Comparison of Histopathologic Coronary Lesions Obtained from Directional Atherectomy in Stable Angina Versus Acute Coronary Syndromes

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The transition of coronary lesions from the stable to unstable state is the pathophysiologic mechanism underlying myocardial infarction and unstable angina pectoris. Angiographic, angioscopic and postmortem pathologic studies suggest that this transition is mainly due to atherosclerotic plaque fissuring and associated thrombus formation.1,2 The present study examines the histopathologic characteristics of the "culprit lesion" obtained during directional coronary atherectomy of patients with acute coronary syndromes. Directional atherectomy provides a unique opportunity for studying the composition of unstable lesions in living symptomatic patients.

Case histories of consecutive patients referred to the University of Michigan Medical Center for directional coronary atherectomy after May 1, 1989 were analyzed. All patients selected for inclusion in this study had angina, objective evidence of myocardial ischemia and cineangiograms showing ≥1 lesion with >50% diameter stenosis of an epicardial coronary artery. The unstable group comprised patients who had experienced ischemic pain at rest accompanied by transient ST-T changes on the electrocardiogram, or acute myocardial infarction during the 2-week period preceding directional atherectomy. The stable group comprised patients who had not had ischemic pain at rest, progressive angina, recent-onset angina or acute myocardial infarction during the 3-month period preceding directional atherectomy.

Directional atherectomy was performed as described previously.3 The atherectomy device (Devices for Vascular Intervention Inc., Redwood City, California) consists of a cylindrical metal housing, with a window opening of a 0.014-inch guide wire through a special housing. The device was advanced to the coronary artery. The unstable region was defined when it contained loose cellular tissue and associated hemorrhage.

Histopathologic analysis of the atherectomy specimen was performed as previously described.4 Briefly, immediately after removal from the atherectomy device, the specimens were fixed, processed routinely and stained with either hematoxylin-eosin or Verhoeff-Van Gieson elastic tissue stain.

The histologic sections were analyzed at a remote pathology core laboratory by an experienced cardiac pathologist (CCH) unaware of the clinical details. The slides were positioned on the stage of a projection light microscope, and the image was projected onto a digitizing tablet (MOP, Carl Zeiss Instr, Germany). Each different tissue component was outlined, measured (µ²) and expressed as a percentage of the total atherosclerotic plaque area.

The different tissue components were defined as follows: Media was characterized by parallel arrangement of smooth muscle cells, located between the elastic lamina. Adventitia was characterized by thick bundles of dense collagen with few interspersed elastin fibers, located exterior to the external elastic lamina.

Atherosclerotic lesion was defined as containing ≥1 of the following components: Atheromatous tissue was defined by extracellular cholesterol crystals and foam cells. Atheromatous tissue often contained necrotic regions and amorphous extracellular matrix. Fibrocellular tissue was characterized by heavy collagen and elastin fiber matrix with scant cellularity. Fibrocellular tissue was defined when the fibrous matrix contained abundant cellularity. The cells consisted of macrophages and spindle shaped cells resembling smooth muscle cells, myofibroblasts and fibroblasts. Organized thrombus was defined when it contained loose cellular tissue in myxomatous stroma with fibrin remnants, occasional platelet aggregates or collagen fibers. The specimens were examined for evidence of plaque fissuring, with or without organized thrombus, and underlying myocardial infarction and unstable angina.

<table>
<thead>
<tr>
<th>TABLE I Patient Characteristics</th>
<th>Unstable (n = 44)</th>
<th>Stable (n = 55)</th>
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</thead>
<tbody>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
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<tr>
<td>Age (years)</td>
<td>60 ± 12</td>
<td>58 ± 12</td>
</tr>
<tr>
<td>Men</td>
<td>29 (66%)</td>
<td>41 (74%)</td>
</tr>
<tr>
<td>Positive family history</td>
<td>23 (52%)</td>
<td>37 (68%)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>21 (48%)</td>
<td>26 (47%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>25 (57%)</td>
<td>37 (68%)</td>
</tr>
<tr>
<td>Severe hypertension</td>
<td>16 (35%)</td>
<td>25 (45%)</td>
</tr>
<tr>
<td>History of diabetes mellitus</td>
<td>4 (9%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>History of PTCI</td>
<td>13 (29%)</td>
<td>12 (22%)</td>
</tr>
<tr>
<td>History of MI</td>
<td>2 (4%)</td>
<td>20 (36%)</td>
</tr>
<tr>
<td><strong>Angiographic</strong></td>
<td></td>
<td></td>
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<tr>
<td>Severity of culprit lesion (% stenosis)</td>
<td>74 ± 13</td>
<td>78 ± 12</td>
</tr>
<tr>
<td>1-vessel disease</td>
<td>27 (61%)</td>
<td>28 (53%)</td>
</tr>
<tr>
<td>2-vessel disease</td>
<td>9 (20%)</td>
<td>15 (27%)</td>
</tr>
<tr>
<td>3-vessel disease</td>
<td>11 (25%)</td>
<td>11 (20%)</td>
</tr>
</tbody>
</table>

No differences were significant (p < 0.05) between patients with unstable and stable angina, except history of myocardial infarction (MI) (p = 0.002).

PTCA = percutaneous transluminal coronary angioplasty.
red blood cells and ingrowing capillaries. Fresh thrombus was characterized and distinguished from thrombus formed during the procedure by its layered organization, aggregates of platelets, fibrin and erythrocytes. When it occupied ≥3000 μ², it was coded as large thrombus.

The frequency of the clinical characteristics, and the histologic evidence of large fresh thrombi were compared in the unstable and stable groups by analyzing contingency table data with the use of chi-square analysis. An unpaired Student’s t test was used to compare the area of each histologic component in the 2 groups. Data were expressed as mean ± 1 SD. A p value <0.05 was considered significant.

One hundred four lesions from 99 patients were studied. The unstable and stable groups were comparable in their clinical and demographic features, except, as expected, for history of acute myocardial infarction, which was more frequent in the unstable group (Table I).

The unstable and stable groups had a similar extent of coronary artery disease (45 and 47% multivessel disease, respectively; p = NS), and severity of the culprit lesions (74 ± 13% and 78 ± 12% stenosis, respectively; p = NS).

The composition of the excised coronary lesion specimens was mainly fibrous tissue (75 ± 25% vs 76 ± 23% area, p = NS). However, lesions excised from the unstable group had a higher frequency of large thrombi (≥3000 μ²) (44 vs 17%; p = 0.02) (Figure 1), and a higher degree of cellularity, expressed as a larger area of fibrocellular component (40 ± 28% vs 29 ± 23% area; p = 0.02) and as a smaller area of fibrosclerotic component (35 ± 22% vs 48 ± 25% area; p = 0.009) (Figure 2).

This is the first study to describe the histopathologic characteristics of coronary lesions in living patients presenting with acute coronary syndrome. Up to the present, the lesion histopathology in acute coronary syndromes was studied in selected populations of patients who died after acute myocardial infarction or unstable angina.1,2,5

Histopathologic analysis showed that coronary lesions, regardless of the clinical presentation, consist primarily of fibrous tissue (75% of the area). Atheromatous material was only a minor component in the composition of atherosclerotic plaques. Similar to the present findings, Kragel et al6 have found, in a quantitative histologic analysis of patients who died of acute myocardial infarction or sudden cardiac death, that fibrous tissue occupied 81% of the area of unstable plaques.

We found that lesions in patients with acute coronary syndrome are associated with large fresh thrombi. The findings are consistent with the data of other investigators, using angiography and pathologic findings, showing an association between unstable lesions and fresh thrombus.1,2,6,7 We found that a relatively high prevalence of large fresh thrombus accompanied the presence of clinical stability (17%). Other investigators have observed this phenomenon while using angiography7 and in postmortem studies.15,16 Thrombus deposition and organization may be an important element in the development of atherosclerotic plaques in humans.8 These observations, together with the observed histologic continuum between organizing thrombus and fibrocellular tissue,9 suggest that the clinically significant fibrous lesions may represent the progression of early lipid-rich lesions that had undergone repeated, in some cases silent, episodes of thrombosis and thrombus organization.8

The data indicate that unstable lesions have a higher degree of cellularity, suggesting that lesions with clinical evidence of recent instability undergo a proliferative phase. Tracy et al9 found a greater degree of cellularity in unstable than in stable plaques in the same patients. Immunohistochemistry of atherosclerotic plaques showed the highest proliferation rate in plaques associated with acute thrombosis.11 Several components of the fresh
Alleviation of Cocaine-Induced Coronary Vasoconstriction with Intravenous Verapamil

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Cocaine use has been associated with a number of cardiovascular complications, including angina pectoris, myocardial infarction and sudden cardiac death. Previous studies in humans have shown that cocaine causes epicardial coronary vasoconstriction, which is mediated, at least in part, by α-adrenergic stimulation. Studies in experimental animals have suggested that cocaine may also cause vasoconstriction by altering calcium transport in vascular smooth muscle, and this can be attenuated by calcium channel blockade. The present study was performed to assess the effect of verapamil, a calcium antagonist, on cocaine-induced coronary vasoconstriction in humans.

Fifteen patients (6 men and 9 women, aged 39 to 65 years) undergoing cardiac catheterization for the evaluation of chest pain were studied. None had a history of prior cocaine use. The protocol was approved by the Human Subjects Review Committee of the University of Texas Southwestern Medical Center, and all patients gave written informed consent. All participants were studied in the fasting state after receiving 5 to 10 mg of oral diazepam. Antianginal medications were discontinued >12 hours before study.

An arterial sheath was placed percutaneously in the femoral artery, through which an 8Fr Judkins catheter was advanced to the left coronary artery. Systemic arterial pressure was measured through the catheter, and heart rate was determined by electrocardiographic monitoring. At baseline, systemic arterial pressure and heart rate were measured, and cineangiography of the left coronary artery was performed in orthogonal (right anterior oblique caudal and cranial) projections. Each subject then received topical, intranasal cocaine, 2 mg/kg. Fifteen minutes later, blood pressure and heart rate measurements and left coronary cineangiography were repeated, and a blood sample was obtained for determination of cocaine concentration by gas chromatography. Immediately thereafter, patients were randomized to receive (1) intravenous saline (group 1; n = 5) or (2) intravenous verapamil, 10 mg over 2 minutes (group 2; n = 10). Three minutes later, heart rate

References: