Virchows Arch A (1986) 410:195–202

Virchows Archiv A

Percutaneous transluminal coronary angioplasty – Histopathological analysis of nine necropsy cases

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Summary. From 1982 to 1984 nine of 300 patients undergoing transluminal coronary angioplasty died. The nine coronary arteries and one saphenous aorto-coronary by-pass graft affected by angioplasty were studied by light microscopy. The following types of lesions were found, frequently in association: rupture of the plaque, circumscribed or reaching to the intimal layer or extending beyond it, dissections (fissures) between arterial layers, intra-plaque haemorrhage, plaque emboli and thrombosis. In two cases the therapeutic approach was considered to be clinically and pathologically successful; the patients survived 24 h (case 6) and forty days (case 4). Case 6 which presented recent lesions indicative of success showed, in contrast with the other non-successful cases, rupture affecting not only the initimal layer but also deeper structures of the arterial wall. There were also more extensive fissures. Case 4 which presented late alterations indicative of success showed a plaque fracture whose borders were kept apart by fibrous tissue. In conclusion, we believe that angioplasty allows the re-establishment of arterial blood flow by provoking deep intimal and medial rupture producing a small fissure between the arterial layers and a widening of the lumen; in cases with good late results these alterations cicatrize leaving a wider arterial lumen.

Key words: Percutaneous coronary angioplasty – Balloon angioplasty – Coronary atherosclerosis

Introduction

Transluminal coronary angioplasty (TCA) represents a therapeutic approach to atherosclerotic obstruction which is becoming widely used. Initial indecision has given way to a very clear trend to progressive increase in the use of TCA especially in patients with one-artery atherosclerotic obstructive lesions (Dotter and Judkins 1964; Grüntzig et al. 1979; Przybojewski and Weich 1984).

Studies that have analysed the coronary arteries of patients who died after having been submitted to TCA are few (Block et al. 1981; Essed et al. 1983; Waller et al. 1983; Mizuno et al. 1984). However, these studies allowed a deeper evaluation of the possible morphological events that occur in atherosclerotic arteries submitted to balloon dilatation. In this series of papers, and in other clinical ones, possible arterial changes produced following transluminal coronary angioplasty are the smashing of a plaque and rupture of the artery wall up extending to the medial layer.

In our institution, TCA is a therapeutic method that is increasingly utilized. The patients submitted to this method who died, for different reasons, were submitted to complete post-mortem study. We made a clinico-pathological correlation, mainly emphasizing the histological alterations observed in the vessels affected by angioplasty. We contribute here new information on this subject which is not well studied, and reinforce lines of interpretation about the origin of the arterial alterations provoked by the therapeutic procedure.

Material and methods

Among 300 patients submitted to TCA in our institution, from July 1982 to August 1984, nine died and were submitted to complete necropsy. All patients were admitted and treated in the course of an acute myocardial infarct of less than three hours evolution.

The nine coronary arteries and one saphenous aorto-coronary by-pass submitted to TCA were carefully dissected, fixed in 10% formalin, eventually decalcified in formic acid and embedded in paraffin in 0.3 cm segments. Histological sections were stained with hematoxylin-eosin and by Verhoeff van-Gieson methods and examined in order to determine the changes

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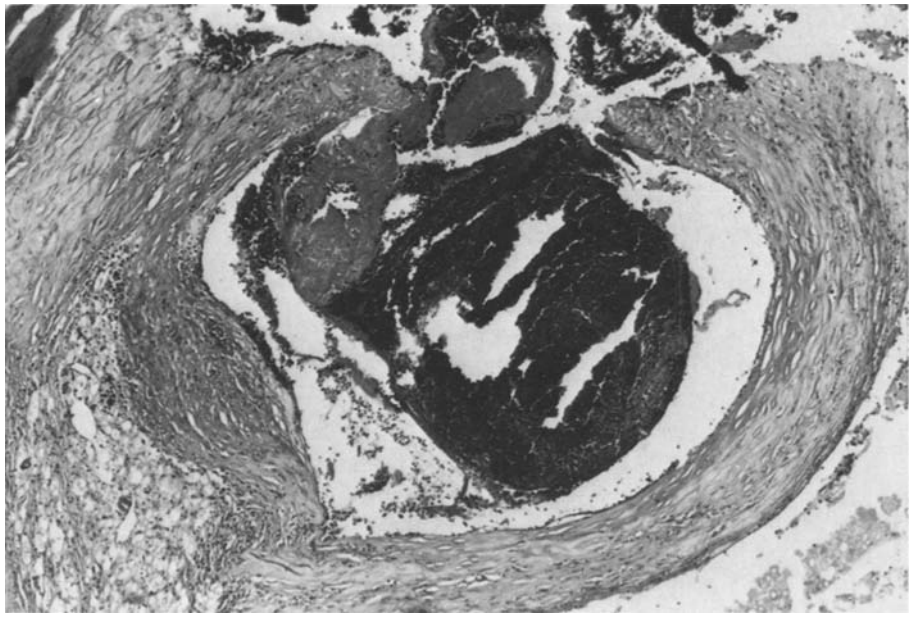

Fig. 1. Segment of the right coronary artery from case 3, submitted to transluminal coronary angioplasty. There is intimal layer rupture with thrombosis. HE × 30

Table 1. Clinical data, results of the T.C.A., time elapsed from T.C.A. to death, cause of the death and explanation for the unsuccess of the 9 cases submitted to T.C.A., W = white; B = black; Y = yellow; T.C.A. = transluminal coronary angioplasty; AMI = acute myocardial infarction; I.L. = inferior and lateral; P.S. = posterior and septal; A.S. = anterior and septal; M.B. = marginal branch

Case No.	Age (years)	Sex	Race	TCA		Death due to	Insuccess due to
				Result	Death after		
1	50	F	W	Unsuccessful	48 h	AMI I.L.	Rupture of the catheter tip, occlusive thrombus
2	66	M	W	Unsuccessful	48 h	AMI P.S.	High grade stenosis, occlusive thrombus
3	57	F	B	Unsuccessful	instantaneous	AMI P.A.	Patient "in extremis", low output, occlusive thrombus
4	56	F	W	*Successful*	40 days	Pulmonary embolism	–
5	69	M	W	Unsuccessful	24 h	AMI A.S.	Insufflation before critical lesion, high grade stenosis
6	54	M	W	*Successful*	24 h	CNS infarction, AMI A.S.	Occlusive thrombus im M.B.
7	52	M	W	Unsuccessful	instantaneous	AMI A.S.	High grade stenosis. No insufflation
8	72	M	Y	Unsuccessful	instantaneous	AMI A.S.	High grade stenosis, intense calcification
9	68	M	W	Unsuccessful	30 days	Bronchopneumonia	High grade stenosis, occlusive thrombus

caused by TCA. Arterial stenosis was measured in histological sections of coronary arteries submitted neither to perfusion-fixation nor to physiological pressure techniques. The histological assessment was by cross sectional area based on lumen and vessel radii. Results were given in four ranges of percentages: 0–25%, 26–50%; 51–75%; 76–100%. The miocardium was examined in slices of approximately 2,0 cm wide, generally with the utilization of nitro-blue tetrazolium reagent for determining recently infarcted areas.

Results

The general clinical data, results of the TCA, time elapsed from angioplasty to death, the cause of death and explanation for the death are exposed in Table 1.

Re-establishment of the coronary circulation with cessation of cardiac symptoms was obtained

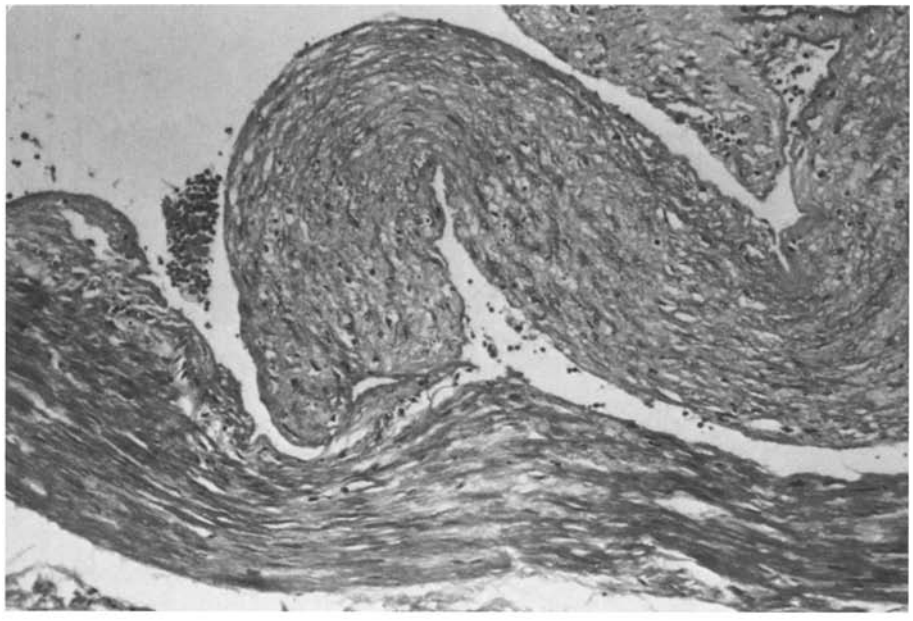

Fig. 2. Case 2 showing in detail plaque rupture and intimal-medial dissection (fissure). HE ×190

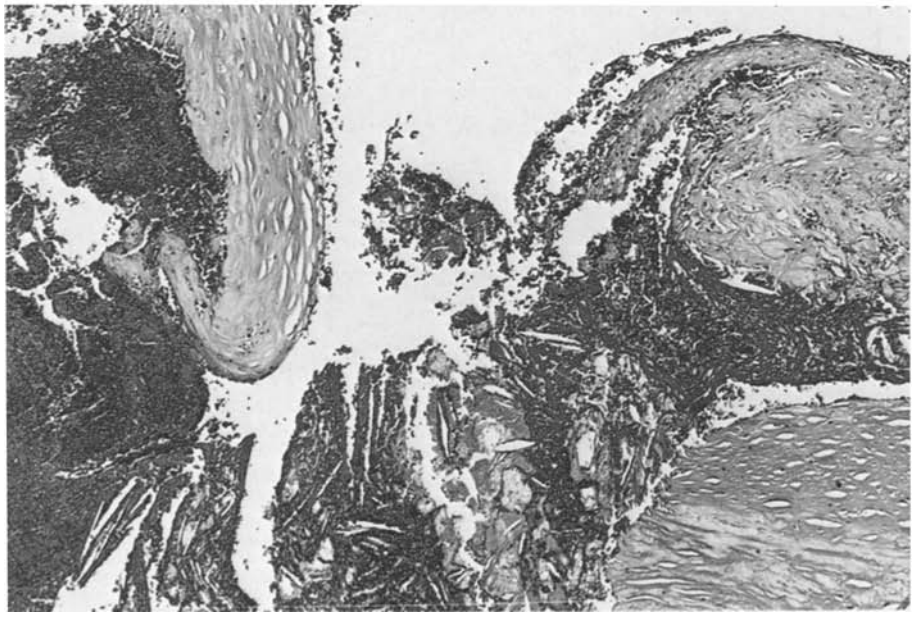

Fig. 3. Segment of right coronary artery from case 2 showing intimal layer rupture, plaque hemorrhage and desquamation of atheroma constituents. HE ×120

in only two of these patients. They died due to causes not related to the angioplasty itself, e.g. pulmonary embolism 40 days after TCA (case 4) and CNS infarct associated with acute myocardial infarct 24 h after TCA (case 6).

In the remaining cases this therapeutic procedure did not work mainly due to occlusive thrombosis (5 cases) and/or plaques that were considered to be too big and too hard (5 cases) (Table 1).

Histological findings are gathered on Table 2. The following types of lesions were found among the cases, frequently in association; rupture of the plaque circumscribed to the intimal layer or extending beyond it (Fig. 1–4), fissures between arterial layers (Figs. 2 and 4), intra-plaque haemorrhage, plaque emboli (Fig. 3) and thrombosis (Fig. 1). It should be stressed that case 7 had an intimal layer rupture caused by the introduction of the balloon only, since this was not insufflated.

The case with re-establishment of the coronary flow and death 24 h after TCA (case 6) showed rupture affecting not only intimal layer but also more than half of thickness of medial layer, together with more extensive fissures (Fig. 4); haemor-

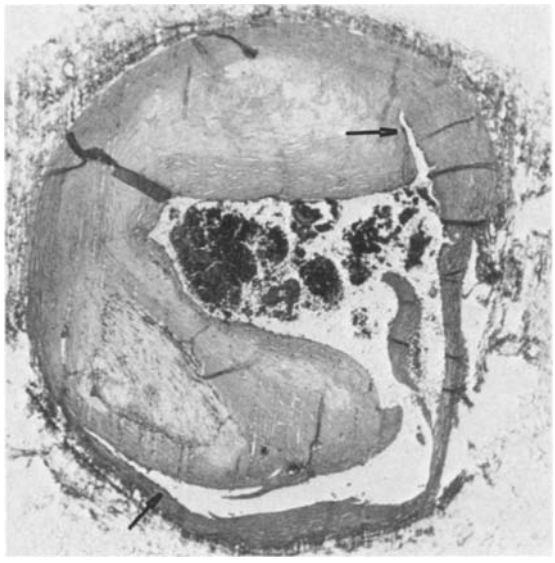

Fig. 4. Anterior descending artery from case 6. There is rupture affecting intimal layer and deeper structures of the arterial wall, with fissure formation. Red blood cells and fibrin can be seen lining the edges of the ruptured plaque as dark spots (*arrows*). HE ×12

rhage into adventitia was not found. The patient was admitted with a 100% obstruction seen by cine angiographic study, affecting the initial segments of the descending anterior artery; after streptokinase infusion the lumen showed an obstruction of 90% and after transluminal coronary angioplasty the obstruction fell to 10%. Pressure gradient before and after angioplasty was 82 and 4 mmHg, respectively.

The case of angioplasty with re-establishment of the coronary flow and death 40 days later (case 4) was found to have a cicatricial lesion in a region interpreted as previously affected by the angioplasty (Fig. 5). This picture was considered to be resolution of an acute lesion like that present in case 6. The borders of the ruptured plaque were kept apart allowing lumen widening; no evidence of haemorrhage into adventitia was found. The patient was admitted with a total obstruction of the initial segment of the anterior descending artery shown by the cineangiographic study; after introduction of streptokinase there was a stenosis

Table 2. Histopathological findings in the segments of the nine vessels submitted to T.C.A. LAD = left anterior descending artery; M.B. = marginal branch; R.C. = right coronary artery; A = adventitial layer; I = intimal layer; M = medial layer; T.C.A. = transluminal coronary angioplasty

Case No.	Vessel	Segment of the vessel submitted to TCA								
		Intimal rupture	Medial rupture	Fissure				Morphology of the plaque	% of arterial stenosis[e]	Complications
				I–I	I–M	M–M	M–A			
1	Saphenous graft	+	–	+	–	–	–	–	A	Occlusive thrombus
2	RC	+	–	+	+	–	–	"Mixed"[a]	D	Plaque haemorrhage Plaque embolus Occlusive thrombus
3	RC	+	–	+	–	–	–	LP[c]	D	Plaque embolus Occlusive thrombus
4	LAD	+	+	–	–	–	–	FP[b]	C	Plaque hemorrhage
5	LAD	–	–	–	–	–	–	FP[d] Calcified	D	–
6	MB	+	+	+	+	+	–	"Mixed"	C	Occlusive thrombus
	LAD	+	+	–	+	+	+	"Mixed"	C	Small thrombus
7	LAD	+	–	–	–	–	–	FP	D	Plaque embolus Small thrombus
8	RC	+	–	+	+	–	–	FP Calcified	D	Plaque haemorrhage
9	RC	+	–	+	–	–	–	FP	D	Plaque haemorrhage Plaque embolus Occlusive thrombus

[a] Plaque in which the "lipid component" was in similar proportion to the "Fibrous and muscular components".
[b] Mainly "Fibrous plaque".
[c] Mainly "Lipid plaque".
[d] Calcified means intense calcification.
[e] Post-mortem assessment: A 0–25%; B 26–50%; C 51–75%; D 76–100%

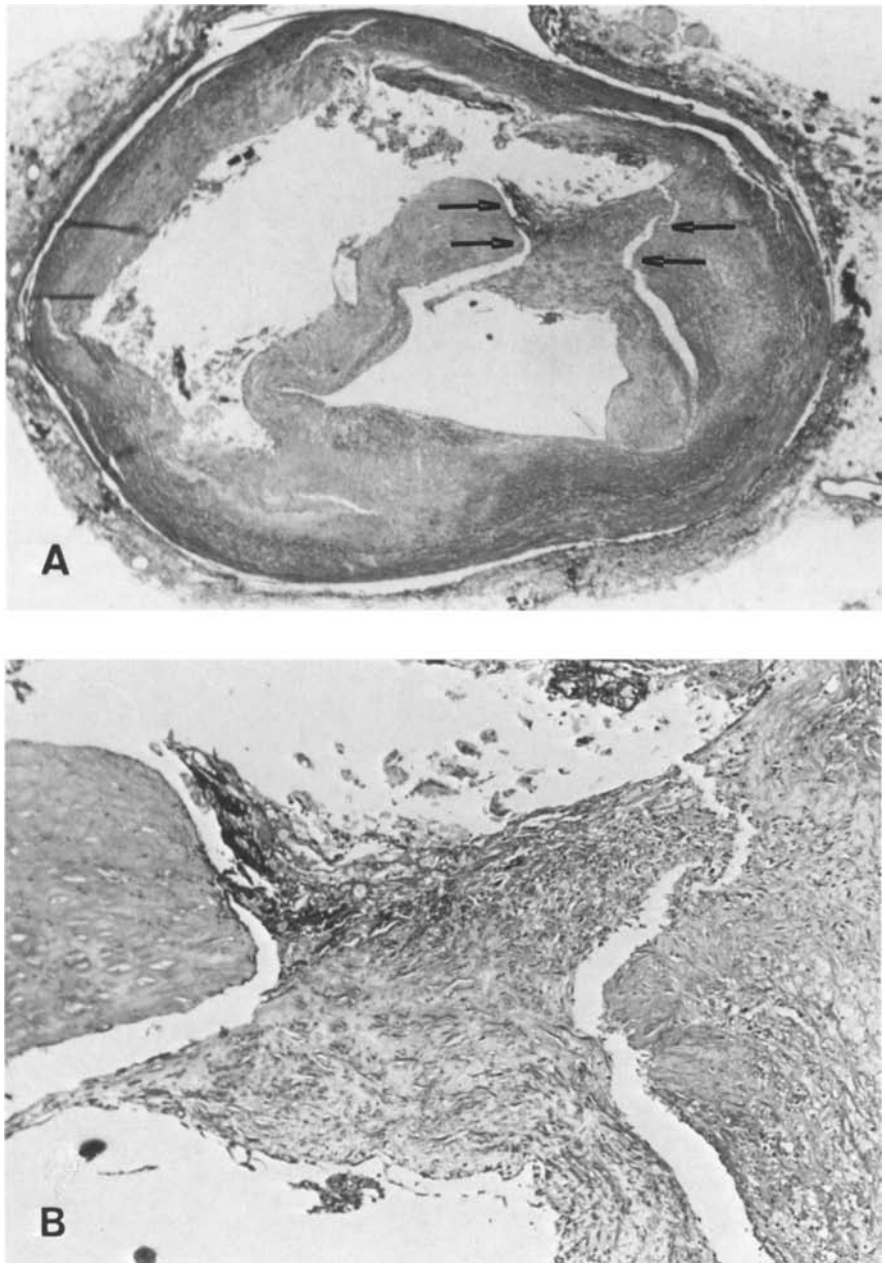

Fig. 5A–D. Anterior descending coronary artery from case 4.
A The atherosclerotic plaque was ruptured and the borders (arrows) kept apart by cicatricial tissue, HE ×12.
B Shows in detail the area of repair of the rupture, HE ×120.

of 90% reduced to 20% after angioplasty; the pressure gradient before and after angioplasty was 37 and 10 mmHg, respectively. One month later the cineangiographic study showed the same degree of obstruction seen after TCA associated with uneveness of the internal profile at the site of angioplasty.

Among the arteries submitted to the angioplasty and without re-establishment of flow, we found lesions in all but one (case 5) where the balloon was not insufflated at the site of lesion. In the remaining cases plaque rupture occured constantly and, in two of them (cases 2 and 8) this feature, extended to the medial layer, with formation of a fissure but without medial rupture (Fig. 2). However, in these cases either occlusive thrombosis occured or the plaques were too big, too hard and did not show enough separation of their borders, preventing a successful angioplasty.

Seven out of the nine patients showed acute myocardial infarction; these were extensive and transmural; four were haemorrhagic.

Compression or remodelling of the plaques were not found; the elastic fibers of the arterial

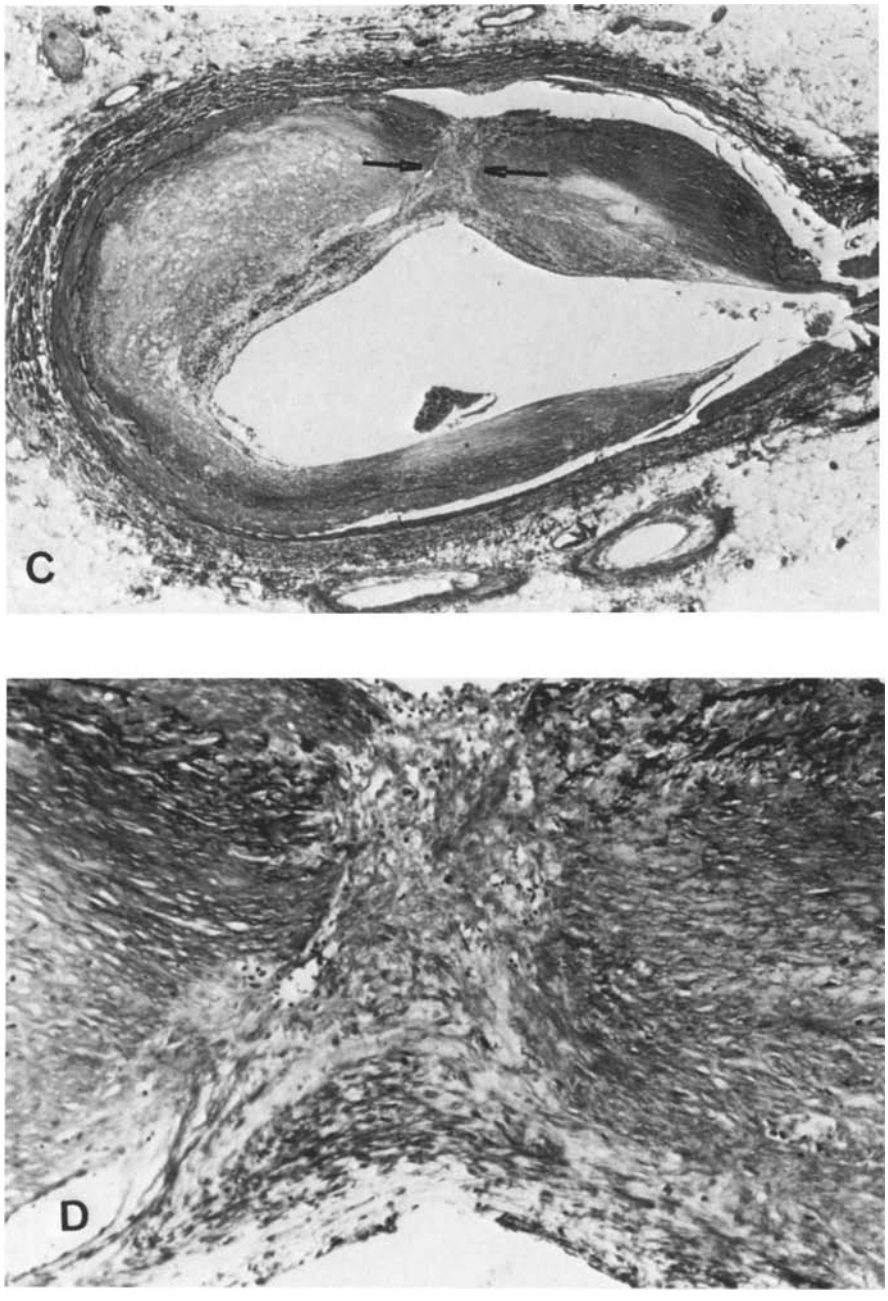

Fig. 5.
In C is shown another level of the artery with plaque rupture and repair by fibrous tissue, HE ×12. **D** is a detail of such lesion, HE ×190. Fissures found in these figures are artefactual since neither red blood cells nor fibrin could be found lining the edges of the ruptured plaque

medial layer did not show signs of distension; there were neither aneurysms nor histological lesions away from the site of the angioplasty.

Plaques at the site of angioplasty were classified as mixed (M) when the "lipid component" was in roughly similar proportion to the "fibrous and muscular components" and as mainly "fibrous" (F) or mainly "lipid" (L). Three arteries were found to have M plaques, five arteries F plaques and only one artery L plaques. The degree of calcification was variable, being intense in two arteries, contributing to the lack of success of the angioplasty.

Discussion

The exact mechanism of angioplasty is not clear. The mechanisms proposed include: plaque compression (Dotter and Judkins 1964; Grüntzig 1977), intimal fractures and plaque rupture (Freudenberg et al. 1978), minimal disruption of the endothelial layer and plaque compression (Lee et al.

1980), disruption and dissection of the atheromatous plaque with desquamation of its elements (Block et al. 1980), intimal fracture, intimal-medial separation and stretching of the medial layer (Castaneda-Zuniga et al. 1980; Baughman et al. 1981; Hoffman et al. 1981), stretching and rupture of the intimal and medial layers (Mizuno et al. 1984; Castaneda-Zuniga et al. 1981) or intimal and medial fractures with hyperdistension of the medial layer elastic fibers (Schmidt-Moritz et al. 1982).

We believe that the morphological findings of our cases are useful in understanding the mechanisms involved in angioplasty. When we consider the histopathological alterations found, we conclude that plaque rupture was a common finding in all recent angioplasty cases. This rupture, of a variable extent affected not only the intima, but also – and specially – the medial layer almost completely (no haemorrhage into adventitia was found) with formation of fissures permitting the widening of the vascular lumen.

Our supposition was reinforced by case 4, which survived 40 days after angioplasty. The finding of a cicatricial lesion affecting the intimal and medial layers of the artery, permitted us to infer that it resulted from the acute intimal-medial process of rupture and fissure.

We did not find histopathological alterations supporting mechanisms like compression or remodelling of the plaque (Waller et al. 1983; Grüntzig 1977) or hyperdistension of the medial layer (Castaneda-Zuniga et al. 1980; Castaneda-Zuniga et al. 1981; Schmidt-Moritz et al. 1982).

Among the complications found, we wish to stress the role of thrombi since they play an important role in most of the unsuccessful cases. Intraplaque haemorrhage was discrete and probably not important in the evolution of the cases since it was observed even in case 6, as an old area of haemorrhage.

The relation of the plaque morphology to the final result of the angioplasty was apparently a controversial matter among our cases, since one successful case (number 4) had a F slightly calcified plaque (theoretically of difficult resolution) (Grüntzig et al. 1979; Block et al. 1981) and unsuccesful cases had L and M non-calcified plaques (easy resolution plaques). However, what must be taken into consideration together with plaque morphology is, of course the degree of the stenosis.

Case 4 deserves special attention since, as far we know, is the first reported where the prolonged evolution of a successful angioplasty has been studied histopathologically. The human cases with prolonged evolution reported hitherto were three patients with 80, 90 and 150 days of evolution (Waller et al. 1983) who, however, did not show lesions at the microscopical level and one case with histopathological alterations apparently due to the complications of the angioplasty (Essed et al. 1983).

Hence, we believe that angioplasty allows reestablishment of arterial blood flow by provoking a relatively deep intimal and medial rupture almost up to the adventitia with a small fissure between the arterial layers; so that acute widening of vascular lumen occured in vessel segments without high grade stenosis. In cases with good clinical results, these alterations cicatrize leaving a wider lumen. Moreover, we also believe that the mechanism of action of the angioplasty is not simply the smashing of the plaque. Furthermore, as was evident in some cases, the rupture of the atherosclerotic plaque resulted in exit and embolization of the central core of the plaque, diminishing its volume, thus contributing to the lumen widening, as has been previously reported (Block et al. 1982).

In conclusion, from the data we gathered it appears that intimal-medial rupture with small fissure formation is the characteristic lesion of angioplasty. Intimal rupture with or without a small area of fissure, may be provoked simply by the passage of the catheter.

Acknowledgements. We sincerely thank Ivany Tavares da Silva and Edgard Augusto Lopes Filho for the photographic work, and Renatha da Silva Pinto for secretarial work.

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Accepted August 31, 1986