**99mTc-HMPAO SPECT studies in traumatic intracerebral haematoma**

M S Choksey, D C Costa, F Iannotti, P J Ell, H A Crockard

Abstract

Traumatic intracerebral haematomas are a common neurosurgical emergency. Their management, particularly the role of surgical removal, is controversial. Deterioration often occurs late, and is unpredictable. Eight patients with traumatic intracerebral haematomas were admitted to the neurosurgical unit to monitor their clinical state. All were studied within 48 hours of admission with single photon emission computerised tomography (SPECT), using the recently introduced radionuclide Technetium-99m-Hexamethyl propylene amine oxime (99mTc-HMPAO). At the time of the SPECT study, all the patients had been clinically stable. Three patients remained so; in the other five, the conscious level deteriorated, necessitating craniotomy and evacuation of the haematoma. In all the patients, the SPECT studies demonstrated perfusion defects that corresponded to the location of the haematoma, as demonstrated by computerised tomography (CT). However, in the five patients who subsequently deteriorated, the perfusion defects seen on the SPECT scan appeared larger than the haematoma, as seen on the CT scan. In addition, there was widespread poor retention of 99mTc-HMPAO in the ipsilateral hemisphere. These differences were quantifiable. Interestingly, these differences were present at a time when the patients were clinically stable, before their deterioration. It is concluded that SPECT studies with 99mTc-HMPAO are of possible use as predictors of late deterioration in the management of traumatic intracerebral haematomas.

With the advent of X-ray computerised transmission tomography (CT) scanning traumatic intracerebral haematomas are recognised more often in life. The clinical course in these patients is variable; some deteriorate, others do not. Not infrequently, this deterioration may be delayed, sometimes by days. The reasons for the delay are unclear: there may be an increase in size of the haematoma due to further bleeding, or alternatively brain swelling and oedema in the surrounding brain may develop and cause brain shift, with secondary ischaemia. This deterioration may occur rapidly in a previously stable patient, and at a rate greater than that at which the clinical services can respond.

One solution is to subject all such patients to immediate surgery. This, however, has its drawbacks, mainly because a large number of the operations would be unnecessary. It also places a large strain on resources, and may result in needless surgical complications. What is required is a method that is capable of differentiating between those patients who will deteriorate and those who will not, on admission. Such a method would be useful in guiding a clinician faced with the choices of controlled ventilation, osmotic diuretics or even pre-emptive surgery.

While CT scanning has provided the ability to visualise these haematomas, to define their anatomical limits and to generate information about their volume, it does not provide functional information on the rest of the hemisphere containing the haematoma. Although patients with large haematomas are more likely to need surgery, this is not an infallible guide. Similarly, the measurement of intracranial pressure is not wholly reliable, as some patients may tolerate high pressures well, and in others deterioration may only be briefly preceded by an acute pressure rise.

Single photon emission computerised tomography (SPECT) studies using Technetium-99m-Hexamethyl propylene amine oxime (99mTc-HMPAO) have been available for four years. Some controversy surrounds the precise mechanism of its uptake and subsequent retention by brain tissue, and there is evidence that it underestimates blood flow at high flow rates. There is, however, good evidence that the eventual distribution of this radionuclide is determined by regional perfusion, and that in pathological states, such as after acute stroke, areas of decreased retention may reflect defects in the local microcirculation. In acute head injury its uptake may be decreased in regions corresponding to the haematoma, its penumbra, and also in regions that appear normal, or minimally oedematous on the CT scan.

As part of a wider study into the outcome in patients with traumatic intracranial haematomas, we investigated the relationship between the clinical course and the 99mTc-HMPAO/SPECT scan appearances in eight patients, to see if these studies contained information complementary to that available on the CT scan.

Materials and methods

Eight patients were studied, and their details...
are given in Table 1. All had traumatic intracerebral haematomas. They had all been transferred to the neurosurgical unit within 24 hours of their injury, had CT scans on admission and were observed closely for deterioration using the Glasgow Coma Scale. Five patients did deteriorate, and required emergency craniotomy for haematoma removal. The timing of this deterioration varied from 48 hours to five days after admission. In two patients, repeat CT scans showed that the haematoma had increased in size (patients 2 and 7). In patients 1 and 6, there was increased brain swelling, to the extent that patient 6 developed a fixed and dilated pupil. Patient 8 had no change in his CT scan appearance, but in view of his falling conscious level and the large size of his haematoma (fig 1), he had a craniotomy.

All the patients survived; the two with large temporoparietal haematomas were left with residual hemipareses at nine month follow up (patients 6 and 8). None of the patients had intracranial pressure monitors inserted preoperatively, and the decision to operate on them when they deteriorated was based on clinical grounds. We report the results of the SPECT studies performed on these patients before any of them deteriorated and required surgery.

**Methods**

**CT scans**

All the patients had CT scans performed on admission, and thereafter as indicated. For the purpose of data analysis it was the initial scan that was used. The CT scans were recorded on standard film, and the dimensions of the haematomas were measured. It was assumed that these haematomas could be treated as ellipsoids; the volume of an ellipsoid is determined by the formula: \( V = \frac{1}{6} \pi abc \), where \( a, b \) and \( c \) are its three mutually perpendicular and concentric diameters. For each haematoma, measurements were obtained of these three mutually perpendicular and concentric dimensions, and the assumption made that they were equivalent to the diameters of an ellipsoid. The approximate volume was now given by the expression: \( V = \frac{1}{6} D_1 \times D_2 \times D_3 \times \pi \) where \( D_{1,2,3} \) are the three mutually perpendicular and concentric diameters, and \( \pi \) is taken to approximate to 3. This reduces to \( V = \frac{1}{2} D_1 \times D_2 \times D_3 \).

Two such haematomas are illustrated in figs

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Table 1 Patients details

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<th>No</th>
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<th>Cause</th>
<th>Site</th>
<th>SPECT</th>
<th>A</th>
<th>B</th>
<th>D</th>
<th>F</th>
<th>Day</th>
<th>Operation</th>
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<td>15</td>
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RTA = Road traffic accident
SPECT = Day of SPECT scan
GCS = Glasgow coma score
Deterioration cause
Operation
Outcome GOS

A = On admission
B = Best score noted
D = Score after deterioration
F = Fall in GCS from best to worst

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Figures 1 and 2  CT and SPECT scans of patient 8. Note the large haematoma size, and the large corresponding perfusion defect on the SPECT scan. There is also low uptake in the ipsilateral hemisphere anteriorly and posteriorly.
Figures 3 and 4 Eight of the 16 transverse SPECT images in patient 5, together with the CT scan. In the SPECT images, right and left are reversed. Note the relatively close coupling between the size of the haematoma on the CT scan, and the perfusion defect on the SPECT scan. In addition, the perfusion in the ipsilateral cortex and basal ganglia is unaffected. This patient did not deteriorate.

1 and 5. The volume of the first, larger haematoma was 75 ml, while that of the smaller was 26 ml.

SPECT studies using $^{99}$Tc$-HMPAO were performed as soon as possible after the patients were admitted. The maximum delay was 48 hours. We used the IGE 400AC/STARCAM gamma camera and computer system, according to a protocol described elsewhere. The reconstructed images consisted of transverse, coronal and sagittal contiguous slices. The transverse sections were parallel to the orbito-meatal line, and their vertical spacing was 0.7 cm, so generating either 15 or 16 slices (figs 3, 4). Only these transverse $^{99}$Tc$-HMPAO/SPET$ images were used for quantitative analysis, according to a system devised by us.

**SPECT image analysis**

The SPECT image analysis fell into two parts. In the first, the volume of the perfusion defect associated with the haematoma was calculated. On each slice, the counts per pixel were measured, and a mask was created around all areas where the count rate was 50% or less than the maximum on that slice. This 50% contour corresponded to the outline of the haematoma as seen on the CT scan. The calculation then proceeded as follows:

The slices in which the perfusion defect was visible were numbered 1, 2, 3, 4...n. The area of the perfusion defect on the nth slice was $D_n$.

The total area of the nth slice was $A_n$.

The percentage ($P_n$) of the slice occupied by the perfusion defect was $D_n/A_n \times 100$.

Then, assuming that each contiguous slice was of unit thickness, summing the areas yielded a measure of the volume of the perfusion defect viz: Volume Index = $P_1 + P_2 + P_3 + \ldots + P_n$.

In the second part, a region of interest was drawn around the remainder of the ipsilateral hemisphere, that is that part which did not contain the haematoma. This region was then compared to its contralateral counterpart, and a perfusion ratio was calculated using the following expression:

$$\text{PERFUSION RATIO} = \frac{\text{Counts/pixel unaffected side} \times 100}{\text{Counts/pixel affected side}}.$$

This yielded a measure of the asymmetry between the hemispheres, where low retention of the radionuclide on the affected side appeared as a value greater than 100.

These two items of information were then combined by multiplying the Volume Index by the perfusion ratio.

Index of Severity = Volume Index $\times$ perfusion ratio

The result was termed the Index of Severity of the haematoma. Here, a large haematoma associated with poor perfusion in the rest of the ipsilateral hemisphere had a high score, while a small haematoma with little perfusion asymmetry had a low score.

**Statistical analysis**

The mean (SD) was calculated for all the groups of results, and the data were analysed using the unpaired Student's $t$ test.
Results
The patients were divided into two groups, those who required surgery and those who did not. In the CT scans, the haematoma volume, presence of midline shift and contralateral ventricular dilatation did not differ significantly between the two groups (Table 2). In all patients, the location of the perfusion defects seen on the SPECT studies corresponded well with the CT scan appearances. Large haematomas appeared as large perfusion defects. There was a statistically significant difference between the two groups of patients (Table 2). The mean (SD) size of defect in patients who deteriorated was 71.4 (11.7), while in the stable group it was 30.7 (13.3), (p < 0.004).

In addition, in seven patients there appeared to be low perfusion in the rest of the ipsilateral hemisphere. When this information was combined with the volume of the perfusion defect, to form the Index of Severity, the mean (SD) in the first group was 87.0 (7.7), while that in the second, stable, group was 34.0 (9.1), p < 0.0001.

Discussion
Traumatic intracerebral haematomas have a poor prognosis, with many series reporting mortality of between 25 and 30%, and severe morbidity of 15 to 25%.

In contrast, the consequences of spontaneous haemorrhage are not so severe—most series quoting mortalities from 10–20%.

Even allowing for differences, such as the rapidity of onset, size and the presence of associated injury, this contrast between the two origins is striking. It is likely that patients with traumatic haematomas may have, in addition, diffuse hemispheric damage that is not readily apparent on a CT scan. This may also account for the delayed development of haematomas in areas of diffusely damaged brain, where the initial CT scan showed no gross abnormality.

In some patients, these insults are tolerated, the oedema subsides, the haematoma is accommodated by shifts of brain and cerebrospinal...
fluid (CSF), the blood pressure increases to maintain perfusion. In most patients, the ICP remains low, or is only moderately raised. In others, however, these compensatory mechanisms are exhausted, and the pathophysiological changes induced by the original trauma continue to progress to a point where they become self-sustaining. This is characterised by a sudden increase in ICP, with subsequent herniation and coning. The precise final trigger for this process is uncertain and may vary from patient to patient. It may be a small increase in haematoma size, the effects of ischaemia or the onset of vasomotor paralysis. Whatever the cause, late deterioration has a grave effect on outcome: in Jamieson and Yelland's series, 15 22 patients were lucid at some stage after their injury, and then became unconscious. Of these, nine died. (40-5%).

Clinical criteria for intervention

The aim in the management of patients with intracranial haematomas should be to identify this high-risk group of patients early, before they deteriorate, and either treat them with intensive conservative measures, or pre-emptive surgery. In the past, the criteria for operative intervention have been clinical deterioration, a low GCS score, large haematoma size, failure to improve, mid-line shift on the CT scan and a high ICP.

Awaiting clinical deterioration, the expectant policy, was advocated by McKissock, et al.,16 and discussed more recently by Solomonik et al.17 The mortality and morbidity are considerable; only 10/35 patients made a good recovery in Solomonik's series, and nine were left moderately disabled. Cooper18 advocated the removal of all large haematomas associated with a depressed conscious level or focal deficit, or high ICP, or mid-line shift.

In a retrospective series of 26 patients with intracranial haematomas, Galbraith and Teasdale6 approached the problem of selective surgery by looking at the role of ICP monitoring. They found that the ICP had been elevated in 12 patients who later needed operations, and so suggested that it was a good criterion for early surgery. Their series, however, contained only five purely intracerebral haematomas, the rest being either mixed with sub-dural blood, or sub-dural haematomas alone. Thus the results may not be strictly comparable. In addition, in their series five patients who required surgery had ICPs in the 20-30 mmHg range, as did five who did not, indicating considerable overlap between the two groups. Interestingly, and in contrast to Cooper,18 they found that mid-line shift was not a strong indicator of late deterioration.

Andrews et al.19 recently considered the role of haematoma volume in 32 patients with traumatic intracerebral haematomas. In their series, a temporal location and a volume greater than 30 ml were high risk factors for deterioration, and they recommended pre-emptive surgery in this group. (In their study they assumed that the volume of a haematoma was given by the product of its mutually perpendicular dimensions, that is, that it approximates to a slab. In our study, we have assumed that it approximates more closely to an ellipsoid, where the volume is half the product of these dimensions.)

Experimental studies

Experimental studies of intracerebral haematoma have shown that surrounding the obvious anatomical limits of the haematoma there is a penumbra of damaged tissue, in which the neurons show evidence of ischaemic damage.17,18 This may be due to the local liberation of vasoactive and histotoxic substances from the haematoma itself, or the adjacent brain. Alternatively, the cells may be damaged by a period of ischaemia, as the local microcirculation is "squeezed" rather as is a sponge, and therefore is incapable of either delivering oxygen or removing the locally liberated mediators of inflammation. A possible delayed consequence is that this ischaemic zone may swell—and such delayed swelling may further increase the local tissue pressure, creating the conditions for a self-sustaining rise in ICP to follow.

SPECT studies

This report stems from the appearances of the SPECT scans in patients with TICH. Here we observed two separate phenomena. First, the haematomas themselves were visualised as areas where the retention of 99Tc-HMPAO was very low. This is in keeping with the findings of Abdel-Dayen et al.,10 who compared the CT scan appearances with SPECT studies after acute head injury, and showed areas of low retention in both the region of the haematoma, and the peri-lesional area, similar to the large defects we have found.

Second, in some patients the remainder of the hemisphere, which looked intact on the CT scan, also had poor retention of 99Tc-HMPAO when compared with the opposite, presumably intact hemisphere. This is shown clearly in the SPECT study of patient 1 (figs 5, 6). What is interesting is that during this particular SPECT study, the patient was alert and orientated, and there was no clinical evidence of any dysfunction in that hemisphere. Yet three days later this patient deteriorated quite abruptly, was found to have marked swelling around his haematoma, and required an emergency craniotomy.

This pattern was repeated consistently in the other seven patients. Simple visual evaluation of the SPECT images revealed that the perfusion defects were larger in patients who later deteriorated. In addition, there appeared to be poor uptake in the ipsilateral hemisphere. This raised the next question: could these differences be in some way quantifiable?

We therefore created our own form of image analysis. First, we defined the perfusion defect attributable to the haematoma and its penumbra as the area within which the retention of 99Tc-HMPAO was 50% of the maximum in either hemisphere. The use of this 50% contour line to delineate a lesion is well-established in SPECT image analysis.10 This enabled us to calculate the area occupied by the perfusion...
defect on each slice. Summing this area for all the slices on which the perfusion defect was apparent provided a measure of the haematoma volume, the Volume Index.

Second, the remainder of the hemisphere, that part not included in the haematoma, had a region of interest (ROI) drawn around it. This was then flipped horizontally, and compared with the opposite hemisphere, in a manner similar to the image analysis described by Black et al. They compared the SPECT images of intracerebral tumours with those of the diametrically opposite normal brain in order to grade their malignancy. Their 201TI Index is similar in concept to our perfusion ratio.

When these two parameters were combined to form an Index of Severity, there was a marked difference between the two groups of patients, with a score of 87.0 (7.7) in those who deteriorated, compared with 34.0 (9.1) in those who did not (p < 0.0001).

We accept the criticism that the form of image analysis that we created is empirical. However, what is important is that it was applied in exactly the same manner to all the SPECT studies, and that the differences we have observed are therefore consistent. Its biological basis is not unreasonable if we accept that 99Tc-HMPAO is an indicator of regional perfusion, and that the penumbra of ischaemic brain demonstrated by these SPECT studies is prone to late swelling.

In conclusion, the precise biological basis of the uptake and subsequent retention of 99Tc-HMPAO in brain tissue is unclear. However, there is a general acceptance that it is related to cerebral perfusion. If we attempt to correlate our observations with the clinical and experimental evidence cited above, we can make the following suggestions:

1. That SPECT studies of intracerebral haematomas with 99Tc-HMPAO demonstrate not just the haematoma, but the haematoma together with the ischaemic penumbra as a single perfusion defect.

2. That a haematoma may appear large on a SPECT study either because it is actually so, or because it has a large ischaemic penumbra.

3. That the ipsilateral hemisphere in these patients may be diffusely damaged, and show low retention of 99Tc-HMPAO, yet appear clinically to be functioning relatively normally.

4. That patients with large perfusion defects corresponding to their haematomas are more likely to deteriorate, possibly due to swelling in the ischaemic penumbra. This may be more likely if there is coexisting poor retention of 99Tc-HMPAO in the ipsilateral hemisphere.

In summary, eight patients with traumatic intracerebral haematomas were studied with 99Tc-HMPAO/SPECT on admission to our neurosurgical unit. In the patients who later deteriorated, the SPECT studies showed significantly larger perfusion defects; there also appeared to be diffuse low retention of 99Tc-HMPAO in the ipsilateral hemisphere. Although the study numbers were small, the results were statistically significant. We propose that SPECT studies with 99Tc-HMPAO may have a possible predictive value in patients with traumatic intra-cerebral haematomas. Further investigation of this is justified.