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Transluminal coronary angioplasty and early restenosis
Fibrocellular occlusion after wall laceration

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SUMMARY Transluminal coronary angioplasty was performed in a 51 year old man with a localised narrowing of the proximal segment of the left anterior descending coronary artery. Initial inflations with a small size balloon catheter were unsuccessful. A second attempt, during the same procedure, using a larger calibre catheter relieved the obstruction but produced a dissection. Angina pectoris reappeared approximately three months later. Another attempt to relieve the obstruction by angioplasty, five months after the initial procedure, induced ST segment elevation before angioplasty, followed by ventricular fibrillation and death.

The necropsy showed a split in the pre-existent sclerotic plaque and a dissecting aneurysm of the media. A proliferation of fibrocellular tissue filled the false channel and almost totally occluded the pre-existent arterial lumen.

The observation suggests that wall laceration with exposure of smooth muscle cells to blood may have initiated the excessive fibrocellular tissue response. This event may be the underlying pathogenetic mechanism for the occurrence of early restenosis after transluminal coronary angioplasty.

The clinical introduction of percutaneous transluminal angioplasty has revolutionised the treatment of obstructive coronary artery disease.[1 2] In patients with angina pectoris and localised stenoses the long term follow-up of the procedure has shown good results,[2] despite the occurrence of occasional early restenosis.[3] In fact, its success is largely determined by the patency rate after three to six months. Despite the favourable clinical results, the morphological substrate that underlies the process of dilatation of the lumen has remained controversial. Animal studies and postmortem experiments indicate that the atherosclerotic lesion is split and dissected,[4–8] rather than being crushed and pushed outwards as initially suggested.[9] Necropsy studies in two patients who died shortly after transluminal angioplasty have recently endorsed this opinion.[10] The conclusion that wall laceration is a "natural" consequence of the procedure is important because, by analogy with aortic wall laceration and dissection, one might expect that at least in some instances a reparative response might be evoked that could lead to early restenosis.

The present report documents a patient who died suddenly, while undergoing a second coronary angioplasty of the left anterior descending coronary artery, five months after the first transluminal dilatation of this vessel. The necropsy showed a severely lacerated wall at the site of the previous angioplasty with obliteration of the lumen by a fibrocellular intimal proliferation.

Case report

A 51 year old man was admitted to hospital for evaluation of effort angina that had developed after myocardial infarction. The coronary angiogram showed multiple wall irregularities in the right coronary artery and the left circumflex artery and a 95% narrowing, over approximately 1 cm, in the proximal part of the left anterior descending coronary artery (Fig. 1A). Percutaneous transluminal angioplasty of the stenosis in the left anterior descending coronary artery was performed four months after the acute episode. The result of the first inflation, using a Schneider-Grüntzig dilatation catheter DG 20–30, was unsatisfactory: the segmental stenosis persisted and, in retrospect, the immediate postinflation angiogram showed a circumscript wall laceration (Fig. 1B). At the time, however,

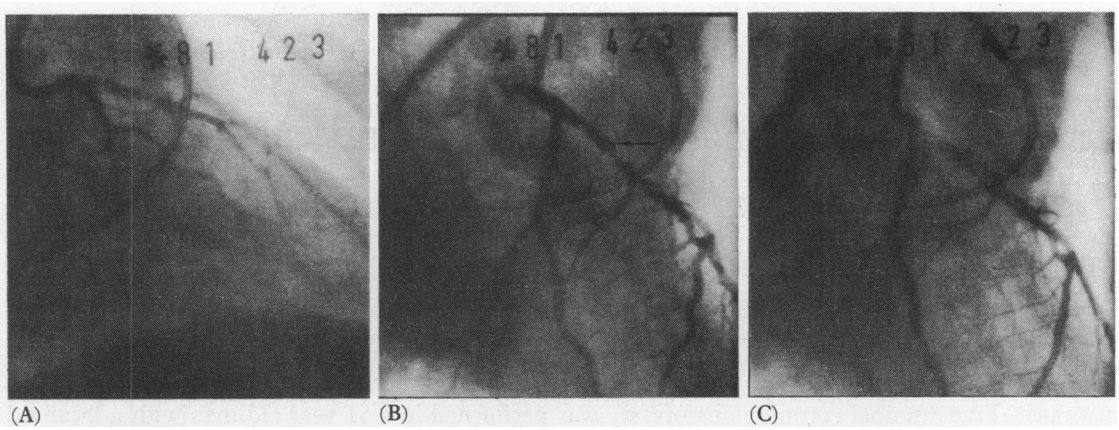

Fig. 1 *Angiograms of the left coronary artery. (A) There is segmental obstruction proximal in the anterior descending artery before angioplasty. (B) Angiogram, in a slightly different oblique projection, after the initial attempt to relief the obstruction. The stenosis is still present. The proximal arterial segment discloses a discrete luminal outpouching (arrow). (C) Angiogram after the second attempt to relieve the obstruction. A dissection is clearly shown.*

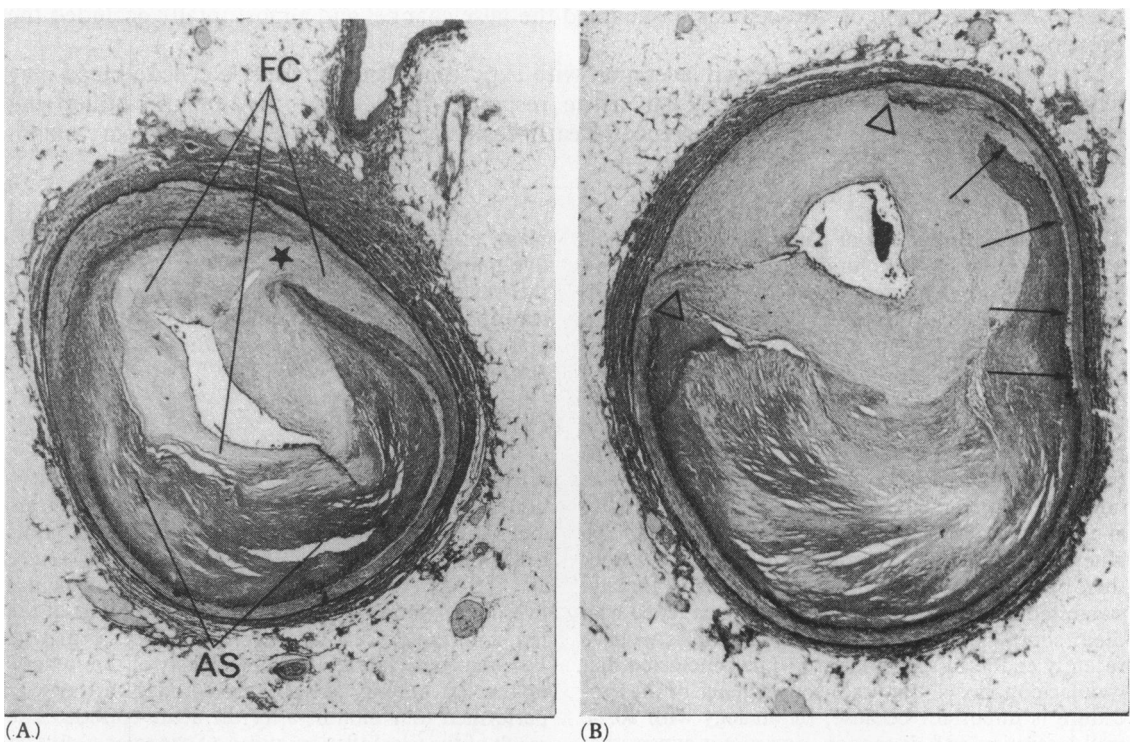

Fig. 2 *Cross-sections through the affected segment of the left anterior descending coronary artery. (A) A disruption of the medial layer (asterisk) is present, which has led to medial dissection. The false channel and the major part of the lumen are filled with fibrocellular tissue (FC). The pre-existent atherosclerotic plaque (AS) is readily identified. (B) A slightly more distal segment of the same artery shows, in addition, dehiscence of the sclerotic plaque from the underlying media (closed arrows). The media shows a localised total interruption (open arrows), with only the outer elastic lamellae and the adventitia left intact.*

the wall abnormality was not appreciated and the procedure was repeated, using a larger calibre Schneider-Grüntzig dilatation catheter DG 20–37. The angiogram which immediately followed the latter procedure showed a distinct dissection (Fig. 1C), but luminal patency was adequate.

The patient was free of complaints for approximately three months, when effort angina recurred. The latter rapidly progressed in severity and a coronary angiogram, four months after angioplasty, showed almost total occlusion of the same segment previously stenosed. At the time a second attempt to dilate the stenosed segment was considered indicated. During the procedure, which was carried out one month later, the patient suddenly developed severe precordial pain with ST segment elevation while the catheter was being positioned; ventricular fibrillation ensued; resuscitation was unsuccessful.

The necropsy showed a severely stenosed and almost totally occluded proximal segment of the left anterior descending coronary artery, corresponding with the stenosed area shown on the angiogram.

Histological sections of the affected artery showed extensive disruption of the media with dissection of the wall, in both proximal and distal directions, and partial absence of the pre-existent muscular layer, giving the artery an expanded diameter (Fig. 2). The initial atherosclerotic plaque was still clearly identified (Fig. 2). The sclerotic lesion, together with fragments of the internal elastic lamina, had become partially detached (Fig. 2). The false lumina were filled with a fibrocellular proliferation, extending over the denuded area where the media was absent. These tissues also covered the atherosclerotic plaque and the lumen was almost totally occluded (Fig. 2). Minor obstructive atherosclerotic lesions were present in the right coronary artery and the left circumflex artery.

The heart showed a healed inferior wall infarct. Histological study of the myocardium disclosed a recent transmural regional anteroseptal infarction corresponding to the area of distribution of the left anterior descending coronary artery.

The necropsy also showed carcinoma of the pancreas with hepatic metastases. There were no signs of general intravascular clotting or non-bacterial thrombotic vegetations.

Discussion

The success of transluminal coronary angioplasty depends on the ability of the inflated balloon to dissect the sclerotic plaque and to expand the media, though the limitations regarding the extent of wall laceration tolerated remain as yet unclear. This uncertainty is clinically relevant since it is well known that laceration of the aortic media and aortic dissection trigger a reparative fibrocellular response that may eventually completely obliterate the false channel and, when evoked in a coronary artery, could easily lead to significant obliteration of the functional lumen, as seen in the present case.

The first inflations of the balloon failed to relieve the obstruction adequately and caused localised wall laceration, which was missed at the time though clearly identified in retrospect. This in itself is important since it is not always easy to recognise wall laceration during the execution of the procedure. The initial trauma was followed by a full blown dissection when a larger sized catheter was advanced and inflated. We re-emphasise the need for extreme caution when readvancing a dilating catheter across a previously acutely dilated segment; repeat inflations in any patient in whom the initial procedure has been unsuccessful may be dangerous. The case also shows that a dissecting haematoma of a coronary artery can be tolerated briefly if anterograde flow is maintained, though late obstruction can be expected.

At histological examination of the left anterior descending coronary artery the severe wall laceration was confirmed. The abrupt disruption of the media with a dissecting aneurysm and the partial detachment of the atherosclerotic plaque from the underlying wall are unequivocally traumatic in origin. The dissection of the atherosclerotic plaque is strikingly similar to the lesions observed in patients who died acutely after coronary angioplasty[10] and those observed after post-mortem procedures[4 8] as well as animal experiments.[5 7] The presence of such a tear in our case thus stresses the point that the luminal patency obtained with angioplasty is probably achieved at the cost of a lacerated plaque. In the present case, however, the procedure had been complicated by a dissecting aneurysm of the media. The histological examination confirmed the traumatic nature of this feature, and also disclosed an exuberant fibrocellular tissue response with almost total occlusion of the lumen. It is of interest, in this respect, that the tissue response is histologically identical to that seen in longstanding cases of dissecting aneurysm of the aorta. The response is probably the result of direct exposure of vascular smooth muscle cells to blood, which triggers the aggregation of platelets and leads to proliferation by the release of a potent growth factor.[11] The histological appearances thus strongly suggest that the complication in our patient was secondary to traumatic dissection of the media. A sclerotic plaque, for its greater part composed of acellular collagen, may be relatively inert in evoking a tissue reaction, though we can conceive that atherosclerotic lesions which still have a fair amount of smooth muscle cells may also produce such a response when exposed.[12] Hence, early restenosis after transluminal

coronary angioplasty may be the result of an exuberant tissue reaction, either because of triggering of cells within a cellular plaque or because of the stimulation of exposed muscle cells of a lacerated media. The fibrocellular proliferation may thus be the pathological substrate of early restenosis in patients who develop recurrence of symptoms within three months after angioplasty. Moreover, since the degree and extent of smooth muscle cell exposure may vary considerably from one case to the other, depending on the nature of the lesion present and the traumatic effect of the procedure performed, the pathogenetic concept could explain why in some patients, but not others, the angioplasty is followed by early restenosis. Additional studies are necessary to evaluate the validity of this concept.

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