Regional cerebral blood flow alterations remote from the site of intracranial tumors

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Regional cerebral blood flow (rCBF) was investigated in 12 patients with brain tumors, using a 254-channel dynamic gamma camera. In nine of the 12 cases, hyperemic regions with loss of autoregulation were seen in sites remote from the tumor (the area around the tumor was in most cases also hyperemic). These remote rCBF abnormalities were found in the lower posterior part of the hemisphere in six cases, and in the frontal region in three. The location of the remote rCBF abnormality seemed to depend on the site of the tumor: cases with frontal and posterior fossa mass lesions had hyperemia in the lower part of the temporooccipital regions, cases with centroparietal mass lesions had hyperemia mostly in the frontal region. This may mean that the remote rCBF abnormality is due to local tissue compression against unyielding anatomical structures, namely, the tentorium and the falx. It is suggested that these abnormalities may constitute evidence of an early stage of a dangerous clinical condition: a state of preherniation.

KEY WORDS □9 regional cerebral blood flow □9 brain tumor □9 remote hyperemia □9 local compression □9 acidosis □9 preherniation

It is well known that the regional cerebral blood flow (rCBF) in brain-tumor patients is abnormal (increased or decreased) in the tumor area and in the brain tissue immediately surrounding it. The rCBF in regions remote from the space-occupying lesion has been found to be normal or diffusely reduced. The hyperemia in perifocal brain tissue probably represents a state of "luxury perfusion" related to vascular dilatation due to brain tissue acidosis.

Autoregulation and CO$_2$ reactivity are impaired focally or globally in nearly all tumor cases. In addition, paradoxical reaction to induced arterial hypertension and CO$_2$ pressure (pCO$_2$) change occurs often in the tumor region. The paradoxical responses may be related to changes of intracranial and/or tissue pressure. Thus the regulation of rCBF in patients with space-occupying intracranial masses is disordered at the site of the lesion and sometimes in the entire brain. These characteristic phenomena have been discussed in detail by Pálvölgyi and others.

In the present study we investigated these rCBF abnormalities using the xenon-133 ($^{133}$Xe) internal carotid injection method and a high resolution 254-channel multidetector gamma camera.

Clinical Material and Methods

A total of 12 patients with brain tumors were investigated. Three patients had a frontal mass lesion, five had a centroparietal lesion, two had a temporal lesion, and two had a posterior fossa lesion. Of the five patients who underwent surgery, rCBF was studied preoperatively in three, and several months...
The tumors included four meningiomas, three metastases, one melanoma, one glioma, one astrocytoma, one epidermoid cyst, and one tumor of unknown type; five involved the left hemisphere and seven the right. The mean age of the patients was 61 years. There were eight men and four women.

The rCBF measurement was performed in connection with carotid angiography under local anesthetic with 1% lidocaine hydrochloride (3 to 5 ml). The common carotid artery was punctured by the Seldinger technique, and a thin polyethylene catheter was inserted into the internal carotid artery. The catheter position in the internal carotid artery was confirmed by noting a blanching of the skin in the ipsilateral supraorbital area when 2 to 3 ml of saline solution was injected rapidly. For each rCBF study, $^{133}$Xe, 5 to 8 mCi dissolved in 3 ml saline, was injected through the catheter into the internal carotid artery.

Autoregulation for CBF was tested by altering the systemic blood pressure. Hypertension was induced by infusion of angiotensin intravenously, elevating the mean arterial blood pressure (MABP) 20% to 50% above the control blood pressure. Hypotension was induced with Arfonad (trimethaphan camsylate). Blood pressure was measured directly via the carotid catheter. Blood samples for pCO$_2$ determinations were taken from the carotid catheter during each flow study. Flow values obtained during rest and during hypertension (and also during the other functional tests except hyperventilation) were corrected to a standard pCO$_2$ of 40 mm Hg, employing a correction of 4% flow changes for each 1 mm Hg of pCO$_2$.

During the studies the patients lay relaxed with closed eyes, plugged ears, and without movement. The head position relative to the camera was noted by using small radioactive markers on the nasion, the external auditory meatus, and upper part of the forehead.

We measured rCBF using the high resolution multidetector scintillation camera with 254 individual detectors recently developed in our clinic. This system can record simultaneous events; it has a maximum counting rate of 4000 cps per channel, and a total camera load of $10^6$ cps, with a coincidence loss of less than 1% in any channel. The sodium iodide crystals measure 8 mm in diameter and are placed in a rectangular matrix with a center-to-center distance of 10 mm. Each crystal is individually connected to a photomultiplier and an amplifier.

Two kinds of collimators, both 40 mm thick, are used. One has parallel holes of 7 mm in diameter, the other has converging holes of 8 mm in diameter, and a focal distance of 22.5 cm from the camera surface. The entire lateral brain hemisphere can be seen with the collimator with parallel holes. With the collimator with converging holes, an amplifying effect of about 30% is obtained, but the anterior and posterior brain poles cannot be seen in all cases, depending on the size of the head.

A special timetable is set by computer for transferring the cumulative counts in the memory system to the core memory of the computer (Varian 620/f). In this way 254 clearance curves are obtained. The initial flow values are calculated by a least square fit and using the equation: 

$$\text{rCBF}_{\text{initial}} = 200 \times \text{D}_{\text{initial}} \text{ml/100 gm/min},$$

where $\text{D}_{\text{initial}}$ is the numerical value of the slope of the clearance curve in base 10 logarithmic system and with time intervals from 15 to 60 seconds after the injection. The results are shown on a color television monitor 2 minutes after injection of the $^{133}$Xe solution. On the display system all the 254 curves and also the initial flow values (the slope of the curves) can be seen with a 16-level color scale.

The normal hemispheric mean flow value with this approach was about 50 ml/100 gm/min in a series of 27 patients without neurological deficits (with pCO$_2$ corrected to 40 mm Hg). The frontal region shows a slightly high perfusion level, 10% to 30% above the hemispheric mean flow value. No significant differences between left and right hemisphere CBF have been found in the resting state. Also, there is no significant difference between the two hemispheres with regard to reproducibility as assessed by two studies made with the patients at rest and 20- to 30-minute intervals between measurements. These studies showed a coefficient of variation for the rCBF values in patients with intact brain $5.5 \pm 2.8\%$ (mean $\pm$ SD) except for the upper frontal region, where the values were $7.6 \pm 3.2\%$. The remarkable constancy of rCBF in neurologically normal subjects was confirmed in studies that showed that neither flow level nor flow pattern responded to changes in blood pressure; this is evidence of intact autoregulation.
rCBF alterations remote from tumor site

### TABLE 1

The correlation between clinical diagnosis, flow distribution, brain scintigraphy and autopsy in 12 patients with brain tumor

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Sex</th>
<th>Remote Hyperemia</th>
<th>Clinical Diagnosis</th>
<th>Hyperemic Foci in Flow Study*</th>
<th>Focus in Brain Scintigraphy</th>
<th>Location of Tumor in Autopsy</th>
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*Dotted line denotes ischemic areas corresponding to tumor/peritumor site.

### Case Reports

**Frontal Lobe Lesions**

Three patients with frontal lobe tumor were studied (Table 1). In all three cases remote rCBF abnormalities were seen with loss of autoregulation in the posterior part of the hemisphere, and in one patient (Case 3) also in the central region. Conventional static brain scintigraphy revealed the mass lesions but failed to show any abnormal isotope uptake in the remote area of disordered rCBF. Intracranial pressure was not measured and there was no ophthalmoscopic evidence of increased intracranial pressure.
Case 1. This 62-year-old man with moderate arterial hypertension was admitted because of a grand mal seizure. After the convulsion, he had a slight right-sided central facial palsy, paresis of the right leg, and slight aphasia. An electroencephalogram (EEG) 8 days after the attack was normal, but a repeat EEG showed a 3- to 5-Hz focus in the left temporal lobe. Left carotid angiography revealed displacement of the anterior cerebral artery to the opposite side and a contrast shadow in the precentral superior region. A meningioma was suspected. Several brain scintigraphic studies with $^{99m}$Tc-pertechnetate were positive; there was no evidence of any other space-occupying lesion in that hemisphere. The patient was given only supportive treatment. Over the following weeks the brain scans and the patient's clinical condition returned to normal.

Studies were done of the rCBF on the left side (Fig. 1). With a resting MABP of 135 mm Hg, marked hyperemia of about 79 ml/100 gm/min was seen in the frontal region corresponding to the site of the suspected meningioma. Two other small hyperemic regions, with flow values of 90% to 100% above that of the rest of the hemisphere are seen in the occipital region remote from the space-occupying lesion. Hypotension (MABP 110 mm Hg), induced by infusion of Arfonad intravenously, disclosed loss of autoregulation in the hyperemic occipital regions. The rCBF in the tumor region was seen to be unchanged.

A few hours after the rCBF study the patient's condition suddenly deteriorated with loss of consciousness and respiratory arrest. He was artificially ventilated and returned to his previous status. He refused surgery.
Case 2. This 52-year-old woman had had an astrocytoma removed from the right frontal region. Several months after the operation she developed a nearly total left-sided hemiparesis and multiple Jacksonian seizures. Brain scintigraphy with $^{197}$Hg-chlormerodrin was positive, and an rCBF study was done on the right side (Fig. 2). With a resting MABP of 100 mm Hg, three areas of focal hyperemia with a flow value of about 70 ml/100 gm/min were seen. One area was in the right upper frontal region corresponding to the tumor site, and the other two were in the lower part of the temporooccipital region. When the MABP was elevated to 128 mm Hg by angiotensin, the flow values in the tumor region did not alter, but a decrease of focal flow was found in the remote hyperemic region, a so-called "paradoxical response" to induced hypertension. Hyperventilation reduced MABP to 93 mm Hg and pCO$_2$ to 26.2 mm Hg and caused a flow increase in the remote hyperemic region (also a paradoxical response); focal flow values did not change in the tumor region.

The patient deteriorated further and died 4 weeks later. At autopsy recurrence of the brain tumor in the frontal region and brain edema were found, but no special mention was made of herniation of the posterior portion of the right hemisphere.

Case 3. This 54-year-old man was admitted because of severe headache, dizziness, and slight left-sided paresis. He had been operated on for malignant melanoma 3 years previously. Right carotid angiography showed a space-occupying mass in the right frontal lobe. Brain scintigraphy with $^{99m}$Tc-pertechnetate revealed abnormally high uptake in the
right frontal and anterior right temporal regions. Ophthalmoscopic studies were normal. An rCBF study was done on the right side. With a resting MABP of 100 mm Hg, the mean hemispheric rCBF value was very low, averaging about 28 ml/100 gm/min. No hyperemic areas were seen and the flow was decreased in the frontal lobe corresponding to the tumor site. Hypertension was induced with intravenous angiotensin infusion (MABP 135 mm Hg) and revealed hyperemia in the centroparietal region and a small area of hyperemia in the occipital region. There was no change in rCBF in the frontal lobe.

The patient died 1 month later. Autopsy revealed a right frontobasal tumor (metastatic malignant melanoma) and two small cavities of recent bleeding in the temporal lobe.

**Parietal Lobe and Central Region Lesions**

Five patients with centroparietal tumors were studied (Table 1). In four of these, two with a meningioma (Cases 4 and 5), and two with a solitary metastasis (Cases 6 and 7), abnormalities of rCBF were seen in areas remote from the lesion: in the frontal region in all four, and also in the occipital region in one of the four (Case 7). One patient with a meningioma (Case 8) showed no remote rCBF abnormalities. Ophthalmoscopic evidence of increased intracranial pressure was found in only one patient (Case 7).

**Case 4.** This 59-year-old man had had grand mal epilepsy for 3 years. After each convolution he suffered temporary right-sided hemiparesis and aphasia. Occasional 3- to 4-Hz activity was shown by EEG in the left premotor and midtemporal area. Brain scintigraphy with 133Xe injection in internal carotid probably represented low flow in the underlying cortex.

Eight days after the rCBF study a meningioma was removed from the parietal region.

**Case 5.** This 65-year-old man had had recurrent focal epileptiform attacks in the left hand and face for 5 months. On admission he had headache and dizziness. An EEG showed sporadic 3- to 4-Hz focal activity in the right parietal region. Right carotid angiography showed a right parasagittal tumor. Brain scintigraphy with 133Xe-chloromerodrin was positive.

An rCBF study was done on the right side. With a resting MABP of 100 mm Hg, moderate focal hyperemia was found in the right centroparietal region, corresponding to the tumor site. Measurement of the mean hemispheric flow showed a subnormal value of about 40 ml/100 gm/min. Angiotensin-induced hypertension (MABP 135 mm Hg) caused a focal flow increase of about 15% to 33% above the resting level in two parts of the frontal lobe, that is, remote from the tumor. Hemispheric mean flow did not change and hyperemia at the tumor site was unchanged. As the tumor was supplied almost solely by the external carotid artery, the high rCBF values over the tumor site may have represented functional hyperemia of the hyperactive (epileptogenic) underlying cortex.

Excision of the meningioma was performed some days after the rCBF study.

**Case 6.** This 66-year-old man was admitted to the hospital with paresis of the right arm, and attacks of clonic seizures in the right extremities. He had been operated on for lung cancer 3 years previously. An EEG showed 2- to 4-Hz activity in the left temporal region. Brain scintigraphy with 99mTc-pertechnetate revealed focal abnormality in the left parietal region. Left carotid angiography revealed a tumor at this site.

An rCBF study was done on the left side. With a resting MABP of 95 mm Hg, low rCBF and relative hyperemia were found around the tumor area, and hyperemia was also seen in the frontal lobe. Angiotensin infusion caused hypertension at an MABP of 118 mm Hg, and disclosed loss of autoregulation in the frontal lobe. As the tumor was mainly supplied by the external carotid artery, the low rCBF values over the tumor region
rCBF alterations remote from tumor site

revealed a solitary metastasis in the left parietal region.

Case 7. This 63-year-old woman was admitted because of headache, vomiting, and paresis of the left arm. The symptoms improved with steroid therapy. An EEG was slightly abnormal. Right carotid angiography showed an intracranial mass lesion in the right parietal region close to the midline. The first brain scintigram with 99mTc-pertechnetate was normal, but repeat scintigrams revealed a solitary tumor in the right parietal region.

An rCBF study was done on the right side under general anesthesia. (All the other cases were studied under local anesthesia only.)

With a resting MABP of 65 mm Hg, and a pCO2 of 24.6 mm Hg, hemispheric flow was very low with values of about 23 ml/100 gm/min. Two small areas of relative hyperemia with flows of about 40 to 45 ml/100 gm/min were found, one in the parietal region corresponding to the tumor site, and one very close to the tumor. In addition, there were two other regions of relative hyperemia, one in the occipital part of the hemisphere, one in the frontotemporal area. An autoregulation test was not performed.

At operation some days after the rCBF study, a solitary metastasis was removed from the right parietal region.

Case 8. This 65-year-old man had suffered frequent focal seizures in the left hand for 2 years, sometimes with loss of consciousness. Several EEG's were normal. Brain scintigraphy with 197Hg-chlormerodrin indicated a pathological process in the right parietal region. Angiography performed via the internal carotid artery was normal, while angiography via the common carotid artery showed a slight tumor blush in the parietal region.

An rCBF study was done on the right side. With a resting MABP of 88 mm Hg, mean hemispheric rCBF was diffusely low, with flow values of about 30 ml/100 gm/min. In the temporal lobe the flow was low in the area corresponding to the tumor site. No focal hyperemia was seen. Functional tests (flicker stimulation, contralateral hand discrimination) did not change the flow pattern in the hemisphere. An autoregulation test was not performed.

Case 9. This 50-year-old man had a 5-year history of grand mal attacks. He was admitted with a slight supranuclear paresis in the left extremities. Right carotid angiography showed a large process in the anterior part of the temporal region. Brain scintigraphy with 197Hg-chlormerodrin showed evidence of an intracranial mass in the right temporal lobe. An epidermoid cyst was subsequently removed from the basal part of the temporal region. Several months after operation the patient was readmitted because of grand mal seizures without loss of consciousness. Brain scintigraphy with 197Hg-chlormerodrin was normal.

An rCBF study was performed on the right side. With a resting MABP of 88 mm Hg, mean hemispheric rCBF was diffusely low, with flow values of about 30 ml/100 gm/min. In the temporal lobe the flow was low in the area corresponding to the tumor site. No focal hyperemia was seen. Functional tests (flicker stimulation, contralateral hand discrimination) did not change the flow pattern in the hemisphere. An autoregulation test was not performed.

Case 10. This 71-year-old man was admitted because of severe expressive aphasia and loss of consciousness for several hours. An EEG was focally abnormal in the left temporal region. Left carotid angiography suggested a vascular tumor, probably a glioma, in the left temporal area. Brain scintigraphy with 197Hg-chlormerodrin disclosed abnormally high isotope uptake in the same region.
An rCBF study on the left side was performed. With a resting MABP of 110 mm Hg, values of about 70 to 75 ml/100 mg/min were seen in the left tempororooccipital region, with many vascular spikes. Angiotensin-induced hypertension with an MABP of 135 mm Hg did not change the flow pattern in that hemisphere.

Posterior Fossa Lesions

Two patients with posterior fossa masses were studied, one with a solitary metastasis from the lung (Case 11), and the other with a tumor of unknown type (Case 12) (Table 1). Focal rCBF abnormalities remote from the lesions were seen in the supratentorial portion of the hemisphere in both cases. There were no ophthalmoscopic signs of increased intracranial pressure in either case.

Case 11. This 54-year-old woman was admitted with severe headache, vomiting, and grand mal seizures, but no focal neurological deficits. She had had inoperable lung cancer for 2 years. She was treated conservatively with steroid therapy. The EEG findings suggested a pathological process in the posterior fossa. Brain scintigraphy with 197Hg-chlormerodrin showed no sign of a tumor.

An rCBF study was done on the left side. With a resting MABP of 75 mm Hg, there was a normal, slightly higher flow, about 20% to 25% above the mean flow value in the frontal region. A study done during a mental calculation test (MABP 75 mm Hg) revealed two hyperemic areas, one in the temporal lobe (as seen in normal individuals), and the other in the lower portion of the temporooccipital region (a distinctly abnormal site of flow increase for this test).

The patient died 1 month later. Autopsy revealed a metastatic cerebellar tumor and brain edema, but no metastasis in the supratentorial portion of the brain.

Case 12. This 76-year-old man was admitted with acute right-sided hemiparesis, aphasia, and seizures of the left side. An EEG was slightly abnormal over the right hemisphere, and showed 1.5- to 2-Hz activity in the bifrontal temporal regions. Right carotid angiography suggested arteriosclerosis, whereas right vertebral angiography demonstrated a cerebellar tumor. Several brain scintigraphic studies with 197Hg-chlormerodrin revealed an abnormally high uptake of isotope in the right posterior fossa.

An rCBF study was done on the right side (Fig. 4). With a resting MABP of 100 mm Hg, subnormal mean flow values and a normal flow pattern were found. Autoregulation test with MABP elevated to 150 mm Hg by angiotensin infusion disclosed two hyperemic areas, one in the central region, and the other in the lower portion of the frontotemporoooccipital region.

Discussion

Origin of Remote Abnormality

In these cases the remote location of rCBF abnormality was not due to mass lesions remote from the primary lesion. This was shown from the results of other clinical examinations in all cases, and confirmed by autopsy in four. In the autopsy record no special mention of herniation was made, but all four had diffuse brain edema. In particular, there were no masses or other gross anatomical changes in the area where abnormalities were detected by rCBF measurement. In the eight other cases, routine clinical examinations, several conventional static brain scintigraphic studies, carotid angiography, and EEG all failed to show abnormalities in the area of remote rCBF disturbance.

For these reasons the remote rCBF abnormality must represent a functional disturbance of cortical tissue. This cortical tissue disturbance is not directly related to a severe rise in intracranial pressure. The intracranial pressure was not measured directly, but ophthalmoscopic signs of papillary edema were found in only one case. It is therefore likely that the remote rCBF abnormalities have developed at an early stage of increased intracranial pressure. If the pressure rises further, this would be expected to cause disturbance of the rCBF in the entire brain.\(^5,18,19\)

Our attention was first called to the existence and probable nature of localized rCBF abnormalities in an area remote from the tumor by the observations made in Cases 1 and 2. Both patients showed such abnormalities in the anterior fossa, namely, in the posterior part of the area of supply of the internal carotid artery. In all, nine of the 12 patients with intracranial masses showed remote rCBF abnormalities consisting of lost autoregulation and sometimes hyperemia at rest. In six of these nine cases, the posterior
part of the injected hemisphere was involved. It is tempting to suggest, therefore, that this finding represents an abnormality of the cortex close to the incisura of the tentorium. Mass displacement due to pressure gradients can be expected to cause local compression at this site in particular.\(^2,12,26\) The compression is probably of an intermittent nature, as judged from the variation of intracranial pressure often seen in such cases.\(^5,18,20\) This speculation accords well with the hyperemia seen in remote areas in control studies at rest, because, if intermittent tissue compression occurs with periods of frank ischemia, then tissue acidosis would result.\(^1,7,27\) Between such periods of compression tissue hyperemia could be expected in the same area. However, if there is permanent local ischemia due to tissue compression against unyielding anatomical structures, then adjacent tissue areas might well show hyperemia and loss of autoregulation due to focal spread of vasoactive stimuli (lactacidosis).

**Relation of Mass Location and Remote Hyperemia Site**

In all three patients with frontal mass lesions (Cases 1, 2, and 3), we found remote abnormalities, usually tissue hyperemia and loss of autoregulation, in the lower part of the posterior part of the hemisphere. The hyperemia was independent of hyperemia in or around the tumor itself. In cases of mass lesion in the frontal lobe, focal clinical symptoms are frequently absent, and when they are recognized clinically the tumor has often already grown to a considerable size with resultant mass displacement of brain tissue over the midline or down into the posterior fossa. Under the moderately increased intracranial pressure and with mass displacement and neuroaxial distortion, the falx and the tentorium will tend to cause sites of intermittent compression. For this reason, remote lesions of the type discussed in this paper are perhaps particularly characteristic of frontal mass lesion.

Our patients with mass lesions in the centroparietal region showed a different type of hyperemia compared with that of the cases with frontal mass lesion. In four of the five cases, remote hyperemia with loss of autoregulation was seen in the frontal region. These hyperemic regions were also independent of the rCBF abnormalities found in or around the mass lesion in most cases. This hyperemia might correspond to local tissue compression around the falx, where the falx gives a counterpressure to the brain tissue and thus produces tissue ischemia and hypoxia at this site.

Our two patients (Cases 9 and 10) with temporal mass lesions did not show remote rCBF abnormalities. This could be due to the location of the mass lesions, which were rather deeply situated and distant from the falx and tentorium.

Both patients with posterior fossa mass lesions had focal rCBF abnormalities in the lower part of the hemisphere, that is, close to the tentorium. This could be due to direct influences of tissue compression through the tentorium from increased volume in the posterior fossa.

It has previously been reported that loss of autoregulation in the entire brain hemisphere\(^5,18,19\) is sometimes observed in cases with mass lesion.\(^1,17,18\) This global effect on rCBF, probably related to more severe and variable intracranial pressure increase, was not seen in our cases. We found focally abnormal rCBF with loss of autoregulation in many of our patients, a phenomenon not recognized by previous authors. The most important reason for our finding is, perhaps, that our rCBF measurement system has fairly high spatial resolution.\(^9,21,24,25\) This allows us to identify changes in focal blood flow in quite small regions.

The areas of abnormal rCBF remote from the lesion are found in fairly specific sites according to the site of mass lesion: if the tumor is situated in the frontal region, remote rCBF abnormalities are probably found in the lower portion of the occipital region; with a centroparietal mass lesion, remote rCBF abnormalities will probably be in the frontal region; and with a posterior fossa mass lesion, remote rCBF abnormalities may be in the lower part of the occipital region. These characteristic rCBF abnormalities are particularly seen in areas that may be related to local tissue compression against unyielding anatomical structures, such as the falx and tentorium. Only mild local compression of brain tissue is needed to elicit the vicious circle of lactacidosis – hyperemia – blood-brain barrier damage – edema – further local compression – further lactacidosis.\(^1,11,12\) It is likely that focal lactacidosis, which provides a chemical
basis for post-hypoxic luxury perfusion, may
be a major factor causing remote rCBF ab-
normalities in the compression site. This
suggestion is supported by the studies show-
ing a focally increased lactacidosis in the sur-
roundings of the tumor.7,8,15

Clinical Observations

The possible relation between clinical
symptoms and remote rCBF abnormalities
must be discussed. In our series, a patient
with a meningioma over the frontal lobe
(Case 1) deteriorated rather suddenly, sugges-
tive of herniation, some hours after the rCBF
study. Fortunately, vigorous treatment in-
cluding artificial ventilation to a low pCO2
gradually restored him to his previous condi-
tion. This observation is consistent with the
above discussion of the possible origin of
remote rCBF changes, and suggests that
remote hyperemia may be taken as a danger
sign: a state of preherniation.

The state of preherniation is clinically well
known. But, it can actually only be diagnosed
accurately in retrospect, that is, after symp-
toms of herniation have developed. In this
context our results may be of special interest,
as so far no other methods have disclosed the
remote abnormality of cortical tissue that can
be expected to precede herniation. Clinicians
have noted that complex symptoms arising
from widely different parts of the brain can
sometimes be found in brain-tumor cases.
Such observations have been interpreted as
evidence of the interruption of neural
pathways by the tumor with consequent func-
tional disturbance of distant cortical areas.6,8,28
Our results suggest that, in addition to direct
tumor effects on pathways, indirect effects
from displacement by the mass should also be
taken into account.

With the more widespread use of com-
puterized axial tomography we shall learn
much more about mass displacement inside
the skull; however, displacement of a struc-
ture may not have any functional effect. In
such cases an rCBF study, or other methods
currently being developed to yield a map of
tissue metabolism, will be needed to identify
functional abnormality that may constitute a
well defined state of preherniation. Conven-
tional static brain scintigrams cannot find the
remote areas of abnormality: no discernible
blood-brain barrier damage was seen at these
sites in any of our patients.

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