EXPERIENCES WITH RIHSA ENCEPHALOGRAPHY

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CONVENTIONAL neuroradiological techniques allow accurate location and fairly accurate identification of intracranial masses. Unfortunately, these procedures necessitate admission to hospital, cause some discomfort, and are not free from danger. Moreover, carotid angiography cannot reliably demonstrate lesions situated posteriorly in the hemispheres and, as it relies mainly on the detection of displaced vessels rather than on outlining the tumour itself, it is apt to miss or underestimate the size of infiltrating gliomas.

Because of these disadvantages, substances known to stain tumours or to be selectively concentrated in them have been studied in the hope of finding a means of outlining the tumour itself. Fluorescein is one such substance. Over 50 years ago it was being used as a vehicle for selenium in chemotherapy (von Wasserman, Keysser and Wassermann, 1911) and more recently it has been used to delineate neoplastic tissue in exposed brain (Moore, 1947). Attempts were then made to detect fluorescein tagged with radioactive iodine through the intact skull, using a Geiger-Muller counter (Moore, 1948). These early attempts at cerebral scanning were disappointing because the equipment used was insensitive, but as techniques improved (Schlesinger, de Boves and Tavernas, 1962) the method became increasingly popular.

Inevitably, once the principal was accepted, other substances were introduced. Chou, Aust, Peyton and Moore (1951) describe how, during plasma volume studies on a patient with a brain tumour, the radio-iodinated (^{131}I) human serum albumin (RIHSA) being used was found to concentrate in the tumour. Since then this substance has been extensively employed (Peyton, Moore, French and Chou, 1952; Dunbar and Ray, 1954; Rhody and Nowlis, 1957; Magalotti and Hummon, 1960; di Chiro, 1961; McAfee and Taxdal, 1961; Schlesinger and others, 1962), and its advantages have been discussed in detail by di Chiro (1961). It has frequently been

suggested that the rate of uptake of this isotope depends upon the vascularity of the particular tumour although Raimondi (1964) has suggested that pinocytosis by glial cells may be the responsible mechanism. RIHSA has also been used to detect spinal blocks (Perryman, Noble and Bragdon, 1958), to study hydrocephalus (Bell, 1957) and in "isotope ventriculography" (di Chiro, Reames and Matthews, 1964) although intrathecal injection occasionally produces side effects (Bell, 1957; Detmer and Blacker, 1965).

Brain scanning has been widely used in the United States in the last few years, a number of different isotopes being employed. Only one previous clinical study has, however, been reported from this country (Bull and Marryat, 1965). Until recently RIHSA has been used for cerebral scanning at Hammersmith Hospital*. It is the purpose of this paper to report the results of 100 consecutive brain-scans using this substance.

Patients investigated and methods

Most of the patients investigated were suspected on clinical grounds of having primary or secondary cerebral tumours. The series also contains cases of epilepsy of late onset, where a tumour—although thought unlikely on clinical grounds—could not definitely be excluded. Some patients with strokes of rather slow onset or with persistent headache were also scanned. All patients in whom there was strong presumptive evidence of a cerebral tumour were later investigated by conventional neuroradiological techniques.

Each patient scanned was given an oral dose of 1 mg. of KI followed, an hour later, by an intravenous injection of 300 μc of RIHSA in approximately 5 ml. of saline. Lateral and postero-anterior scans were recorded 24 hours later with a colour dot scanner (Mallard and Peachey,

* ^{197}Hg labelled chlormerodrin (Neohydrin) is currently used.

1959; Morrison, 1965) utilizing a sodium iodide crystal (5" in diameter and 1" thick) and a 37-hole collimator focussed at 6" from the collimator face.

No discomfort or side effects were produced, and difficulties were only encountered when restlessness or confusion prevented the patient from lying still for the two periods of forty minutes involved. On the basis of simple visual assessment the scans were reported as positive, equivocal or negative.

Results

A definite diagnosis of cerebral tumour was established in 38 patients and of cerebral infarction in 14 patients. The incidence of positive, doubtful and negative scans in these 52 patients (and in 48 other patients) is summarised in Table 1.

All 7 supratentorial meningiomas were unequivocally shown. A meningioma at the foramen magnum, clearly shown on the scan, was overlooked until a myelogram demonstrated the site of the lesion.

Four of the 7 astrocytomas were unequivocally seen, but two others were only seen in retrospect. (One was a grade III temporal tumour, the other a grade II tumour of the corpus callosum, which had been irradiated.) One small grade I astrocytoma was not shown up, although its presence was subsequently demonstrated at angiography, by minimal upward displacement of a short segment of the left middle cerebral artery. One cerebellopontine angle tumour was also missed.

In 14 out of 22 patients with secondary deposits, lesions were detected on the postero-anterior scan but few were clearly visible on the lateral scan.

Fourteen patients had had cerebrovascular accidents. Only one (with a thrombotic episode

less than four weeks old) produced a clearly abnormal scan. Two scans in patients with recent infarction gave equivocal results.

On the remaining 48 patients, 1 showed a well-marked focal uptake soon after the drainage of an intracerebral haematoma and 1 a focal uptake at the site of an old cerebral abscess. Four doubtfully positive scans were obtained in patients suffering, respectively, from epilepsy of late onset, an unusual form of unilateral rigidity, probably Parkinsonian, and severe, unexplained headache (2 cases). In these patients full neuroradiological investigation had excluded cerebral tumour with virtual certainty, although it is not impossible that further follow-up may compel us to revise this opinion. No positive scans were seen among 4 cases of gross cerebral atrophy, or 14 cases of epilepsy of late onset of as yet undetermined aetiology.

Comment

Radioisotope scanning using RIHSA is a safe, painless, economical procedure which can be performed on out-patients. It is a technique by means of which the majority of primary supratentorial tumours can be confidently detected after a minimum of training. We agree with the general experience that virtually all meningiomas and 80% of hemisphere gliomas are located (Dunbar and Ray, 1954; Rhody and Nowlis, 1957; di Chiro, 1961; McAfee and Taxdal, 1961; Schlesinger and others, 1962) and are convinced of its value.

Certain failings must, however, be recognised. Some well-differentiated gliomas or gliomatous cysts may be missed, possibly due to scanning too soon after the injection of isotope. Schlesinger and others (1962) have suggested that if scanning were delayed for 2, 3 or 4 days some of these lesions might be found. Magalotti and

TABLE 1
INCIDENCE OF POSITIVE, EQUIVOCAL AND NEGATIVE SCANS IN 100 CONSECUTIVE CASES.

SCAN	TUMOURS					CEREBRAL INFARC- TION	OTHERS
	Supratentorial			Infratentorial			
	Meningiomas	Gliomas	Secondaries	Meningioma	Cerebello-pontine angle tumour		
Positive	7	4	14	1	0	1	2*
Equivocal	0	2	1	0	0	2	4
Negative	0	1	7	0	1	11	42
Total	7	7	22	1	1	14	48

* 1 old abscess 1 post-craniotomy

Hummon (1960) point out that the detection of secondary deposits is also unsatisfactory, and suggest this is due to their small size. Although other workers have had considerable success in this field we only indentified metastases in some two-thirds of the cases in which they were present.

Unequivocal 'false positive' scans (i.e. positive scans in the absence of tumour) were obtained in 3 of our patients: 1 with a recent infarct, 1 who had recently undergone a craniotomy, and 1 with an old cerebral abscess. Similar 'false positive' uptakes have been reported by a number of observers but seldom occur in circumstances in which there is real difficulty in making a clinical diagnosis.

Observations on RIHSA scanning of patients with cerebral infarction are scanty. Dunbar and Ray (1954) report negative results in 2 cases of carotid occlusion and 1 case of anterior cerebral occlusion. Rhody and Nowlis (1957) studied 6 patients with diffuse cerebrovascular disease and 3 patients with focal vascular lesions. All the scans proved negative. On the other hand McAfee and Taxdal (1961) state that patients scanned within 2 weeks of the occurrence of a cerebrovascular accident may 'sometimes' show a positive uptake, whereas scans performed on patients with cerebrovascular accidents of several months standing are 'nearly always' negative. Di Chiro (1961) reports 2 positive scans in patients with internal carotid occlusion and 1 each in cases of anterior and middle cerebral occlusion (the time lapsing between the occurrence of the occlusion and scanning is not mentioned)*. He emphasises that 'extravasated blood has a high radioactive uptake'. Positive scans after recent craniotomy (van Vliet, Tauxe, Svien and Jenkins, 1965) and with cerebral abscess (di Chiro, 1961; McAfee and Taxdal, 1961) have also been previously described. McAfee and Taxdal (1961) also found that angiography per se may sometimes cause confusion by producing a focal uptake 'for several days'.

Equivocal 'false positive' scans were obtained in 4 further patients in our series. None of these

patients were thought to be harbouring space-occupying lesions. It should be stressed that in these 4 cases opinion was divided as to whether the scan was in fact abnormal. In the present state of our knowledge it is our practice only to place reliance on scans which show an unequivocal focal uptake.

Others workers have shown that with a carefully standardised technique and a detailed knowledge of the normal scan pattern of various radio-isotopes the majority of primary intracranial tumours, including those in the cerebellar hemispheres and cerebellopontine angles may be detected although pituitary and deep midline tumours are usually missed. Familiarity with the uptake patterns of various types of cerebral tumour may enable the experienced observer to suggest the nature as well as the site of many intracranial neoplasms, and with immediate scanning even arteriovenous malformation can be detected. There are conflicting reports (Dunbar and Ray, 1954; McAfee and Taxdal, 1961) about the diagnosis of subdural haematoma by scanning techniques but here, as with angiomata, the rapid and excellent results of angiography are unlikely to be bettered.

The only practical problems encountered, that of scanning a restless patient, may eventually be solved by the γ camera which has a high sensitivity and allows completion of the scan in a short time.

Summary

The value of brain scanning using radioiodinated human serum albumin is considered on the basis of a survey of the literature and of a study of 100 patients.

Nearly all meningiomas and most astrocytomas are easily detected. The method is less reliable for secondary deposits. With experience laterally placed posterior fossa tumours may be detected but the method is unreliable with deep midline tumours.

Doubtfully positive results occasionally occur in the absence of a space-occupying lesion. Cerebrovascular accidents may produce a focal uptake and recent craniotomy and cerebral abscesses may give unequivocal positive scans. Unequivocal false positives were not encountered in our series, however, in the absence of either a cerebral tumour, or of one or other of the conditions just mentioned.

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*Using different isotopes (^{203}Hg and ^{197}Hg) Glasgow, Currier, Goodrich and Tutor (1965) have recently reported their experience in scanning large numbers of patients with cerebrovascular disease. They found that the highest incidence of positive scans was in the third week following an infarct, when a positive scan was found in 18 out of 25 cases. The incidence shortly after an infarct was much lower, as was the incidence several months later. By repeat scanning on some of the patients an 'evolutionary pattern' of focal uptake was demonstrated.

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