Intracranial Metastasis of Prostate Cancer: Report of Two Cases

Po-Hui Chiang, MD, PhD; Tao-Chen Lee[1], MD; Chao-Cheng Huang[2], MD

Metastases from prostate cancer to the brain are very unusual and are seldom reported in the clinical literature. We report 2 cases of advanced stage prostate cancer with intracranial metastasis. One patient developed intracranial metastasis 5 years after step-up treatment. He had hormone refractory prostate cancer with a high level of prostate specific antigen (PSA). Unfortunately, he died of sepsis 3 weeks after craniotomy. The other patient with various neurologic symptoms and a normal PSA level responded to hormone therapy well. He had an uneventful postoperative course and has survived for more than 21 months after surgery. We also reviewed the literature and suggest that aggressive treatment, including neurosurgery, could improve the survival of certain patients with advanced prostate cancer with intracranial metastasis. *(Chang Gung Med J 2004;27:770-6)*

Key words: prostate neoplasm, brain metastasis, hormone deprivation therapy.

We report two rare cases of advanced stage of prostate cancer with intracranial metastasis. One died of sepsis and the other has been uneventful after craniotomy. From the experience of our second case and literature review we suggest neurological intervention may be considered in prostatic cancer patients as it could improve the survival rate in certain cases.

CASE REPORT

Case 1

A 61 year-old man was first seen with dysuria and hematuria in June, 1997. Transurethral resection of the prostate and bladder was performed and pathological examination showed moderately differentiated adenocarcinoma. Computerized tomography revealed multiple enlarged lymph nodes at the prevertebral space. Initial treatment at another hospital was supportive only. However, chest radiograph (Fig. 1A) and bone scan revealed multiple lung and bone metastases, respectively, in April, 1998. The PSA value was 816.8 ng/ml (normal 0-4 ng/ml) at that time. The treatment was then stepped up to steroidal antiandrogen (Cyproterone acetate) and LH-RH analogue (Goserelin). Complete resolution of lung metastasis (Fig. 1B) two months after the androgen deprivation therapy was noted. The PSA value declined to 12.74 ng/ml in Sep., 1998. The clinical course had been uneventful until the PSA value increased to 368.2 ng/ml in July, 1999. Radiotherapy (6000 Rad.) of the pelvis and lumbar spine was initiated when the PSA value increased to 920.4 ng/ml and the patient complained of right hip pain in Sep., 1999. Castration was performed in Jan., 2000. However, lung metastasis was noted again and the PSA value increased to 1762 ng/ml in Dec., 2000. Flutamide and estrogen were used as second-line endocrine management. The PSA value decreased to 483 ng/ml one month later. The clinical course was uneventful until the PSA value increased

From the Department of Urology, [1]Department of Neurosurgery, [2]Department of Pathology, Chang Gung Memorial Hospital, Kaohsiung.
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Address for reprints: Dr. Po-Hui Chiang, Department of Urology, Chang Gung Memorial Hospital. No. 123, Dabi Rd., Niaosung Shiang, Kaohsiung, Taiwan 833. R.O.C. Tel.: 886-7-7317123 ext. 8094; Fax: 886-7-2357210; E-mail: cphtem@yahoo.com.tw

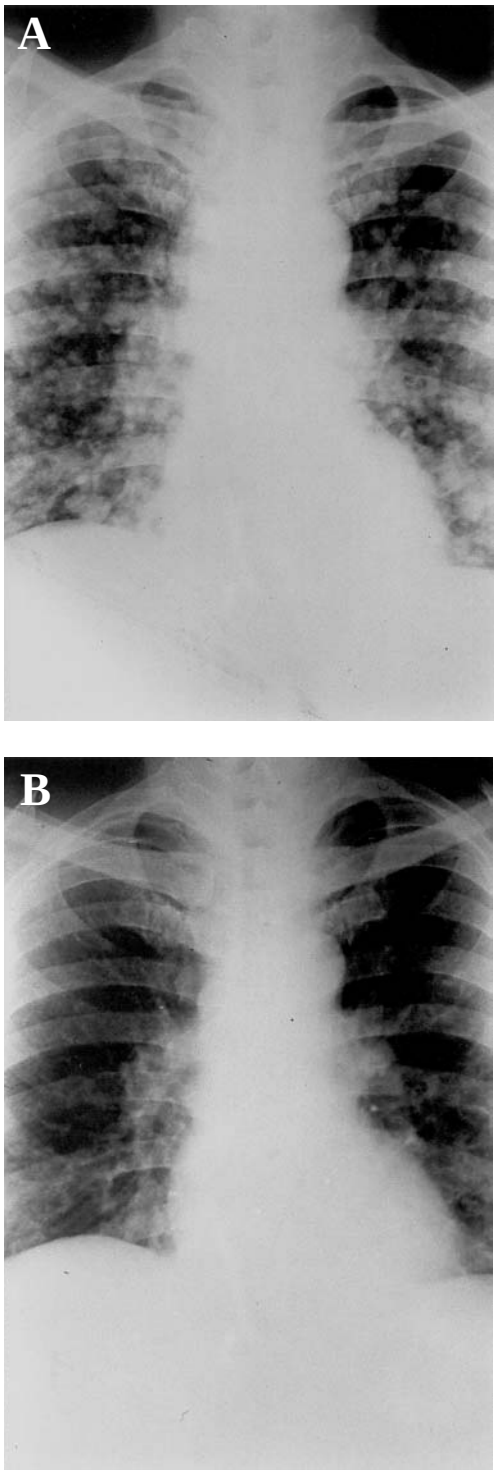

Fig. 1 (A) Chest X-ray showing multiple pulmonary metastases before androgen deprivation therapy. (B) Complete resolution after androgen deprivation therapy.

to 2668.1 ng/ml in Oct., 2001. Magnetic resonance imaging revealed multiple vertebral metastases with severe compression at the L1-L2 level. The patient suffered a left subtrochanteric pathological fracture at that time. Withdrawal of flutamide resulted in a fall in the serum PSA to 1660 ng/ml. However, the PSA value increased to 4052.48 ng/ml 4 months later. Thereafter, chemotherapy with mitoxantrone (12 mg./m^2 IV q3wk) and docetaxel (75 mg./m^2 IV q3wk) was prescribed for 4 and 2 courses, respectively. The PSA value decreased to 514 ng/ml in Aug., 2002. Persistent ileus was noted and an ileostomy was performed in Jan., 2003. The PSA value increased to 812 ng/ml at that time. Sudden onset of dysarthria, seizure and confusion was noted two weeks after the operation. Cranial CT revealed a left frontal mass with heterogenous density and left lateral ventricle compression (Fig. 2). Craniotomy and complete resection of the left frontal tumor were done in January, 2003. The histology showed metastatic adenocarcinoma and a positive immunohistochemical stain for PSA (Fig. 3). Estramustine was then prescribed. Postoperatively, the patient had an intermittent high fever with wound infection, bacteremia and right obstructive uropathy with pyonephrosis. Although he received empiric antibiot-

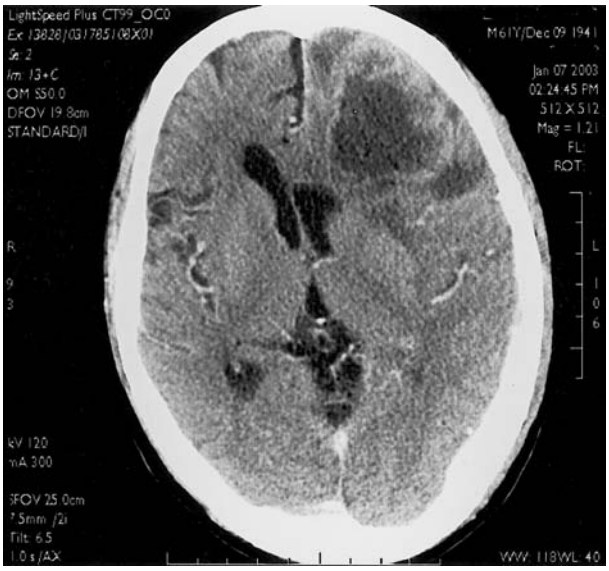

Fig. 2 Brain CT demonstrating a left frontal mass with heterogenous density and left lateral ventricle compression.

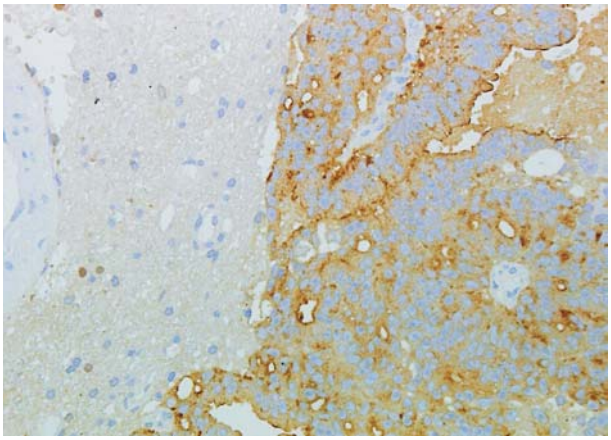

Fig. 3 Brain tumor showing positive staining for adenocarcinoma (brown color) and for prostatic specific antigen (×300).

ic treatment and a right percutaneous nephrostomy, he died of sepsis with multiple organ failure three weeks after the operation. The chronological history is shown in Figure 4.

Case 2

A 62 year-old patient with prostate cancer with known 8th thoracic spine bony metastasis received a thoracotomy and radiotherapy in 1998. He was admitted in December, 2002 due to weakness in the right extremities and poor memory since October, 2002. Furthermore, he complained of ataxia with blurred vision for several months. His PSA level was within normal limits (1.63 ng/ml, normal 0-4 ng/ml) under androgen deprivation therapy (steroidal antiandrogen and LH-RH analogue). Brain CT revealed a left parietooccipital tumor with perifocal edema and calcification (Fig. 5). Resection of the brain tumor

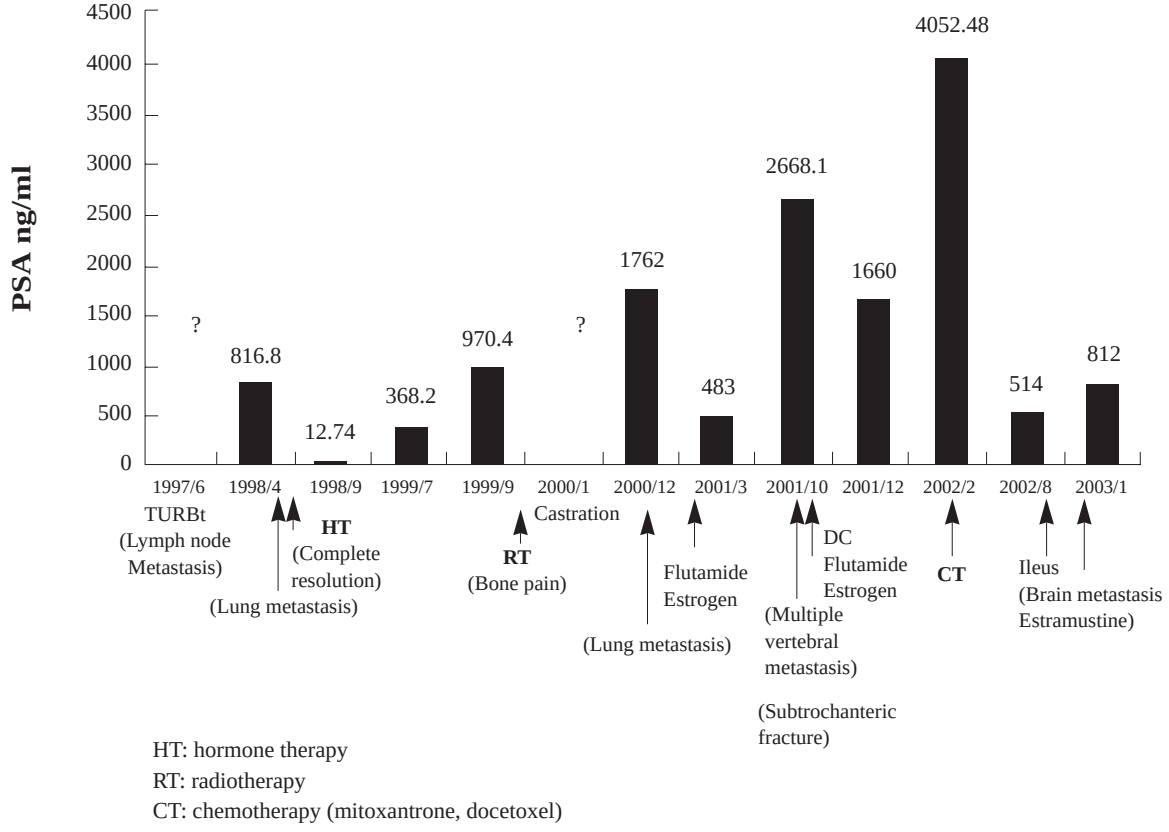

Fig. 4 Chronological history of the first case.

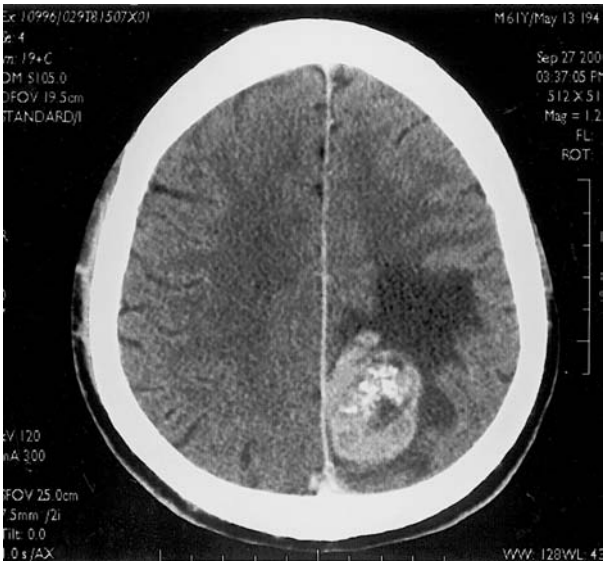

Fig. 5 Brain CT demonstrating a left parietal occipital tumor with perifocal edema and calcification.

was carried out and the pathology report showed adenocarcinoma with positive PSA staining. The postoperative course has been uneventful. He has survived for more than 21 months after surgery.

DISCUSSION

The most common sites of prostate cancer metastasis include the bone, lung and liver.[1] Brain metastasis is very rare.[1] The reported incidence at autopsy was 0.6% to 4.4% and mostly involved the leptomeninges (67%), followed by the cerebrum (25%) and cerebellum (8%).[1,2] Antemortem diagnosis of intracranial metastases has been achieved in only 0.1% of cases.[3] Routes of dissemination of advanced stage prostate cancer to the central nervous system include direct extension from a skull lesion, lymphatic spread and vascular embolization.[4]

Two different pathways of brain metastasis have been postulated.[1] One is through secondary tumor seeding from the bone and lung and the other is direct access through the paravertebral venous plexus, thus avoiding the bone and the viscera. Multiple metastases in the spine, femur, lymph node and lung were diagnosed in our first patient. Our second patient had an 8th thoracic spine bony metastasis and had received a thoracotomy. The first pathway was likely for both patients.

Neurologic findings are variable (Table 1) and include headache, seizure, motor deficits, intracranial hemorrhage, subdural hematoma, mental status changes, gait disturbance, vertigo, multiple cranial nerve palsies and inappropriate secretion of antidiuretic hormone syndrome.[2] The neurologic deficits in our two patients varied greatly and were distinctive.

Large scale prospective studies have reported an overall survival of 2-3 years in stage D2 prostate cancer with any combination regimen. Our first patient was treated initially by less effective means. His treatment was then stepped up to androgen blockade, palliative radiotherapy and castration, followed by second-line hormone therapy, antiandrogen withdrawal and chemotherapy. The various treatments resulted in complete or partial responses although treatment resistance developed afterwards. This patient suffered from lymph node, lung, bone and brain metastases and spinal cord compression and finally died of sepsis. The benefit of craniotomy can not be assessed in this patient with disseminated prostate cancer. However, this patient had indeed survived for 69 months. We herein report and add supportive evidence to the concept of a step-up approach.[5]

Treatments available for intracranial metastasis include neurosurgery, external beam radiation and hormonal manipulation.[1,4] Kohri et al. reported the benefits of daily administration of estramustine phosphate sodium leading to regression of a brain metastatic lesion in a patient who survived for more than two years.[6] Our first patient had received the above regimen but with little improvement, possibly due to the short interval of usage.

Some reports showed that the prognosis of brain metastasis is poor with a one year survival rate of 18% and an average survival of 7.6 months.[7] Our second patient survived for more than 21 months post intracranial surgery. He is presently receiving hormonal therapy and his condition is stable.

Generally, radiation therapy and surgery are believed to be standard options for brain metastases. Table 1 shows the reported cases of intracranial metastasis of prostate cancer in the literature. In the series of Catane et al., 2 patients treated with radiation therapy survived for only three and four weeks.[9] On the contrary, other series have reported survivals

Table 1. Summary of Reported Cases of Intracranial Metastasis from Prostatic Carcinoma

Case no. & source	Age (yr)	Tumor site	Symptoms	PSA (ng/ml)	Diagnosis tool	Treatment	Survival time
1. Case 1	61	Left frontal	Dysarthria seizures *Consciousness disturbance	812	CT	Craniotomy Estramustine	3 weeks
2. Case 2	62	Left parietal occipital	Ataxia blurred vision	1.63	CT	HT Craniotomy	> 21 months
3. Fervenza et al.,[1] 2000	61	Right frontal	Confusion		MRI	Brain RT Craniotomy	> 8 months
4. Sutton et al.,[2] 1996	70	Right parietal	Dizziness	> 100	CT	Craniotomy Orchiectomy	> 6 months
5. Sutton et al.,[2] 1996	62	Right pons	Left sided weakness Nausea anorexia	11.70	CT	Brain RT	> 1 month
6. Zhang et al.,[3] 1997	72	Right frontal	Transient unconsciousness	40.6	CT	Craniotomy	19 months Estramustine
7. Kunkler et al.,[4] 1993	71	Right parietal	Left hemiparesis		CT	Craniotomy HT	> 24 months
8. Kohri et al.,[6] 1998	62	Left frontal	Left visual defect		CT MRI	Estramustine Orchiectomy	> 24 months
9. Gupta A et al.,[8] 1994	55	Left pons/Left cerebral penduncle	Face fullness, headache	11.5	MRI stem RT	Brain & brain	> 2 months
10. Catane R et al.,[9] 1976	51	Intracerebral (multiple)	Right complete hemiplegia		Cerebral blood flow Brain scan	Dexamethasone Brain RT	3 weeks
11. Catane R et al.,[9] 1976	43	Right cerebral hemisphere	Drowsiness vomiting, loss of memory left hemiparesis		EEG	Brain scan Brain RT	4 weeks
12. Rao KG [10] 1982	75	Left cavernous sinus, posterior to int. carotid artery	Headache, left eyelid ptosis, pain behind the left eye		nil	Craniotomy, Orchiectomy, Stilbestrol	> 24 months
13. Chang et al.,[11] 1998	68	Left temporal	Unsteady gait Slurred speech		CT	Craniotomy	2 weeks

Abbreviations: HT: hormone therapy; RT: radiotherapy

of up to two years after intracranial tumor surgical resection.[4,10] We reviewed eleven reported cases in addition to our two cases.[1-4,6,8-11] Five of the 8 patients (63%) receiving craniotomy survived longer than 8 months. However, only one of five patients (20%) who did not receive craniotomy survived longer than 8 months. However, the case number is too small to make a conclusion. Aggressive treatment including neurosurgery could be done as it has been shown to improve the survival of certain patients with advanced prostate cancer with intracranial metastasis.

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攝護腺癌之顱內轉移：兩病例報告

江博暉 李道眞[1] 黃昭誠[2]

攝護腺癌顱內轉移不常見並且臨床文獻報告不多。我們報告2例末期攝護腺癌顱內轉移病例。一位以逐步進階治療之末期攝護腺癌經5年治療後發生顱內轉移，病人之PSA指數偏高並爲荷爾蒙抗性，顱內腫瘤切除術後3星期死於敗血症。另一病例表現不同神經學異常但有正常之PSA指數，並對荷爾蒙治療反應良好，此病例術後恢復良好，至今存活超過21個月。回顧文獻及第二例經驗，我們認爲積極接受顱內腫瘤切除對某些病例可改善存活率。(長庚醫誌2004;27:770-6)

關鍵字：攝護腺癌，顱內轉移，荷爾蒙治療。

長庚紀念醫院 高雄院區 泌尿科，神經外科[1]，病理科[2]
受文日期：民國92年7月28日；接受刊載：民國92年12月22日。
索取抽印本處：江博暉醫師，長庚紀念醫院 泌尿科。高雄縣333鳥松鄉大埤路123號。Tel.: (07)7317123轉8094; Fax: (07)2357210; E-mail: cphtem@yahoo.com.tw