Hypersensitive Carotid Sinus Reflex
Associated with Spontaneous, Transient Complete Heart Block

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A patient with transient, intermittent, complete heart block had periods of asystole, accompanied by syncope, whenever his cardiac rhythm shifted spontaneously from regular sinus rhythm to complete auriculoventricular dissociation. Similar clinical and electrocardiographic findings were produced by carotid sinus pressure when there was regular sinus rhythm. During the periods of heart block carotid sinus stimulation produced no effects. Physiologic studies suggested that the site of sensitivity of the hyperactive carotid sinus reflex was located at the effector end of the reflex arc. The possibility of structural damage to the heart from repeated stimulation of a hyperactive carotid sinus reflex is considered.

This is a study of a patient with syncopal attacks due to ventricular arrest which, on occasion, were found to occur when the cardiac rhythm shifted spontaneously from normal sinus rhythm to complete heart block and which, on other occasions, followed stimulation of the right carotid sinus. The observations to be reported permitted an evaluation of the relative importance of the organic and neurogenic factors in the causation of these attacks and offered an opportunity to study the mechanism of transient heart block.

Case Report

The patient, a 73 year old Chinese man, was admitted to Bellevue Hospital following a fall in the street. He gave a one-month history of dizziness and fainting which had resulted in almost daily falls with consequent minor injuries. Unconsciousness usually lasted only a few seconds and was not related to head movement, neckwear, activity, or change of position. There were no aura, nausea, vomiting, tongue-biting, or incontinence of urine or feces. Chest pain, symptoms of diminished cardiac reserve, and previous heart disease or hypertension were denied. He did recall two episodes of palpitation during the three months prior to admission. System review and past history were otherwise noncontributory. The patient had been a heavy wine- and whiskey-drinker for many years but had entirely discontinued drinking alcoholic beverages two months before admission.

Physical examination showed a well-developed, well-preserved elderly Chinese man in no apparent distress. The rectal temperature was 98.6 F., respiratory rate 24 per minute, pulse rate 56 per minute, and blood pressure 200/90. There were bilateral arcus senilis, right periorbital swelling and edema, and a laceration 2 inches in length over the right eye. No abnormalities of the carotid arteries or adjacent tissues were noted. The heart sounds were distant; the aortic second sound was louder than the pulmonic; and a soft, medium-pitched, blowing systolic murmur was heard over the entire precordium, maximal in the third intercostal space at the left sternal border. The rhythm was regular with the ventricular rate equal to the pulse rate at 56 beats per minute, except for brief periods of five to seven seconds of irregular rhythm terminating in complete ventricular arrest, following which the heart resumed activity at a regular rate. The remainder of the physical and neurologic examination revealed no abnormality.

The urine was normal; its specific gravity was 1.015. Complete blood count showed: red blood cells—4,800,000 per cu. mm.; hemoglobin—12.9 grams per cent; white blood cells—9,250 per cu. mm. with a normal differential count. The Mazzini reaction was negative. Blood chemical analyses gave the following values: fasting blood sugar—81 mg. per 100 cc. of blood; calcium—12.4 mg. per 100 cc.; chlorides—328 mg. per 100 cc.; phosphorus—3.09 mg. per 100 cc.; albumin/globulin ratio—4.5/2.4; nonprotein nitrogen—94 mg. per 100 cubic centimeters. There were no parasites in the stool. The icteric index was 9. On lumbar puncture the initial pressure of the spinal fluid was 130 mm.; the Pandy reaction was negative; there were 900 red blood cells

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per cu. mm. of spinal fluid (traumatic tap); the Wassermann reaction was negative; and the colloidal gold curve read 112210000. Posteroanterior

Four days after admission while attempting to climb into bed the patient fell to the floor. The pulse rate was reported as 35 beats per minute with

x-ray film of the chest showed the lungs clear and the heart not enlarged. Roentgenograms of the skull showed no abnormality.

a rise to 60 beats per minute an hour later. Two days later, testing of the right carotid sinus reflex by digital pressure produced asystole and syncope fol-

FIG. 1.—A, Control tracing, normal sinus rhythm. B, Left carotid sinus pressure with massage; arrow indicates release of pressure, which at this point had been maintained for twenty seconds. C, Right carotid sinus pressure with massage, ventricular asystole, and convulsion. Pressure was applied during the interval between the arrows. (The unlettered strip is continuous with the strip immediately above.)

FIG. 2.—A, Normal sinus rhythm. Right carotid sinus pressure with massage, ventricular asystole, and convulsion. Pressure was applied during the interval between the arrows. B, Three minutes later. Periodic appearance of normally conducted beats of supraventricular origin indicates that, although A-V block was high grade, it was not complete. This probably represents the last vestige of normal A-V conduction. C, Ten minutes later. Stabilization in complete A-V block (compare with fig. 4, C). (The unlettered strip is continuous with the strip immediately above.)
lowed by a few convulsive movements (fig. 1, C). During the next few weeks the patient was observed to exhibit normal A-V conduction at times and complete heart block at other times. Spontaneous attacks of dizziness and syncope occurred. At this stage the nature of his cardiac rhythm and the cause of the syncopal attacks were not clear, and studies were undertaken to clarify the relationship between the carotid sinus reactivity and the spontaneously occurring heart block in the genesis of the syncopal attacks.

**Fig. 3.**—A, Control tracing, A-V block. B, Right carotid sinus pressure with massage applied during the interval between the arrows. Three seconds after the application of pressure the atrial rate decreased from 70 per minute to 66 per minute without alteration in ventricular rate. C, Atropine sulfate (2.0 mg.) injected intravenously during interval between the arrows. D, Thirty seconds after injection of atropine. (Each unlettered strip is continuous with the strip immediately above.)

Clinical Studies. When the cardiac rhythm and A-V conduction were normal, carotid sinus stimulation on several occasions gave the responses indicated in figures 1 and 2. Pressure on left carotid sinus produced a negligible response (fig. 1, B); but pressure over the right carotid sinus produced atrial slowing with change in the shape of the P waves and ventricular asystole which led to a convulsion (fig. 1, C). The ventricular asystole produced by right carotid sinus stimulation was followed by a high-grade, but not complete, A-V block (fig. 2, B). Approximately ten to thirty minutes later this rhythm changed to that of complete A-V block (fig. 2, C).

In contrast, whenever A-V conduction was blocked (fig. 3, B), right carotid sinus pressure produced usually a slowing of the atrial rate of 10 to 15 beats per minute, and occasionally no effect. However, carotid sinus pressure on either side failed to produce ventricular asystole on any occasion, whether the atrium was slowed or not. The failure of the atrium to slow on a few occasions during right carotid sinus pressure cannot be explained; the pressure was applied always by the same observer who made every effort to keep the intensity, location, and duration of stimulation constant at all times. During these observations, both with and without A-V block, the blood pressure ranged from 90–144/40–62; and at no time did carotid sinus stimulation produce a primary depressor response.

The demonstration of carotid sinus hypersensitivity during periods of normal sinus rhythm but not during periods of A-V block is to be anticipated, since a neurogenic (vagal) effect, which is manifested by a sudden interruption of A-V conduction, is not to be expected when A-V conduction is already blocked.

On several occasions the patient was observed in a period of spontaneously shifting rhythms. At these times complete A-V block predominated with a ventricular rate of 34 beats per minute. Every five
to ten minutes there was a temporary restoration of A-V conduction and normal sinus rhythm ensued with a ventricular rate of 60 beats per minute. After one to three minutes of the normal sinus rhythm a spontaneous ventricular arrest of three to ten or more seconds occurred, following which there was reactivation of an idioventricular center with complete A-V block (fig. 4). During the asystole the patient became pale, and if the asystole was prolonged, he had a mild generalized convulsion. On recovery of consciousness he was momentarily con-
changes in A-V conduction than the result of a hypersensitive carotid sinus reflex.
Several studies made during complete A-V block pointed to an organic rather than functional basis for the block. Normal A-V conduction could not be restored by any of the following procedures: (1) The administration of 2 mg. atropine sulfate intravenously increased the atrial rate briefly from 88 beats per minute to 114 beats per minute, and the idioventricular rate from 31 beats per minute to 34 beats per minute, but did not alter the A-V block (fig. 3,
fused. A-V block then continued until normal con-
duction was resumed spontaneously, and the cycle repeated. Such a change in conduction occurred approximately three or four times in the half hour that he was observed before his rhythm became stabilized in A-V block. These attacks were all spontaneous; the patient lay supine in bed with his face directly upwards. There was no turning of the head preceding an attack. After the asystole there was a period of incomplete A-V block with occasional normal conduction of supraventricular beats. This rhythm gradually yielded to complete A-V block. Thus the events following spontaneous ventricular asystole were the same as after ventricular asystole induced by right carotid sinus stimulation (compare figs. 4, C and 2, C).
It was now considered that the patient's sponta-
neous syncopeal attacks were more likely the result of ventricular arrest associated with the spontaneous

Fig. 4.—Spontaneously changing cardiac rhythm. Tracings taken with the patient lying flat in bed without movement. A, Ventricular asystole followed by convulsion. B, Ventricular asystole is not prolonged enough to produce a convulsion. C, Stabilization in complete A-V block (compare with Fig. 2, C). (Each unlettered strip is continuous with the strip immediately above.)

C). (2) The right carotid sinus was blocked with 10 cc. of 1.5 per cent procaine; a mass block was effected and produced hoarseness and Horner's syndrome on the right side but did not affect the ventricular rate or A-V conduction. (3) Inhalation of 100 per cent oxygen flowing continuously at 6 liters per minute failed to affect the complete A-V block.
In view of the carotid sinus hypersensitivity demonstrated by applying digital pressure from without, an attempt was made to stimulate the carotid sinus from within by elevating the arterial pressure. The cold pressor test was chosen for this purpose. On two separate occasions, when A-V conduction was normal, immersion of the forearm in ice water produced a marked rise in blood pressure from 134/74 to 202/92 and from 104/58 to 204/102. On each occasion, as the blood pressure reached its peak, ventricular asystole occurred (fig. 5, A). On one occasion, following the ventricular asystole, normal
A-V conduction was resumed immediately. Then, after removal of the forearm from the cold water, there followed a period during which the blood pressure fluctuated widely. Ventricular asystole occurred whenever the blood pressure became elevated above 160/80 (fig. 5, B); but as the blood pressure fell below this level, normal A-V conduction returned. On the other occasion ventricular asystole was followed by a period of A-V block before A-V conduction returned and normal sinus rhythm again ensued. Again there followed a period during which the blood pressure fell irregularly with occasional spikes above 160-80; and again ventricular asystole occurred whenever the blood pressure became elevated. When the blood pressure stabilized at its initial level, A-V conduction returned and normal sinus rhythm was re-established.

These asystolic episodes cannot be attributed unequivocally to carotid sinus stimulation by the increased arterial pressure, because of the possibility that they could have been due to decreased circulation to the A-V bundle during the pressor test. An attempt to decide between these two alternatives by repeating the cold pressor test after abolishing vagal influence was unsuccessful because on this occasion complete A-V block occurred immediately after 2.5 mg. atropine sulfate were injected intravenously.

Course. After a number of spontaneous Adams-Stokes attacks the patient stabilized in heart block. Novatropine (0.005 Gm., four times a day) and atropine sulfate (0.0004 Gm., four times a day), were given by mouth. Atropine was increased to tolerance in the hope of breaking the A-V block, but without success. Heart block with a ventricular rate of 34 beats per minute became established and the patient was discharged to be followed in the outpatient cardiac clinic.

During his repeated visits to the clinic complete A-V block was usually observed. However, on three visits normal sinus rhythm with rates of 60 to 66 beats per minute was noted. On one occasion he complained of attacks of dizziness but denied fainting or unconsciousness. The next morning an electrocardiogram was made; this revealed the same spontaneously changing A-V conduction that had been noted four months previously. For the next two years (May 1947 to June 1949) the patient visited the clinic at frequent intervals and on all occasions.

Fig. 5.—A, During cold pressor test, blood pressure 204/102 at onset of ventricular asystole. B, Two minutes after removal of hand from ice water, blood pressure 192/82 at onset of ventricular asystole. (Each unlettered strip is continuous with the strip immediately above.)

he was observed to have complete A-V block with a ventricular rate of 32 to 40 beats per minute. During this period he has been free of Adams-Stokes seizures. Cardiac reserve and general condition appear about the same as two and one-half years previously when he was first admitted to the hospital.

Discussion

Transient Heart Block. Complete heart block alternating with normal conduction is a relatively infrequent occurrence. In 1934 Weiss and Ferris reported two cases of transient complete heart block in association with the Adams-Stokes syndrome and cited only fourteen other cases in the previous literature, including those collected by Carter and Dieulaide in 1923. In the more recent literature, transient complete
heart block has been reported in association with congenital heart disease2-4 and as a result of the acute myocarditis of rheumatic fever,5 diphtheria,6 mumps,7 and scarlet fever.8-

Unique cases of congenital heart block with transitory periods of normal sinus rhythm were described by Smith9 and by Calandre.10 Smith's patient had complete heart block which was unaffected by exercise or atropinization, but A-V conduction could be restored with a return to normal sinus rhythm by forced expiration. The author suggested that this change might be explained mechanically by lessening of traction on the conduction system owing to the altered position of the heart during forced expiration. Calandre's patient also exhibited complete heart block, except when in absolute repose at which time conduction was normal.

In most cases the transient heart block ultimately changed to permanent heart block and postmortem examination revealed underlying anatomic lesions within the cardiac conduction system. In a few cases of transient heart block, evidence of a neurogenic origin was present; and in this group Weiss and Ferris included their own three cases of vagovagal reflex Adams-Stokes syndrome,1 the similar cases of Flaum and Klima,11 and of Gluch,12 and the cases due to hyperactivity of the carotid sinus.13 Our patient belongs with that group of cases14-18 with anatomic lesions which incompletely sever the cardiac conduction system and in which a sudden increase in vagal tonus precipitates the development of complete A-V block.

Site of Hypersensitivity of the Hyperactive Carotid Sinus Reflex. The site of hypersensitivity of a hyperactive carotid sinus reflex may be in the afferent nerve endings of the sinus, in the medullary synapses of the central nervous system, or in the efferent nerve endings such as the vagal endings in the heart, alone or in combination. Observations13, 19-21 in cases with local abnormalities of the carotid artery and adjacent tissues on the side of a hyperactive reflex suggested that the hypersensitive carotid sinus reflex results from a pathologic lesion within or impinging upon the sinus itself. On the other hand, there has accumulated clinical22a, 22b, 23, 24 experimental,25 and morpholo-

gic evidence in favor of the view that the site of hypersensitivity in the "vagal" or cardioinhibitory type of reflex is predominantly, if not entirely, at the effector end of the reflex arc. The observations in the patient here reported may be interpreted in support of this viewpoint. The persistence of P waves (at a rate never less than forty-four per minute) throughout ventricular asystole indicates that potential stimuli for ventricular contraction were present during asystole but were blocked in propagation to the ventricle. This suggests that the site of carotid sinus hypersensitivity in this patient was located primarily in the vicinity of the A-V node and bundle, which coincides with the site of the lesion as inferred from the later development of permanent A-V block.

Permanent A-V Block Precipitated by Carotid Sinus Pressure. The development of permanent A-V block in this patient raises the question of structural damage to the heart as a consequence of carotid sinus sensitivity. Such reports have not been found in the literature, although cerebral damage following carotid sinus stimulation has been observed.7-27 There is clinical and experimental evidence21-25 that the coronary circulation and myocardium may be adversely affected by the carotid sinus reflex. Glenn and Read21 reported a case of coronary artery disease in which anginal pain, similar to the patient's spontaneous symptoms, could be reproduced by carotid sinus stimulation. Friedman22 observed two young adults without cardiovascular disease in whom anginal pain occurred following carotid sinus stimulation but not following severe exertion. Stella24 observed a decreased coronary blood flow following elevation of pressure within the perfused carotid sinus of a dog's heart-lung-head preparation. Hall, Ettinger, and Banting27 reported that repeated intravenous infusions of acetylcholine produced myocardial damage, and that vagal stimulation alone could cause myocardial degeneration, small infarcts, and electrocardiographic changes.

This evidence is indirect, but nevertheless indicates the possibility that stimulation of the hyperactive carotid sinus reflex may result in some subtle structural alteration in addition to the transient dramatic asystole. Such altera-
tion would escape clinical detection unless it involved a critical area such as the cardiac conduction system. The absence of clinical symptoms in the patient here reported until shortly before his hospital admission reflects "the large reserve in the conducting capacity of the A-V bundle, which structure may be considerably encroached upon before conduction is measurably impaired. Thus, with only a few intact fibers serving to carry on the normal conduction process, an increase in vagal activity and/or a small local decrease in circulation may result in failure of these few remaining fibers to function." Such a loss of function would result in permanent A-V block if the anatomic lesion were extended through these last intact fibers. It is at least possible that in the patient here studied some such progressing change may have resulted from repeated stimulation of his hypersensitive carotid sinus reflex. As a consequence the remaining few intact fibers of the A-V conduction system may have been obliterated with the result that the initially transient complete heart block became permanent.

It is a matter of pure speculation whether repeated carotid sinus stimulation hastened the establishment of permanent heart block in this case, or whether the block resulted from the natural progress of the primary disease. Nevertheless, whatever its cause, the development of permanent block was beneficial to the patient. With this conduction system precariously near the point of complete severance, he was imminently susceptible to the onset of complete A-V block and ventricular standstill; but with the establishment of permanent A-V block with an idioventricular rhythm, the pacemaker of which was located below the site of vagal susceptibility, he was freed from his asystolic episodes and syncopal attacks. This change would have been valueless if the idioventricular focus were prone to retardation or to periods of complete inactivity. In this patient the complete A-V block, with an idioventricular rhythm at a rate of 32 to 40 beats per minute, has been present for two years during which he has been active and free of symptoms. In this sense the development of permanent heart block has been of benefit to him.

Summary

1. A case of transient complete heart block is described in which there were present a hyperactive cardioinhibitory carotid sinus reflex and a probable organic lesion of the A-V conduction system.

2. During periods of A-V conduction with normal sinus rhythm, carotid sinus stimulation produced asystole; during periods of complete A-V block, carotid sinus stimulation was without effect.

3. Several clinical studies indicated that the region of the anatomic lesion (vagus endings or His bundle) represented the site of greatest sensitivity of the hyperactive reflex in this patient.

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