Ruptured Atheromatous Plaques in Saphenous Vein Coronary Artery Bypass Grafts: A Mechanism of Acute, Thrombotic, Late Graft Occlusion

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SUMMARY    Although early occlusion of saphenous vein coronary artery bypass grafts is usually thrombotic, late occlusion is most often a result of progressive intimal fibromuscular proliferation or atheromatous formation in the implanted vein. We describe another mechanism of late graft occlusion: atheromatous plaque rupture with superimposed occlusive thrombosis. Four men, ages 48-67 years underwent repeat bypass surgery for recurrent angina. Six of eight vein grafts excised 5-8 years after original bypass showed complete luminal occlusion by recent thrombus superimposed on ruptured atheromatous plaques. Similar findings were present at autopsy in two of three vein grafts from a 66-year-old man who died 7 years after bypass. These lesions are indistinguishable from those that occur in native coronary arteries of many patients with acute myocardial infarction. Unlike previously described graft occlusions, the present lesion represents a mechanism of acute, thrombotic, late graft occlusion. If recognized early, it may be amenable to nonsurgical intervention by angioplasty or thrombolysis.

SAPHENOUS VEIN aortocoronary artery bypass grafts may undergo a variety of morphologic changes that lead to graft occlusion.1,4 Early graft occlusion is usually caused by technical factors6-9 or compromised anatomic runoff10-12 and is almost always thrombotic.11 In contrast, late graft occlusion is usually a result of structural changes within the graft itself and is not usually associated with occlusive thrombosis.10-14 Progressive fibrous or fibromuscular intimal proliferation10, 11, 14-16 and, less frequently, atheromatous plaque formation,10, 10, 10-18 are the most common pathologic changes found in grafts that become occluded late after coronary artery bypass surgery. Recurrent symptoms of myocardial ischemia sometimes necessitate revascularization.10-21

Excision of occluded grafts at reoperation has enabled us to study the pathologic changes responsible for acute late graft occlusion. In this communication we describe a lesion that has not been previously emphasized in saphenous vein grafts, although it is well recognized in native coronary arteries: atheromatous plaque rupture with superimposed occlusive thrombosis. This lesion, which we observed in five patients, represents a mechanism of graft occlusion that appears to occur as an acute event late after coronary artery bypass grafting. This lesion may be amenable to nonsurgical correction by percutaneous, intravascular, thrombolytic22, 23 or angioplastic techniques.24

Patients

Patient 1    RW, a 53-year-old, obese, hypertensive male, presented with recurrent angina pectoris 5 years after saphenous vein coronary artery bypass. Angiography showed occlusion of grafts to the left anterior descending and the circumflex coronary arteries. At reoperation, new vein grafts were placed. The occluded grafts were excised and submitted for pathologic examination.

Histologic sections of the vein graft to the left circumflex coronary artery showed complete luminal occlusion by recent thrombus superimposed on a ruptured atheromatous plaque (fig. 1). Thrombotic and atheromatous material were mixed. Although the plaque was composed primarily of fibrous tissue, numerous lipid-laden cells, cholesterol clefts, chronic inflammatory cells and focal calcifications were present. The media was focally fibrotic and thinned. These findings are indistinguishable from atherosclerotic plaques that occur in native arteries. In some areas, the atheromatous material extended from intima to adventitia. Some regions showed a marked inflammatory reaction to the lipid, including foreign body giant cells. Adventitial fibrosis was also present.

Histologic examination of the graft to the left anterior descending coronary artery also showed marked luminal occlusion. In this vessel, however, a small focal thrombus was superimposed on a markedly fibrotic, thickened intima. Atheroma with lipid-laden cells and calcification was present in only a small region of the graft. Medial and adventitial fibrosis was marked.

Patient 2    JL, a 67-year-old, obese, hypertensive male with a history of heavy smoking, presented for evaluation of recurrent refractory angina pectoris 8 years after bypass surgery. Angiography showed occlusion of the
showed increased collagen and decreased smooth muscle content. Thus, this lesion was morphologically identical to atherosclerosis that occurs in native arteries. Previous rupture of the vein graft (fig. 2C) through a discontinuity in the media had resulted in extravasation of atheromatous material into the perivascular soft tissue. A marked granulomatous and chronic inflammatory response was localized to the saphenous vein graft to the left anterior descending coronary artery. At reoperation a 3.5-cm segment from the proximal portion of the occluded graft was excised. The patent graft to the right coronary artery was not disturbed, but an additional saphenous vein graft to the left circumflex coronary artery was placed.

Histologic examination of the excised saphenous vein graft showed complete luminal occlusion by thrombus, which was mixed with material from an underlying circumferential atheromatous plaque (fig. 2A and B). The plaque was composed of collagen, elastic tissue, calcium deposits, lipid-laden and inflammatory cells and cholesterol clefts. The thinned media

**FIGURE 2.** Saphenous vein graft to left anterior descending coronary artery from patient 2. (A) Histologic section from occluded segment of graft shows hemorrhage into atheroma (A), disruption of fibrous cap (between asterisks), and thrombotic occlusion of residual lumen (L). Atheromatous material (lighter staining) and hemorrhage (darker staining) are present deep in the vessel wall (arrows). Masson trichrome stain; original magnification × 3. Inset shows admixture of atheromatous (lighter) and thrombotic (darker) material evident on cut section of the graft. (B) Higher magnification shows disruption of plaque (between asterisks). Cholesterol clefts are present in the atheroma and in the defect. Atheromatous plaque (A) contains a mixture of darker-staining blood and lighter-staining atheromatous material. Some atheromatous material has entered the lumen (L), which also contains thrombus. Masson trichrome stain; original magnification × 16. (C) Histologic section showing rupture of atheromatous material through vessel wall (between asterisks) with confinement only by a thin layer of adventitial collagen (A). Masson trichrome stain; original magnification × 16.
rupture site. There was diffuse adventitial fibrosis; this fibrosis may have prevented severe hemorrhage.

Patient 3
M.R., a 48-year-old, hypertriglyceridemic, hypercholesterolemic male with a 50-pack-year history of cigarette smoking, was admitted for evaluation of rest angina 5 years after saphenous vein grafts had been placed to the left circumflex—marginal and right coronary arteries. Angiography showed complete occlusion of both grafts. He underwent reoperation for placement of new grafts and excision of the occluded grafts.

Pathologic examination of the resected graft to the right coronary artery showed complete luminal occlusion by relatively dense collagenous tissue. Multiple recanalized channels were present. No lipid or calcium deposits were present. The findings suggested recanalization and organization of an old thrombus.

The graft to the circumflex system was occluded by thrombotic material superimposed on and mixed with atheromatous material from an underlying ruptured atheromatous plaque that contained collagen, calcium deposits, chronic inflammatory cells, lipid-laden cells and cholesterol clefts (fig. 3). There was marked focal thinning, fibrosis and chronic inflammation of the media as well as adventitial fibrosis.

Patient 4
L.M., a 65-year-old male with a history of heavy smoking and myocardial infarction, presented with severe angina 7 years after coronary artery bypass surgery. Angiography showed complete occlusion of saphenous vein grafts to the right, left circumflex, and a diagonal branch of the left anterior descending coronary arteries. At reoperation, segments of the grafts were excised for pathologic study.

All three grafts showed similar histologic findings. There was complete luminal occlusion by thrombus superimposed on ruptured atheromatous plaques (fig. 4). Atheromatous material was mixed with thrombotic material. The atheromatous plaques contained collagen, elastic tissue, foam cells, cholesterol clefts and a chronic inflammatory cell infiltrate. The latter was presumably a reaction to the lipids released from the plaque. Each vessel showed focal disruption of the thinned and fibrotic media with spillage of atheromatous material into the adventitial tissues. A foreign body giant cell granulomatous reaction surrounded the lipid material, which had extravasated outside the vessel. There was also diffuse adventitial fibrosis.

Patient 5
B.L., a 66-year-old, obese, hypertensive, diabetic smoker, was admitted with sudden onset of severe angina and myocardial infarction 7 years after three-vessel saphenous vein coronary artery bypass surgery. He died 1 week after admission. At autopsy, ruptured atheromatous plaques with thrombosis identical to those described in the other four patients were present in the occluded grafts to the left anterior descending and left circumflex coronary arteries (fig. 5).

Discussion
In 1906, Carrell and Guthrie described the intimal changes that lead to luminal narrowing in veins implanted within the arterial system. Subsequent light and electron microscopic studies have demonstrated that the usual intimal proliferation noted consists of collagen fibers, elastic fibers and ground substance synthesized by smooth muscle cells that have migrated from the media. These substances are present in varying amounts, depending on several factors, including the duration of implantation. Fibrin deposition, inflammatory cell infiltration and proliferation of small vessels have also been observed. The intimal lesions in some grafts are indistinguishable from the atheromatous plaques of arterial atherosclerosis. Although the factors that lead to progressive intimal proliferation with or without
atheroma formation are unclear, the same factors that influence naturally occurring atherogenesis are probably important in saphenous vein grafts as well (e.g., age, hypertension, hyperlipidemia, and diabetes).

Eight of 11 grafts in the patients of this study were occluded by thrombus superimposed on ruptured atheromatous plaques. These lesions are histologically identical to those described in coronary arteries as the precipitating event in acute transmural infarction. The thrombosis is thought to result when plaque disruption (endothelial injury) leads to the release of thrombogenic substances from the plaque. As with rupture of native coronary artery plaques, the cause of rupture of saphenous vein bypass graft plaques is uncertain. In three of five patients, rupture of plaques with thrombosis occurred synchronously in two or more vessels, suggesting that the process was not due only to local factors within the graft, but to some unknown predisposing factor common to all the vein grafts in these patients. In six of the 11 grafts, the atheromatous plaques had destroyed the media and extended into the adventitia, focally eliciting an inflammatory response that included foreign body giant cell formation and fibrosis. Preexistent adventitial fibrosis, common to all implanted vein grafts, may have prevented hemorrhage and exsanguination through such a rupture.

This striking morphologic alteration has not been emphasized previously, although many implanted saphenous veins have been studied at necropsy. Most of these grafts were probably studied long after acute thrombosis had occurred. Few vein grafts are excised by surgeons and examined by pathologists at revascularization procedures, and probably even fewer are excised soon after a sudden deterioration in a patient’s condition.

Even if this lesion occurs infrequently, it is of practical importance because it represents a mechanism of acute, late, cardiovascular deterioration after a long, sometimes symptom-free, postoperative period. Prompt intervention may prevent myocardial injury. The recognition of late thrombotic atherosclerotic graft occlusion may allow appropriate nonsurgical intervention to reopen the acutely occluded vessel by thrombolytic therapy, or increase luminal patency by angioplasty therapy. Intravascular thrombolytic therapy and transluminal angioplasty have been used to treat coronary arterial narrowing and, in a few cases, early thrombotic vein graft occlusion.

Addendum

Since recognition of this lesion and submission of the manuscript, surgeons at our institution have more regularly excised occluded coronary grafts. As a result, we have studied seven additional aorto-coronary saphenous vein bypass grafts that showed similar lesions. Six such grafts were excised from men 45–74 years old and one was excised from a 71-year-old woman. The occlusions occurred 5–9 years after bypass. In addition, Kern and associates recently provided additional documentation of this lesion.

References

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