The Syndrome of Bilateral Hemispheric Border Zone Ischemia

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Symptoms compatible with vertebrobasilar ischemia have been reported in patients with unilateral or bilateral carotid occlusive disease. Intracranial steal phenomena have been proposed to explain the symptoms. In a review of 54 patients with angiographically documented severe bilateral carotid stenosis (≤2 mm residual lumen) or occlusion, eight had symptoms suggesting vertebrobasilar insufficiency. Five patients were identified retrospectively, and the other three were evaluated prospectively. Symptoms included various combinations of hemodynamically mediated, transient bilateral motor, sensory, or visual impairment. Dysarthria, dysphagia, and diplopia were generally absent. Each patient also described additional symptoms compatible with transient hemispheric or retinal ischemia. The anatomic regions subserving the bilateral vertebrobasilar-like symptoms could be correlated with angiographically estimated arterial border zones in both hemispheres and may thus represent bilateral hemispheric border zone ischemia rather than brain stem ischemia. An intracranial steal need not be invoked. (Stroke 1990;21:1668-1673)

The clinical and angiographic aspects of carotid1-3 and vertebrobasilar4-6 territory transient ischemic attacks (TIAs) and stroke are well known. Some cerebral hemispheric processes, such as epileptic lesions or electrical stimulation of the superior temporal or parietal cortex, produce vertigo7-8 and suggest posterior circulation ischemia. Since coexistent arterial occlusive lesions are present in 27-34% of cases,9-11 it may therefore be difficult to distinguish unilateral or bilateral hemispheric dysfunction from brain stem dysfunction on clinical grounds in some patients.

Investigators have postulated that the origin of vertebrobasilar-like symptoms in some patients with carotid artery disease is due to an intracranial steal phenomenon,12-22 that is, that blood flows anteriorly though the posterior communicating arteries to supply ischemic anterior-circulation structures, leading to brain stem/cerebellar hypoperfusion and vertebrobasilar-like symptoms. The concept of the totality of cerebral blood flow (i.e., that correction of an occlusive lesion increases blood flow to ischemic and nonischemic tissues through an intact circle of Willis) has prompted numerous reports ascribing relief of vertebrobasilar-like and/or nonspecific symptoms to treatment with carotid endarterectomy or bypass operations.23-26 However, these studies do not demonstrate that anterior circulation revascularization eliminated the vertebrobasilar-like symptoms by normalizing the posterior circulation blood flow. Therefore, it is difficult to conclude that the mechanism of intracranial steal explains the production of symptoms in all cases.

An alternative explanation is that symptoms are produced by failure of autoregulation in the distal field of a vessel bearing a hemodynamically significant (flow-limiting) lesion. Since the microcirculation in this terminal region may be maximally dilated, a subtle alteration in posture, blood pressure or blood flow might elicit hemodynamically mediated TIAs mimicking vertebrobasilar TIAs, particularly if the ischemia is bilateral.27 Patients with multiple hemodynamic lesions of the extracranial vessels may be especially susceptible to such attacks.

We examined the spectrum of symptoms compatible with published criteria for vertebrobasilar TIA in patients with severe bilateral carotid occlusive disease and correlated the symptoms with angiographic lesions, patterns of collateral flow, and computed tomographic (CT) data.

Subjects and Methods

We retrospectively and prospectively reviewed the cerebral angiography files of the University of Virginia Medical Center from January 1, 1982, to May 15, 1988, for consecutive cases of severe, flow-limiting (residual lumen diameter of ≤2 mm) bilateral carotid
stenosis and/or occlusion. Complete medical records of 54 patients were available for this investigation. Patients were classified as having carotid or vertebrobasilar TIAs based on criteria of the Joint Committee for Stroke Facilities.1 Other transient neurologic symptoms (e.g., dizziness, confusion, syncope) that did not meet standard criteria for a TIA were classified as nonspecific symptoms.

Cerebral angiographic studies were reviewed by the investigators and a neuroradiologist unaware of the patient's clinical history. The standard transfemoral route was used in most cases; in some studies, retrograde brachial angiograms were necessary. Arch and selective cerebral arteriograms with multiple views were obtained in most cases. The origins of all extracranial vessels, the intracranial circulation (i.e., the anterior cerebral artery [ACA], middle cerebral artery [MCA], and posterior cerebral artery [PCA]), and patterns of collateral blood flow were sought and tabulated. Specifically, the presence and contribution of external carotid–to–internal carotid (EC–IC) flow, cross flow (across the anterior communicating artery to the opposite ACA and/or MCA), or forward flow (from the posterior circulation to the anterior circulation via the posterior communicating arteries) and the pattern of leptomeningeal collaterals were evaluated. Demonstration of intracranial collateral patterns was adequate for analysis in all cases.

Angiographic data were used in an attempt to identify the border zone regions (Figure 1). The distal field (or far field, "die letzten Wiesen")28 was defined as the most distant portion of a cerebral artery territory seen on angiography.29 An arterial border zone was defined as a region of potentially increased susceptibility to hypoperfusion between the distal fields of two or more cerebral arteries. We assumed that the arterial border zone in a patient with hemodynamically significant carotid occlusive disease corresponds to a region of decreased blood flow demonstrable by microangiographic30 or physiologic techniques.

Locations of the arterial border zones were estimated according to correspondence with known angiographic patterns and anatomic foci of border zone ischemic infarcts by CT or pathologic criteria (Figure 1). The anterior (ACA/MCA) border zone was assigned if only the internal carotid artery filled the ipsilateral ACA and MCA or if forward flow was the predominant collateral supply to the hemisphere of interest. If a leptomeningeal collateral from the PCA territory was the major supply to a hemisphere, then the posterior (ACA/PCA and/or MCA/PCA) border zone(s) was (were) designated. Both anterior and posterior border zones were assigned in each hemisphere if cross flow was the major collateral supply since tissue perfusion at all distal supratentorial sites might be compromised. Clinical symptoms and angiographic findings were correlated based on comparison of the location of brain regions subserving an anatomic function suggested by motor/sensory homunculi with the border zones estimated from angiography (Figure 2).

We hypothesized that anterior border zone ischemia would produce sensorimotor symptoms whereas posterior border zone ischemia would produce sensory/visual symptoms.

Results

Among the 54 cases reviewed, eight patients described symptoms that met the Joint Committee for Stroke Facilities criteria1 for vertebrobasilar TIAs. Five patients (cases 1–3, 5, and 6) were identified after retrospective chart review and the other three (cases 4, 7, and 8) were evaluated prospectively. The five men and three women had an age range of 53–75 (median 62) years (Table 1). All patients had unilateral carotid territory symptoms in addition to vertebrobasilar-like symptoms that included transient ret-
inal ischemia (cases 2, 5, and 8) or infarction (case 1), unilateral (cases 2, 3, 5, and 6) or bilateral (cases 4, 7, and 8) transient hemispheric ischemic attack, and unilateral hemispheric infarction (case 8). Nonspecific symptoms were present in four patients.

Vertebrobasilar-like symptoms included bilateral or alternating weakness or motor dysfunction in three patients (cases 1, 3, and 4), gait abnormalities in three (cases 2, 6, and 7), bilateral or alternating sensory phenomena in five (cases 1, 4–6, and 8), bilateral visual blurring in three (cases 5, 7, and 8), and vertigo in one (case 4). Postural sensitivity (i.e., occurrence of symptoms after orthostatic or positional changes) was noted in all eight patients. Symptoms were produced by erect posture (sit/stand) in three patients (cases 3, 6, and 7), changes in head or neck position in three (cases 4, 5, and 8), exertion (walking or exercise) in three (cases 1, 2, and 7), and documented orthostatic hypotension in one (case 6). One patient (case 7) had symptoms provoked by sitting upright and walking. Only one patient (case 7) complained of dysarthria; the others denied diplopia, dysarthria, or dysphagia. The mechanism of symptom production was inferred to be hemodynamic in all eight cases.

Neurologic signs included mental changes in four patients (cases 1, 2, 6, and 7), motor dysfunction in six (cases 2, 4–8), and sensory disturbances in two (cases 7 and 8). Abnormalities in speech or language were noted in two patients; case 1 had frontal lobe signs and dysarthria, while case 7 had dysarthria and minimal fluent aphasia. Cases 2 and 7 had abnormal tandem walking that was not clearly localizable to the nervous system. Case 6 had left dysmetria; whether this was due to cerebellar dysfunction or related to frontopontocerebellar tract dysfunction in the contralateral hemisphere was unclear. No patient had Wallenberg's syndrome or other classic brain stem signs. In no case did CT show brain stem or cerebellar infarction.

### Table 1. Syndrome of Bilateral Hemispheric Border Zone Ischemia: Demographics and Clinical Features in Eight Patients

<table>
<thead>
<tr>
<th>Case/age/sex</th>
<th>Carotid</th>
<th>Presenting symptoms</th>
<th>Vertebrobasilar-like</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/59/M</td>
<td>L central retinal artery occlusion</td>
<td>B sensorimotor, decreased mentation</td>
<td></td>
</tr>
<tr>
<td>2/62/M</td>
<td>R TMB, L THA</td>
<td>Change in level of consciousness, ataxic gait</td>
<td></td>
</tr>
<tr>
<td>3/61/M</td>
<td>L THA</td>
<td>B (R&gt;L) UE, LE weakness</td>
<td></td>
</tr>
<tr>
<td>4/66/F</td>
<td>B THA</td>
<td>Vertigo, alternating UE numbness, B LE weakness</td>
<td></td>
</tr>
<tr>
<td>5/60/F</td>
<td>L TMB, L THA</td>
<td>B visual blurring, B LE sensory</td>
<td></td>
</tr>
<tr>
<td>6/74/M</td>
<td>L THA</td>
<td>B UE sensory, dizziness, confusion, falling</td>
<td></td>
</tr>
<tr>
<td>7/75/F</td>
<td>B THA</td>
<td>Dizziness, staggering gait, B visual blurring</td>
<td></td>
</tr>
<tr>
<td>8/53/M</td>
<td>R TMB, THA, stroke; L THA</td>
<td>B visual blurring, B UE sensory, dizziness</td>
<td></td>
</tr>
</tbody>
</table>

M, male; F, female; L, left; R, right; B, bilateral; TMB, transient monocular blindness; THA, transient hemispheric ischemic attack; UE, upper extremity; LE, lower extremity.
The carotid lesions included bilateral stenosis in four patients (cases 1, 3, 6, and 7), stenosis/occlusion in two (cases 5 and 8), and bilateral occlusion in two (cases 2 and 4). Of the 16 external carotid arteries, nine were normal, six were stenotic, and one was occluded. Important EC-IC collaterals were bilaterally present in two patients (cases 4 and 8). Cross flow occurred in five patients, to the left in three (cases 1, 5, and 7) and to the right in two (cases 2 and 5). Forward flow was unilateral in two patients (cases 1 and 5) and bilateral in two (cases 2 and 4). Leptomeningeal collaterals were unilateral in two patients (cases 3 and 5) and bilateral in one (case 7). None of the eight patients had hemodynamically significant intracranial vertebrobasilar occlusive disease (residual lumen diameter of ≤2 mm). In cases 5 and 8, the vertebral artery origins were not imaged. In two patients (cases 2 and 3), no vertebrobasilar artery disease was documented.

Border zones were designated from the angiographic data using the method described above. In two patients (cases 2 and 4), bilateral anterior border zones were observed. In the other six patients (cases 1, 3, 5–8), bilateral anterior and posterior border zones were noted.

Vertebrobasilar-like symptoms were analyzed in relation to the presence and nature of arterial lesions, the pattern of collateral circulation, and the designated border zones. Correlation of clinical symptoms with angiographically determined border zones (Table 1) revealed the following patterns. In the patients with bilateral motor dysfunction (cases 1–4, 6, and 7), all six (100%) had bilateral anterior border zones. Of the patients with bilateral visual symptoms (cases 5, 7, and 8), all three (100%) had bilateral posterior border zones. In the patients with bilateral/alternating sensory symptoms (cases 1, 4, 5, 6, and 8), four of five (80%) had bilateral anterior and posterior border zones. Forward flow was demonstrated in four patients (cases 1, 2, 4, and 5; Table 2), affording the opportunity for intracranial steal in only half of the cases.

Vertebral artery origin disease was demonstrated in four of eight patients with vertebrobasilar-like symptoms (50%; Table 2). In the 46 patients without vertebrobasilar-like symptoms, vertebral artery origin disease occurred in 15 cases (32.6%). This difference was not significant (p=0.285, Fisher’s exact test). The severity of occulsive vertebral artery origin disease did not correlate with the type of vertebrobasilar-like symptoms (Tables 1 and 2).

All patients with vertebrobasilar-like symptoms underwent either carotid endarterectomy (seven) or bypass of arterial lesions (one). The putative surgical effect (i.e., increased blood flow) was unilateral in three patients (cases 4, 7, and 8), bilateral in four (cases 1, 3, 5, and 6), and a shift in border zone in one (case 2). Results were favorable (i.e., associated with abolition of symptoms) in four patients (cases 1, 3–5), unfavorable in three (cases 2, 6, and 7), and uncertain in one (case 8 was lost to follow up). Perioperative myocardial infarction with complicating embolic stroke (in two patients) and postoperative hemispheric stroke ipsilateral to the bypass surgery (in one) accounted for the unfavorable outcomes.

<table>
<thead>
<tr>
<th>Case</th>
<th>EC-IC</th>
<th>Cross flow</th>
<th>Forward flow</th>
<th>Leptomeningeal collaterals</th>
<th>Vertebral artery origin disease</th>
<th>Location of border zones</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>O</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>Bilateral S (moderate)</td>
<td>B anterior, B posterior</td>
</tr>
<tr>
<td>2</td>
<td>S</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>None</td>
<td>B anterior</td>
</tr>
<tr>
<td>3</td>
<td>O</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>None</td>
<td>B anterior, B posterior</td>
</tr>
<tr>
<td>4</td>
<td>O</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>L S (mild)</td>
<td>B anterior</td>
</tr>
<tr>
<td>5</td>
<td>O</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>B anterior, B posterior</td>
</tr>
<tr>
<td>6</td>
<td>S</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>L S (severe)</td>
<td>B anterior, B posterior</td>
</tr>
<tr>
<td>7</td>
<td>S</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>L irregularity</td>
<td>B anterior, B posterior</td>
</tr>
<tr>
<td>8</td>
<td>S</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>?</td>
<td>B anterior, B posterior</td>
</tr>
</tbody>
</table>

L, left; R, right; EC-IC, external carotid to internal carotid flow; O, occlusion; S, stenosis; -, absent; +, present.

Nature of the carotid lesions, collateral blood flow, presence of vertebrobasilar arterial disease, and designated border zone regions are shown in Table 2. The carotid lesions included bilateral stenosis in four patients (cases 1, 3, 6, and 7), stenosis/occlusion in two (cases 5 and 8), and bilateral occlusion in two (cases 2 and 4). Of the 16 external carotid arteries, nine were normal, six were stenotic, and one was occluded. Important EC-IC collaterals were bilaterally present in two patients (cases 4 and 8). Cross flow occurred in five patients, to the left in three (cases 1, 5, and 7) and to the right in two (cases 2 and 5). Forward flow was unilateral in two patients (cases 1 and 5) and bilateral in two (cases 2 and 4). Leptomeningeal collaterals were unilateral in two patients (cases 3 and 5) and bilateral in one (case 7). None of the eight patients had hemodynamically significant intracranial vertebrobasilar occlusive disease (residual lumen diameter of ≤2 mm). In cases 5 and 8, the vertebral artery origins were not imaged. In two patients (cases 2 and 3), no vertebrobasilar artery disease was documented.

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Discussion

Several investigators have reported clinical series of patients with unilateral or bilateral carotid stenosis or occlusion,22,32,42 with severe bilateral carotid artery disease in from 0.9%36 to 2.4%42 of the cases. Verteobasilar-like symptoms in patients with severe carotid artery disease have been described in a number of studies.17,22,34,41 Clinical-angiographic correlations have infrequently been reported.22,35,42 In two studies,22,42 some patients had “vertebrobasilar symptoms” with positional provocation and normal vertebrobasilar angiograms, while other patients had a variety of documented lesions or forward flow. These studies describe a small yet heterogeneous subgroup of patients with carotid artery disease. Surgical procedures alleviated the symptoms in some cases, but evidence that the benefit occurred due to increased blood flow
to the posterior fossa structures potentially responsible for the symptoms is not clear.

Diverse studies suggest that hemodynamic failure of the cerebral hemispheres may cause vertebrobasilar-like symptoms. In a monkey model of MCA occlusion, a more rapid onset of characteristic ischemic microcirculatory changes in the ipsilateral cerebral hemisphere occurred after the induction of significant hypotension. Correlative clinical–pathologic or clinical–CT studies support the hypothesis that the distal field28 of a cerebral arterial territory is most susceptible to hypoxic-ischemic injury.46-52 In patients with systemic hypotension, initial damage occurs in the border zones of all three major cerebral arteries and, with increasing severity, spreads asymmetrically into the border zones between the ACA and MCA.29

Recent clinical reports of patients with hemodynamically significant occlusive disease document the occurrence of orthostatic or positional cerebral ischemia in the retinal, hemispheric, and vertebrobasilar circulations.33-60 Investigations using xenon-133 inhalation60 and positron emission tomography61 of patients with severe unilateral60,61 or bilateral60 carotid artery disease have demonstrated a severe reduction in cerebral blood flow and an increase in the oxygen extraction fraction in the ipsilateral61 and bilateral60 anterior border zones, respectively. Several series of patients with severe unilateral or bilateral carotid occlusive disease have demonstrated hypodense lesions corresponding to anatomic border zones.50-52 Signs suggestive of the medial medullary syndrome have been documented in a patient with severe bilateral carotid occlusive disease and bilateral anterior border zone infarcts.62 These data suggest that hemodynamic reserve is lowered in the hemispheric border zones and that postural/positional changes produce cerebral ischemia or infarction.59,60

We found a correlation between the described bilateral motor, sensory, and visual symptoms and the border zones estimated by angiography. The uniform occurrence of postural sensitivity, the absence of specific intrinsic brain stem symptoms or signs, the correlation of the symptoms with the estimated angiographic border zones, and the favorable response of half of the patients to anterior circulation surgery support the hypothesis that the vertebrobasilar-like symptoms were mediated by ischemic dysfunction of anterior circulation structures. While four of the eight patients had angiographic evidence of vertebral artery origin (and not intracranial vertebral artery or basilar artery) disease, the occurrence of symptoms with changes in body position or posture imply that the symptoms occurred due to compromised collateral blood flow to the distal field, that is, to both cerebral hemispheres. This mechanism may explain the production of symptoms in one prospective (4) and two retrospective (1, 6) cases; in one patient (case 6), the potential for intracranial steal (forward flow to the cerebral hemispheres) was not present. Moreover, in four patients (retrospective cases 3 and 6, prospective cases 7 and 8), forward flow to the cerebral hemispheres ("steal-vertebrobasilar ischemia") was not present. Finally, the occurrence of unfavorable surgical results in three patients (37.5%) confirm that persons with bilateral hemodynamically significant carotid artery disease may comprise a high-risk surgical subgroup.

In conclusion, subtle alterations in perfusion pressure in patients with severe hemodynamic lesions of both internal carotid arteries could provoke simultaneous bilateral border zone ischemia, a syndrome of bilateral motor and/or sensory symptoms with facial sparing (lack of ischemia in brain region[s] subserving facial functions62), gait (bilateral lower extremity) disturbances,60 or bilateral visual phenomena52 but no intrinsic brain stem symptoms. In rare cases, the occurrence of diplopia22 might reflect parieto-occipital dysfunction due to posterior border zone (MCA/PCA) ischemia as opposed to intrinsic brain stem ischemia. Correlation of the symptoms and the mechanism of their production with the angiographic vascular anatomy suggests the possible hemispheric origin of such vertebrobasilar-like symptoms. However, description of a larger series of patients with detailed clinical, angiographic, and cerebral blood flow analyses is needed to determine the validity of this hypothesis and distinguish it from intracerebral steal as the cause of vertebrobasilar-like symptoms.

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References


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