ANGIOGRAPHIC CHANGES IN THE CORONARY ARTERY ASSOCIATED WITH CYCLICAL REDUCTIONS OF CORONARY BLOOD PRESSURE

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Morphological changes associated with cyclical reductions of blood pressure in the partially constricted coronary artery of anesthetized dogs have been examined. In the constricted coronary segments, smooth and diffuse spasm, rosary-like spasm, a localized narrowing indicating a platelet aggregate or thrombus, and no obvious change were observed during the pressure reductions in 3, 5, 2 and 5 of 15 trials of 12 preparations, respectively. In the distal segments of the same preparations, segmental spasm and diffuse spasm were observed during the pressure reductions in 8 and one trial, respectively. The changes in the constricted and distal segments appeared simultaneously or independently. The change which indicates obstruction of the distal segments with platelet aggregates or thrombi was observed in none. The results indicate that spasm, but not platelet aggregates or thrombi, in the constricted segments and/or distal segments plays the major role in the cyclical reductions of blood pressure in the partially constricted coronary artery.

CYCLICAL reductions of blood pressure and flow in the partially constricted coronary artery of anesthetized dogs were observed by Uchida, et al. and by Folts. This phenomenon was frequently associated with cyclical ST elevation of surface electrogram and therefore closely resembles Prinzmetal's variant angina pectoris. Uchida, et al. suggested participation of coronary spasm in this phenomenon since segmental or diffuse narrowing was observed in the coronary segments distal to the constricted portion. On the other hand, Folts suggested obstruction of the constricted portion with platelet aggregates since platelet aggregates were found histologically in the removed constricted portion. Thus, the opinion on the mechanism(s) of this phenomenon is still unsettled. Therefore, we examined angiographically the morphological changes not only in the constricted but also in the distal coronary segments.

METHODS

1. Twelve beagle dogs were anesthetized with intravenously administered sodium pentobarbital (35–40 mg/kg). The trachea was intubated for artificial positive pressure respiration with air. The upper 7 ribs on the left side were removed. After pericardiotomy, the proximal segment of the left circumflex artery was dissected free of surrounding tissues. A rigid cylindrical plastic tube 3 mm in length and with a longitudinal slit was placed on the coronary segment for partial constriction. The tube was covered with another plastic tube to keep the segment inside the former tube. A catheter was introduced in retro-
RESULTS

1. Changes in the Constricted Coronary Segments

The diameter of the constricted coronary segment angiographically examined immediately after partial constriction ranged from 10 to 60 percent of that of the adjacent non-constricted proximal segment. During a decrease of peripheral coronary blood pressure, a further and smooth narrowing from the proximal end to the distal end of the constricted segment was observed in 3 of 15 trials of 12 preparations. During the succeeding increase of the pressure, the narrowing disappeared in 2 and remained, although reduced in its magnitude, in the remaining one (Fig. 2). A rosary-like narrowing was observed in the constricted segment in 5 trials. In these trials, both sides of the walls of two to four small portions of the segment protruded forwards symmetrically (Fig. 3). The changes, however, was not observed during the succeeding increase of the pressure. A localized narrowing in the constricted segment was also observed in 2 trials. In these trials, a small portion of one side of the wall, the middle portion in one and the distal portion in another, protruded inwards as if something attached to that portion (Fig. 4). In the remaining 5 trials, no obvious change was observed in the constricted segment even during the pressure decrease (Fig. 6).

2. Changes in the Distal Coronary Segments

During the pressure decrease, narrowings in the distal segments were observed in 9 of 15 trials. Both sides of the walls of one to 3 distal segments protruded inwards symmetrically in all these trials. During the succeeding pressure increase, the narrowings disappeared in 5 and remained, although reduced in their magnitude, in 4 trials. The narrowings in the distal segments were associated with smooth and diffuse narrowing in the constricted segment in 2, with rosary-like narrowing in the constricted segment in one and with no obvious change in the constricted segment in 5 trials. A diffuse narrowing from the constricted segment to the distal segments was observed in one trial (Figs. 5, and 6).

In one of the same preparations, angiography was repeated during a pressure decrease. In this preparation, a narrowing appeared in a distal segment at the beginning of the pressure decrease and additional narrowings appeared in two other
distal segments in later phase of the pressure decrease (Fig. 5). Angiography was performed in two pressure decreases in 2 preparations. The rosary-like narrowing which was observed during a decrease was replaced by a localized narrowing during another decrease in one (Figs. 3 and 4). In another preparation, the smooth and diffuse narrowing in the constricted segment disappeared.
Fig. 3. Left half: During an increase of coronary blood pressure. Right half: A rosary-like narrowing in the constricted segment (arrows) during a decrease of coronary blood pressure. No obvious change in the distal segments.

and a narrowing in a distal segment appeared during another pressure decrease. The changes observed in these 3 preparations are included in Fig. 6.

3. Relationship between the Site of Narrowing and the Pattern of the Changes in Coronary Blood Pressure

As shown in Fig. 7, the peripheral coronary blood pressure showed one type of cyclical changes in the preparations in which the narrowing was observed in either the constricted or the
distal segment. On the other hand, two or three types of the pressure changes were observed in the preparations in which the narrowings were observed in both constricted and distal segments (Fig. 8).

The patterns of the cyclical changes in the peripheral coronary blood pressure were examined in 50 preparations in which coronary angiography was not performed. One type of the pressure changes was observed in 24, two types in 31 and three types in the remaining 5 preparations (Figs. 7 and 8). Fusion and dissociation of the different types of the pressure changes were frequently observed in the preparations in which more than one type of the pressure changes were observed (Fig. 8).

DISCUSSION

The results in this study indicate that narrowings in the constricted and/or the distal coronary segments appear during cyclical reductions of peripheral blood pressure of the partially con-
Fig. 5. Left: During an increase of coronary blood pressure. Middle: At the beginning of a decrease of coronary blood pressure. A narrowing in a distal segment (the arrow labelled with 2). Right: Additional narrowings in the distal segments (the arrows labelled with 1 and 3), but no obvious change in the constricted segment.

stricted coronary artery.

There are at least three possible explanations for the narrowings observed in this study: narrowings with thrombi or platelet aggregates, those by vasospasm, and combination of both. In case of the smooth and diffuse narrowing in the constricted segment, it is unconceivable that platelet aggregates or thrombi attached to the inner surface of the segment uniformly and smoothly during the pressure decrease and all of them detached within a short time at the beginning of the pressure increase. It is also unconceivable that platelet aggregates or thrombi attached to the inner surface smoothly and symmetrically causing rosary-like narrowing in the constricted segment. Likewise, it is also unconceivable that platelet aggregates or thrombi caused symmetrical and smooth narrowings in the distal segments. These smooth and symmetrical narrowings closely resembles clinically observed coronary spasm. Therefore, we consider that these narrowings were due to vasospasm.

A localized narrowing in the constricted seg-
Fig. 6. Angiographic changes associated with cyclical reductions of coronary blood pressure. A: A smooth and diffuse narrowing in the constricted segment. B: A rosary-like narrowing in the constricted segment. C: A localized narrowing in the constricted segment. a: Narrowing(s) in the distal segment(s) with no change in the constricted segment. b: Narrowing(s) in the distal segment(s) with a smooth and diffuse narrowing in the constricted segment. c: Narrowing(s) in the distal segment(s) with a rosary-like narrowing in the constricted segment. d: Diffuse narrowings from the constricted segment to the distal segments. No. = number of trials in which the changes appeared/number of trials.

Fig. 7. A representative pattern of the cyclical changes in coronary blood pressure observed in the preparations in which a narrowing was observed in either the constricted segment or a distal segment. From top channel: peripheral coronary blood pressure (CBP), coronary blood flow (CBF), systemic blood pressure (SBP), heart rate (HR), surface electrogram (ECG) and left ventricular contractile force (CF). A: before coronary constriction. B: during coronary constriction.

ment was observed less frequently. A small portion of one side of the inner surface protruded inwards as if something attached to that portion. Such a change is unusual for vasospasm. Therefore we consider that this type of narrowing was due to adhesion of a platelet aggregate or thrombus to the inner surface. An obstruction of the constricted or the distal segment showing "cut-off" sign which is usually observed in case of thromboembolism was observed in none. Therefore, it is unlikely that embolism with thrombi or platelet aggregates which were formed elsewhere participated in the narrowings observed in this study.

Since the narrowings which indicate vasospasm were observed in the majority of experiments, we consider that vasospasm played the major role in the cyclical reductions of blood pressure in the partially constricted coronary artery.

Two or more types of the changes in coronary blood pressure were observed in the preparations in which narrowings were observed in more than one coronary segment. In addition, different types of the pressure changes fused or dissociated with each other. It is likely that vasospasm of different magnitude and of different duration occurred independently, causing different types of the pressure changes and fusion or dissociation of the pressure changes.

The exact mechanism of coronary vasospasm is not well known. In our studies, the cyclical reductions of blood pressure and flow in the partially constricted coronary artery were eliminated by synthetized prostaglandin I$_2$ (prostacycline) and were induced by tranylcypromine that inhibited synthesis of prostaglandin I$_2$. Therefore, the changes in production or wasting of prostaglandin I$_2$ in the coronary wall or the changes in concentration of circulating prostaglandin I$_2$ may have caused cyclical coronary vasospasm and/or platelet aggregates or thrombi, leading to cyclical reductions of blood pressure and flow in the partially constricted coronary artery.

REFERENCES


*Japanese Circulation Journal Vol. 44, March 1980*


