Temporal Profile of Vertebrobasilar Territory Infarction
Prognostic Implications

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SUMMARY To determine the type and prognostic significance of the various temporal profiles of vertebrobasilar territory infarction, 39 consecutive patients were studied.

The following temporal profiles were identified: 1) coma from onset, 5 patients; 2) sudden onset followed by stabilization, 12 patients; 3) gradual onset reaching stabilization within 24 hours, 7 patients; 4) gradual onset with progression beyond 24 hours, 2 patients, and; 5) delayed worsening after stabilization, 13 patients. Patients in Group 1 and those with unstable courses, Groups 4 and 5, had poor outcomes with mortality of 100 and 27 percent, respectively. Mortality for Groups 2 and 3 was 5 percent. Overall, hospital mortality was 25.6 percent.

Demographic data, risk factors, presenting symptoms and type of neurologic deficit, other than coma, had no correlation with mortality, degree of disability and long term survival. At follow up of 6 to 52 months, median 24, only 7 percent of the survivors had recurrent cerebrovascular events; 2 patients (7%) died due to nonvascular causes and 72 percent of patients re-examined (20 of 28) were either neurologically normal or had only minimal deficits.

DESPITE EXTENSIVE LITERATURE on the clinical and pathological characteristics of vertebrobasilar infarction (VBI),1,2 the prognostic significance of the various temporal profiles of the neurological deficits remains unclear. As is the case in patients with carotid artery territory infarction (CTI), patients with VBI may present with a fixed, stable neurologic deficit from onset or with an unstable deficit that is either progressive or has remissions and exacerbations.1,3,4 To date, however, there is only one study dealing specifically with the temporal profile of VBI.3 In order to determine the prognostic significance of various temporal profiles of VBI the present investigation was undertaken.

Materials and Methods

The hospital records of all patients diagnosed as having suffered from VBI, hospitalized at St. Paul Ramsey Medical Center from January, 1975, through December, 1978, were reviewed. All patients were personally seen by one or more of the authors. VBI was defined as neurologic deficit believed to be caused by dysfunction in the brainstem, cerebellum, and/or occipital lobes of sudden, gradual, or stepwise onset lasting 24 hours or more. Excluded from the study were patients in whom deficits resolved in less than 24 hours, patients with subjective symptoms and no objective findings, patients with nystagmus as the only finding, and patients in whom VBI was thought to have been a complication of trauma, cerebral angiography, or a result of prolonged systemic hypotension. Patients who presented with "pure motor hemiplegia" were also excluded because of the difficulty in clinically establishing the location of the lesion in the internal capsule,5 the pons,6 or elsewhere.7,8,9,10,11 Diagnosis was established by history and examination and confirmed by laboratory investigations (CSF examination, EEG, CT scan); 7 patients had cerebral angiography, one patient had surgical decompression of the posterior fossa. In 5, the diagnosis was confirmed at autopsy.

The following information was obtained from the records for analysis:
1) demographic data and risk factors;
2) mode of onset, presenting symptoms and time elapsed between onset and examination or hospitalization;
3) initial neurological findings, severity of neurological deficit and clinical localization of anatomic site of lesion;
4) clinical course of neurologic deficits and outcome at time of hospital discharge;
5) treatment and its possible relationship to course and outcome;
6) neurologic deficit at subsequent follow up.

Neurologic deficit was defined as mild in the alert patient whose cranial nerve, cerebellar, and/or sensorimotor impairment did not interfere with independence in ambulation and activities of daily living (ADLs). Patients with moderate neurologic deficits required assistance in ambulation and ADLs; alteration in level of consciousness (LOC), if present, was slight (patient arousable with verbal or non-painful stimulus). Neurologic deficits were considered severe when paralysis of cranial nerves, severe ataxia, or plegia made ADLs impossible and/or there was severe...
depression in LOC (painful stimulus necessary to arouse patient) or coma.

The temporal profile was categorized as stable when the neurologic deficit became maximal within 24 hours of onset, remaining fixed or improving through the hospitalization. An unstable course was characterized by deterioration in the severity and/or distribution of deficits extending beyond 24 hours or beginning after a period of stabilization of 24 hours or more. During hospitalization, the temporal profile of the neurologic deficits was documented by serial examinations at intervals of no more than 24 hours.

Follow up examinations were performed by one of the authors or other neurologists in all but 3 patients; for the latter only telephone contact was possible.

Results

Thirty-nine patients met the criteria for VBI, ages ranging from 40 to 95 years, including 27 males (mean age 66 years) and 12 females (mean age 70 years). Risk factors were identified in 34 patients (table 1). In 14 patients, 2 or more risk factors were identified. In 12 patients a cardiac source of embolus was present. Three patients were found comatose and details of the onset of their illness were unknown. Of the remaining 36, 27 had sudden and 9 had either gradual or stepwise onset of symptoms. Table 2 shows the symptoms at onset in order of frequency. Seven patients had only one symptom; 5 were in coma and two complained of ataxia. The most common symptom was weakness, followed by ataxia and vertigo.

Thirty patients were examined within 24 hours of onset of symptoms, 6 within 4 days and 3 during the second week of illness. Neurological findings on first examination are shown in table 3. Of the 17 patients with an altered level of consciousness, 5 were in coma from onset and 3 of them had decerebrate posturing. Extraocular movement disorders included internuclear ophthalmoplegia, skew deviation, and gaze palsy as well as isolated sixth and third nerve palsies.

Localization of the VBI was clinical; it was confirmed by surgery in one patient and at autopsy in 5. CT scan and cerebral angiography provided additional diagnostic support by confirming cerebellar infarction (4 patients) and basilar artery occlusion (3 patients), and by excluding hemorrhage.

The neurologic deficit was mild in 14, moderate in 13, and severe in 12 patients at first examination. The time profile and its relationship to the degree of deficit at first examination and at time of hospital discharge are shown in table 4.

Seventeen patients reached the peak of the neurologic deficit at onset of symptoms. Five were in coma at onset and all died. The other 12 remained stable or improved; of these, one patient died due to aspiration pneumonia, and another had a severe deficit and remained unchanged. Another 7 patients reached maximal deficit within 24 hours and then remained stable or improved throughout hospitalization. Two patients had gradual onset of neurologic
deficits that progressed for more than 24 hours. One described progressive ataxia over 7 days before hospitalization; the other progressed for 48 hours, then had a fluctuating course, became septic and expired on the seventh hospital day.

The remaining 13 patients developed progressive neurologic impairment after the original deficit had been stable for 24 hours. Eight progressed on day 2 (2 died), 2 on day 3, and one each on days 4, 6, and 7 (1 died). Table 5 shows the relationship of the clinical localization of the infarction with the clinical profile and degree of neurologic deficit.

Mortality for the whole group was 25.6 percent (10 patients). However, for the 34 patients who were not in coma from onset, mortality was only 14.7 percent (5 patients). Of the 29 surviving patients, 19 (65.5%) were either neurologically normal or had only mild deficits, 9 (31%) had moderate and one had a severe deficit at the time of hospital discharge.

Treatment consisted of supportive measures with parenteral adjustment of fluids and electrolytes in all patients. Thirty-one patients received additional treatment during the acute phase of illness. Twenty-eight received continuous intravenous heparin; in 7, the treatment was started more than 24 hours after onset of symptoms or progression. Seven patients appeared to extend their neurologic deficits while being treated but at the time of discharge 5 of the 7 showed an improvement in their deficit from that recorded on admission. Among the heparin treated patients, 6 died (one due to aspiration pneumonia); 8 survived with moderate and 9 with mild deficits and 5 (one of whom had a severe deficit at onset) were essentially normal at hospital discharge (table 4). Eleven patients who were not heparinized fit one of 2 patterns. At the time of admission they had mild deficits of at least 3 days' duration or they presented in coma with flexor or extensor responses.

### Table 4. Time Profile and Outcome of Vertebrobasilar Infarction (35 patients)

<table>
<thead>
<tr>
<th>Time Profile</th>
<th>Deficit at Onset</th>
<th>Deficit at Final Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Severe</td>
<td>Normal</td>
</tr>
<tr>
<td>Coma at onset</td>
<td>5 pts</td>
<td>0</td>
</tr>
<tr>
<td>Stable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At onset</td>
<td>Mild</td>
<td>3 pts</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>3 pts</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>2 pts</td>
</tr>
<tr>
<td>By 24 Hours</td>
<td>Mild</td>
<td>2 pts</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>3 pts</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>2 pts</td>
</tr>
<tr>
<td>Unstable</td>
<td>Mild</td>
<td>5 pts</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>7 pts</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>3 pts</td>
</tr>
</tbody>
</table>

h = number of patients treated with continuous intravenous heparin.

### Table 5. Relationship of the Location of VBI to Temporal Profile and Degree of Neurologic Deficit at Onset

<table>
<thead>
<tr>
<th>Temporal profile</th>
<th>Deficit at onset</th>
<th>Number of pts.</th>
<th>Location of VBI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coma from onset</td>
<td>Severe</td>
<td>5*</td>
<td>3 pons</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 pons, midbrain</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 pons, midbrain, occipital</td>
</tr>
<tr>
<td>Stable course</td>
<td>Mild</td>
<td>7</td>
<td>2 medulla, pons</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4 pons</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>3</td>
<td>1 medulla*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 pons</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>2</td>
<td>1 pons, midbrain</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 midbrain, cerebellum</td>
</tr>
<tr>
<td>By 24 hours</td>
<td>Mild</td>
<td>2</td>
<td>1 pons</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 midbrain</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>3</td>
<td>2 medulla, pons, cerebellum</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 midbrain</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>2</td>
<td>1 pons</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 pons, occipital</td>
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<td>Unstable course</td>
<td>Mild</td>
<td>5</td>
<td>1 medulla</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 pons</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 pons, cerebellum*</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>7</td>
<td>1 medulla, pons, cerebellum*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 pons</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 midbrain, occipital</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>3</td>
<td>2 pons*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 cerebellum</td>
</tr>
</tbody>
</table>

*Deaths.
Follow up was possible in 28 of the 29 survivors. Median follow up time was 22 months with a range from 6 to 52 months. Two patients (7%) died of non-vascular causes at 14 and 30 months after their VBI. Two patients (7%) suffered CTI at 2 and 8 months after their VBI, and one with a previous history of VB TIAs had a questionable TIA during follow up. There was further improvement after discharge from hospital in 11 patients.

Discussion

The different syndromes occurring as a consequence of VBI have been well defined[13-18] as have their correlation with the vascular anatomy of the vertebro-basilar arterial system.[19, 20] Instability and fluctuation in the neurologic deficits have been recognized since Kubik and Adams' classic paper on "Thrombosis of the Basilar Artery,"[12] and other authors have stressed the variability in the clinical course of this condition.[21-25] The same has been reported in patients with lateral medullary syndrome.[26-28]

In the present study 17 patients reached their maximum neurologic deficit at onset and 7 did so within 24 hours. Of these 24 patients, 5 were in coma at onset and died while the others remained stable and improved. Their prognosis was excellent with only one death (5%) due to aspiration pneumonia in a patient with a lateral medullary syndrome whose deficit was improving.

The remaining 15 patients had an unstable course. One progressed over 7 days outside the hospital, while another had a documented 48 hours of progression followed by late worsening. The other 13 had an acute onset and were stable for at least 24 hours before worsening. Exacerbation or worsening occurred up to 7 days after the initial event. Four of these 15 patients died in hospital (26.7%).

It has been said that VBI cannot be considered stable until at least 96 hours have elapsed from onset of symptoms.[29] Our data show that instability and late exacerbations can be expected for as long as 7 days after onset of symptoms.

In Jones' et al. study, 54 percent of the patients, including some comatose on admission, suffered an unstable course characterized by a progressive or remitting relapsing profile.[30] If our patients who were in coma on admission and subsequently died are added to the group of 15 unstable patients, then a comparable 51 percent of our patients had a progressive temporal VBI profile.

The temporal profile of the neurologic deficit and the mortality of VBI are expressions of the availability of collateral circulation. Patients in whom the infarction is so extensive as to cause coma from onset have a dismal prognosis; however, if the infarcted area is smaller and collateral circulation is established early (within 24 hours) and the needs remain stable, an excellent prognosis can be expected. There is another group of patients in whom collateral circulation fails after a period of apparent stability and in them the prognosis is much more serious.

Risk factors, presence of a source for emboli, and symptoms at onset other than coma, show no correlation with the severity of the neurologic deficit or with the time profile of the illness. Other than the negative effect of coma on survival, no other clinical parameters could be identified as having prognostic value. Severity of neurological deficit in the absence of coma did not serve as an absolute prognostic finding. Three out of 4 "locked-in syndromes" survived and one even returned to a normal level of functioning. However, 6 out of 9 patients with clinical evidence of cerebellar infarction had a progressive or fluctuating course and the majority had a moderate to severe neurologic deficit at the time of examination; 3 died and one was saved by emergency posterior fossa decompression.

Since this study was not prospective and most of our patients received treatment with heparin on a non-randomized basis, no valid conclusions can be drawn from results of this treatment modality. However, knowledge of the incidence of an unstable course in VBI (38.5%) may have important implications in patient care. Mild vertebrobasilar deficits may herald a more devastating brainstem event and immediate hospitalization may be indicated even if the patient's course has been stable for 24 hours. Close monitoring of the patient's neurologic status at the time of admission and for several subsequent days may reduce the risk of complications. Aspiration pneumonia is a particular problem, especially if the patient develops increasing somnolence or bulbar signs; oral feeding should be withheld for several days and, when allowed, extreme care should be exercised. Monitoring respiratory patterns is also advisable in the event that need for assistance should arise.

Decompressive surgery for large cerebellar infarctions has been reported.[31] Since cerebellar infarctions have a tendency to act as a posterior fossa mass, this type of therapy would seem recommendable when cerebellar involvement is associated with fluctuation or progression of the neurologic deficit. In Jones' et al. study 4 of 5 patients with clinical symptoms of acute cerebellar infarction died.[32] None had had surgical intervention. One of our patients had a successful posterior fossa decompression. In another, surgery was delayed and the patient died of a large cerebellar infarction with upward transtentorial herniation and brainstem compression documented at autopsy.

Prognosis for survival after VBI is variable. Clinical pathological studies suggest that thrombosis of the basilar artery usually results in fatal brainstem and/or cerebellar infarctions. However, Archer described 5 patients with angiographically proven basilar artery occlusions who survived the event[33]; Fields et al.[34] and Kaplan[27] have also reported patients with basilar artery occlusion who had minimal residua or no neurologic deficit at all. Of our 3 patients with angiographically demonstrated basilar artery occlusions, 2 died and one had an excellent recovery. Basilar artery thrombosis was found at autopsy in yet another patient.

Overall, in our population, information obtained
over a median 22-month follow up would seem to indicate a good prognosis for patients surviving VBI. Life table analysis of follow up data at 42 months demonstrates 16 percent mortality resulting from causes unrelated to vascular disease. The same type of analysis shows identical figures for the recurrence of cerebrovascular disease; 2 patients had a cerebral infarction at 2 and 8 months, respectively (fig.). This is comparable with previously reported data.

Conclusions

VBI presents with various temporal profiles. Patients who are in coma from onset have a dismal prognosis. In other patients, onset is either acute or gradually progressive with stabilization of deficits in 24 hours; in these patients, prognosis is excellent and it can be assumed that they have adequate collateral circulation that establishes itself early. Finally, there is a group of patients who do not stabilize in 24 hours. Either gradual progression continues or, after an apparent period of stability of 24 to 48 hours, secondary deterioration occurs, presumably due to failure of collateral circulation. For these patients the prognosis is serious. Patients with progressive cerebellar infarction may benefit from early posterior fossa decompression.

There is a need for a randomized study of treatment for patients suffering from VBI to establish the role of heparin, corticosteroids and other measures commonly used in the treatment of this condition.

References

Effect of Unilateral Common Carotid Artery Occlusion on Levels of Prostaglandins D₂, F₂α and 6-Keto-Prostaglandin F₁α in Gerbil Brain

ROBERT J. GAUDET, PH.D. AND LAWRENCE LEVINE, Sc.D.

SUMMARY The concentrations of the arachidonic acid metabolites, PGD₂, PGF₂α, and 6-keto-PGF₁α, were measured in the cerebral hemispheres of gerbils subjected to unilateral carotid occlusion. Approximately 37 percent of the animals with occlusion had symptoms of cerebral ischemia. In those animals PGD₂ and PGF₂α levels were elevated in both hemispheres. The levels of 6-keto-PGF₁α increased only slightly. There was no change of prostaglandin levels in asymptomatic animals. Indomethacin inhibited the increase in the levels of these arachidonic acid metabolites but did not alter brain swelling as judged by a decrease in specific gravity after 6 hours occlusion.

CEREBRAL ISCHEMIA is known to cause rapid changes in brain chemistry and function. When circulatory arrest occurs, brain energy reserves quickly become depleted, neuronal membranes depolarize, extracellular fluid shifts into the intracellular compartment and neuroelectric activity ceases. Ischemia also stimulates the activity of cellular lipases, whose actions cause deacylation of brain phospholipids and release of free fatty acids. 1,3 Arachidonic acid (A.A.) is one of the predominant fatty acids released in brain after ischemia. 4-6 A.A. is the primary substrate for the synthesis of prostaglandins, thromboxanes and prostacyclin. The availability of non-esterified A.A. is generally thought to be the rate limiting factor in the production of most prostaglandins. 8 Only small changes in the levels of prostaglandins in brain occur after interruption of the cerebral circulation in gerbils following bilateral common carotid occlusion. 7,8 Most likely, depletion of tissue oxygen in severely ischemic brain limits A.A. conversion to PGD₂

endoperoxides by cyclooxygenase, a step requiring the addition of molecular oxygen. 9

Previously we reported that reperfusion of the brain, after episodes of brief ischemia, resulted in a large accumulation of A.A. metabolites in brain tissue. 1 Presumably, re-establishment of blood flow restores tissue oxygen and permits the conversion of A.A. released during ischemia. We suggested that "non-total" ischemia can promote A.A. metabolism if residual flow provides enough O₂ for enzymatic conversion to endoperoxides. Furthermore, A.A. could diffuse from areas of focal ischemia to non-ischemic areas and be metabolized. These considerations could explain the elevated levels of PGF₂α and PGE₂ found in spinal fluid of patients with stroke. 9,10

The effect of unilateral common carotid artery (CCA) occlusion on the levels of PGD₂, PGF₂α, and the stable prostacyclin product, 6-keto-PGF₁α, in the cerebral hemispheres of Mongolian gerbils was studied. PGD₂ and PGF₂α are major A.A. metabolites produced by brain tissue; 11-15 and prostacyclin is the predominant A.A. metabolite produced by vascular tissue, microvessels, and endothelial cells. 16-18 Unilateral common carotid artery (CCA) occlusion

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