TECHNETIUM BRAIN SCANS IN TUBEROUS SCLEROSIS

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Positive brain scans resulting from giant cell subependymal astrocytomas were found in 3 of 18 patients with tuberous sclerosis. All three tumors were vascular at carotid angiography, and two showed abnormal draining veins and some AV shunting. This vascularity may be related to the tumor's propensity for concentrating 99mTc similar to that seen with meningiomas. The other 15 patients had normal scans. Even when very large, benign gliotic tubers were not associated with concentration of the radionuclide.

The most common of the hereditary neurocutaneous disorders, tuberous sclerosis (TS), is a dominantly transmitted disease clinically characterized by mental retardation, seizures, and distinctive skin lesions including adenoma sebaceum, achromatic spots, and shagreen patches (1,2). Retinal phakomas are also diagnostically important (3). Although lesions in the brain clinically predominate in the usual case, diversity of pathologic involvement is a hallmark of the disease. Thus, tumors in the heart, lung, and other viscera are common, and renal angiomylipomas are particularly frequent (4-7).

Roentgenographic abnormalities have been described in the kidney (8-13), lung (14,15) and bone (16-18). Neuroradiographic findings in TS include intracranial calcifications, sclerosis of the calvarium, and candle guttering demonstrated pneumoencephalographically (19). Hydrocephalus resulting from occlusion of the foramen of Monro or cerebral aqueduct may also be found. Despite the extensive radiographic literature, no description could be found of brain scans in TS, and standard nuclear medicine references and atlases do not mention this disease. The study reported here was therefore undertaken to determine what abnormalities, if any, occur in brain scans of patients with TS.

PATIENTS AND METHODS

Eighteen patients ranging in age from 6 to 30 years with proven TS were included in the study. Seventeen were institutionalized and all but two were moderately to severely retarded. Sixteen patients had a history of seizures. Clinical deterioration had been noted in six cases. Seventeen had intracranial calcifications present on the plain skull films. Several had involvement of other organs.

Following the intravenous injection of 10 mCi of 99mTc-pertechnetate, static brain scans were obtained with a Pho/Gamma scintillation camera and low-energy collimator. Anterior, posterior, and both lateral views were obtained in all patients 1 hr after injection.

RESULTS

Abnormal scans were found in three patients. In each the abnormality consisted of a large, well demarcated area of isotope concentration in the frontal region.

Case 1. The patient was a 20-year-old woman with a history of seizures and mental retardation. She was admitted to the hospital because of a progressive visual and intellectual deterioration. Seizures had been controlled. The patient was noted to have intracranial calcifications on the plain skull film including one in the region of the foramen of Monro. The brain scan showed an area of increased activity in the region of the foramen of Monro which lay in the midline and extended slightly to the right. The lesion was identifiable in all four views (Fig. 1). Bilateral carotid arteriograms showed a large, slightly vascular tumor mass in the region of the foramen of Monro and extending to the right of the midline. In addition, pneumoencephalography also showed the mass originating from the lateral wall of the right lateral ventricle and extending through the foramen of Monro into the third ventricle. Some obstruction was produced at this level. The right lateral ventricle was dilated more than the left.

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foramen of Monro, which lay in the midline and extended to the right (Fig. 3). The lesion was identifiable on all four views. Plain skull films showed intracranial calcification with some in the region of the scan lesion. Plain skull films also showed separation of the sagittal, coronal, and lambdoid sutures and a marked increase in digital markings when compared with films of 2 years earlier. There were also changes in the sella turcica indicative of increased intracranial pressure. Bilateral carotid arteriograms showed a vascular tumor in the region of the foramen of Monro and extending into the right lateral ventricle. Pneumoencephalography also outlined the large mass that arose from the lateral wall of the right lateral ventricle and extended through the foramen of Monro into the third ventricle. The right lateral ventricle was larger than the left.

**DISCUSSION**

Tuberous sclerosis derives its name from the distinctive tuber found in the cerebral convolutions and subependymal regions. Microscopically, the tuber consists of an enormous proliferation of glia including giant astrocytes and large, bizarre neurons. Sometimes attaining huge size, these nodules are histologically benign; however, a slow increase in size can be shown in some cases. When strategically located near the interventricular foramen, obstructive hydrocephalus can result. The nosology of this unusual lesion remains somewhat unsettled. Although considered a type of hamartoma by some (20), the tuber is classified by most neuropathologists as a unique form of dysgenetic developmental abnormality (21,22). In addition to the tuber, dense gliosis of white matter is often present, and heterotopic gray matter is occasionally conspicuous. Calcium and ferrous deposits in the gliotic nodules and blood vessels account for the roentgenographic calcifications.

Although uncommon, neoplasia is a recognized complication of TS (22–24). Even though a previous
estimate of a 3.4% incidence of neoplastic development may be too low (6), it is unlikely that any frequency of neoplasia found in the present study (17%) reflects an accurate assessment of the actual incidence because of bias in patient selection. Furthermore, it has become increasingly clear that many patients with TS have incomplete forms of the disease, and many are of normal intelligence (10,25). Thus, unless seizures develop, a significant number of these individuals never come to the attention of a physician.

The usual neoplasm found in patients with TS is a subependymal giant cell astrocytoma (22,26). This term has gained favor because it serves to distinguish accurately the nature of the tumor from other glial neoplasms. Some histologic features including marked vascularity, multinucleated cells, and pseudorosettes mimic to some extent the characteristics of malignant tumors and account for occasional confusion in microscopic interpretation of surgical specimens. A remote similarity of the ventricular tumor of TS to ependymomas has also been cited (26). The biologic behavior of the subependymal astrocytoma, however, is quite different, and long survival is to be expected in most cases. Subtotal surgical removal of the tumor was performed in Cases 1 and 3. The tumor was not resectable in Case 2. In each, microscopic examination revealed typical subependymal astrocytomas exhibiting large fusiform cells with uniform nuclei and perivascular pseudorosettes.

Abnormal brain scans have been described in a variety of non-neoplastic conditions (27–36). However, the abnormalities cited in these studies were caused by lesions quite unlike those found in TS. In one study a reference is made to a positive scan resulting from a subependymoma, but the tumor is not further described and no relationship to TS was stated (29).

The results of this study indicate that positive brain scans in patients with TS should be interpreted as evidence of neoplasia, which in most cases will be a subependymal giant-cell astrocytoma. No patient in this study with negative brain scans has developed evidence of tumor in an average followup period of 20 months. Two patients with normal brain scans died after completion of the study. At autopsy, numerous large tubers were found in both, some measuring up to 5 cm in diam. Technetium-99m-pertechnetate was selected as the scanning agent since it is felt to have superior properties in comparison with other available radiopharmaceuticals for brain scanning, and it is in wide use (37–40). No attempt was made to determine whether the use of other tracers would produce different results, but the propensity of 203Hg to concentrate in low grade astrocytomas would justify its trial in this disease.

REFERENCES


