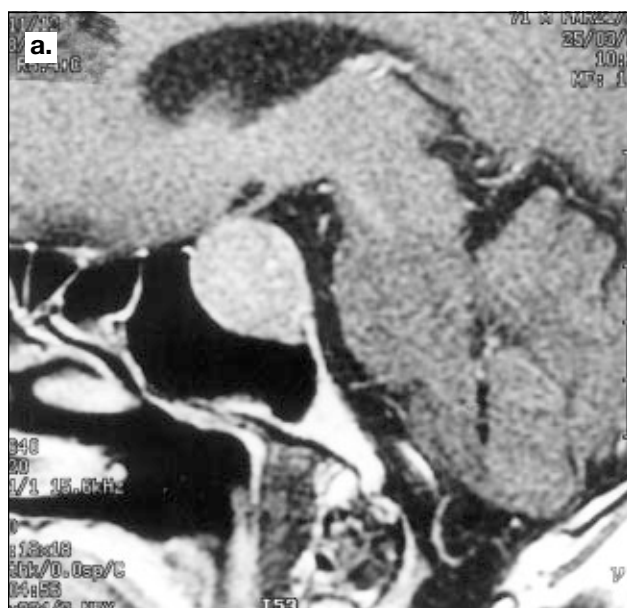


Fig 2. Sagittal (a), axial (b), and coronal (c) T1 weighted magnetic resonance images with gadolinium injection showing a pituitary lesion, with sphenoid sinus invasion

The serum alpha fetoprotein level, however, was elevated to 695 mg/L, and the hepatitis B virus surface antigen status was positive. Endocrinological tests were normal with the exception of the serum prolactin level, which was slightly elevated to 795 mIU/L. An MRI brain scan depicted a 16.7 x 36.6 x 17 mm tumour in the pituitary region, with an enlarged pituitary fossa (Fig 2). The tumour was also indenting the optic chiasma, with lateral extension into the cavernous sinus. Radical resection of the tumour was subsequently undertaken using a sublabial transphenoidal approach. Histology reported the frozen section specimen to be a pituitary adenoma. The postoperative period was uneventful and the patient's ocular symptoms improved. He was given cortisol therapy—20 mg in the morning and 10 mg in the evening.

Histological review of the resected specimen revealed a metastatic HCC. The serum alpha fetoprotein level was elevated to 15 000 mg/L and examination of the abdomen

demonstrated a palpable liver 3 cm below the right subcostal margin. Subsequent ultrasound of the abdomen revealed a lesion of 5.5 cm in diameter in the right lobe of the liver. A CT scan of the abdomen depicted a tumour in the right lobe of the liver, with metastasis to the left adrenal gland. Features of HCC were also seen in the hepatic angiogram. A surgeon specialising in hepatobiliary procedures recommended conservative treatment. After receiving radiotherapy (4500 cGy) for his pituitary lesion, the patient was seen at the neurosurgical out-patient clinic regularly and remained symptom-free for 8 months. He then reported epistaxis, which subsided with conservative treatment. A month later, the patient experienced a further episode of epistaxis and the recurrence of visual symptoms. An MRI brain scanning indicated recurrence of the pituitary lesion, with compression of the right cavernous sinus and displacement of the right internal carotid artery. The tumour had obliterated the sphenoid sinus, destroying the sella floor, and extended to the roof of the nasal cavity. The patient underwent sphenoidotomy and temporalis muscle packing. Subsequent follow-up MRI studies showed a significant increase in the size of the pituitary lesion. The patient's clinical condition deteriorated and he died almost a year following first presentation. No autopsy was performed.

Discussion

Metastasis to the pituitary gland is a relatively common finding in autopsy series of cancer patients, but involvement of the skull base is rare. The majority of reported patients, however, were either asymptomatic or died without identification of the pituitary metastasis because of overwhelming systemic complications of malignancy.^{1,4} Cases of pituitary metastases from renal cell carcinoma mimicking an adenoma have been reported. In one patient,

the correct histological diagnosis was confirmed only at autopsy, with two consecutive tumour specimens obtained 1 year apart, reporting a finding of pituitary adenoma.^{5,6} The Memorial Sloan-Kettering Cancer Center's report of clinical cases identified pituitary metastases in 3.6% of autopsy series and pituitary adenomas in 1.8%.⁷ The most common primary sources for metastasis were breast and lung cancer, and the median survival was approximately 12 months. Other primary sources reported include endometrial carcinoma, and rarely bronchial carcinoid tumours.⁸

Patients with metastases arising from breast, lung, or bladder cancer frequently present with central diabetes insipidus.^{3,4,9} In a study of 37 patients undergoing transphenoidal hypophysectomy for diffuse metastatic breast carcinoma, nine patients were found to have metastatic pituitary carcinoma resulting in diabetes insipidus. Pathology reports confirmed that the anterior lobe of the pituitary was involved in the majority of cases.⁴ When a patient with known metastatic cancer develops diabetes insipidus with radiographic evidence of a pituitary mass, the diagnosis of metastasis is thus highly probable.¹⁰

The optic chiasm may be compromised by suprasellar extension of a pituitary metastasis or by infiltration from an infundibular or hypothalamic metastasis. In the patients in this study, however, the tumour invasion was in the direction of the skull base and in particular, the cavernous sinus.^{2,6} The current patients presented with retro-orbital pain or headache, and diplopia—a presentation similar to that due to metastasis from thyroid follicular adenocarcinoma, though with a poorer apparent prognosis. Weight loss was also a significant feature seen in both patients. Hypopituitarism and visual disturbance have been more frequently reported in metastases arising from renal cell carcinomas than from other primary tumours.¹¹ Although patient survival of 3 to 5

years has been reported after metastasis to the skull from primary renal or colon tumours or plasmacytomas, patients with a pituitary metastasis from the pancreas have a survival of approximately 3 months.¹ Metastasis to the pituitary gland from an HCC has been the subject of a single report in the literature to date, and survival time was not mentioned.¹ The two patients in this study survived for only 3 months and 12 months, respectively. Despite the poor prognosis, relief of symptoms was deemed to justify surgical intervention in each case.

References

1. Morita A, Meyer FB, Laws ER Jr. Symptomatic pituitary metastases. *J Neurosurg* 1998;89:69-73.
2. Cohen MM, Lessell S. Chiasmal syndrome due to metastasis. *Arch Neurol* 1979;36:565-7.
3. Clavier H, Poiraudou S, Le Gros V, Tourani JM. Pituitary metastasis of a small cell bronchial carcinoma responsible for diabetes insipidus and disclosed by corticosteroid therapy [in French]. *Rav Mal Respir* 1987;4:185-6.
4. Oi S, Ciric IS, Mayer TK. Metastatic breast carcinoma in the pituitary gland [in Japanese]. *No To Shinkei* 1978;30:69-73.
5. McCormick PC, Post KD, Kandji AD, Hays AP. Metastatic carcinoma to the pituitary gland. *Br J Neurosurg* 1989;3:71-9.
6. Buonaguidi R, Ferdeghini M, Faggionato F, Tusini G. Intracellular metastasis mimicking a pituitary adenoma. *Surg Neurol* 1983;20:373-8.
7. Max MB, Deck MD, Rottenberg DA. Pituitary metastasis: incidence in cancer patients and clinical differentiation from pituitary adenoma. *Neurology* 1981;31:988-1002.
8. Rossi ML, Bevan JS, Fleming KA, Cruz-Sanchez F. Pituitary metastasis from malignant bronchial carcinoid. *Tumori* 1988;74:101-5.
9. Kawamura J, Tsukamoto K, Yamakawa K, Tazima K, Tochigi H. Diabetes insipidus due to pituitary metastasis from bladder cancer. *Urol Int* 1991;46:217-20.
10. Sioutos P, Yen V, Arbit E. Pituitary gland metastases. *Ann Surg Oncol* 1996;3:94-9.
11. Koshiyama H, Ohgaki K, Hida S, et al. Metastatic renal cell carcinoma to the pituitary gland presenting with hypopituitarism. *J Endocrinol Invest* 1992;15:677-81.