C-Reactive Protein in Patients With Acute Myocardial Infarction

To the Editor:
Sano et al. investigated the relation between lesion morphology as seen under preintervention intravascular ultrasound and C-reactive protein (CRP) in the acute phase of acute myocardial infarction (AMI). They found that elevated CRP concentrations may be related to the presence of ruptured plaque and concluded that in the setting of AMI, elevated CRP levels may reflect the inflammatory activity of a ruptured plaque.

The presence of inflammatory infiltrates in unstable coronary plaques suggests that inflammatory processes may contribute to the pathogenesis of acute coronary syndromes. In patients with acute coronary syndromes, coronary atherosclerotic plaques are characterized by the presence of macrophages and, to a lesser extent, T lymphocytes at the immediate site of either plaque rupture or superficial erosion. The risk of plaque rupture depends more on the number and the activation status of macrophages, the principal inflammatory cells in atherosclerotic plaques, than on plaque size.

However, experimental studies have shown that short periods of ischemia (as short as 15 minutes) followed by reperfusion elicit a cascade of proinflammatory reactions that include production of oxygen-derived free radicals, activation of the complement system, adherence of neutrophils to the coronary endothelium, leukocyte-mediated injury of the myocardial cells, and production of cytokines, including interleukin-6 and interleukin-1, which are the major determinants of acute-phase protein production.

We recently examined temporal variations in plasma levels of CRP during AMI to investigate whether ischemia-reperfusion injury causes this acute-phase response. We found that CRP is significantly increased in patients with AMI shortly after the onset of symptoms, supporting the hypothesis that, in addition to plaque rupture, acute-phase markers of inflammation may also be elevated as a result of reperfusion injury caused by abrupt closure of the infarct-related artery and by initiation of a thrombolysis or revascularization procedure in patients with AMI.

Thus, temporal variations in plasma levels of CRP during the acute phase of AMI may be important when data addressing the relation between lesion morphology and CRP are being interpreted.

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Response

We thank Dr Auer and colleagues for their comments concerning our manuscript. We, too, considered the time from the onset of acute myocardial infarction to blood sampling as an important point for clarifying the relationship between lesion morphology and C-reactive protein (CRP).

Dr Auer and his colleagues measured CRP concentrations 4 times (at 0, 12, 24, and 72 hours) in acute coronary syndrome subjects and reported that CRP increased after a period of 12 hours compared with baseline; on the basis of these results, they argue that ischemia-reperfusion also generates CRP.

As we mention in our manuscript, CRP is mainly synthesized and secreted by hepatocytes 6 hours after an acute stimulus. In this study, to exclude the promotive effect of myocardial necrosis on CRP generation, we carefully included acute myocardial infarction patients who were “within 6 hours” of the onset of symptoms. Similarly, even if ischemia-reperfusion did stimulate production of CRP, it would have played a small part in elevated CRP at the time of admission, because it requires >6 hours for hepatocytes to synthesize and secrete CRP. Furthermore, all of our patients presented with ST-segment elevation-type myocardial infarction. Therefore, both elevated CRP patients and normal CRP patients had some ischemia, and possibly ischemia-reperfusion, at least at admission.

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