A Case of Sudden Cardiac Death Due to Isolated Eosinophilic Coronary Arteritis*

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Spontaneous coronary artery dissection is a very rare event and occurs most often in young women following childbirth. It is also known as a rare focal complication in Churg-Strauss syndrome. Here, we present the case of a 43-year-old woman who died after spontaneous dissection of all three coronary arteries. The microscopic examination of coronary vessels showed severe eosinophilic infiltrations, whereas all extracardiac (medium-vessel and large-vessel) arteries were intact and free of inflammatory cells. Her history did not reveal allergy, asthma, or eosinophilia. To the best of our knowledge, this is the first case of spontaneous coronary dissection involving all coronary arteries without a history of Churg-Strauss syndrome or hypereosinophilic syndrome. (CHEST 2005; 128:1047–1050)

Key words: arteritis; Churg-Strauss syndrome; sudden death

Abbreviations: LAD = left anterior descending; LV = left ventricle; PAN = panarteritis nodosa

Inflammation of the vessel wall occurs in a number of disorders, including Kawasaki disease, Churg-Strauss syndrome, Behcet syndrome, rheumatoid arthritis, syphilis, tuberculosis, and autoimmunity to heat-shock protein 65. Dissections of coronary arteries are increasingly recognized as a cause of sudden cardiac death in apparently healthy individuals. Women are affected more frequently (85% of cases reported), and approximately 35% of coronary artery dissections occur < 3 months postpartum. Dissections most often occur in the left coronary artery system (approximately 75%), primarily the left main artery or left anterior descending (LAD) artery (approximately 80%). Eosinophilic infiltration of the coronary arteries has been described as a limited form of Churg-Strauss syndrome in patients with a lifelong history of allergies to (often) numerous agents. Panarteritis nodosa (PAN), a medium-sized-vessel vasculitis, has been described as a cause of myocardial infarction and angina. However, PAN also involves, at the same time, other than the coronary arteries. In most of the arterial inflammatory disorders, cystic necroses in the vessel wall can be found. There have been numerous case reports on inflammatory alterations in coronary arteries as a cause of sudden cardiac death. Rarely, the affected coronary arteries develop aneurysms. Previously, cases of strictly isolated eosinophilic coronary arteritis have been reported; however, these occurrences were preceded by signs or symptoms of allergy, asthma, and dyspnea. The causes of inflammatory diseases of the coronary arteries, as reported in the literature, are mainly PAN, Takayasu arteritis, and rheumatic disease. Giant cell arteritis affects persons > 50 years of age almost exclusively, and the disease risk is highest among those who are > 75 years of age. Systemic inflammation is present in almost all patients with giant cell arteritis. Here, we report a case in which the patient had none of the alterations described as predisposing a person to spontaneous coronary dissection.
Case Report

A 43-year-old woman died of multiple spontaneous coronary artery dissections caused by eosinophilic arteritis in all three major coronary arteries. Six years prior to death, she had presented with stress-induced dyspnea and a history of hypertension, and was referred to a cardiologist. There was no history of asthma or a positive family history of coronary artery disease. A physical examination was without pathologic findings, and especially, no heart murmur was present (cardiovascular risk factors were obesity and hypertension, but there was no history of diabetes and the total cholesterol/high-density lipoprotein ratio was normal). No enzyme defects related to collagen metabolism were noted. Echocardiography revealed a dilated left ventricle (LV) [ie, end-diastolic diameter, 67 mm] with slightly impaired LV function and mild mitral valve insufficiency. ECG showed sinus rhythm and left-axis deviation at a resting heart rate of 61 beats/min. No bundle branch block was seen. An exercise stress test was performed to a 100-W workload with an adequate heart rate and a hypertensive BP response, and no signs and symptoms of angina, ST-segment depression, or rhythm disorders.

One year later, the exercise stress test was repeated, and the patient was again asymptomatic at 75 W. Because of atypical chest pain, a heart catheterization was performed, which revealed normal hemodynamics. All coronary arteries were free from visible atherosclerotic lesions. The patient received therapy with a combination of beta-blocker, diuretic, and angiotensin-II receptor blocker. Furthermore, she started to receive therapy with aspirin (100 mg/d).

The patient had planned to undergo an abdominal hysterectomy because of uterus myomatosus with polymenorrhea; therefore, aspirin therapy was discontinued. Five days before hospital admission, the patient’s hemoglobin level was 13.6 g/dL but was found to be 8.6 g/dL when the patient was hospitalized. C-reactive protein level and erythrocyte sedimentation rate were normal on hospital admission. The patient underwent two blood transfusions and was operated on successfully the following morning. The day after surgery, she complained about chest pain (right-sided pressure, not typical for angina). An ECG was performed, which showed no changes compared with previous ECGs. Blood tests for myocardial necrosis markers (ie, creatinine kinase, creatinine kinase-MB, and troponin I) had negative results. No specific therapy was initiated at that time. Regular postoperative care was continued. Two days later, the patient was found dead in her bed at 4:00 AM. An autopsy revealed a regular status after the hysterectomy without signs of infection or bleeding. The abdominal organs were without pathologic findings, especially without signs of necrotizing vasculitis, granulomas with eosinophilic necrosis, or tissue infiltration by eosinophils. There was acute pulmonary congestion. The heart showed LV dilatation and compensatory hypertrophy, with a heart weight of 470 g. No valve diseases or anomalies of the coronary arteries were seen. An examination of the external surface of the heart revealed perivascular hemorrhage overlying all three epicordial arteries (Fig 1). There was no evidence of atherosclerosis either in the coronary vascular bed, or in the aorta or large aortic branches. Coronary artery dissection was confirmed histologically in serial transversal sections of all three vessels with a similar histology. The lumina

Figure 1. Hemorrhage overlying all three coronary arteries: top, A: right coronary artery [RCA]; middle, B: Ramus interventricularis anterior [RIVA]; bottom, C: Ramus circumflex [RCX].

Figure 2. Sections from the coronary arteries (left, A, right coronary artery; middle, B, RCX; right, C, RIVA) showing dissecting hematoma (H) in false lumina between adventitia (A) and media (M), collapse of the true lumina (L), false channel (FC) and inflammatory cell infiltrate within adventitia is remarkable (hematoxylin-eosin, original ×1.25). See Figure 1 for the definition of abbreviations not used in the text.
were occluded due to proximal dissection between the media and adventitial layer with large intramural hematomas (Fig 2). The adventitial tissue was found to be infiltrated with inflammatory cells, predominantly eosinophils (Fig 3, 4). There was no fibrinoid necrosis of arterial walls, and no microorganisms were identified. There was also no evidence of cystic medianecrosis of the aorta or of the coronary arteries, and no visceral eosinophilia, extracardiac necrotizing arteritis, or granulomatosis were evident.

In addition, the LAD artery revealed ferrous deposits under Perls staining (Prussian Blue stain), indicating a previous rupture of this branch leading to stenosis. The combination of LAD artery narrowing together with LV hypertrophy had caused ischemic cardiomyocyte damage, which was evidenced by the presence of abnormal CD56 positivity\(^23\) and diffuse irregular interstitial myocardial fibrosis.

**DISCUSSION**

The case of fatal isolated eosinophilic coronaritis presented here is of interest for several reasons. First, our histopathologic findings confirm the findings of a previous report,\(^8\) which suggested that changes, mainly in the media of the coronary arteries, predispose the patient to dissection, and that these changes are likely to be associated with eosinophilic infiltration. Eosinophils are capable of releasing cytotoxic substances and matrix metalloproteinases into the adjacent adventitia and media of the arteries, causing substantial weakening and focal necrosis (not present in this case). Nonlaminar shear forces may cause subsequent intimal disruption and mural dissection. In most cases, the etiology of an eosinophilic infiltrate remains elusive; however, it seems to be part of a systemic process. Contrary to previously described cases,\(^24,25\) no systemic involvement was seen in the case presented here. There have been reports of spontaneous carotid artery dissections, but in these cases no such histopathologic findings have been reported.\(^26\) Second, the case demonstrates the occurrence of noncontiguous dissections in all three main coronary arteries, suggesting a profound underlying change in vascular biology only in the affected vascular beds. The reasons for such a change are poorly understood in patients with conditions other than atherosclerosis, which to date has been considered to be a local inflammatory disorder of the vessel wall accompanied by a systemic inflammatory response. The fact that spontaneous coronary artery dissection is linked to the postpartum period suggests the involvement of endocrine factors. It has been postulated that hormonal changes associated with pregnancy weaken the coronary arterial wall. Subsequently, the strain of delivery may initiate fissuring in the intima, which proceeds slowly to dissection over a few days or weeks, and eventually coronary flow becomes compromised and fatal arrhythmia or myocardial infarction occurs.\(^7\) In the present case, the woman was not postpartum; however, she had delivered four children (ages, 4 to 11 years), and, as we could show by Prussian blue staining, coronary arteries might have been affected through recurrent inflammation of the vessel wall and were prone to rupture. In summary, the etiology and precise mechanisms involved in the pathogenesis of eosinophilic arteritis of the coronary arteries is unknown but, in this case, does not appear to be a part of a systemic vascular process. Hypersensitivity or an elusive autoimmune mechanism may be causative.

**REFERENCES**


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*Figure 3.* Adventitia and media of the RCX. Inflammatory infiltration (I) is localized in the adventitia (hematoxylin-eosin, original \(\times 10\)). See Figures 1 and 2 for abbreviations not used in the text.


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Expiratory Flow Limitation Is Associated With Orthopnea and Reversed by Vasodilators and Diuretics in Left Heart Failure*

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Background: In patients with acute left heart failure (LHF), orthopnea has also been related to the occurrence or worsening of expiratory flow limitation (EFL) in the supine position. We wished to assess whether short-term treatment with vasodilators and diuretics was able to abolish supine EFL and whether this could help to control orthopnea in patients with acute LHF.

Methods: In nine nonobese (ie, mean ± SD body mass index, 24 ± 5 kg/m2), never-smoker patients (two men and seven women; mean age, 77 ± 7 years) with acute LHF (mean ejection fraction, 43 ± 15%), we assessed EFL by the negative expiratory pressure method and dyspnea by the Borg scale, with patients in both the seated and supine positions, before and after short-term treatment with vasodilators and diuretics until hospital discharge. Orthopnea was defined as a positive difference in the Borg score between measurements made with the patient in the supine and seated positions. Postural variations in the end-expiratory lung volume were inferred from changes in inspiratory capacity (IC) that were measured under the same circumstances.

Results: Before treatment, with the patient in the

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