Nonacute Coronary Syndrome Anginal Chest Pain

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Anginal chest pain is one of the most common complaint encountered by family physicians, internists, and emergency room physicians. Patients with escalating chest pain symptoms, electrocardiographic (ECG) abnormalities consistent with acute myocardial ischemia or infarction, or hemodynamic instability suggestive of an acute coronary syndrome (ACS), which includes unstable angina (UA), ST-elevation myocardial infarction (STEMI), and non–ST-elevation myocardial infarction (NSTEMI), should be triaged to the emergency department. Non-ACS anginal chest pain, termed chronic stable angina (CSA), can also have devastating consequences; therefore, a considerable amount of time and resources is appropriately spent in risk stratifying the patient who complains of chest pain in an office-based setting. The challenge for the clinician is to determine cardiac from noncardiac chest pain, and use a systematic approach for testing and therapy based on patient risk factors and characteristics. This review focuses on our current understanding of non-ACS anginal chest pain, its pathophysiology, diagnostic modalities, and treatment.

PATHOPHYSIOLOGY

The acute reduction in coronary blood flow (CBF) leads to a decline in oxygen supply, resulting in development of an ACS. Similarly, a chronic limited ability to increase

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oxygen supply to the myocardium in the setting of increased oxygen demand results in CSA.[1] Because myocytes already extract about 75% of the oxygen in coronary blood at rest, a higher demand is primarily met by increasing CBF.[2,3] Myocardial ischemia results from hypoxia, which disrupts oxidative metabolic pathways; cellular anaerobic pathways are activated and mediators such as lactate are produced, which results in the sensation of pain.[4]

Coronary Atherosclerosis and Obstructive Coronary Artery Disease

In the largest diameter epicardial coronary vessels, CBF is primarily limited due to obstructive atherosclerotic coronary artery disease (CAD). Originally thought to be dominantly a lipid storage disease, our current understanding of the pathogenesis of atherosclerosis implicates endothelial injury and inflammation.[5–9] Inflammation-induced atherosclerosis does not occur linearly.[10] Instead, bursts of atherosclerotic plaque progression occur and are accompanied by physical disruption to endothelial cells, hemorrhage into the plaque, clot formation, and vascular remodeling. Studies of vessels at autopsy show that as the number of atheromatous plaques increases, deposition occurs principally within the vascular wall, with compensatory enlargement of the external vessel.[11] This process permits maintenance of the lumen size. Once this compensatory mechanism is exhausted, the plaque begins to bulge into the lumen, causing obstruction to CBF during periods of increased oxygen demand.[1,6,11] As a result, atherosclerosis produces symptomatic chest pain relatively later in its course of development.

While elevated low-density lipoprotein (LDL) cholesterol still remains a major contributor to atherosclerosis and adverse ischemic heart disease (IHD) events, effective therapies that target LDL reduce coronary events by only 33% over a 5-year treatment period.[6] This observation has led to the conclusion that additional chemical and mechanical insults also trigger endothelial injury, including altered sheer stress, high oxidative stress, smoking, and insulin resistance.[8,9]

Microvascular Coronary Dysfunction

Myocardial ischemia can produce anginal chest pain without angiographically obstructive CAD, often due to microvascular coronary dysfunction (MCD). A relatively common occurrence of MCD appears to be in women who present with evidence of myocardial ischemia, identified by a myocardial infarction (MI) or abnormal stress testing in the absence of obstructive CAD. Autopsy reports in patients with normal angiograms and angina have revealed myointimal proliferation, endothelial degeneration, and lipid deposits in the microvasculature.[12] Multiple angiographic studies have demonstrated abnormal endothelium-dependent function in subjects with angina, evidence of ischemia, and no obstructive CAD.[13–15] Patients with angina and MCD have elevated levels of serum inflammatory markers, such as C-reactive protein (CRP), suggesting an underlying inflammatory process as well.[16] There is a significant peri- and postmenopausal female predominance in this condition, leading to a suspected pathogenic role of estrogen deficiency[17]; however, this remains controversial.

Coronary Artery Spasm

Additional causes of anginal chest pain to consider include coronary artery vasospasm (CAS),[18] also known as Prinzmetal angina,[19–21] which involves epicardial coronary vasoconstriction secondary to smooth muscle dysregulation, and may lead to transient reduction in myocardial oxygen supply. Again, inflammation is thought to initiate damage as patients with CAS tend to have higher levels of circulating leukocytes, CRP, and interleukin-6 (IL-6) compared with control populations.[22,23]