

### *Clinical Study*

## **Solitary brain metastases from carcinoma of the bladder**

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### **Summary**

We report 6 cases of solitary brain metastasis from bladder carcinoma. Although systemic metastases from this cancer are frequent, central nervous system metastases are rare. Analysis of our material and of published cases shows that the tumor is resistant to therapy and the prognosis is consequently very poor.

### **Introduction**

Carcinoma of the bladder accounts for about 2% of malignant tumors [6, 11]. About 80% of bladder carcinomas are superficial (stages A-B1) but 20% are invasive (stages B2-D) [12]. Invasive carcinoma gives rise to distant metastases, which settle chiefly in the lymph nodes (45%–65% of cases), lung (24%–36%), liver (21%–35%) and skeleton (10%–25%) [7]. Brain metastases are rare (0.3%–8%) [9, 10, 17, 21].

We report 6 cases of solitary brain metastasis from bladder carcinoma and discuss the clinical features and treatment.

### *Material and method*

Six patients with brain metastasis from bladder carcinoma received surgical treatment in the Neurosurgery Section of the Neurological Sciences Department of 'La Sapienza' University of Rome between 1962 and 1988.

The clinical and therapeutic characteristics of 6 patients were reported in Table 1. All were treated according to the protocol for the treatment of the primary tumor: cystectomy (with lymphadenectomy in 1 of them), a course of local radiotherapy (to-

tal dose 4500 rads); 2 patients received a course of systemic chemotherapy (methotrexate and cyclophosphamide). Clinical status was rated pre- and post-operatively on the Karnofsky Performance Status scale (KPS) (Fig. 1). The radiological diagnosis was established by pneumoencephalography and angiography in the patients who were treated before 1975 (2 cases) and by angiography and CT scan since then. Systemic radiological examinations were done in all cases to elicit any other cancerous lesions present (plain films, total body CT, urography, ultrasound and radionuclide scanning, . . .). All the systemic examinations were negative. All patients received surgical treatment and radiotherapy for the brain metastasis.

### **Result**

Of the 6 patients 4 were male and 2 female (M/F ratio; 2 : 1) and their mean age was 65 years (range 55–72 years).

The mean interval between diagnosis of the bladder carcinoma and onset of the brain metastasis was 5.9 months (range 1–13 months). The mean duration of the clinical history was 2 months (range 1 week – 4 months). The most frequent presenting clinical symptom was intracranial hypertension (5

Table 1. Summary of our cases

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Sex	m	f	m	f	m	m
age (yrs)	55	57	63	71	72	72
Mean clinical history of bladder carcinoma (mos):	12	8	6	4	5	4
Presenting signs (%)	h-d	h-d	h-d	h-d	h-d	h-d
Treatment:	cy/r	cy/r/ch	cy-1/r/ch	cy/r	cy/r	cy/r
Grading:						
clinical	b2	c	d1	b2	c	c
histological	III	II	III	II	III	III
Mean intervall between diagnosis of the bladder carcinoma and onset of brain metastasis (mos):	5.1	8.1	3.1	7.1	6	6
Mean clinical history of brain metastasis (mos):	1	3	2	1	2	2
Presenting signs:	hi	hi/se	hi	hi/se	hi	hi
KPS:	90	60	70	80	80	70
Site:	RG-fr	RG-t	LT-fr	RG-fr	LT-t	RG-p
Treatment:	s/r	s/r	s/r	s/r	s/r	s/r
(year)	1963	1970	1969	1976	1980	1987
Survival since brain surgery (mos):	8.2	3	2	6.1	7.8	5.9

Abbreviation: ch/chemotherapy; cy/cystectomy; d/dysuria; f/female; fr/frontal; h/hematuria; hi/intracranial hypertension; KPS/Karnofsky Performance Scale; l/lymphadenectomy; LT/left; p/parietal; r/radiotherapy; RG/right; s/surgery; se/seizures; t/temporal.

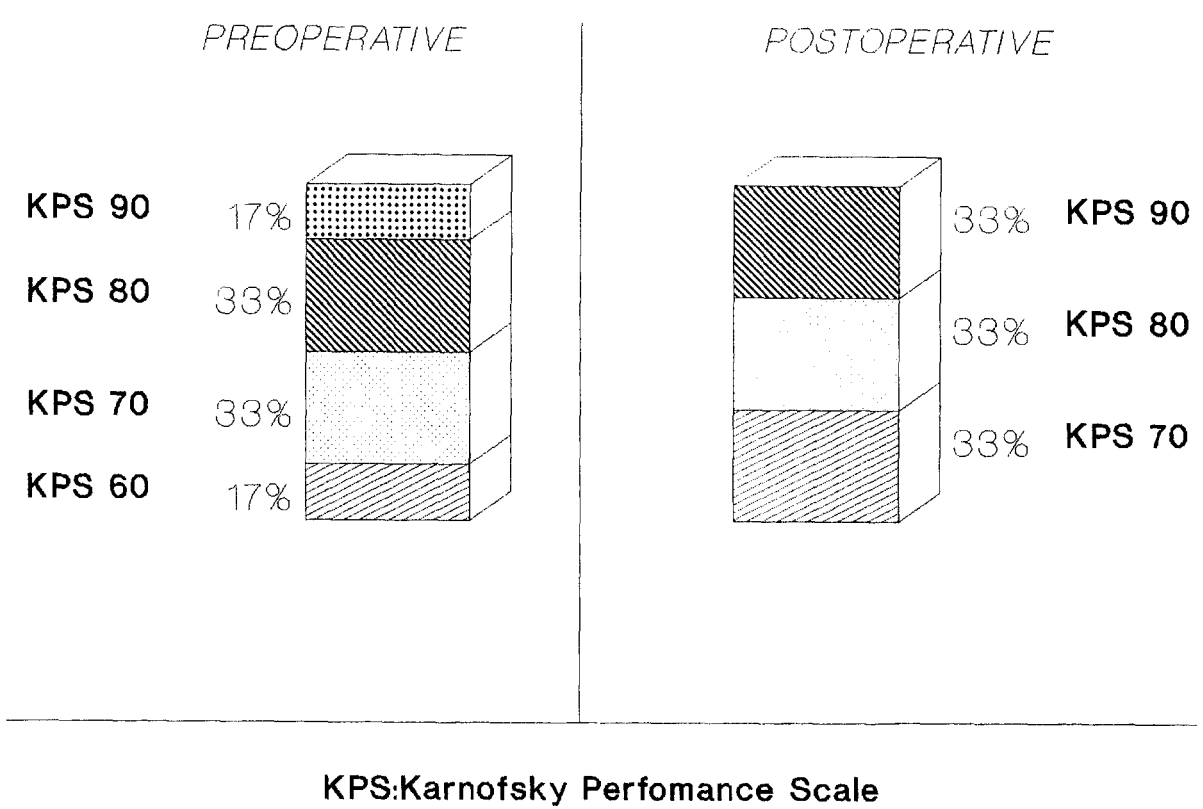


Fig. 1. KPS: Karnofsky Performance Scale.

cases) and epileptic seizures (1 case). All patients had a KPS > 60 on admission (Fig. 1). Pneumoencephalography and cerebral angiography supplied indirect signs of a space-occupying brain lesion (hydrocephalus and noninjection of the ventricles by the former and vessel displacement and pathological blood supply by the latter). CT brain-scans revealed a roundish cystic lesion with ring enhancement and perilesional edema in every case. The metastasis was single in all cases. This was not revealed by the plain films in the first 2 cases (seen before 1975) but was later proved by the fact that the cause of death was found to be progression of the systemic disease and by autopsy, at which no other brain lesions were found. The tumor site was frontal in 3 cases (50%), temporal in 2 (33%), parietal in 1 (17%). None of the patients presented radiological or clinical signs of other systemic lesions at the time of examination for the brain metastasis.

All the patients underwent surgical tumor removal, grossly total in every case, supplemented by postoperative whole brain radiotherapy (total dose 40–45 Gy). The histotype was transitional carcinoma in all cases: grade II and 2 in grade III in 4 cases. Treatment of the brain lesion resulted in KPS improvement, even though transient, in all cases (Fig. 1). The improvement was maintained for 2/3 of the residual life. Mean survival was 5.5 months (range 4–25 months). The cause of death was progression of the systemic disease in 5 out of 6 cases and the onset of 3 new brain metastases in one. Brain relapse occurred in 2 other cases but it was not the direct cause of death.

## Discussion

Metastases from bladder carcinoma are multiple in 60%–80% of cases and solitary in 20%–40% [3, 7]. Solitary brain metastases from carcinoma of the bladder are rare. Only 31 cases without evidence of other metastatic disease have been reported in detail (including the 6 reported here) [1–5, 8, 13–15] (Table 2). In the majority of cases (90%) the brain metastases developed within one year of treatment for the primary tumor. The factors relevant to their manifestation seem to be the extent and histolog-

ical grade of the primary tumor [12, 13]. The brain metastases were present in the cases in which the cancer had invaded the tunica muscularis of the bladder. It has been shown that the risk of invasion of the vascular and lymphatic structures and hence the manifestation of metastases depends strictly on a high degree of malignancy of the primary tumor [12]. The histological grade of the primary, when reported (21 of the 31 published cases of brain metastases), was always above I. Although rare, brain metastases from bladder carcinoma have been on the increase for the past decade. They may well develop as a result of treatment for the primary tumor. Patients with bladder cancer, especially if invasive, undergo surgical removal of the tumor, radiotherapy and systemic chemotherapy [1, 3, 13, 20]. This combination may control the cancer [20], but the systemic chemotherapy might be indirectly related to the onset of brain metastases, partly because the drugs are thought to damage the blood-brain barrier and partly because their effect on the brain compartment might be limited and not enough to prevent the progression of micrometastases [13].

Table 2. Summary of 25 cases reported in literature [1–5, 8, 13–18]

Total number	25
M/F ratio	1.2 : 1
Mean age (yrs)	62
Mean interval between diagnosis of the bladder carcinoma and onset of brain metastasis (mos):	4.9
Mean clinical history (mos):	2.1
Presenting Signs (%):	
Intracranial hypertension	80
Focal	65
Seizures	20
Site (%):	
Cerebellum	33
Frontal	24
Temporal	22
Few lobes	15
Parietal	5
Retro-orbital	1
Treatment for brain metastasis:	
Surgery	25
Radiotherapy	23
Chemotherapy	8
Mean survival (mos):	7.2

Patients with metastases had a mean clinical history of 2.1 months (range 2 weeks – 8 months), 80% presenting signs of intracranial hypertension, 65% focal signs and 20% epileptic seizures. The radiological diagnosis is based nowadays on CT and MRI, which image a cystic lesion with ring enhancement in 85% of cases. In 15% of cases the lesion presents patchy enhancement. MRI after administration of gadolinium has proved consistently superior to CT in staging the brain lesions (single or multiple), which is necessary for more accurate therapeutic classification [6, 8, 9, 19]. Solitary metastases are treated by surgical removal and radiotherapy plus, recently, chemotherapy [17, 19].

In 12 cases the contemporary presence of the primary tumor without evidence of other metastatic disease was reported. The tumor site was cerebellum in 33% of cases, a frontal lobe in 24%, a temporal lobe in 22%, more than one lobe in 15%, a parietal lobe in 5% and retro-orbital in 1%. Delattre [6] in a study of 288 brain metastases, 27 of which originated from abdominal and pelvic cancers, noted that the frequency of solitary metastases from pelvic and abdominal cancers was significantly higher in the infratentorial compartment (50% vs 10%;  $p = 0.003$ ). In our series, by contrast, the metastases were supratentorial.

The outcome of treatment was very poor with a mean survival of only 7.2 months (range 1 week – 27 months). The cause of death in 71% of patients was progression of the systemic disease and in 19% brain relapse. In our series 50% of patients recurred even after whole-brain radiotherapy. These results show that these lesions are more resistant to treatment than are other metastases from other primary cancers when brain metastases are present [9, 17, 19, 21].

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