Temporal Profile (Clinical Course) of Acute Vertebral Basilar System Cerebral Infarction

H. Royden Jones, Jr., M.D., Clark H. Millikan, M.D., and Burton A. Sandok, M.D.

SUMMARY Records of 37 consecutive patients with acute brain infarction from vertebrobasilar artery disease, admitted to the cerebrovascular hospital service within 36 hours of the onset of symptoms, were studied to define the temporal profile of clinical events during the first week of illness. A stable course with unchanged neurologic deficit was found in 11% (4 patients). Progressive improvement in symptoms occurred in 35% (13 patients). Progressive disability occurred in 43% (16 patients). A remitting-relapsing course was noted in 11% (4 patients). In these latter 2 groups, stabilization of the clinical course occurred in the majority within 48 hours after the initial symptom; however, definite changes continued to develop up to 96 hours in a significant number of patients. Mortality at the conclusion of the first week was 27% for the entire group. This was 2.5 times greater than the 10.6% previously reported for a group of 179 patients with acute brain infarction due to carotid system disease who were concomitantly studied.

THE DEFINITION of an expected natural history for a series of patients presenting with acute cerebral infarction has important therapeutic and prognostic implications. We have previously defined the clinical course in 179 consecutive patients with brain infarction in the area of the carotid system (CSI) and categorized their neurologic status during the first week of illness as stable (39%), improved (35%), progressive deficit (19%), and remitting-relapsing (7%). As supplement to this, 37 patients were seen concomitantly who had brain infarction in areas supplied by the vertebrobasilar system (VBI).

Definitions

Patients having non-hemorrhagic cerebrovascular disease are commonly divided into categories of transient ischemic attack (TIA), progressive stroke, and completed stroke. This categorization does not imply severity of deficit but rather refers only to the temporal aspect of each event. The actual natural history or temporal profile of the initial course of patients having an acute stroke, that is, the risk of progression or remission-relapse versus those patients whose course is static or improving, has not been defined clearly in a large series until our initial report on carotid system disease. Similarly, many large series of patients having VBI have been reported, but review of the actual acute course seems unclear from the data available to date.

Literature Review

In 1946, Kubik and Adams fully described the clinical pathology of brain stem infarction due to basilar artery disease. Of 22 patients, in 18 the disease was fatal, and the diagnosis was confirmed at postmortem examination; another 4 patients had a clinical picture which seemed compatible with a non-fatal VBI. The variable clinical spectrum of brain stem infarction from basilar artery occlusion was well defined. This was primarily a postmortem study, and an overall perspective of the various temporal profiles was not reported. However, their detailed clinical case descriptions were reviewed by us, and the course of these patients could be categorized in the 18 fatalities as progressive in 12 (67%) and remitting-relapsing in 6 (33%). Of the 4 non-fatal cases, 2 were progressive, 1 was static, and 1 improved from the onset.

Millikan and Siekert in 1955 emphasized the importance of TIA in the vertebrobasilar system. They also reported 28 fatal cases of brain stem infarction from basilar artery occlusion with TIA occurring in 71%, principally in the preceding 10 months. Many patients had progressive development of symptoms with 22 dying within the first week and 12 within the first 48 hours.

In 1961, McDowell and associates reported a comparison study of patients with CSI and VBI. In 32 untreated patients with VBI the mortality was higher after 1 month (25%) and later on in 1 year (50%) in comparison to the results in patients with CSI. Williams and Wilson reviewed their records of patients with basilar occlusion and brain stem infarction syndromes, but no comments were made about the temporal profile.

Fields and co-workers reported the variable status of 8 patients with angiographically proven basilar artery occlusion emphasizing the importance of good collateral circulation, but no analysis of the actual progression of symptoms was provided. A series of 22 consecutive patients with angiographically proven vertebrobasilar occlusion was reported by Archer and Horenstein. In this selected population, the temporal profile can be summarized as follows: progressive course, 12 (54%); remission relapse, 1 (5%); unchanged, 7 (32%); and improved, 2 (9%). A 23% mortality was noted during the first week of illness. In another angiographic study, Caplan and Rosenbaum emphasized the variability in outcome in relationship...
to multiple characteristics of the vascular supply. In 6 patients (60%) the symptoms were progressive, a remitting-relapsing course was noted in 2 patients (20%), and a static course was found in 2 patients (20%). Three deaths occurred (30%). Although a high mortality is apparent in most studies, the possibility of a benign course has also been emphasized.11

The largest series of patients with brain stem infarcts (141 patients) was reported from Helsinki.12 The initial mortality of 7 (4.9%) suggests that this may have been a highly selective group with the most severely ill patients staying in their local hospital. No analysis was reported of the temporal profile of any of these patients.

Thus, in reviewing the various studies of acute VBI reported to date, the major series have either been autopsy or angiographic studies with little emphasis on the actual clinical course. No specific study has been primarily directed at a definition of the natural history or temporal profile of these patients. The need to understand prognosis in the individual patient presenting with acute symptoms of VBI is obvious. Such information has important bearing in judging effectiveness of the results of various therapeutic modalities. For these reasons, we decided to review our patients further.

Methods

Methodology was identical to that previously outlined in the CSI group.7 The charts were reviewed of every patient admitted to the neurology cerebrovascular service during a 3-year period who sustained a cerebral infarct within the immediately preceding 36 hours. Patients excluded from this study were those with any form of intracranial hemorrhage, acute TIA not producing cerebral infarction, and various inflammatory and collagen vasculitides.

Each patient's historical, physical, laboratory data, and neurologic investigative studies were reviewed. Emphasis was placed on localization of the infarct and the hospital course with changes in physical findings.18 In reference to patients receiving anticoagulants, any patient receiving a dose or more of heparin or sodium warfarin (Coumadin) was included as having received such therapy even though most patients were not taking either drug on a long-term basis, and many who received it for an acute episode took it for only a few doses.

Results

Records of 219 patients were reviewed. In the paper on CSI, 220 were reviewed: 179 with CSI, 38 with VBI, and 3 with an indeterminately localized infarction. Upon detailed study of records of the original patients with VBI, we found that 1 patient actually sustained a cerebellar hemisphere hemorrhagic infarction and therefore was excluded from the current reported data. The 37 patients (17%) clinically believed to have the locus of their cerebral ischemia in the brain supplied by the vertebrobasilar system form the group analyzed in this paper.

Table 1 outlines the historical and cardiovascular data of the VBI group. Age and sex distribution are essentially the same as noted in the CSI group. Hypertension was noted with greater frequency (51%) than with CSI (37%). Cardiac lesions were much less conspicuous, particularly those with embolic potential.

The various types of cerebrovascular events, which preceded the admission under study, are outlined in table 2. Of 37 patients, 12 had at least 1 preceding TIA, and in all but 1 it was localized to the brain stem. None of these patients received anticoagulant or antiplatelet treatment before the TIA. Five patients had a cerebral infarction, 3 in the brain supplied by the carotid system, and 2 in the brain supplied by the vertebrobasilar system. The onset of the neurologic deficit was precipitous in 30 (81%) but was insidious and slowly progressive in 7 (19%).

The patients were placed in clinical categories according to the evolution of the neurologic deficit during the first week of illness (table 3). Four distinct temporal profiles again emerged: stable or essentially unchanged, improved deficit, progressive worsening, and remission relapse.

No significant change in the neurologic deficit was noted during the first 7 days of the illness in 4 patients (11%). These deficits were variable in degree, ranging from a mild ataxia to bilateral loss of motor and sensory function with no evidence of loss of conscious awareness.

A course characterized by continued improvement without any neurologic exacerbation was noted in 13 of the 37 patients (35%). However, only 3 of these 13 patients had a neurologically normal status at the end of the first week.

A progressive deterioration in neurologic function was noted in a larger group, 16 of 37 patients (43%),

<table>
<thead>
<tr>
<th>Findings</th>
<th>Number</th>
<th>Percent</th>
<th>Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>19</td>
<td>51</td>
<td>67</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>4</td>
<td>11</td>
<td>41</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>1</td>
<td>3</td>
<td>19</td>
</tr>
<tr>
<td>Recent myocardal infarction</td>
<td>1</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3</td>
<td>8</td>
<td>—</td>
</tr>
</tbody>
</table>

Table 1. Acute Vertebrobasilar System Infarction in 37 Consecutive Patients. Historical and Cardiovascular Background.
TABLE 2  Prior Cerebrovascular Events in Acute VBI Site of Prior CVA

<table>
<thead>
<tr>
<th>Type of prior cerebrovascular accident (CVA)</th>
<th>Vertebobasilar</th>
<th>Carotid</th>
<th>Total VBI</th>
<th>Total CSI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>Percent</td>
<td>Number</td>
<td>Percent</td>
<td>Number</td>
</tr>
<tr>
<td>TIA</td>
<td>11</td>
<td>30</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Completed infarction</td>
<td>2</td>
<td>5</td>
<td>3</td>
<td>8</td>
</tr>
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TABLE 3  Characteristics of Clinical Course During First Week of Illness. Acute VBI

<table>
<thead>
<tr>
<th>Clinical course</th>
<th>Alive</th>
<th>Dead</th>
<th>Total VBI</th>
<th>Total CSI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>Percent</td>
<td>Number</td>
<td>Percent</td>
<td>Number</td>
</tr>
<tr>
<td>Deficit</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improved</td>
<td>13</td>
<td>—</td>
<td>13</td>
<td>35</td>
</tr>
<tr>
<td>Progressive</td>
<td>8</td>
<td>8</td>
<td>16</td>
<td>43</td>
</tr>
<tr>
<td>Unchanged</td>
<td>4</td>
<td>—</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>Remission relapse</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
<td>—</td>
<td>27</td>
<td>—</td>
</tr>
</tbody>
</table>

During the same time period, mortality in this subcategory was high since half of the patients died — 2 patients per day on each of the first 4 days of the illness. The maximal degree of deficit of those who lived was reached in 48 hours in 6 of the 8 survivors. The remaining 2 patients reached their worst degree of dysfunction on days 3 and 4 respectively.

Four patients (11%) had a course characterized by at least 1 definite remission of the focal neurologic deficit followed within a few hours to a few days by a further exacerbation of the neurologic deficit. In each of these 4 patients, remission occurred in the first 24 hours. Relapse occurred on the first day in 2 and on days 2 and 3 in the other 2 patients. In 2 of these 4 patients, relapse proved fatal.

Loss of consciousness occurred during the first week of illness in 13 patients. Six were in coma at the onset of the illness, and 4 of these 6 died within the first week. One remained in a vegetative state and died 13 months later. Only 1 patient in this group showed even a modest improvement in function. Seven patients initially alert after the VBI became comatose during the first week, all within 4 days. A fatal outcome occurred in all 7 of these patients. Five died within the first week, another during the second week, and the last 2.5 months after the onset of the illness.

Symptoms and findings compatible with a clinical diagnosis of lateral medullary syndrome were found in 4 of the 37 patients. Two had an excellent recovery. One continued to have swallowing difficulty but otherwise had no neurologic symptoms at the end of the first week. The 1 patient who died had initially shown an improvement until the third day when extension of the infarct proved fatal. At postmortem, thrombosis of the left posterior inferior cerebellar artery and vertebral artery was demonstrated with consequent infarction of the lateral medulla, cerebellum, and brain stem. Although a more benign course in the patient with lateral medullary syndrome has been reported previously, in some patients the syndrome may progress to a fatal outcome.

Five of the 37 patients had clinical symptoms of cerebellar infarction, that is, progressive ataxia, gaze palsies, vomiting, and changes in level of consciousness. One of these initially had a lateral medullary infarct as noted previously. None was treated surgically. Four of these 5 patients died during the acute stages. Postmortem examination confirmed the diagnosis in both patients in whom it was performed. Gradual improvement was noted in only 1 patient treated conservatively.

Anticoagulants were given to 18 of the 37 patients (49%) at some time during the acute stages of their infarction (table 4). No randomization of selection for these drugs was carried out. When patients with an unstable course characterized by either a progressive increase in neurologic deficit or an early remission and subsequent relapse are considered, 12 patients received anticoagulants and 4 of them died. No anticoagulants were given to 8 others with a progressive course, and 6 died including all 4 who were comatose on admission. The question of effectiveness of anticoagulants in preventing late progression or relapse in those patients whose course was characterized by continued improvement without progression or relapse, could not be evaluated as equal numbers during the same time period. Mortality in this subcategory was high since half of the patients died — 2 patients per day on each of the first 4 days of the illness. The maximal degree of deficit of those who lived was reached in 48 hours in 6 of the 8 survivors. The remaining 2 patients reached their worst degree of dysfunction on days 3 and 4 respectively.

Anticoagulant therapy

<table>
<thead>
<tr>
<th>Temporal profile of deficit</th>
<th>Anticoagulant therapy</th>
<th>No anticoagulant therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total patients</td>
<td>Dead</td>
</tr>
<tr>
<td>Unchanged</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Improved</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Progressive</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Remission relapse</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

*2 comatose at onset.
received anticoagulants or no therapy. The numbers are not large enough in any of these groups to allow a meaningful statistical comparison as to the effectiveness of anticoagulant therapy in unstable, acute vertebrobasilar system progressive infarction. A universally beneficial effect was not observed.

None of the 12 patients with TIA reported in this paper had been given anticoagulant therapy before the acute VBI. Thus, no comment can be made about specific therapy in this important group.17

Autopsies were performed in 5 of the 10 patients whose course was acutely fatal. Vertebrobasilar system non-hemorrhagic infarction was found in each one. As previously mentioned, 2 had predominant unilateral cerebellar infarction with associated medullary or pontine infarcts. Three had basilar artery infarcts with bilateral cerebellar infarctions in 2. Three of the 5 autopsied patients had evidence of preceding cerebral infarcts, 2 with bilateral occipital lobe lesion pointing to preceding VBI, and 1 with an infarct of the basal ganglia.

Discussion

Interesting data are noted in looking at the temporal profile of patients with VBI in comparison to those with CSI. Patients with VBI have a higher incidence of hypertension than patients with CSI (51% vs 37%). In contrast, possible cardiac embolic sources were much less common in VBI (17%) vs CSI (40%).

Of the patients with VBI, 11 of 37 (30%) had had a prior TIA in the vertebrobasilar system. The TIA occurred no more than 3 months before the VBI in 9 of these 11 patients. Thus, although some authors14 have suggested that vertebrobasilar TIA may be a relatively benign lesion, such was not the case in this study, and our findings agree with another large study recently reported.12 Furthermore, a previous survey from Rochester, Minnesota, demonstrated no significant difference in the probability of occurrence of stroke after a TIA in either the carotid or vertebrobasilar system.21 However, a larger percentage of strokes occurred during the first year among patients with vertebrobasilar TIA. None of the patients with vertebrobasilar TIA in this present study had received anticoagulants or antiplatelet therapy before their VBI.

An unstable course characterized by either a progressing or a remitting-relapsing temporal profile was twice as common in VBI (54%) as compared to 26% in CSI. While it was distinctly unusual for progression of neurologic deficit to continue beyond 48 hours in patients with CSI, 16% of patients with VBI continued to experience new symptoms more than 48 hours after the onset of their illness, and their period of instability may last as long as 96 hours.

The presence of a significant decline in the level of consciousness was an ominous sign with a 92% mortality (12 of 13 patients) in comparison to the CSI series where 41% of such patients died.

The mortality rate for acute VBI was 27.5% (table 5), which was 2.5 times greater than that seen with CSI (10.6%). Follow up data were available for 16 of the 27 patients who survived the first week of illness. Four more died without any recovery from the initial severe VBI — 2 in another 2 weeks, 1 in 2.5 months, and 1, the last, in 13 months. Fatalities occurred in 3 more patients during the next 14 months — 1 had a severe CSI, another had cardiac arrest, and in the third the cause of death was not available. Three others had a non-fatal cerebrovascular accident. In 2 this was in the carotid system — 1 had a TIA in 3 months and 1 a completed stroke 2 weeks after the VBI. A third patient had another VBI 2 weeks after the first episode. Only 6 of 16 of the initial survivors in whom follow up information was available were reported to be alive and without further vascular problems over the next year. No follow up study was available on 11 patients.

No clinical subset of signs and symptoms emerges that will ensure the patient of a predictably benign outcome. Even in patients with a lateral medullary syndrome, late progression was noted. The clinician must, therefore, remain alert for such worsening in all patients with VBI for at least 96 hours. Untreated acute cerebellar infarction emerged as a syndrome with a particularly unfavorable prognosis, and alteration in the level of consciousness was found to be an even more ominous prognostic sign with death occurring in 92% of such patients.

Although a study of this type provides the clinician with certain factors to judge the natural history and efficacy of various forms of treatment for VBI, conclusions as to appropriate therapeutic intervention are few. However, based on our observations, a reduction in morbidity and mortality due to VBI might be attained by the following: aggressive and early treatment of hypertension, which was noted in 51% of our patients; recognition and treatment of TIA, which was present in 30% of our entire series and in 60% of patients with fatal VBI; appropriate pharmacologic agents, which might favorably alter the progressive clinical course seen in 43% of our patients and prevent the late relapse of symptoms seen in 11%. These should be considered for use during the first 96 hours of acute VBI, and in those patients with a progressive course secondary to acute cerebellar infarct, aggressive surgical intervention may be indicated.

### Table 5: Clinical Status on Follow Up Over 14-Month Period After Acute VBI

<table>
<thead>
<tr>
<th>Clinical status</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death in first week</td>
<td>10</td>
<td>27.5</td>
</tr>
<tr>
<td>Death secondary to original VBI but occurring after first week</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>Death secondary to new vascular accident</td>
<td>3*</td>
<td>8</td>
</tr>
<tr>
<td>Subsequent non-fatal CVA</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Improved, with no new CVA symptoms</td>
<td>6</td>
<td>16</td>
</tr>
<tr>
<td>Lost to follow up</td>
<td>11</td>
<td>30</td>
</tr>
</tbody>
</table>

*Cerebral infarct, 1; myocardial infarct, 1; acute, probable vascular lesion not otherwise defined, 1.
References

Bilateral Nothnagel Syndrome
Clinical and Roentgenological Observations
IRAJ DERAKHSHAN, M.D., MANUCHEHR SABOURI-DEYLAMI, M.D., AND BENJAMIN KAUFMAN, M.D.

SUMMARY The clinical features of a patient with bilateral oculomotor palsy, ataxia, disturbance of memory, and hypokinesia are described. Pneumography and CT scanning showed dilatation of the posterior portion of the third ventricle, indicating involvement of the postero-medial thalamic structures. The relation of this finding to the patient's amnesia and hypokinesia is briefly discussed. It is concluded that the patient suffered an infarction within the region served by penetrating branches which arise from the cephalad end of the basilar artery, probably including the mesencephalic artery.

ACUTE BILATERAL THIRD NERVE palsy of midbrain origin is rare. This report concerns the clinical features of a patient who had sudden development of bilateral ophthalmoplegia due to bilateral third nerve paralysis, ataxia, hypokinesia, and memory disturbance. The patient was studied with computerized tomography (CT), pneumoencephalography, and angiography.

The patient was a 50-year-old farmer, previously in good health. Following the acute onset of vertigo and vomiting (lasting 1 to 2 hours) he became unresponsive and remained so for about 48 hours. Upon regaining consciousness, he was unable to open his eyes or to keep his balance while walking. Vomiting and vertigo did not recur. There was no history of fever, trauma or headache. He was admitted to Dariush-Kabir Hospital (Tehran, Iran) 4 months after the episode. According to family members, he had lost control of urination 3 weeks prior to admission. Otherwise, there had been no change in his condition.

On repeated examinations he was alert and oriented to person and place but not to the date. He knew what season it was but could not remember or retain any new information such as the date or the name of the
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