Extensive metabolic and neuropsychological abnormalities associated with discrete infarction of the genu of the internal capsule

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Abstract

Objective—The clinical presentation of capsular genu infarct varies. Prominent faciolingual weakness and subcortical dementia are the rule, but symptoms depend on the precise location and extension of the lesion beyond the genu. The aim was to characterise the radiographic, electroencephalographic, and neuropsychometric abnormalities in a woman who had a history of recurrent transient memory loss.

Method—Case report.

Results—Magnetic resonance imaging showed infarct in the genu of the left internal capsule. Positron emission tomography scan demonstrated decreased metabolic activity in the ipsilateral temporal, occipitotemporal, and contralateral cerebellar hemispheres. Electroencephalography showed intermittent rhythmic delta activity in the left frontotemporal region, and findings on neuropsychometric evaluation were consistent with cognitive impairment. Follow up evaluation 7 months after the stroke showed improvement in some areas of the cognitive domain, but residual neuropsychometric and neurophysiological abnormalities persisted.

Conclusion—This case illustrates that cerebral and cerebellar diaschisis may contribute to the symptomatic presentation and recovery from capsular genu infarct, although its precise role remains elusive.

Key words: capsular genu infarct; amnestic syndrome; diaschisis

Clinicoanatomical correlation of capsular genu infarct implicates the disruption of corticopontine and corticobulbar fibres as the cause of faciolingual and motor deficits often seen in these patients.1 The cognitive impairment is attributed to interruption of the inferior and anterior thalamic peduncles2 or diaschisis.3 In one of the largest case series, Tatemoni et al4 reported that profound acute frontal lobe syndrome was manifested by fluctuating alertness, inattention, memory loss, apathy, abulia, and psychomotor retardation with minimal involvement of pyramidal and corticobulbar tracts. Some patients, however, had infarcts beyond the capsular genu. In a series by Bogousslavsky and Regli,5 the most prominent findings were contralateral facial and lingual hemiparesis with dysarthria. Amnestic syndromes may result from lesions of the medial temporal lobe1 and diencephalon.7 Transient global amnesia5 can be easily distinguished from other amnestic syndromes on clinical grounds.

Recurrent transient amnesia limited to recent memory and culminating in ischaemic infarct of the genu of the internal capsule has not been reported. We report on a woman with infarction of the capsular genu who presented with episodic marked cognitive impairment associated with major verbal memory and language deficits. Results of detailed clinical, neuropsychological, and functional imaging studies suggest that cerebral and cerebellar diaschisis may contribute to the presentation and recovery from capsular genu infarction.

Case report

A 71 year old right handed woman with 12th grade education presented after acute onset of short term memory loss. Eleven years earlier, she had coronary artery bypass grafting for acute myocardial infarction. Over the previous 2.5 years, she had five discrete episodes of stereotypical short term memory loss, each lasting 15 to 20 minutes and completely resolving. Her fifth spell, 7 months before presentation, was evaluated by brain CT, transoesophageal echocardiography, and carotid duplex ultrasonography at another institution. No abnormality was found, and a diagnosis of transient global amnesia was made. Two days before presentation, while at church, her husband noted that she was unable to follow the service. Later that day, she could not remember her daughter’s name or what day it was. The next day, she could not remember the events of the previous 24 hours and asked repetitive questions. Evaluation at the local emergency department a day later disclosed no other focal neurological symptoms. Results of a general physical examination were normal. Abnormal findings on neurological examination were disorientation to time and place and impaired 5 minute delayed recall. Results of laboratory studies, such as glucose, sodium, calcium, leucocyte count, haemoglobin, electrolyte, and urinalysis, were normal. A diagnosis of transient global amnesia was made, and an outpatient neurological consultation was arranged.

Neurological evaluation 7 days after the onset of her symptoms disclosed no change in her symptoms. She was alert and cooperative but disoriented to place and time. She offered no spontaneous speech. Her response to questions was fluent but notable for delayed...
response latency and word finding difficulties. Comprehension of conversational language was impaired, but she was able to follow a simple one step command. There were marked perseveration, apathy, and psychomotor retardation, with prominent frontal release signs (glabellar, palmomental, and snout). Motor examination showed normal gait with decreased right arm swing, mild drift, and decreased rapid alternating movements of the right hand. There was a mild upper motor neuron right facial weakness. Muscle stretch reflexes were hyperactive, with an extensor plantar response on the right.

She was admitted to hospital, and brain MRI showed T2 weighted and fluid attenuated inversion recovery hyperintense signals in the genu of the left internal capsule and periventricular and subcortical white matter.

Figure 1 Fluid attenuated inversion recovery magnetic resonance image showing hyperintense signals in the genu of the left internal capsule and periventricular and subcortical white matter.

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She was admitted to hospital, and brain MRI showed T2 weighted and fluid attenuated inversion recovery hyperintense signals in the genu of the left internal capsule and periventricular and subcortical white matter (fig 1). Gradient echo MRI was negative for cerebral amyloid angiopathy. Electroencephalography showed left frontotemporal intermittent rhythmic delta activity. Transoesophageal echocardiography and magnetic resonance angiography of the intracranial and extracranial vessels yielded normal findings. Cerebrospinal fluid analysis showed 4 white cells and 6 red cells/µl, protein concentration of 41 mg/dl, and glucose concentration of 53 mg/dl (serum, 109 mg/dl). Results of CSF index, synthesis rate, oligoclonal bands, and fungal and viral cultures were negative.

A neuropsychological examination performed 2 weeks after the onset of her symptoms documented substantial cognitive compromise (table 1). Her performance on an expanded measure of mental status (dementia rating scale) was severely impaired for her age, with markedly deficient performances on subtests of attention (for example, digit span, visual scanning), initiation/perseveration (for example, word fluency), conceptualisation (for example, identifying oddities and similarities among verbal and visual stimuli), and memory (for example, orientation and immediate memory for words and figures). She was unable to retain information presented in the form of a word list from the Consortium to Establish a Registry for Alzheimer’s Disease neuropsychological test battery or geometric designs from the Wechsler memory scale, revised (visual reproduction). Severe expressive and receptive language deficits were also evident. She had marked difficulty following auditory-verbal commands on the token test of the multilingual aphasia examination and comprehending short stories on the complex ideational material subtest of the Boston diagnostic aphasia examination.11 Her ability to provide the names of line drawings of objects was also severely impaired (Boston naming test),12 with errors characterised primarily by substitution of semantically similar words (for example, “arrow” for “dart,” “dice” for “dominoes”). Her written mathematical skill and ability to recognise and pronounce written words were mildly impaired (wide range achievement test, 3rd edition).13 Her comprehension of the meaning of written sentences was more severely impaired (Peabody individual achievement test, revised; reading comprehension). By contrast, the patient showed relatively intact phrase repetition, spelling ability, and visuospatial constructional abilities. She endorsed moderate symptoms of depression on the geriatric depression scale.14

13F-2-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) scan of the brain performed 7 weeks after symptom onset showed decreased metabolic activity in the left temporal, occipitotemporal, and right cerebellar hemispheres (fig 2). The PET scanner used an ADAC vertex coincidence camera with a
Discussion

Remote focal metabolic effects in the brain, commonly referred to as diaschisis, are attributed to depressed synaptic activities at sites distant from, but neurally connected with, the damaged area. Several PET studies have demonstrated these remote metabolic effects in patients with large frontoparietal and thalamocapsular strokes, but the precise relation to patients’ symptoms and the prognostic value remain obscure. Some investigators have reported that cerebellar diaschisis does not resolve. Others have suggested that cerebral and cerebellar diaschisis is a transient phenomenon with potential for reversibility of the alterations and recovery of the deficits resulting from it. Bowl et al investigated the contribution of diaschisis to clinical deficit in human cerebral infarction and concluded that diaschisis does not independently add to clinical deficit after stroke. However, other investigators have found that crossed cerebellar diaschisis is greater with larger infarcts, but whether the degree of crossed cerebellar diaschisis correlates with clinical stroke severity remains controversial. Speculations that these remote effects underlie the neuropsychological deficits of subcortical origin and contribute to diffuse symptoms of acute supratentorial strokes, such as confusion, agitation, and coma, have been difficult to prove.

Frontotemporal cortices have extensive connections with ipsilateral anterior thalamic nuclei and contralateral cerebellar hemisphere via the anterior and inferior thalamic peduncles. Corticothalamic and thalamocortical fibres form the thalamic peduncles. These fibres enter and exit the thalamus at its rostral and caudal poles and along the dorsal surfaces. The inferior thalamic peduncle carrying fibres connecting the ventromedial thalamus with the orbitofrontal, insular, and temporal cortices passes through the posterior capsule in the region of the genu. Damage to this white matter tract may occur with infarction in the region of the inferior genu, causing severe amnesia from disruption of the basolateral limbic system. Interruption of the anterior or inferior thalamic peduncle, or both, in the region of the capsular genu has been proposed as the mechanism underlying the abrupt cognitive impairment seen in these patients.

Functional brain imaging in our patient demonstrated hypometabolic activity in the temporal cortex ipsilateral to the capsular lesion, supporting the view that cognitive changes probably occurred by functional disruption, perhaps related to diaschisis. Periventricular and subcortical T2 signal abnormalities (leukoaraiosis) were present on brain MRI in our patient. Leukoaraiosis or white matter rarefaction has been reported to occur at a higher frequency in subjects with mild cognitive deficits and decreased mental processing. According to one study, about one sixth of patients with stroke had pre-existing dementia previously undiagnosed, and leukoaraiosis and other factors were found to be independent...
Table 2  Summary of case reports of isolated capsular genu infarcts

<table>
<thead>
<tr>
<th>Authors, year</th>
<th>No. of patients</th>
<th>Symptoms at presentation</th>
<th>Recurrent symptoms</th>
<th>Location of lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tattemichi et al, 1992(^2)</td>
<td>1 of 6</td>
<td>Right hemiparesis, confusion</td>
<td>No</td>
<td>Left capsular genu</td>
</tr>
<tr>
<td>Bogousslavsky and Regli, 1990(^1)</td>
<td>5</td>
<td>Faciolingual weakness, dysarthria, dysphagia</td>
<td>No</td>
<td>Right (2) and left (2) capsular genu</td>
</tr>
<tr>
<td>Rousseaux et al, 1987(^3)</td>
<td>1</td>
<td>Left hemiparesis</td>
<td>No</td>
<td>Right capsular genu</td>
</tr>
<tr>
<td>Iwata, 1984(^4)</td>
<td>1</td>
<td>Right hemiparesis</td>
<td>No</td>
<td>Left capsular genu, corona radiata</td>
</tr>
<tr>
<td>Schneider et al, 1986(^5)</td>
<td>1</td>
<td>Confusion, amnesia</td>
<td>No</td>
<td>Right capsular genu, anterior thalamus</td>
</tr>
<tr>
<td>Yamakawa et al, 1994(^6)</td>
<td>2</td>
<td>Abulia</td>
<td>No</td>
<td>Right (1) and left (1) capsular genu</td>
</tr>
<tr>
<td>Moreau et al, 1996(^7)</td>
<td>1</td>
<td>Abulia, confusion, right facial weakness</td>
<td>No</td>
<td>Left capsular genu</td>
</tr>
<tr>
<td>Lai et al, 1990(^8)</td>
<td>1</td>
<td>Amnesia</td>
<td>No</td>
<td>Left capsular genu</td>
</tr>
<tr>
<td>Terao et al, 1991(^9)</td>
<td>1</td>
<td>Amnesia</td>
<td>No</td>
<td>Left capsular genu</td>
</tr>
<tr>
<td>Yamadori, 1990(^10)</td>
<td>1</td>
<td>Aphasias</td>
<td>No</td>
<td>Left capsular genu</td>
</tr>
<tr>
<td>Spertell and Ransom, 1979(^11)</td>
<td>1</td>
<td>Dysarthria, clumsy hand syndrome</td>
<td>No</td>
<td>Left capsular genu</td>
</tr>
<tr>
<td>Kooistra and Heilman, 1988(^12)</td>
<td>1</td>
<td>Memory loss</td>
<td>No</td>
<td>Left capsular genu</td>
</tr>
<tr>
<td>Markowitz et al, 1990(^13)</td>
<td>1</td>
<td>Aphasias, right hemiparesis</td>
<td>No</td>
<td>Left capsular genu</td>
</tr>
<tr>
<td>Chukwudeluzu et al, present case</td>
<td>1</td>
<td>Amnesia</td>
<td>Yes (&lt;5)</td>
<td>Left capsular genu</td>
</tr>
</tbody>
</table>

Abnormalities associated with capsular genu infarct

In a case report by Moreau et al\(^2\) with persistent abnormal neuropsychological findings, there was a major presenting feature in four\(^10\) cases. A lesion was seen in the left genu of the internal capsule in three of the four patients. Table 2 summarises the literature review of cases. Tattemichi et al\(^2\) reported detailed clinical and neuropsychological long term follow up (10 weeks to 2 years) findings in four of their six patients with capsular genu infarct. Resolution of acute dementia syndrome occurred in only one patient 2 years after stroke. Results of initial brain functional imaging studies (SPECT) were abnormal in all patients, but follow up studies were not reported. Schneider et al\(^5\) reported on a patient with persistent abnormal neuropsychological testing results 7 months after a capsular genu stroke. In a case report by Moreau et al\(^3\), PET demonstrated hypometabolism in the left frontotemporal region, left caudate, left thalamus, and right cerebellar cortices 2 months after a left capsular genu infarct. Follow up SPECT studies in two patients reported by Yamakawa et al\(^6\) showed persistent abnormality in one and resolution in the other 4 and 6 months after stroke, respectively. Kooistra and Heilman\(^11\) and Markowitz et al\(^13\) reported similar cases with persistent cognitive abnormalities on neuropsychological testing 2 years and 9 months after capsular genu infarction. Our case report is similar to previously reported cases, but in addition to long term follow up with detailed clinical and neuropsychological testing, we showed that clinical and neuropsychological findings were correlated with those of PET studies.

In our patient, the relevant lesion lies in the distribution of arterioles perforating from the apex of the internal carotid artery\(^14\) or the anterior cerebral artery. The essential features of this capsular genu “cognitive syndrome” resemble the clinical profile found in unilateral polar thalamic infarction\(^15\) or the dementia syndrome of bilateral paramedian thalamic infarction. Among 100 patients with lacunar infarcts in the territory of deep perforators of the carotid system identified by CT, Ghika et al\(^5\) found neuropsychological deficits in up to 34%. Thus, capsular genu infarct causing acute cognitive impairment may need to be uncommon and may be underreported.

A chance association between the infarct and our patient’s presentation cannot be excluded with certainty. Her underlying cardiac condition may have contributed to her memory loss. It is also possible that our patient had transient epileptic amnesia\(^14\) and that the infarct was coincidental. A trial of anticonvulsant drugs and ambulatory electroencephalography were not performed.

Although our patient’s disorientation, aphasia, psychomotor retardation, and mood and some of her cognitive functions improved 7 months after the stroke, neuropsychological evaluation and PET studies showed persistent abnormalities beyond the area of the structural lesion. The infarct was limited to the white matter without involvement of the adjacent grey matter structures. No mass effect to adjacent structures was demonstrated on brain MRI. The implications are that the cerebral and cerebellar diaschisis in this patient may have contributed to her inadequate clinical recovery. This case supports the phenomenon of cerebral diaschisis as a possible contributing mechanism to poor recovery from a small but strategically placed ischaemic infarct.
