Cardiac Arrhythmias and Sudden Death in Subarachnoid Hemorrhage

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Abstract: Life-threatening cardiac arrhythmias can occur in patients with subarachnoid hemorrhage secondary to rupture of intracranial aneurysms. The arrhythmias are secondary to acute dysfunction of the central nervous system and possibly to sudden increase in intracranial pressure. The autonomic nervous system is the mediator in the production of these disorders. The clinical significance of these rhythm disorders is discussed, particularly in regard to the sudden, unexpected death seen in this type of patient. The possible mechanisms of production are analyzed and their therapeutic implications are stressed.

Additional Key Words
intracranial aneurysms
autonomic nervous system
electrocardiographical abnormalities

The functional relationship between heart and brain is an ancient topic. It has been known since 1947 that primary, spontaneous subarachnoid hemorrhage (SAH) and other acute intracranial events can precipitate dramatic changes in the morphology of the waves of the electrocardiogram (ECG). A wealth of literature has been published since that time on this subject. Distinctive electrocardiographical abnormalities associated with this intracranial event include a prolonged QT interval (the importance of this change will be discussed later), large upright or deeply inverted T waves, elevation or depression of ST segments, prominent U waves and a marked increase in the amplitude of the U waves in postextrasystolic beats. The time course of these abnormalities has not been adequately documented. These ECG changes may closely resemble an acute myocardial infarction. The most widely accepted view is that they represent disturbances of ventricular repolarization. It is likely that the ECG changes are secondary to a derangement in the autonomic control of the heart. A large body of experimental and clinical evidence exists to support this view. Many of the patients who had abnormal ECGs and who died of central nervous system lesions had normal hearts at autopsy. On the other hand, there is experimental and clinical evidence that shows that many of these patients have acute structural changes in the myocardium, and furthermore that this myocardial damage appears to be secondary to brain lesions. Connor demonstrated structural changes of the myocardium in patients dying with a variety of diseases of the brain. These changes consisted of focal myocytolysis, myofibrillar degeneration, lipofuscin pigment deposition in the myofibrils and sparse collections of histiocytes in the area of necrosis. The mechanism responsible for these pathological myocardial changes produced by intracranial lesions is not known. However, it appears that the autonomic nervous system and its various chemical mediators play a role in its pathogenesis.

In contradistinction to the abundance of information concerning ECG changes in SAH, there is hardly any mention of disturbances of cardiac rhythm in the neurological and cardiological literature. Scattered reports on this subject have been published; nevertheless, there is a dearth of information concerning the incidence, time of appearance, clinical importance and methods of prevention and treatment of these feared events. No mention of arrhythmias is made in the standard textbooks of neurology and the condition is merely regarded as a curiosity at best. However, the presence of these disorders of the heart beat is likely to have great clinical importance, particularly as it pertains to the distressingly common, sudden and now somewhat expected death so unfortunately frequent in these patients. Moreover, when there is a concomitant impairment of consciousness and no clinical history, the disturbance of the cardiac rhythm may appear to be the primary illness of these patients. Parizel described two cases of spontaneous SAH, both of which developed several different arrhythmias within a short period of time: supraventricular tachycardia, short bursts of ventricular premature beats, multifocal ventricular tachycardia, ventricular flutter and ventricular fibrillation necessitating D.C. countershock and intravenous antiarrhythmic drugs. Both patients survived. His comments are enlightening: "Life-threatening arrhythmias can occur in patients with subarachnoid hemorrhage. Our two patients would undoubtedly have died without the prompt resuscitative measures made possible by their admission to a coronary care unit. Their death would have been attributed to their
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nervous system disease." Prior to this report the seriousness of these events had not been emphasized. Plum and Posner described a 44-year-old man who presented with arrhythmias of various sorts: 2:1 block, sino-atrial block, sinus arrhythmia, intermittent complete atrioventricular block, supraventricular tachycardia and finally ventricular tachycardia. This patient was mistakenly diagnosed as having a myocardial infarction, but postmortem examination showed a massive SAH from rupture of an aneurysm of the anterior communicating artery. No mention was made of the state of the heart. The transient nature of these disorders and the fact that many of these patients are not under careful cardiac monitoring during the acute illness are also additional factors in the poor documentation of these arrhythmias. A prospective study of electrocardiographical changes associated with SAH does not mention the presence of cardiac arrhythmias. We have recently seen two cases of acute SAH secondary to rupture of intracranial aneurysms in whom life-threatening cardiac arrhythmias were present. In only one case was it possible to obtain full documentation of the disorder.

Case 1

A 61-year-old white man was brought to the emergency room of the Baltimore City Hospitals in a stuporous state. Cardiac examination disclosed a very fast apical rate with a varying first sound. ECG revealed ventricular flutter at a rate of 250 per minute (fig. 1) that spontaneously reverted to normal sinus rhythm in about 30 seconds. Over the next few minutes he had multiple premature atrial contractions (PACs), intermittent 2:1 block, multifocal premature ventricular contractions (PVCs), and short episodes of bigeminal rhythm. Fifty milligrams of intravenous xylocaine were given with restoration of normal sinus rhythm. Following these events the patient was lethargic, but easily arousable, and oriented. He complained of a severe headache. He related that he was standing on the street when he suddenly became dizzy and then "blacked out." He did not recall falling or having a headache prior to losing consciousness. The next memory he had was that of waking up in the ambulance with a severe headache; he remembered he suddenly lost consciousness again upon entering the emergency room. His past medical history was unremarkable except for mild hypertension of ten years' duration, for which he had been treated intermittently with 50 mg of hydrochlorothiazide daily. An ECG taken one year prior to his admission was within normal limits and a chest x-ray taken at the same time was normal as well. He denied any history of heart disease. He denied angina or symptoms of congestive heart failure. He did not smoke or drink, and stated that his general health prior to this incident had been excellent.

Physical examination on admission revealed a man in acute distress complaining of a severe headache. He was lethargic but easily arousable and oriented. Blood pressure when the patient was in normal sinus rhythm was 200/120 mm Hg, respiratory rate was 25 per minute and regular, and pulse 110 per minute and regular. Rectal temperature was 101°F. General physical examination showed no evidence of jugular venous distention, the lungs were clear, the heart was not enlarged. There was grade 1 hypertensive retinal changes (Keith-Wagener classification) and normal peripheral pulses. Neurological examination revealed slight neck stiffness and the presence of an incomplete left third nerve palsy, with 50% palpebral ptosis, and a left pupil which was 2 mm larger than the right and sluggishly reactive to light. There was paresis of left medial rectus, inferior oblique and superior rectus. There were no hemipareses, sensory deficits or visual field defects. A lumbar puncture showed an opening pressure higher than 300 mm H2O. The CSF was grossly bloody with a xanthochromic supernatant and a hematocrit of 6%. The urine showed no protein or sediment. No red or white cells. An ECG taken one hour after admission revealed a sinus rhythm of 85 per minute, first degree AV block, left axis deviation (-15°), and a QT interval of 0.44 second. There were no U waves but the T waves were slightly depressed in lead III. The blood sugars and the electrolytes were normal, including potassium. Continuous monitoring over the next 48 hours did not reveal the presence of a serious cardiac arrhythmia. The ECG remained unchanged. Serial arterial blood gases were normal. An arteriogram revealed a left posterior communicating artery aneurysm at the point of junction with the left internal carotid artery.

Case 2

A 29-year-old black man was admitted to the Johns Hopkins Hospital because of sudden onset of severe, generalized headache that developed while the patient was having intercourse. His previous health had been good and his family history was negative for neurological or cardiac diseases. His general physical examination on admission was negative. Neurological examination showed moderate
neck stiffness and a Kernig sign, but was otherwise negative. While he was being examined by the house staff he suddenly developed multifocal PVCs and runs of ventricular tachycardia each lasting a few seconds. These arrhythmias were directly observed on the cardiac monitor. They subsided spontaneously after a few minutes and no therapy was given. At no time was there evidence of shock or decreased cerebral perfusion. Electrolytes, arterial blood gases, chest x-ray and an ECG taken one hour after this episode were within normal limits. Lumbar puncture showed an opening pressure of 400 mm of CSF and was grossly bloody with a xanthochromic supernatant. Cerebral angiography proved the presence of a right posterior communicating artery aneurysm, again at the point of junction with the internal carotid artery.

Discussion

PATHOPHYSIOLOGY

The neural mechanisms by which these arrhythmias are produced are not clearly understood. However, in recent years some physiological information has accumulated which sheds some light upon this subject.19-25 An excellent review of this somewhat confusing topic was made recently by Mauck.32 In the experimental animal, cardiac arrhythmias can be induced by electrical stimulation of several cortical and subcortical areas. These include the frontal lobes, the limbic system, the amygdaloid nuclei, the hypothalamus, the mesencephalon and other areas in the brain stem.29 These arrhythmias are in all likelihood mediated through the autonomic nervous system.32 In another study, Hockman et al.34 induced a spectrum of ectopic ventricular rhythms by electrical stimulation of some areas of the mesencephalon and diencephalon. Observed in sequence were ventricular tachycardia, both unifocal and multifocal, ventricular premature contractions in bigeminal pattern, and finally return to sinus rhythm. Bilateral vagotomy had no effect on the response; however, it was completely abolished by beta-adrenergic blockade with propranolol. They concluded that the type of arrhythmia observed was directly related to the intensity of the sympathetic discharge and that all abnormal ventricular complexes observed in the clinic could be elicited experimentally. On the other hand, Smith and Rau33 were able to provoke various cardiac arrhythmias in anesthetized dogs by rapid increase in intracranial pressure or by instantaneous release of previously elevated intracranial pressure. Both the administration of atropine and vagotomy eliminated or prevented the arrhythmias. These animals also developed cardiac arrhythmias after injections of isoproterenol. More recently it has been shown39 that if hypoxia is present the frequency of these problems is increased. Thus, the experimental evidence appears to indicate that both the sympathetic and the parasympathetic systems are implicated in the production of these rhythm disturbances. That sudden increase of intracranial pressure can precipitate cardiac arrhythmias is of particular clinical interest. Wong and Cooper37 published a case of SAH with atrial fibrillation and ventricular slowing in which a lumbar puncture, presumably by decreasing the increased intracranial pressure, abolished the cardiac arrhythmia. Also, the prolongation of the QT interval so frequently seen in these patients has been associated with sudden death.36 According to James,36 “Prolongation of the QT interval represents delayed ventricular repolarization and an increase in the duration of the vulnerable period with greater susceptibility to the development of a ventricular dysrhythmia. In a patient with a prolonged QT interval, therefore, it is particularly important to prevent the occurrence of premature ventricular beats or supraventricular dysrhythmias.” Smith36 published a case of SAH associated with a prolonged QT interval and ventricular bigeminy and quadrigeminy. He stated that the cardiac arrhythmias were clearly related to a prolonged QT interval. The prolonged QT interval appears to be secondary to a non-uniformity in the rate of repolarization of these cells.37, 38

Intracellular studies of the sino-aortic node (SA node) have shown that the firing rate of the SA node is modified by both sympathetic and parasympathetic nervous systems. It is well established that the rate of depolarization of the SA node is greatly influenced by neural mechanisms.39 For example, vagal discharges depress the pacemaker by slowing the rate of depolarization; on the other hand, an increase in sympathetic discharge increases the slope of depolarization. By reciprocal effects on the rate of depolarization in the transmitter tissue, conduction through the atrioventricular node (AV node) is either increased or decreased. Sudden changes in discharges of either vagal or sympathetic systems could produce a number of cardiac arrhythmias. In addition to the aforementioned neural factors, pre-existing heart disease, changes in electrolytes, and pH of the blood or Pao2 may be of significance in the production of these arrhythmias. However, neither abnormalities in the above-mentioned factors nor an increase in circulating catecholamines has been found to be consistently associated with the electrocardiographical abnormalities of SAH.40 The role of the myocardial lesions secondary to acute brain lesions in the genesis of these problems is not known.41

RELATION OF ARRHYTHMIAS TO THE SUDDEN UNEXPECTED DEATH SYNDROME

An important point that naturally arises is the possible relationship between the cardiac arrhythmias and the sudden unexpected death of some patients with primary SAH. It has been estimated that as many as 15% of the patients with spontaneous SAH die before reaching the nearest hospital.42 Twenty percent more will die within 48 hours after the onset of symptoms.43 Hamman44 found that 8% of all patients who died suddenly had some sort of cerebral hemorrhage. Others45 have found SAH to be responsible for 4.7%
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of all sudden deaths. In a remarkable study Secher-Hansen analyzed 115 cases of autopsy-proved spontaneous subarachnoid hemorrhage, all of which fulfilled the criterion for sudden unexpected death (all deaths ranging from "instantaneous" to the first 24 hours) and found that 75% of his cases had died instantaneously!

The mechanisms of death in these patients are not entirely clear and are doubtless multiple. Acute destruction or compression of vital centers operates in some cases. According to Helpert et al., the most common postmortem finding is a diffuse subarachnoid hemorrhage covering the base of the brain. Also, Crompton has shown that blood may rapidly distend vessels and resultant diencephalic ischemia. This can bring as a consequence impairment of vegetative functions. It is entirely possible that the incidence of cardiac arrhythmias is greater when an aneurysm ruptures in the base of the brain, but there is not enough clinical information to decide upon this point.

There is no satisfactory explanation for the initial loss of consciousness that usually accompanies SAH. There is no evidence that extravasation of blood in the subarachnoid space can, by itself, cause unconsciousness. Hemorrhage into the brain, infarction or arterial spasm have been incriminated, but the clinical fact that many patients recover consciousness with intact nervous system function militates against this thesis. Some of these patients may have seizures, albeit the incidence of seizures at the time the aneurysm ruptures is not known. It should be stressed that patients with SAH should have cardiac monitoring in a place in which proper treatment is available.

In regard to the treatment of these disorders, the few arrhythmias reported in the literature responded well to the standard methods of treatment for arrhythmias of other causes. However, chemical blockage of the sympathetic and parasympathetic systems with atropine and propranolol has been advocated for the prevention of myocardial damage in patients with intracranial hemorrhage. It is probably significant that these patients and three others reported in the literature had bizarre atrial and ventricular arrhythmias similar to those reported in the experimental animal by Hockman et al. Also, from the cases isolated from the literature in which the location of the aneurysm was known, two cases had aneurysms of the anterior communicating artery, and at least three cases (and those reported here) had aneurysms of the posterior communicating in the junction with the internal carotid. The fact that these aneurysms were located in the base of the brain may imply an important relationship between the location of an intracranial hemorrhage and its potential pathogenicity; however, more studies are needed to clarify this point and many others in this important medical problem.

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