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Correlation Between Brain Tumor Detectability on Brain Scan
and Protein Levels of the Spinal Fluid

STEVEN M. PINSKY, M.D., PAUL B. HOFFER, M.D., RICHARD FLOM, M.D.,
JAMES L. QUINN III, M.D., and ALEXANDER GOTTSCHALK, M.D.

From the Department of Radiology (Section of Nuclear
Medicine), University of Chicago (S.M.P., P.B.H., A.G.); The
Argonne Cancer Research Hospital (operated by the University of
Chicago for the United States Atomic Energy Commission) (P.B.H.,
A.G.); and the Nuclear Medicine Laboratory, Chicago Wesley
Memorial Hospital (R.F., J.L.Q.), Chicago, Ill.

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ABSTRACT--Fifty-eight patients with brain tumors were reviewed. Each patient had spinal fluid protein determinations and pertechnetate brain scans before surgery. Twenty-five patients had elevated spinal fluid protein levels. Of this group, 22 had positive scans. Thirty-three had normal protein levels and 17 had positive brain scans. In patients with brain tumors and elevated spinal fluid protein levels 88% had positive scans, if the protein level was normal, only 52% had positive scans. The differences are statistically significant. Thus, there is a positive correlation between brain tumor detectability on brain scans and spinal fluid protein levels.

INDEX TERMS: Brain scans * Brain tumors * Spinal fluid protein *
Brain tumor detectability

The successful diagnosis of intracranial tumors by brain scanning has been reported as ranging from 65-90% with 80% accepted as the usual accuracy rate (1, 2). Diagnostic accuracy is noted to be high for meningiomas, metastatic lesions, and rapidly growing gliomas (3). More slowly growing astrocytomas and cystic tumors have a considerably lower probability of being visualized on the brain scan.

The exact mechanism whereby the various nuclides utilized in brain scanning are localized in a tumor is not known. Indeed, the mechanism is probably not the same for all agents. It is assumed, however, that isotope localization within brain lesions is associated with interruption of the blood brain barrier. We have postulated that scanning agents such as pertechnetate-99m, which is loosely bound to serum protein (4), may localize in brain tumors by passive or active diffusion of protein into the lesion through an interrupted blood-brain barrier. Since it is known that the cerebrospinal fluid accurately reflects the contents of the extracellular fluid space of the brain (5), it follows that if protein leakage through an altered blood-brain barrier causes pertechnetate localization within a tumor, there is a high probability that protein levels of the cerebrospinal fluid may also be elevated in such patients. In other words, if about 80% of all brain tumors are localized by pertechnetate brain scans; and if the localization is in large part due to protein-bound pertechnetate diffusing into the extracellular space through an altered blood-brain barrier; then, granting that

the extracellular space protein and CSF protein are comparable, approximately 80% of all patients with brain tumors should also show an increase in CSF protein. The CSF protein levels, however, have been found to be elevated in only about 40-50% (6) of all patients with brain tumors, a major factor which detracts from this theory. With this apparent paradox in mind, we undertook to determine if there was any correlation between cerebrospinal fluid protein levels and the detectability of brain tumors by brain scanning.

MATERIALS AND METHODS

Records of patients with proven primary brain tumors were reviewed from the University of Chicago Hospitals for the period January 1964 to December 1969 and the Chicago Wesley Memorial Hospital for the period January 1966-December 1969. The series consisted of 58 cases representing all tissue-proven brain tumors for whom both pertechnetate scans and spinal fluid protein determinations were available. A dose range of 10-20 mCi of pertechnetate-99m was utilized for scanning, and for approximately the second half of this series, doses of 0.4-1 gm of perchlorate were used to premedicate the patients. Patients with meningiomas were eliminated from the study because of the high incidence of neovascularity in these lesions, which would introduce a second probable localization mechanism. In addition, acoustic neuromas were excluded from this study. This was done because of the frequent association of markedly elevated cerebrospinal protein with this tumor. In fact, our experience and that

of others indicates that these tumors are highly detectable by brain scan (7).

RESULTS

Protein levels were elevated in 25 (43%) of the 58 patients. The normal value for spinal fluid protein levels at both institutions is considered to be below 45 mg %. Of the 25 patients with elevated spinal fluid protein levels, 22 had abnormal brain scans. Among the 33 patients with normal protein levels, only 17 had abnormal brain scans. Thus, if the protein level was elevated the brain scans were positive for tumor in 88% of the patients, while if the protein levels were within normal ranges only 52% were positive for tumor. These two groups of data are significantly different at the .005 level by Chi-Square test.

Two major histologic tumor types were present in large enough numbers for the cases to be considered individually. The largest group consisted of astrocytomas, of which there were 34 cases. Of the 13 cases with elevated protein levels, 11 had abnormal scans; while of the 21 patients with normal protein levels, only 12 had abnormal brain scans. For astrocytomas, therefore, 85% were detected when protein levels were abnormally elevated, while only 57% were detected with normal protein levels. The other histologic group of significant size consisted of glioblastomas, which included 17 cases. Of the 9 patients with elevated spinal fluid protein levels, 8 had abnormal brain scans, while of the 8 patients with normal protein levels, only 4 had abnormal brain scans. Other histologic types in the study

included 4 medulloblastomas and one case each of oligodendroglioma, chordoma, and craniopharyngioma. These results are summarized in TABLES I, II AND III.

DISCUSSION

We have also analyzed the records of 10 patients from whose tumors cystic fluid was aspirated at the time of operation. All 10 of these cases had grossly positive brain scans. The protein levels of these cystic fluids were markedly elevated, ranging between 2700 and 6200 mg/%. Spinal fluid protein determinations were performed in only 4 of the 10 cases, and in all cases the protein was less than 16 mg/%. In these instances, a highly positive brain scan was proven to correlate with regional protein accumulation, but because of the normal CSF protein the 4 cases were described in the overall results as being unassociated with increased protein levels. If we exclude these 4 cases, only 13 of 29 patients (45%) with normal protein levels had abnormal brain scans.

The brain scan localized only 67% of the tumors in the entire series. This low value is related to two factors. First, meningiomas and metastases were excluded from the study; second, the cases were highly selected, consisting exclusively of patients who were able to have a preoperative spinal tap. There was presumably less clinical evidence of markedly elevated intracranial pressure in the group, therefore, the tumors were likely to be smaller and therefore more difficult to localize on the scan than those in an ordinary series of brain scan patients.

CONCLUSION

This series shows a definite correlation between the accuracy of detection of primary intracranial tumors on brain scans and the cerebrospinal fluid protein level. When the cerebrospinal fluid protein is elevated, there is a high probability of localization on brain scan (88%). If, however, the cerebrospinal fluid level is less than 45 mgm% the probability of detecting the lesion is only 52%. The difference is statistically significant. These data support the concept that tumor localization of pertechnetate-99m is often protein mediated.

Alexander Gottschalk, M.D.
Argonne Cancer Research Hospital
950 East 59th Street
Chicago, Illinois 60637

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TABLE I

All Cases			
	CSF Protein Below 45 mg %	CSF Protein Over 45 mg %	TOTAL
Abnormal Brain Scan	17	22	39
Normal Brain Scan	16	3	19
TOTAL	33	25	58

TABLE II

	Astrocytomas		TOTAL
	Normal CSF Protein (Below 45 mg %)	Elevated CSF Protein (Over 45 mg %)	
Abnormal Brain Scan	12	11	23
Normal Brain Scan	9	2	11
TOTAL	21	13	34

TABLE III

Glioblastomas			
	Normal CSF Protein (Below 45 mg %)	Elevated CSF Protein (Over 45 mg %)	TOTAL
Abnormal Brain Scan	4	8	12
Normal Brain Scan	4	1	5
TOTAL	8	9	17