Correlation of Cardiac Arrhythmias With Brainstem Compression in Patients With Intracerebral Hemorrhage

Traugott Stober, MD, Semi Sen, MD, Thomas Anstätt, MD, and Ludwig Bette, MD

Neurogenically caused cardiac arrhythmias and their correlation to lesions within the central nervous system were examined prospectively in 54 patients with spontaneous intracerebral hemorrhage. All patients were examined neurologically daily for 3 weeks, with special attention given to signs of brainstem compression resulting from transtentorial herniation. Electrocardiograms were continuously recorded over an average of 5 days. A significant correlation was established between the clinical manifestations of brainstem compression and sinus arrhythmias, multifocal premature ventricular contractions, couplets, and ventricular tachycardias. An explanation for this correlation may be found in the localization of the autonomous cardiovascular centers in the hypothalamus and brainstem. Transtentorial herniation frequently leads to a bilateral lesion of these structures. However, the cardiac arrhythmias are only a partial phenomenon within a complex cardiovascular reaction. (Stroke 1988;19:688-692)

Although disturbances in cardiovascular regulation are a well-recognized complication of intracerebral hemorrhage, there are only a few reports on the incidence of cardiac arrhythmias. This is because most studies were not based on continuous electrocardiographic (ECG) recordings. We report on extensive ECG recording in intracerebral hemorrhage, placing particular emphasis on previous cardiac diseases, neurologic complications, and localization of the hemorrhage.

Subjects and Methods

We included 54 patients (mean age 55.7 ± 12.4 years) with spontaneous intracerebral hemorrhage in our prospective study. Table 1 shows localization of the hemorrhage, neurologic complications, risk factors, and previous cardiac disease. In 90% of the cases, a motor or sensory hemisyndrome was present. Two thirds of the patients were hospitalized on the day of the hemorrhage, one sixth on the subsequent day, and the remainder on the second or third day after the event. We excluded any patients admitted later. The day on which the hemorrhage occurred was defined as Day 0, the subsequent day as Day 1, etc.

The diagnosis was always confirmed by computed tomodraphy. Angiography was performed when the patient's age, localization of the hematoma, and absence of hypertension suggested an angioma or aneurysm as a possible cause of the hemorrhage. Patients with bleeding into an infarction or tumor were excluded. All patients were examined neurologically daily, with special attention being given to the level of consciousness and midbrain symptoms. According to McNealy and Plum, disturbances in ocular motility such as absence of bulbar movements, divergent and/or conjugated and nonconjugated floating eyes, respiratory disturbances in the sense of Cheyne-Stokes respiration, periodic breathing, rhythmic hyperventilation or apnea, flexion and stretch mechanisms as well as a general increase in muscular tonus were assessed as indications for a transtentorial herniation. Although differences in pupil size were recorded, they were not taken as a sign of a midbrain syndrome as such alterations could also have been the result of mere local compression of the third cranial nerve. The examination period extended over 22 days if the patients did not die sooner.

Blood pressure was monitored hourly during the acute phase and at 4-hour intervals in uncomplicated cases during the chronic stage. Hypertension was defined as blood pressure of > 160/95 mm Hg. In the majority of cases, hypertension was treated with clonidine alone or in combination with dihydralazine and/or diuretics. Thirteen patients also received digoxin. All patients were strictly confined to bed and relaxed. For sedation barbiturates were preferred, but in a few cases tranquilizers or neuroleptic drugs were administered. In three cases with known alcohol abuse, chlor thalazol was given. Serum electrolytes were monitored daily.

Over an average of 5 days, continuous ECG recordings in addition to daily twelve-channel standard ECG recordings were performed in all patients. The continuous ECG was recorded using a Reynolds two-channel Medilog recorder (Hertford, England). The bipolar precordial lead CM5 was always used, and selection of the second lead was based on the greatest possible QRS deflection and smallest T amplitude. Special attention was paid to the application of the electrodes; once the skin was degreased they were securely fastened to prevent lifting due to tension or...
movement. Artifact periods of <500 seconds within a 24-hour recording were sought.

The ECG evaluation was performed semiautomatically under visual control using the Reynolds pathfinder system. Subsequent to identification on the oscilloscope, all rhythm disturbances were printed out using a chart speed of 25 mm/sec. Heart rates of >100 beats/min were defined as tachycardia and those of <50 beats/min as bradycardia. Repeated variations in heart rate of >20% of the initial rate, when occurring within 12 seconds, were defined as sinus arrhythmias. Asystole was defined as pauses lasting for >2 seconds. Premature supraventricular contractions (PSVCs) were diagnosed when a premature QRS complex of >90% of the prevailing RR interval with the same QRS configuration was registered. Frequent PSVCs were defined when >100 were recorded per hour. Ventricular arrhythmias were classified according to Lown and Graboys. Bigeminy was assumed when a minimum of four successive normal complexes were each followed by a premature ventricular contraction (PVC). Lown Class I was defined as unifocal PVCs of <30/hr. Three or more successive PVCs with a rate of >100 beats/min were defined as ventricular tachycardia. Torsade-de-pointes-type ventricular tachycardia was diagnosed according to the criteria of Soffer and colleagues. Yates' correction was used for random samples of >20.

Statistical analysis was carried out using spss. Yates' correction was used for random samples of >20. Values are percent.

Results

During long-term ECG registration, various cardiac arrhythmias were detected in all but one patient. The incidence of tachycardia, bradycardia, sinus arrhythmias, single PVCs, and ventricular pairs (couplets) are shown in Table 2. Ventricular bigeminy, atrioventricular dissociation, atrioventricular block, atrial fibrillation, a right and left bundle branch block, and torsade de pointes were also intermittently observed.

Sinus bradycardia, couplets, and ventricular tachycardia were detected more often and sinus tachycardias, sinus arrhythmia, and asystole less often in patients with a history of cardiac disease than in those without such a history (Figure 1). However, the differences were not significant.

Sinus tachycardias, sinus bradycardias, and frequent PSVCs attained a maximum on Day 1. The frequency of these arrhythmias subsequently declined until Day 3 or 4, increasing once again after Day 6 or 7. With one exception, no sinus bradycardia was registered after Day 7. There was a great increase in the number of patients with sinus tachycardias from Day 8 to Day 10. In contrast, multifocal PVCs and couplets decreased in frequency from Day 0 until Day 1 or 2, attaining a maximum on Day 3. The subsequent course was not uniform.

The form and incidence of arrhythmias were independent of blood pressure. There was no uniform relation between the occurrence of ventricular arrhythmias and blood pressure or heart rate. The only exception was an increase in PVCs after a decrease in blood pressure, accompanied by an increase in heart rate, in most patients with signs of brainstem compression. Ventricular arrhythmias were often preceded by PSVCs. An abrupt diminution of arrhythmias, often in conjunction with an increase in heart rate, was noted in some patients. In the majority of cases the arrhythmias occurred in a more continuous manner, and no correlation with blood pressure or heart rate was discernible.

All forms of cardiac arrhythmias excluding bradycardia and low-frequency unifocal PVCs were observed more frequently in patients with ventricular extension. However, this difference was significant only in multifocal PVCs (p<0.05). There was no

<table>
<thead>
<tr>
<th>Localization of hemorrhage</th>
<th>No.</th>
<th>Mor-</th>
<th>Ven-</th>
<th>Tran-</th>
<th>Risk factors</th>
<th>Previous cardiac diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>tality</td>
<td>tricular</td>
<td>tentorial</td>
<td>Hypertension</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Pons and cerebellum</td>
<td>4</td>
<td>50.0</td>
<td>50.0</td>
<td>0.0</td>
<td>25.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Putamen and thalamus</td>
<td>20</td>
<td>45.0</td>
<td>60.0</td>
<td>60.0</td>
<td>60.0</td>
<td>15.0</td>
</tr>
<tr>
<td>Lobar (frontal, parietal, temporal, occipital)</td>
<td>30</td>
<td>26.7</td>
<td>13.3</td>
<td>30.0</td>
<td>46.7</td>
<td>3.3</td>
</tr>
<tr>
<td>Total</td>
<td>54</td>
<td>35.2</td>
<td>33.3</td>
<td>37.0</td>
<td>50.0</td>
<td>7.4</td>
</tr>
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Values are percent. PSVCs, premature supraventricular contractions; PVCs, premature ventricular contractions; VT, ventricular tachycardia (≥3 PVCs with rate of >100 beats/min).
correlation discernible between the localization of the hematoma and cardiac arrhythmias (Tables 1 and 2).

Intermittent or continuous signs of bilateral brainstem compression were present in 21 of 54 cases with trans-tentorial herniation. All forms of arrhythmias except low-frequency unifocal PVCs were more numerous in those patients with this complication (Figure 2). Significant correlations were demonstrable with sinus arrhythmias \((p<0.05)\), frequent PSVCs \((p<0.01)\), multifocal PVCs \((p<0.0001)\), and ventricular tachycardias \((p<0.0001)\). This relation was confirmed in two cases by pathologic examinations in which hemorrhages and infarctions in the mesencephalon, pons, and medulla oblongata were demonstrated.9

Simultaneous with long-term ECG registration, intracranial pressure (ICP) was monitored in one female patient, using an extradural device. Together with a hemisyndrome, distinct signs of brainstem compression were observed. The phases of increasing ICP were initially followed by an increase in PSVCs and PVCs.10 Subsequently, these arrhythmias ceased abruptly despite further elevation in ICP.

An intermittent hypokalemia was observed in the first week in 24.1% of the patients. The mean minimum potassium value was 3.11 ± 0.26 mval/l. An increase in PSVCs and PVCs is to be expected in hypokalemia, especially in cases of bradycardic basic frequencies. The question is to what extent the observed arrhythmias were influenced by these electrolyte disturbances. All forms of cardiac arrhythmias were more frequent in those patients with intermittent hypokalemia, but these differences were significant only for asystole \((p<0.05)\) and PSVCs \((p<0.01)\). A further analysis revealed that this statistical relation was a secondary one, as these cardiac arrhythmias were registered either only on those days when the potassium level was
normal or when the same type of arrhythmia was also present during a normal potassium level phase.

Discussion

In 1902 Cushing delivered the first quantitative description of the cardiovascular reaction, with rising blood pressure and bradycardia accompanied by irregular respiratory as a result of increased ICP. Regional cerebral blood flow measurements elucidated the Cushing response. Progressive ischemia, beginning in the cerebral hemispheres and progressing in a rostrocaudal direction to the pons, medulla oblongata, and spinal cord was observed. This advancing ischemia was closely related to alterations in the cardiovascular parameters. Respiratory arrest, a decrease in heart rate, and a rise in blood pressure were registered the moment ischemia reached the lower pons. Further advance of the ischemic front into the lower medulla oblongata led to an abrupt change from bradycardia to tachycardia.

No clinical data are available concerning the development of cardiac arrhythmias during progressive brainstem compression. There are, however, a few experimental reports using ICP increase. In the majority of cases an increase in ICP of 50–70% over ventricular contractions and ventricular tachycardia degenerative discogenic diseases, peripheral neuropathies, less severe in patients with direct brainstem lesions group in a study of cardiac arrhythmias subsequent to hemorrhage involves some basic methodologic problems. The selection of a suitable control group is difficult. Patients with meningiomas, meningitides, 20 peripheral neuropathies, 21 and psychic stress. 22–24 A comparison with clinically normal subjects does not give a correct standard, either, as the incidence of cardiac disorders is expected to be higher in patients with intracerebral hematomas. These problems can be partly overcome only if long-term ECG registration is carried out. This ensures that each patient is his own control so that alterations observed can be correlated with functional disturbances within the central nervous system.

Patients with previous cardiac disorders were excluded from some studies of neurogenic ECG alterations. 25–28 However, autonomic influences have a greater effect if cardiac lesions are already present. This clinical situation corresponds to that obtained by experimental ligation of the coronary arteries in conjunction with various manipulations of the autonomic nervous system in the production of arrhythmias. 29,30 Patients with previous cardiac disease were therefore included in our study.

Antihypertensive treatment with clonidine and, in a few cases, with dihydralazine, presents a further methodologic problem as both drugs affect the autonomic system. 31,32 A direct relation between arrhythmias and administered antihypertensive agents was, however, not demonstrable. Since uniform antihypertensive treatment was used, a substantial influence is unlikely. The small proportion of bradycardia in our study compared with others in which medication was not mentioned strengthens this supposition.

The administration of barbiturates and tranquilizers remains to be discussed. These substances also have a modulating influence on the autonomic system. 34,35 In our study, barbiturates were administered in small dosages, the barbiturate plasma level being approximately that used in antiepileptic therapy. It is, therefore, debatable whether a reduction in arrhythmias or a significant increase in heart rate could be related to these medications.

Prognostic significance has been attributed to various ECG alterations subsequent to subarachnoid hemorrhage. 22 However, after intracerebral hemorrhage we found a close connection between various forms of cardiac arrhythmias and brainstem lesions due to transtentorial herniation. Hence, their prognostic significance must be regarded as secondary and as another indication of progressive brainstem dysfunction. The complex, mainly hierarchical organization of the cardiovascular regulatory centers from the amygdala to the medulla oblongata and their close connections with hormonal regulatory mechanisms of catecholamines and the renin-angiotensin and vasopressin systems does not allow a topical localization on the basis of arrhythmia type. The relation is further complicated by the often rapid progression of the successive rostrocaudal involvement of the autonomic structures during transtentorial herniation.

Since these cardiac arrhythmias are related to herniation, treatment necessitates a reduction in ICP. The extent to which these arrhythmias need to be treated from a cardiologic point of view remains unclear. In many patients with sufficient cardiac reserve, some
arrhythmias would be without consequences due to their short duration. Hemodynamic deterioration could result in patients with impaired cardiac function or with long-lasting tachycardia. In such cases intervention to lower the sympathetic tone with agents like β-blockers may be desirable. The resultant risk of reduction in blood pressure could lead to reduced cerebral perfusion when ICP is elevated. Parasympathetic activity must also be taken into consideration. Vagally caused arrhythmias, such as bradycardias, asystoles, atrioventricular block, atrioventricular rhythms, atrioventricular dissociation, atrial fibrillation, and sinus arrhythmias, were also recorded in 60–85% of patients with sinus tachycardia and ventricular arrhythmias; these are a contraindication for β-blocker therapy. On a theoretical basis, centrally acting substances, such as clonidine, may be more efficacious in lesions involving the cardiovascular regulatory centers.

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References
27. Smith M, Ray CT: Cardiac arrhythmias, increased intracranial pressure, and the autonomic nervous system. Chest 1972; 61:125–133
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