BRAIN SCANNING IN THE DIAGNOSIS OF ASTROCYTOMAS OF THE BRAIN

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The diagnosis of intracranial tumors no longer depends solely on findings such as papilledema in a patient with a "non-febrile, progressive deterioration of nervous function" as Percival Bailey noted in 1933 in *Intracranial Tumors,* or on the onset of seizures in an adult. Patients with suspected intracranial lesions can now be promptly investigated by safe and reliable diagnostic procedures such as radionuclide imaging which enhance the probability of an earlier diagnosis and treatment.

The overall accuracy of radionuclide scanning in the detection of brain tumors is about 80%. Previous reservations about the detection of posterior fossa tumors have been largely overcome since the introduction of short-lived isotopes such as ^{99m}Tc-pertechnetate which have improved the images. Diagnostic methods such as arteriography, pneumoencephalography, and ventriculography detect intracranial masses by demonstrating displacement of normal structures and abnormalities of blood vessels and cerebrospinal fluid spaces. Direct visualization of intracranial masses is revealed by radionuclide imaging, and in an increasing number of cases, as the patterns are recognized, suggestions can be made regarding the etiology of the mass. In certain instances, similar information can be obtained by arteriography ("tumor stain," etc.).

Astrocytomas comprise a large segment of brain neoplasms and range from relatively benign to one of the most malignant tumors in man. The classifications of gliomas is still controversial, and until a few years ago there were doubts about the prognostic value of the various classifications (*1–5*). The value of radionuclide imaging in the detection of brain tumors has been the subject of several reports (*6–8*). In most of these studies, the accuracy of this method in diagnosing low-grade astrocytomas has been disappointing. The purpose of this study was to (A) evaluate the different diagnosis of astrocytomas, and (B) correlate the clinocopathologic features of patients with astrocytomas.

MATERIALS AND METHODS

During the period April 1964 to December 1968, 80 patients were seen at the Johns Hopkins Hospital with proven astrocytomas of the brain; the patients had radionuclide brain scans and cerebral arteriograms before surgery. Other diagnostic studies including pneumoencephalography, ventriculography, and electroencephalography had been performed in many of these patients.

The brain scans were done shortly after the intravenous injection of 10–15 mCi (adult dose) of ^{99m}Tc-pertechnetate. Potassium perchlorate (200–400 mg adult dose) was given orally 1 hr before the administration of the radionuclide. Scans were done in the anterior, posterior, and both lateral positions. In many cases, vertex views were also performed, and in these instances 1 mg/70-kg body weight atropine sulfate was given intravenously at the same time and in the same syringe as the pertechnetate dose. The vertex projection is done first since in this view the atropine effect is most necessary. Rectilinear scanners were used in all cases, and complementary views with the Anger camera were made in some.

The medical histories of these patients were reviewed, and the symptoms, signs, evolution, and mode of presentation were correlated with the malignancy of each tumor. The brain scans and radiographic studies were reviewed in order to localize and characterize the lesions. However, the original interpretations were used in the evaluation of the diagnostic accuracy of these studies.

Histologic material was available in all cases. It was reviewed by one of the authors (FHD) and graded for dedifferentiation, cellularity, vascularity, and necrosis. Kernohan's classification of astrocy-

Received Sept. 23, 1970; original accepted Oct. 29, 1970.

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TABLE 1. INCIDENCE OF MAJOR NEUROLOGICAL FINDINGS IN ASTROCYTOMAS: COMPARISON OF DIFFERENT SERIES

	Low-grade astrocytomas (I–II)				High-grade astrocytomas (III–IV)				
	(Early) Gol (19)	(1928–39) Elvidge-Martinez-Coll (13)	(1945–60) Gonzalez-Elvidge (16)	(1951–61) Paillas (11)	(1970) Moreno-DeLand*	(1924–52) Frankel (14)	(1928–53) Roth-Elvidge (15)	(1967) Jelsma-Bucy (10)	(1970) Moreno-DeLand*
Seizures	56%	72%	48%	74%	56%	32%	26%†	35%	32%
Motor weakness—									
limb	41%		38%		46.6%	44%	60%	43%	68%
face	55%								
Mental impairment	28%			32%†	50%	47%		40%	60%
Intracranial hypertension	59%‡		28.9%	48%	33%	80%¶	66.3%	32%	26%

* Present study.
† Psychic.
‡ Papilledema.
¶ L.P. + 180 mm H_2O.

tomas was used (*1*), i.e., Grade I and Grade II astrocytomas (astrocytoma and astroblastoma), Grade III astrocytoma (astrocytoma with glioblastomatous changes), and Grade IV astrocytoma (glioblastoma multiforme).

RESULTS

The incidence of the four common neurological signs found in our patients is compared with results from previous studies (Table 1). In accord with previous reports we found that seizures were more commonly associated with the lower-grade tumors, and mental deterioration and motor weakness with the higher-grade tumors. However, the incidence of intracranial hypertension was significantly lower for all grades than has been reported in most previous studies, documenting the progress made in earlier diagnosis.

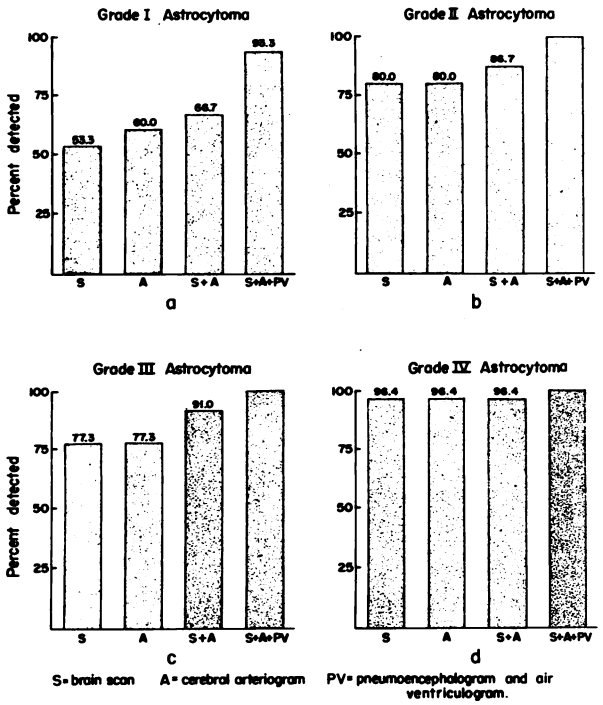

FIG. 1. Detection rate of astrocytomas by radionuclide scanning and radiologic procedures.

The accuracy of brain scanning and cerebral arteriography in the detection of astrocytomas, and the increasing accuracy of diagnosis with combinations of diagnostic studies, is shown in Fig. 1. The brain scans were performed before the cerebral arteriograms. When both the brain scan and the arteriogram were positive, air contrast studies were rarely done; however, if either the scan or the arteriogram was negative or if both were negative in the presence of a suspicious clinical picture, air contrast studies were usually performed. The detection rate of astrocytomas by either brain scanning or cerebral arteriography was similar, regardless of tumor grade. For Grade I astrocytomas detection was relatively poor, whereas for Grade IV tumors it was excellent. The detection rates for Grades II and III were about 80%, the same that has been reported for all types of brain tumors.

Of the 80 cases in this study, all but one were detected by the combination of brain scanning, arteriography, and air contrast procedures. In this instance, surgery was performed on the basis of a persistent temporal lobe focus revealed by electroencephalography. A Grade I astrocytoma was found.

Although the overall accuracy for the detection of astrocytomas by brain scanning (80%) or cerebral arteriography (81.3%) was similar, supratentorial lesions were most frequently detected by

TABLE 2. DETECTION OF SUPRATENTORIAL TUMORS

Malignancy	Scan	Arteriogram
Total	58/72 (80.6%)	62/72 (86.1%)
Grade I (14 cases)	7/14	9/14
Grade II (12 cases)	9/12	10/12
Grade III (18 cases)	15/18	16/18
Grade IV (28 cases)	27/28	27/28

TABLE 3. DETECTION OF INFRATENTORIAL TUMORS

Malignancy	Scan	Arteriogram
Total	6/8 (75%)	3/8 (37.5%)
Grade I (1 case)	1/1	0/1
Grade II (3 cases)	3/3	2/3
Grade III (4 cases)	2/4	1/4
Grade IV (0)	0/0	0/0

arteriography and infratentorial tumors by radionuclide imaging. Of 72 supratentorial astrocytomas, 62 (86.1%) were seen by arteriography and 58 (80.6%) by radionuclide imaging (Table 2). Of eight infratentorial tumors, three (37.5%) were detected by arteriography and six (75%) by scanning (Table 3).

The astrocytomas were graded histologically for vascularity and necrosis on an arbitrary scale of 0–4. There was a direct relationship between malignancy and the degree of vascularity and necrosis. However, the degree of vascularity and necrosis was similar for both positive and negative arteriograms and scans (Tables 4 and 5). Therefore, the histologic study did not offer any evidence of why the radionuclide would concentrate in some tumors and not in others.

In Table 6 the concentration of radionuclide in the different grades of astrocytomas is compared with the frequency that "tumor stain" was seen on the arteriogram. Except for Grade IV astrocytomas, there is a marked disparity between the two procedures. We believe that this is further evidence that the mechanism of a radionuclide concentration in a tumor is related to changes in the blood brain barrier (*9*).

TABLE 4. RELATIONSHIP OF TUMOR VASCULARITY (GRADED 0–4) TO BRAIN SCANS AND CEREBRAL ARTERIOGRAMS

Grade of astrocytoma	Mean vascularity	Brain scan		Arteriogram	
		Positive	Negative	Positive	Negative
I	0.9	0.9	0.8	0.9	1.0
II	1.6	1.4	1.7	1.3	1.7
III	2.8	2.9	2.6	2.8	3.0
IV	3.5	3.5	2.0*	3.5	2.0*

* One case.

TABLE 5. RELATIONSHIP OF TUMOR NECROSIS (GRADED 0–4) TO BRAIN SCANS AND CEREBRAL ARTERIOGRAMS

Grade of astrocytoma	Mean necrosis	Brain scan		Arteriogram	
		Positive	Negative	Positive	Negative
I	0.6	0.6	0.5	0.5	0.8
II	0.8	0.7	1.0	0.7	1.0
III	1.4	1.9	1.4	1.2	2.0
IV	2.8	2.8	1.0*	2.8	1.0*

* One case.

TABLE 6. INCIDENCE OF RADIONUCLIDE CONCENTRATION AND "TUMOR STAIN" IN ASTROCYTOMAS

	Tumor grade			
	I	II	III	IV
Abnormal activity on radionuclide scan	53%	80%	77%	96%
Tumor stain on cerebral arteriography	0	0	36%	96%

DISCUSSION

In our patients, the more common signs of astrocytomas in decreasing frequency were: motor weakness, mental deterioration, seizures, and intracranial hypertension. We found that the incidence of these signs agreed with previous reports (*10–16*) except for one significant variation, i.e., a lesser incidence of increased intracranial pressure in our series. During the past 40 years, there has been a progressive decrease in patients presenting with increased intracranial pressure. This is particularly true in cases of Grade III–IV astrocytomas (glioblastoma multiforme); from 80% in Frankel (*14*) series to 26% in ours.

Seizures were the most common reason why these patients sought medical help. Although seizures were the most common initial sign, motor and mental changes had developed by the time these patients were seen by the physician. Seizures occurred more frequently in the lower-grade tumors and were usually of relatively recent onset. However, seizures had been present for 11 years in one of our patients,

and Gonzalez and Elvidge (*16*) reported a 30-year history of seizures in one case. The complete evaluation of a patient with seizures by means of the electroencephalogram and, if indicated, arteriogram and air contrast studies was suggested by Culbreth and Walker in 1950 (*17*). The results of this study reinforce this concept since 98.7% of all astrocytomas were detected by radionuclide and radiographic studies.

The most frequent sign associated with astrocytomas was motor weakness, and the incidence was directly related to the grade of the tumor; i.e. the greater the malignancy, the greater the frequency of motor dysfunction. In Grade IV astrocytomas, the motor disturbance was often rapidly progressive and in several cases, it resembled a cerebrovascular accident by its abrupt presentation.

Increased intracranial pressure (IIP) was found in about 30% of the patients. It occurred slightly more often in the low-grade astrocytomas because they occur more frequently in the posterior fossa. The relatively low incidence of increased intracranial pressure found in this study contrasts with the higher incidence reported in earlier studies as can be seen in high-grade astrocytomas and 81% in low-grade. that he explored surgically for glioblastoma in 1911 were all blind (*18*). Alpers and Rowe (*3*), in a series of patients from 1930 to 1935, reported an incidence of increased intracranial pressure of 100% in high-grade astrocytomas and 81% in low-grade. Gol (*19*) found that the frequency of IIP was 59% in a series published in 1961. The incidence of papilledema has been progressively decreasing in later reports.

An abnormal accumulation of radionuclide was seen in only half of the scans of patients with Grade I astrocytomas. In nearly all of the positive scans the concentration of ^{99m}Tc-pertechnetate was very poor and the lesion ill defined. The accuracy of cerebral arteriography was only slightly better. The detection of Grade II, III, and IV astrocytomas by brain scanning was much higher than in Grade I astrocytomas, and the lesions were better defined. The overall accuracy of the brain scan for the astrocytomas was similar to figures reported for all brain neoplasms by different authors—81.5% by Witcofski and Maynard (*20*), 84% by Overton (*6*), and 84% by Goodrich (*21*).

Although the overall accuracy for the detection of astrocytomas was nearly identical for scanning and arteriography, there was a difference with respect to location. The detection of brain tumors by arteriography in the absence of "tumor stain" usually depends upon the displacement or abnormal filling of the vessels. These changes are much more difficult to assess on posterior fossa tumors than in supratentorial lesions. The ability to detect lesions by radionuclide imaging depends on the concentration of activity within the tumor, not the location of the tumor. The accuracy of detection for the same type of tumor should be uniform throughout the brain, and in our series we found this to be true (Table 4).

Since studies by electron microscopy have revealed that the blood vessels in the low-grade astrocytomas appear similar or identical to those of normal brain tissue (*22*), the lower concentration of radioactivity in the better differentiated astrocytomas may be related to this qualitative difference in the vessel walls. We could not relate the ability of a tumor to concentrate radioactivity to the number of vessels present (Table 5) nor could this be related to the amount of necrosis in the tumor.

SUMMARY AND CONCLUSIONS

The clinical and diagnostic characteristics of 80 patients with astrocytomas of the brain were evaluated. The neurological findings suggested the possibility of a brain tumor in every case. Seizures and papilledema were more commonly associated with the low-grade astrocytomas; motor weakness and mental deterioration with the high-grade tumors. The incidence of papilledema was appreciably less than has been previously reported.

The accuracy of brain scanning and arteriography were similar for the detection of astrocytomas; both were relatively poor for low-grade tumors and acceptable for high-grade. The correct diagnosis was established in 99% of the cases when air contrast studies were done in addition to scanning and arteriography.

The histologic variations in these tumors (other than dedifferentiation) did not appear to correlate with the ability of the tumor to concentrate radionuclides.

ACKNOWLEDGMENT

We would like to express our appreciation to Fred Hodges, Associate Professor of Radiology at the JHH, for his advice and help in this study and to acknowledge that most of the neuroradiological procedures were performed under his supervision. This study was supported by USPHS Grant GM-10548.

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