Eosinophilic Coronary Monoarteritis

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• Eosinophilic coronary monoarteritis is an unfamiliar cause of acute myocardial ischemia. Most commonly, it presents as a left-sided chest pain or sudden death in middle-aged women with no traditional risk factors for coronary artery disease. Because the abrupt onset leaves almost no time for intervention, the symptoms readily lead to death, and most cases are diagnosed at necropsy. Dissection of the coronary artery wall with resultant occlusion of the lumen, which commonly affects the left anterior descending artery, is a consistent gross finding. An inflammatory infiltrate, which is predominantly composed of eosinophils in the tunica adventitia and tunica media and is often accompanied by a hematoma in between these 2 layers, is observed histologically. The etiology remains unclear, but an increase in the activity of eosinophils because of hormonal interactions during pregnancy has been suggested. Interplay of hormones is thought to culminate in the release of histolytic agents by the eosinophils, which initiate the dissection process. Currently, there is no specific treatment for eosinophilic coronary monoarteritis, but cyclophosphamide and prednisone have shown positive results in the treatment of spontaneous coronary artery dissection with unspecified periadventitial inflammation. Percutaneous coronary procedures have also resulted in favorable outcomes in a subset of patients. Because of the high, sudden death rate in eosinophilic coronary monoarteritis, deciphering the underlying pathophysiology of this almost invariably fatal disease remains both a challenge and a key to developing screening methods that will allow timely detection and thus treatment.

(*Arch Pathol Lab Med.* 2014;138:979–981; doi: 10.5858/arpa.2012-0610-RS)

Eosinophilic coronary monoarteritis (ECM) is a rare event characterized by the presence of an inflammatory infiltrate, predominantly of eosinophils, in the tunica adventitia and tunica media of the coronary artery.[1,2] In most cases, ECM selectively affects the left anterior descending artery, but involvement of the left main coronary, left circumflex, and right coronary arteries has also been documented in a few reported cases.[1,2]

Eosinophilic coronary monoarteritis was first recognized when cases of spontaneous coronary artery dissection (SCAD) were reviewed and carefully examined in an attempt to determine the etiology.[3–5] Spontaneous coronary artery dissection is a rare cause of acute myocardial infarction, with an incidence of 0.1% to 0.28%, as documented in previous angiographic studies.[4] In those cases of SCAD with prominent inflammatory infiltrate, a common observation was the presence of periadventitial accumulation of eosinophils with associated hematoma between the outer medial wall and the tunica adventitia accompanied by dissection of the medial layer with resultant narrowing of the vascular lumen. Acute myocardial ischemia is the immediate consequence of the cascade of events that leads to the cessation of blood flow to the myocardium because of blood vessel lumen compression.[3–5] Because of that, ECM has, since then, been regarded as a distinct and significant entity associated with SCAD and a neglected cause of sudden cardiac death because of the lack of awareness of its existence.[6,7]

CLINICAL FEATURES

Most affected individuals were previously healthy, asymptomatic, middle-aged women without history of heart disease or any identifiable risk factors for coronary artery disease.[6] In most cases, patients with ECM present with left-sided chest pain or sudden death, which mimics the classic symptoms of acute myocardial infarction.[3,4,6] Although less frequent, ECM has also been found in men of similar age and with similar clinical presentation.[1,2] Occasionally, cigarette smoking, hypertension, hypercholesterolemia, obesity, and family history of acute coronary syndromes are reported as coronary artery disease risk factors present in the affected individuals.[2]

Although uncommon, coronary periarteritis, with eosinophils as the predominant inflammatory cell component, has been identified in hypereosinophilic syndromes or systemic vasculitis, such as Churg-Strauss syndrome and Wegener granulomatosis.[2] Furthermore, a marked eosinophil and mast cell infiltrate at the site of dissection was identified in a patient who died of severe drug hypersensitivity reaction. In these settings, however, the clinical history was deemed helpful, and the presence of eosinophils in the coronary artery wall was not an isolated phenomenon.[5]

In one study, ECM was implicated as a component of peripartum heart disease, in combination with myocarditis, because it was diagnosed in a group of women who died shortly after giving birth.[4,7]

Accepted for publication July 10, 2013.

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The authors have no relevant financial interest in the products or companies described in this article.

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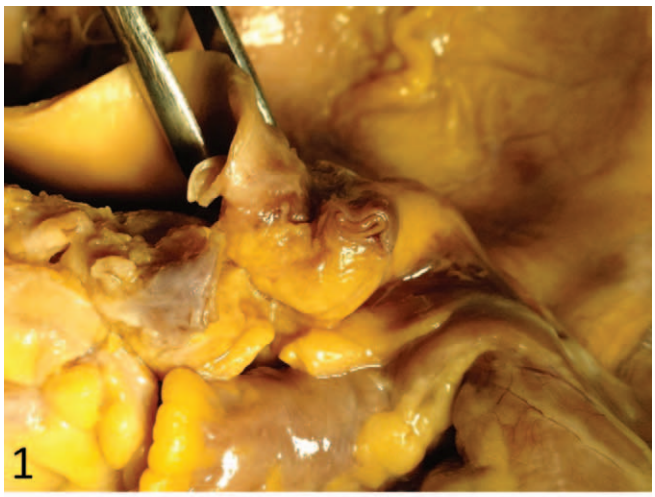

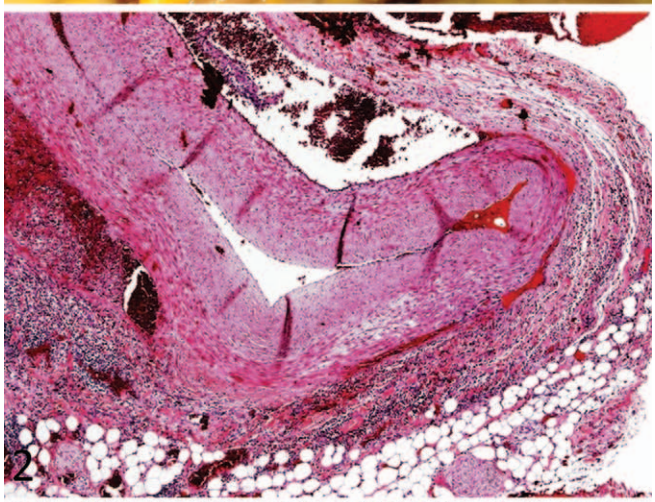

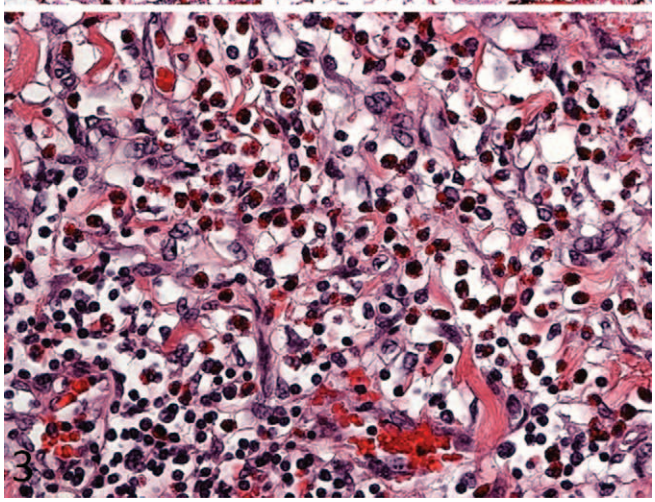

Figure 1. *Dissection of the proximal left coronary artery wall that causes significant narrowing of the vessel lumen.*

Figure 2. *Proximal left coronary artery featuring inflammatory infiltrate in the tunica adventitia and tunica media, with dissection of tunica media and resultant narrowing of the vessel lumen (hematoxylin-eosin, original magnification ×200).*

Figure 3. *Inflammatory infiltrate consists predominantly of eosinophils (hematoxylin-eosin, original magnification ×400).*

Because of the abrupt onset of symptoms and the lack of perceivable clinical signs and symptoms for possible premortem detection, diagnosis is frequently made at necropsy as an isolated finding.[1–3,6]

GROSS PATHOLOGY

Segmental dissection and thrombosis of the left proximal anterior descending coronary artery, as the only finding, is most common (Figure 1). As already mentioned, involvement of the left main coronary and left circumflex arteries and, very rarely, the right coronary artery, has been described.[1,2,6] Furthermore, multivessel involvement is possible, which is usually a combination of left anterior descending artery and right coronary artery or left anterior descending artery and left circumflex artery.[2,6] Moreover, the cardiac weight (280–340g) at autopsy frequently lies between the upper end of reference weight or slightly heavier than the upper range of the expected weight (reference range, 200–280 g), but without any other grossly identifiable abnormalities.[1,6] Although ECM sometimes affects isolated segments of the coronary arteries, the actual length of the involved segment has never, to our knowledge, been documented.

HISTOPATHOLOGY AND IMMUNOHISTOCHEMISTRY

Histologic evaluation of the affected segment discloses variable degree of intimal fibrosis accompanied by an inflammatory cell infiltrate, which is predominantly composed of eosinophils admixed with some lymphocytes and involves the tunica media and adventitia. Resultant dissection of the tunica media with occlusion of the vessel lumen is a consistent feature (Figures 2 and 3). A hematoma in between the tunica media and tunica adventitia may sometimes be observed[1,7]

Intimal fibrosis has been observed in several reported cases, which led to the assumption that coronary artery disease could be a contributing factor or that a possible relationship exists between the two.[2] The dissection of the coronary artery wall in ECM has been postulated to be due to the disruption of the vasa vasorum, which also explains the presence of hemorrhage between tunica adventitia and tunica media that displaces the inner artery wall toward the lumen. In the presence of atheroma, the blood vessels in the vasa vasorum are thought to be increased and more fragile and, therefore, are more susceptible to rupture. On the contrary, an atheroma may create a stenting effect, which makes the vessel wall rigid and less susceptible to luminal compression in contrast to normal coronary arteries. This hypothesis, in turn, provides a plausible explanation for the occurrence of ECM in healthy individuals without coronary artery disease.[5,6]

Cystic medial necrosis, intimal tear, and angiomatosis are some of the infrequent, associated microscopic findings.[5,6] In one study, immunohistochemical staining with antitryptase antibody highlighted the significant distribution of mast cells within the involved area, although it has not been a consistent finding with hematoxylin-eosin stain.[2]

PATHOGENESIS

The exact etiology of ECM has yet to be determined but is believed to be complex and multifactorial, especially in women. Several hypotheses have been formulated, with special attention to the role of eosinophils in the dissection process and the possible reason behind recruitment of eosinophils during the postpartum stage.[6]

The etiologic hypothesis involves the postpartum period and its dramatic shifts in hormone levels, which are a prerequisite for successful uterine involution and eventual return of menstrual cycle. These changes in hormone levels are said to influence the activity of eosinophils, which have been shown to infiltrate the cervix during the involution process, with evidences of degranulation and collagen breakdown. Furthermore, eosinophil is thought to be sensitive to steroid-hormone–mediated events, and estrogen and progesterone have been shown to induce degranulation of already migrated eosinophils. Concomitant localization of eosinophils in the coronary arteries and myocardium in these patients is thought to be a systemic counterpart of the physiologic events during the involution process and may be a normal physiologic phase, or an exaggerated or idiosyncratic pathologic reaction.[6] In addition, the interplay of hormones during pregnancy, especially the exposure to high estrogen levels, may result in reticulin fiber fragmentation, loosening of ground substance, and smooth muscle hypertrophy in the blood vessels, which substantially increases the chances of incurring dissection and, at the same time, places multiparous women at higher risk.[3,5,7]

Although eosinophils secrete tissue-damaging enzymes (collagenase, peroxidase, acid phosphatase, alkaline phosphatase, arylsulphatase ribonuclease, and β-glucuronidase) and major basic proteins that are cytotoxic and known to induce myocardial damage, the specific role of eosinophils with respect to the actual timing of events in the pathophysiology of ECM remains to be understood. The inherent properties of eosinophils, however, support the strong possibility of their involvement in the dissection of the medial layer, a mechanism that may be entirely different from those cases of SCAD that occur in the absence of eosinophilic infiltrate.

DIFFERENTIAL DIAGNOSES

Based on the clinical signs and symptoms, with chest pain and sudden death as the most common,[1,2,6] *acute myocardial infarction* is the clinical diagnosis given at the time of presentation. However, because of its invariably fatal nature, which allows no time for diagnostic procedures, most cases never receive a comprehensive premortem workup to determine the underlying cause.[2,5,6] The isolated finding of coronary artery wall dissection during gross examination at autopsy, or, in rare instances, during radiographic imaging of the coronary vessels, temporarily places this entity under the umbrella of SCAD, but the microscopic features that are appreciated in hematoxylin-eosin–stained sections pinpoint the definitive diagnosis of ECM.

The diagnosis of SCAD, on the other hand, is rendered after the exclusion of the more common secondary causes of coronary artery dissections, which include atherosclerosis, coronary angiography, percutaneous coronary intervention, bypass surgery, blunt chest trauma, and Marfan syndrome. These disease entities need to be considered primarily when wall dissection of the coronary artery is found grossly.

PROGNOSIS, TREATMENT, AND FUTURE DIRECTIONS

Because of its poorly understood etiology, specific treatment options for ECM have never been fully explored, but favorable outcomes with immunosuppression using prednisone and cyclophosphamide have been documented in a few cases of SCAD with periadventitial inflammation.[8] Moreover, in those cases of SCAD that were diagnosed antemortem by coronary angiography, methods of treatment included medical therapy and revascularization procedures using percutaneous coronary intervention or coronary artery bypass graft surgery. The choice of treatment modality is largely dependent on clinical presentation, the extent of dissection, and the amount of ischemic myocardium present. The use of thrombolytic agents has been controversial because it resulted in extension or worsening of the dissection in some studies.[3,4] Successful results using glycoprotein IIb/IIIa inhibitor therapy with significant resolution of dissection, as observed by angiography performed at approximately 20 hours posttreatment, have been documented.

Because of the high sudden death rate in ECM, the overall prognosis of this condition is dismal.[1,4,6] At present, the biggest challenge is to determine the underlying pathophysiology of this disease, which, in turn, may disclose previously unrecognized but potentially useful clinical or laboratory features. Because of its abrupt onset and short interval for a successful intervention, identifying possible risk factors is crucial and must be pursued to develop and institute a screening method, which may be more effective in saving high-risk individuals because of the poor chances of survival even with definitive treatment.

More important, whether at the emergency department or at autopsy, the diagnosis of ECM must be entertained in a patient who is at low risk for atherosclerotic heart disease but who presents with symptoms of acute myocardial infarction.[5]

References

1. Stoukas V, Dragovic LJ. Sudden deaths from eosinophilic coronary 204 monoarteritis: a subset of spontaneous coronary artery dissection. *Am J Forensic Med Pathol*. 2009;30(3):268–269.
2. Arena V, Valerio L, Arena E, et al. Isolated eosinophilic coronary arteritis [letter]. *J Clin Pathol*. 2010;63(5):469–471.
3. Almeda FQ, Barkatullah S, Kavinsky CJ. Spontaneous coronary artery dissection. *Clin Cardiol*. 2004;27(7):377–380.
4. Aqel RA, Zoghbi GJ, Iskandrian A. Spontaneous coronary artery dissection, aneurysms, and pseudoaneurysms: a review. *Echocardiography* 2004;21(2):175–182.
5. Kearney P, Singh H, Hutter J, Khan S, Lee G, Lucey J. Spontaneous coronary artery dissection: a report of three cases and review of the literature. *Postgrad Med J*. 1993;69(818):940–945.
6. Basso C, Morgagni L, Thiene G. Spontaneous coronary artery dissection: a neglected cause of myocardial ischaemia and sudden death. *Heart*. 1996;75(5):452–454.
7. Borczuk AC, van Hoeven KH, Factor SM. Review and hypothesis: the eosinophil and peripartum heart disease (myocarditis and coronary artery dissection)—coincidence or pathogenetic significance? *Cardiovasc Res*. 1997;33(3):527–532.
8. Koller PT, Cliffe CM, Ridley DJ. Immunosuppressive therapy for peripartum-type spontaneous coronary artery dissection: case report and review. *Clin Cardiol*. 1998;21(1):40–46.