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Brain metastasis in hypernephroma*

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Abstract

Of 926 patients with hypernephroma, 36 (3.9%) had metastasis to the brain. The median age at presentation was 61 years (range, 34 to 82). Nineteen patients had a single lesion metastatic to the brain, and 16 of these lesions were supratentorial. In 28% of the patients, computed tomography showed hyperdense lesions before contrast material was injected. All patients, except 2 with incomplete records, had evidence of widespread disease involving bone, liver, or lung. The median time interval between the initial diagnosis and the discovery of brain metastasis was 65.5 weeks (range, 0 to 462), with only 2 patients initially presenting with brain metastasis. Twenty-five of the patients who received only radiation therapy had a median survival of 13 weeks (range, 4 to 146), while 7 selected patients who underwent surgical resection and postoperative radiation had a median survival of 66 weeks (range, 18 to 260). In 5 of the 7 patients, scans demonstrated recurrent tumor from 6 to 23 weeks postoperatively. One patient had a pronounced reduction in the size of the tumor after radiation therapy only. This study shows that brain metastasis is usually a late complication of hypernephroma and is associated with a poor prognosis.

Introduction

The incidence of hypernephroma is approximately 7.5 per 100000 persons in the United States, with nearly 15000 new cases each year (1, 2). Although nearly one-third of the patients have widespread disease at presentation, one of the gravest prognostic signs of this cancer is metastasis to the brain (3, 4). Despite several autopsy studies, as well as reports of solid tumors metastasizing to the brain, there are few clinically oriented reports of a large series of hypernephroma metastasis to the brain (5–12).

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Materials and methods

The medical records of 926 patients with hypernephroma who were seen at the Mayo Clinic between 1975 and 1982 were reviewed. The records of patients with documented metastasis to the brain were analyzed. Patients were included in the study if they had computed tomography (CT) scan or radionuclide scan and there was autopsy evidence of an intracranial mass. Several patients had well-established diagnoses when seen, but additional pertinent information was needed from referring physicians. The data extracted from the chart included neurologic signs and symptoms, radiologic findings, treatment for the primary tumor, treatment for the brain metastasis, and the length of survival.

Results

Thirty-six (3.9%) patients had documented metastasis to the brain. The median age at neurologic presentation was 61 years (range, 34 to 82), and the male-to-female ratio was 6:1. The site of the primary tumor was the right kidney in 16 patients and the left kidney in 20. Surgical resection of the primary tumor was attempted in 31 patients. Twenty-one patients were treated initially with systemic chemotherapy. Only 6 of the 32 patients who received radiation treatment to the brain had initial radiation treatment to the site of the previously resected kidney.

Two patients had incomplete records. All others demonstrated evidence of bone, liver, or lung involvement. Fifteen patients (42%) had involvement of at least two of these sites, with the lung involved most frequently (89%). Only 2 patients were seen initially with metastasis to the brain, and both also had widespread systemic disease.

The onset of clinical symptoms was sudden in 21% of the patients, including 1 patient with seizures. Subsequent to the initial diagnosis, 8 patients had acute neurologic events (paresis, dizziness, gait change, vision loss, or paraesthesias) and 5 additional patients had seizures during the course of their disease. No patient had a symptomatic intracerebral hemorrhage. In general, neurologic symptoms are reported to be more frequent with other types of tumors (13, 14). Complete documentation, however, was lacking for some of our patients, and not all patients were examined by a neurologist.

All available CT scans of the head were reviewed. Two patients had positive radionuclide head scans only. One patient who was studied early in 1975 had a negative CT scan but a positive radionuclide scan. This discrepancy between a radionuclide scan and the early CT scans has been reported (4). Nineteen patients had CT scans with contrast medium, and 10 had CT scans that showed hyperdense lesions before the administration of contrast medium. Sixteen patients (44%) had more than one metastatic lesion to the brain, and 1 patient had a second lesion which, on a CT scan, was equivocal for metastasis. CT scans showed that the lesion was located supratentorially in 23 patients (64%), infratentorially in 5 (14%), and in both sites in 7 (20%); in 1 case, CT scan was done elsewhere and was not available for review, but autopsy confirmed brain metastasis.

For the 32 patients with complete follow-up (4 patients are still alive), the median survival time after initial diagnosis was 74.5 weeks (range, 8 to 526) (Table 1). After the identification of brain metastasis, the median survival was only 17 weeks (range, 4 to 260). The median latency interval (the time between initial diagnosis and the discovery of brain metastasis) for all 36 patients was 65.5 weeks (range, 0 to 462).

Seven patients underwent surgical resection and received radiation therapy postoperatively. These patients survived for a median period of 66 weeks (range, 18 to 260). Each of the 7 patients was selected for operation because of stable systemic disease, an accessible single metastatic lesion, and the belief that the tumor could be totally resected. In 5 of the 7 patients, CT scans demonstrated a recurrent tumor (from 16 to 23 weeks after operation). In 2 of these patients, the recurrence was at the site of the previous resection.

For the 25 remaining patients who received radiation therapy alone, the median survival was 13 weeks (range, 4 to 146). In 1 of these patients, CT scan revealed a pronounced reduction in the size of the tumor after radiation treatment – a finding that also has been documented by others (8) (Fig. 1). Of 5 other patients who had CT scans immediately after radiation therapy, 2 had some

Table 1. Median survival of patients with hypernephroma metastatic to the brain.

Survival	Patients		
	Total (36 pt)[a]	Surgery and radiation (7 pt)	Radiation only (29 pt)
After initial diagnosis (wk)	74.5	128	67
After diagnosis of brain metastasis (wk)	17	66	13
1-year (%)	28	57	22

[a] Four of the 36 patients are still alive.

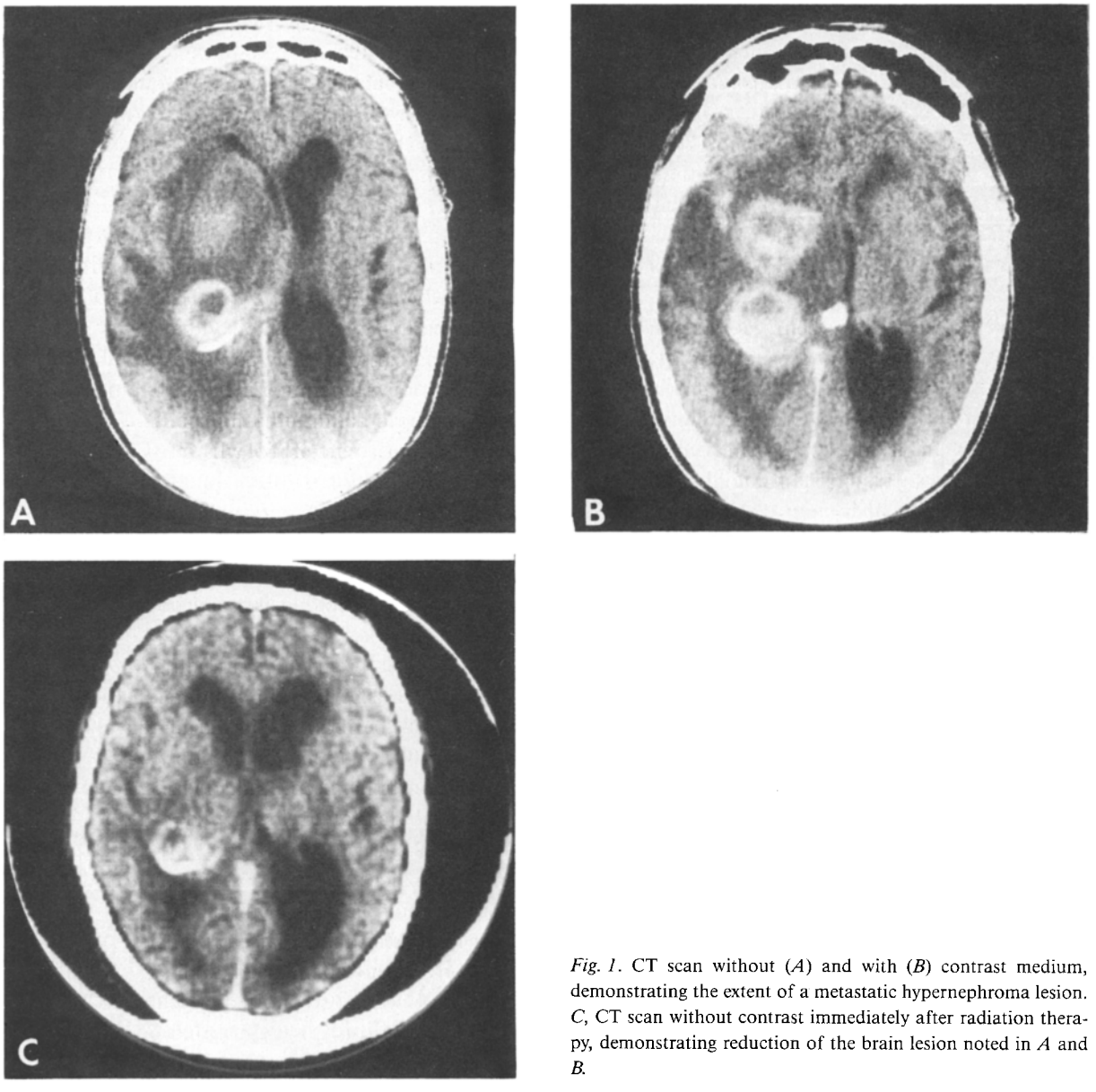

Fig. 1. CT scan without (*A*) and with (*B*) contrast medium, demonstrating the extent of a metastatic hypernephroma lesion. *C*, CT scan without contrast immediately after radiation therapy, demonstrating reduction of the brain lesion noted in *A* and *B*.

reduction in the size of the tumor and three had no change, as demonstrated on CT scan. All but 1 patient also received steroids.

The 1-year survival for all patients was 28%. The 1-year survival was 57% for patients who underwent surgery and 22% for those who did not. There was no difference in survival time when age at diagnosis, latency interval, and location or number of lesions metastatic to the brain were compared.

Discussion

In the present study, the incidence of parenchymal metastasis to the brain in patients with hypernephroma is 3.9%. This percentage is less than that noted in recent reports (6, 8). Several authors have suggested that the incidence of brain metastasis is increasing, possibly because of improved diagnostic methods and longer survival with better treat-

ment of the primary malignant lesion (7, 13, 15). However, this increase was not shown in our study. Autopsy studies have noted an even larger incidence of brain metastasis in patients with hypernephroma – as much as 10% to 20% (Table 2) (6, 8, 10, 17). This high rate supports the hypothesis that many patients may have clinically unrecognized intracranial disease and often have greater morbidity and mortality related to systemic metastasis rather than to brain metastasis (18).

The unexpectedly large proportion of males with brain metastasis in our study is of uncertain significance. Males repeatedly have a higher incidence of hypernephroma, with the sex ratio ranging from 2:1 (1, 19) to 3:1 (10), although a recent large autopsy study suggested that the frequency of metastasis was similar in men and women (8). The median age of the present group of patients at the time of diagnosis of intracranial disease was similar to that in other reports (9, 18, 19).

Of patients with brain metastasis from all types of solid tumors, nearly a third (31%) have neurologic symptoms at initial presentation (13, 14). However, when seen initially, only 2 (6%) of our patients had neurologic complaints due to brain metastasis. In addition, the vast majority of patients described in other reports (11, 13, 18, 20) had evidence of widely metastatic disease at the initial diagnosis. Hypernephroma that metastasized to the brain exclusively is usually demonstrated only in autopsy studies, where the incidence may approach 7% (8).

In our series, there were nearly as many patients with a single metastatic lesion as with multiple lesions. This is similar to that noted in a large series of patients with all types of tumor, in which 50% have multiple metastatic lesions (6, 13, 21). The distribution of metastatic lesions in the brain in our study also was similar to that observed by others for hypernephroma and all tumor types, with nearly three to four times as many supratentorial lesions (5, 8, 11, 13). This predilection may reflect either differences in regional blood flow, proportional to relative brain mass, or more dramatic cerebral symptoms, leading to earlier recognition of tumor metastasis (7).

Table 2. Reports of hypernephroma metastasizing to brain.

Author	Year	Patients	
		With hypernephroma	With brain metastasis
Abrams (3)	1950	34	8 (24%)
Murphy (16)	1961	42	4 (9.5%)
Posner (6)	1978	52	11 (21%)
Saitoh (8)	1982	1828	177 (9.7%)
Present	1985	926	36 (3.9%)

Several modes of access of systemic malignancy to the brain have been proposed. Tumor emboli may traverse the spinal epidural venous circulation and vertebral veins, as demonstrated by Batson in 1940 (22). Metastasis to the lungs was commonly noted in the present study as well as in other studies, and some theorize that neoplastic cells may enter the central nervous system by communication with the pulmonary arterial circulation (7, 13). Direct invasion from bone also has occasionally been described (7).

Seizures in patients with parenchymal metastasis to the central nervous system vary with the type of primary solid tumor (14, 20). About 50% of patients with melanoma metastatic to the brain have seizures during the course of their disease (23). In the present study, seizures were less common, being seen in only 17% of patients. The reason for such variation in seizure activity is unclear.

Acute changes in the clinical course of patients with solid tumor metastasis to the brain are believed to be related to intracerebral hemorrhage. No patient in our study had symptomatic intracerebral hemorrhages. Ten patients had hyperdense lesions noted on CT scan before the injection of contrast medium. It is not clear from our study whether these abnormalities on CT scan represent hemorrhage or simply an increased packing density of metastatic hypernephroma cells. However, 5 patients with hyperdense lesions did have surgery. No comment was made by the pathologist to indicate that there was hemorrhage in the tumor.

In the present study, the median survival time of all patients after diagnosis was in close agreement with the 14 to 24 weeks reported by other authors (11, 13). The median survival when radiation thera-

py was given was 13 weeks, while in 7 selected patients who had both surgical resection and radiation, median survival was 66 weeks (see Table 1). One patient had a verified response to radiation, as noted on serial CT scans. In a recent nonrandomized study, the mean survival of patients with radiation-treated renal brain metastasis was 8.6 months compared to 3.2 months for those who did not receive radiation. Patients treated surgically had a mean survival of 13.8 months (12).

Several factors that may affect survival after treatment were examined. Age, systemic involvement, and number of lesions metastatic to the brain did not correlate with the length of survival. This lack of correlation agrees with other reports noting that age, extent of systemic involvement, and multiplicity or location of brain metastasis do not correlate with survival (7, 12, 13, 17, 18, 24). Neurologic impairment at the diagnosis of brain metastasis was not evaluated in our study, but such impairment has been shown to be a reliable predictor of survival (13, 17). The latency interval remains a controversial prognostic indicator (7, 17, 24) and was found not to be related to survival in our study.

Patients undergoing surgical resection of lesions metastatic to the brain have a longer median survival than those treated with radiation therapy alone, but selection biases obviate direct comparison of the group with radiation alone and the group with surgery and radiation. Neurologic function and the quality of life often can be improved if both forms of therapy are used (25).

Patients with renal cell cancer metastatic to the brain have a poor prognosis. In our study, brain involvement was usually a late and ominous event. However, radiation therapy can be beneficial, as can radiation therapy combined with surgery in selected patients (26).

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