Review Article

Electrocardiographic Abnormalities After Nontraumatic Subarachnoid Hemorrhage

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Summary: Electrocardiographic (ECG) abnormalities and rhythm disorders are frequently observed in the acute phase after spontaneous subarachnoid hemorrhage (SAH). These abnormalities are benign and transient in most cases; however, in some patients they can take the form of life-threatening arrhythmias such as ventricular flutter/fibrillation and torsade de pointe. Among the ECG abnormalities observed, prolongation of the Q-T interval, especially if associated with hypokalemia, deserves particular attention because it is frequently present in those patients who will develop life-threatening ventricular arrhythmias. In some cases, the ECG abnormalities mimic those observed in the setting of acute myocardial infarction. Elevated creatine phosphokinase-myocardial fraction isoenzyme, suggesting underlying cardiac damage, has also been reported. The pathophysiology of these abnormalities is related to an imbalance of autonomic cardiovascular control. Because some electrical and morphological heart abnormalities are experimentally induced by catecholamine injection, the role of circulating catecholamines has been investigated in depth. Pathologically, the hearts of patients who die after SAH can show a peculiar morphological lesion defined as "myocytolysis." Intramyocardial hemorrhages have also been described. These observations confirm the utility of continuous cardiac monitoring in patients with SAH. Key Words: Electrocardiogram—Abnormalities—Subarachnoid hemorrhage.

With improving microsurgical techniques in the last 2 decades, the operation for intracranial aneurysms can be performed with acceptable mortality and morbidity (1,2). Overall results, though, are still disappointing due to rebleeding, vasospasm, and systemic complications (3,4). In addition, it has been calculated that 15% of the patients with subarachnoid hemorrhage (SAH) die before reaching the hospital (5), and sudden death as well as loss of consciousness are well-known manifestations of SAH. Cardiac rhythm disturbances can be the cause of such features (6). Indeed, electrocardiographic (ECG) abnormalities in the presence of SAH are frequently observed. Although much literature in recent years has been published on this subject, the practical consequences of ECG abnormalities on the acute care of the patient with SAH remain unclear.

ECG ABNORMALITIES

ECG changes after SAH have been observed in 50–90% of the cases (7–15); this difference is mainly attributed to the different methodology used to detect the changes and the time elapsed from the hem-
ECG ABNORMALITIES AFTER NONTRAUMATIC SAH

Orrhage. If patients are followed with serial ECGs, abnormalities occur in 100% of the cases (13,14). The most frequent ECG abnormalities observed are a depressed or elevated S-T segment, Q-T prolongation, T-wave abnormalities, and U waves >0.1 mV (16–22).

The ECG changes are observed primarily in the acute phase (72 h or less) after SAH (14). The duration of these abnormalities varies. The ECG usually returns to normal in a few days (9,14), although changes can persist up to 4–8 weeks after the initial insult (23–25). The same type of ECG abnormality can be observed in the same patient if rebleeding occurs (26–28).

Among the ECG changes observed after SAH, prolongation of the Q-T interval deserves particular attention because it is often present in those patients who will develop life-threatening ventricular arrhythmias (29–37)\(^1\). Prolongation of the Q-T interval is a consequence of altered ventricular repolarization, increasing the susceptibility to ventricular arrhythmias. Q-T prolongation, therefore, may play a critical role in the genesis of arrhythmias, especially when other possible cofactors such as catecholamine overstimulation and hypokalemia are present (29,30). Both factors predominate in the acute period after SAH.

In several cases, the ECG changes can mimic those observed in acute myocardial infarction (13, 38–45). Indeed, a thallium scan performed after a mean of 3 days post-SAHI is abnormal in 32% of the patients, suggesting that abnormal myocardial perfusion and possibly myocardial ischemia occur frequently after SAH (46). These changes, however, are often transient, not necessarily indicative of underlying myocardial damage or ischemia, and are secondary to SAH. Postmortem examination of some of these hearts, in fact, showed pathologically intact myocardial tissue with patency of the coronary arteries (38,40).

**CARDIAC ARRHYTHMIAS**

Cardiac arrhythmias have been reported to occur in 91% of patients followed by Holter monitoring after the onset of SAH (10,29,31), whereas arrhythmias are diagnosed only in 28% of normal individuals without any history of cardiovascular diseases (47). These arrhythmias tend to be transient, occur mainly in the acute phase after SAH, and are no longer present if Holter monitoring is repeated (29).

The arrhythmias observed after SAH can take the form of life-threatening disturbances of the ventricular rhythm such as ventricular tachycardia (32,34, 48), ventricular flutter (32), ventricular fibrillation (35), and torsade de pointe (30,36,37,49–51). Continuous Holter monitoring of patients after SAH has shown that 4% of the patients can have such life-threatening arrhythmias (29). Severe cardiac arrhythmias are more frequent in older patients and within 24 h after SAH (29).

Coexistent hypoxia possibly due to altered ventilation in patients with SAH increases the likelihood of developing arrhythmias (52). A slightly lower potassium level is also frequently found in those patients who develop ventricular arrhythmias compared with those who do not (29). Other factors such as the clinical condition of the patient apparently do not influence the development of arrhythmias. In fact, serious rhythm disorders have been observed in patients who were in good clinical condition as well as in those who were comatose. No association exists between the incidence of arrhythmias and the extent of intracranial hemorrhage evaluated by computed tomography (CT). The type of lesion, arteriovenous malformation or aneurysm, also does not affect the development of rhythm disorders (29).

In the case of life-threatening arrhythmias, prompt recognition of the abnormality and conversion to a normal rhythm in some cases have saved the patient’s life (29,35). In other cases, though, the brain damage due to the consequences of arrhythmia resulted in patient death (29). Therefore, continuous ECG monitoring is suggested after SAH in view of its potential role in alerting to the need for treatment (29).

**MARKERS OF MYOCARDIAL DAMAGE**

Abnormally high levels of creatine phosphokinase–myocardial fraction (CK-MB) are found in 37–80% of patients after SAH (53–56). Elevated levels of CK-MB are associated with higher mortality (53,55) and higher incidence of vasospasm (54). The significance of the CK-MB increase observed after

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SAH is debated (53,57,58). The peak activity of CK-MB has been observed 16 h after the onset of neurological symptoms (53), a time course similar to that reported in patients with myocardial infarction (59). Indeed, up to 71% of the patients with CK-MB activity can have pathological ECG changes suggestive of acute cardiac injury (53). Other authors, however, failed to confirm these findings (58).

Another marker of myocardial injury, abnormal levels of myoglobin, has been reported in 85% of the cases after SAH. Coma and in-hospital deaths seem more likely to occur in those patients with the largest myoglobin elevation (more than three times the normal value) (56). The persistence of elevated myoglobin for a few days after SAH despite the rapid renal clearance of myoglobin suggests progressive cardiac damage (56).

PROGNOSTIC VALUE OF ECG ABNORMALITIES

Certain ECG abnormalities can serve as prognostic indicators after SAH. Pathologic Q waves and raised ST segment are associated with a poor prognosis (60). Other abnormalities such as tachycardia (>100 beats/min), P mitrale, and ST-segment depression >1.0 mm or elevation >2.5 mm are more frequently observed in patients dying within 7 days after the bleeding (61). It should be noted that tachycardia and P-wave abnormalities can be a consequence of left ventricular failure, which can lead to pulmonary edema. Indeed, pulmonary edema is a complication frequently encountered in patients with SAH (4,61).

Q-T prolongation (>450 ms) and signs of left ventricular hypertrophy as determined on resting ECG also seem to be associated with a poor prognosis (62). Mortality has been reported to be 10% in patients with a normal Q-T interval and 43% in those with a prolonged interval (62). Among those patients with ECG signs of ventricular hypertrophy, mortality can be as high as 43%, compared with only 4.5% in patients who do not exhibit such a pattern (62). Individual ECG abnormalities, however, seem not to be related to the amount of cisternal or intraventricular blood on the baseline CT scan or to specific complications such as infarction, rebleeding, or acute hydrocephalus (14).

PATHOGENESIS OF CARDIAC ABNORMALITIES

ECG abnormalities seen after SAH reflect an impairment of the balance normally present between sympathetic and parasympathetic stimuli (63). This results in an alteration of the depolarization/repolarization process and facilitation of ectopic foci activity (31).

There is convincing evidence connecting some of the ECG abnormalities observed after SAH to circulating and local catecholamines. The myocardial lesions observed by electron and light microscopy after SAH are similar to those described after catecholamine-induced injury (64–66) and similar changes have been observed after exogenous administration of catecholamines to normal individuals or in patients with pheochromocytoma (67). A causal role of catecholamines is also suggested by experimental studies in which the ECG changes and the myocardial damage occurring after SAH could be prevented by either C2 cordotomy (68), adrenalectomy (69), or propranolol administration (70–73). In addition, norepinephrine can affect the heart indirectly by producing an acute elevation of blood pressure (74). Thus, the concomitant increase in left ventricular pressure generates left ventricular strain and ischemia of subendocardial tissue (7).

Neil-Dwyer et al. investigated the relationship between plasma catecholamines and normal or abnormal ECG after SAH (75). They observed that in patients with normal ECGs, catecholamine levels were within or marginally above the normal range throughout the study (75). This was in contrast to patients with abnormal ECGs where levels remained above the normal range (75). In addition, the same authors observed that certain types of ECG abnormalities such as short PR intervals, large T waves, long QT intervals, and large U waves were found to be associated with significantly higher levels of urinary catecholamine values (75).

It is suggested that the cellular level increased catecholamines cause cellular hypermetabolism and electrolyte displacements detectable in the mitochondria (76). The ECG changes that follow represent the electrical expression of the intracellular/extracellular ion-balance modifications (76).

Sympathetic overstimulation can be a consequence of hypothalamic dysfunction after SAH. Hall et al. (77) stimulated the posterior hypothalamus in conscious dogs and observed that immediately on stimulation all dogs had a sinus tachycardia that persisted during stimulation. During and immediately after stimulation, other ECG changes occurred in three dogs (77). These included T-wave inversions, subsequent increases in T-wave amplitude, and multifocal, premature ventricular contractions (77). All are abnormalities that have been described after SAH. Other types of arrhythmias including ventricular fibrillation have also been induced by stimulation of the diencephalon in experimental animals (78). Indeed, damage of the hypothalamus is frequently present on pathological examination of patients who die after SAH (28, 75, 79). The hypothalamic lesions consist of small perivascular hemorrhages, perforating vessel distention with small ball hemorrhages, and vessel wall edema involving the endothelial cells with perivascular cuffing of polymorphonucleates, microinfarction, and in a few cases, complete infarction of the hypothalamus (75).

Vagal stimulation has also been shown in dogs to cause changes in the ECG, signs of cardiac decompensation, and myocardial infarction (80). In addition, the myocardial damage observed after SAH in mice can be prevented by the administration of atropine (69). Unlike the sympathetic discharge that seems to be mediated mainly by diencephalic structures, the vagal effect is mediated by telencephalic structures as well (81). Destruction of the telencephalic centers, in fact, attenuates slightly the sympathetic reaction without suppressing it, whereas it abolishes completely the parasympathetic reactions more directly controlled by the telencephalon (81).

A rapid change in intracranial pressure is critical in inducing the ECG abnormalities seen after SAH (33, 82). Various cardiac arrhythmias can be induced in anesthetized dogs either by a sudden increase in intracranial pressure or by instantaneous release of previously elevated intracranial pressure (84). Even though cardiac arrhythmias are much more frequent in SAH than in other intracranial disorders (20, 33), blood itself does not play a causal role. Such arrhythmias and/or myocardial damage can be experimentally induced by the injection of the same amount of saline (83), cerebrospinal fluid (84), or air into the ventricles (85).

Hypokalemia of varied degree is often observed in association with the ECG changes observed after SAH (29–31). It results from vomiting, increased levels of circulating catecholamines, and hypercortisolism (60). Moderate hypokalemia (<3.5 mEq/L) is present in patients with malignant ventricular arrhythmias (29–31). In general, hypokalemia facilitates the occurrence of ventricular arrhythmias through an increase in the duration of the electrical systole (31).

**MYOCARDIAL FUNCTION FOLLOWING SAH**

Echocardiography (86–88) or ventriculography (89) have shown that kinetic abnormalities of the cardiac walls can be present after SAH, although the relationship between the ECG changes and the functional abnormalities remains obscure. Yuki et al. (89) have reported on a patient in whom the ECG was compatible with acute myocardial infarction and left ventriculography showed anterior wall akinesis. These cardiac abnormalities resolved after surgical clipping of the aneurysm, and the patient recovered well from the operation. She died 2 months later of cancer. Postmortem examination at that time revealed no evidence of myocardial necrosis (89). The condition seemed to correspond to the so-called "stunned myocardium," which has been defined as reversible posts ischemic myocardial dysfunction (90).

Echocardiography abnormalities such as reduced global and segmental left ventricular systolic function have also been reported in four patients with SAH and neurogenic pulmonary edema (86). Cerebral infarction due to vasospasm occurred in all four patients and resulted in two deaths (86). The kinetic abnormalities observed were transient, and follow-up echocardiography demonstrated normal left ventricular function 26 and 42 days after SAH in both survivors (86).

The dysfunction observed on echocardiography after SAH seems to be related more to the degree of neurologic compromise than to specific ECG changes (87). Davies and co-workers performed echocardiography in 45 patients who had no known chronic cardiac disease and who had a SAH (87). Four patients were found to have wall motion abnormalities. All four had severe neurological dysfunction but only minimal ECG changes. Patients with other ECG abnormalities, including deep in-
version of the T wave usually associated with SAH, had normal echocardiograms. In their study, ECG was not an accurate predictor of myocardial function after SAH, and myocardial dysfunction was related more closely to the severity of neurological condition (87). Other authors have reported similar findings (88).

**PATHOLOGIC FEATURES**

In 1969, Connor (91,92) described pathological myocardial lesions found in 8% of 231 neurological autopsies as "myocytolysis." These lesions can be found in 80% of the patients dying after SAH (93). Connor described the lesion as "... an area in which the muscle fibers have been removed, leaving an 'empty' sarcolemmic sheath, muscle nuclei, lipofuscin pigment, and some histiocytes. Coagulative necrosis and polymorphonuclear leukocytes were not seen" (92). Primarily, these abnormalities were found in patients who had intracranial hemorrhage (91,92). This pathological appearance was usually present in those patients who survived 4-6 days after the onset of the disease (92). This observation is consistent with the assumption that the histological damage does not immediately become apparent (91,92). Subendocardial hemorrhages have also been observed (94).

The myocardial lesions observed after SAH are not uniformly distributed. Baroldi (95) examined hearts removed from 14 patients who died of documented brain hemorrhage. In all, foci of coagulative myocytolysis were present; however, a variation in terms of the number of foci and damaged myocardial cells was seen (95). The left ventricle was involved in all cases, the interventricular septum in all but one case, and the right ventricle in nine cases (95).

**CONCLUSIONS**

ECG abnormalities and frank rhythm disorders are frequently observed in patients after SAH. These abnormalities tend to be more frequent immediately after the hemorrhage and are likely to contribute to the initial loss of consciousness and the sudden death that can be observed after SAH. Life-threatening ventricular arrhythmias such as ventricular fibrillation, ventricular flutter, and torsade de pointe have been reported and seem to occur more frequently if factors such as advanced age, hypokalemia, and QT prolongation are present. These observations confirm the utility of continuous cardiac monitoring, especially during the first 72 h after SAH.

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