available at http://ajws.elsevier.com/tcmj

Tzu Chi Medical Journal

Review Article

Coronary Artery Ectasia

*Chih-Ta Lin, Chih-Wei Chen, Tin-Kwang Lin, Chin-Lon Lin**

Division of Cardiology, Department of Internal Medicine, Buddhist Dalin Tzu Chi General Hospital, Chiayi, Taiwan

Article info

Article history:
Received: November 28, 2007
Revised: January 7, 2008
Accepted: January 25, 2008

Keywords:
Angina pectoris
Atherosclerosis
Coronary artery ectasia

Abstract

This review on coronary artery ectasia (CAE) explores what is currently known about its classification, etiology and pathogenesis, clinical manifestations, methods of diagnosis, treatment and prognosis. CAE is not a rare coronary anomaly. Its prevalence is about 0.3–12% in autopsies and during coronary angiography or multidetector computed tomography (MDCT). Its etiology is varied and its pathophysiology is not completely understood. More than half of CAE cases is due to coronary atherosclerosis, and the right coronary artery is most commonly affected. Angina pectoris is the most common clinical manifestation. Unstable angina, acute myocardial infarction, heart failure, ventricular tachycardia/fibrillation, and sudden death have also been reported. Myocardial ischemia is possibly caused by coexisting significant coronary stenosis, slow flow, microvascular dysfunction, thrombus formation, coronary spasm or spontaneous coronary dissection. Coronary angiography, intravascular ultrasound, and MDCT are the current major diagnostic tools for CAE. The prognosis of CAE has shown improvement when it is treated with aggressive medical therapy, modern revascularization techniques, and state-of-the-art equipment. (*Tzu Chi Med J* 2008;20(4):270–274)

*Corresponding author. Division of Cardiology, Department of Internal Medicine, Buddhist Dalin Tzu Chi General Hospital, 2, Min-Sheng Road, Dalin, Chiayi, Taiwan.
E-mail address: cllinmd@mail.tcu.edu.tw

1. Introduction

Coronary artery ectasia (CAE) has been observed by pathologists and cardiologists for more than two centuries. This coronary anomaly was first described by Morgagni in 1761 (1). Bourgon was the first to describe the postmortem finding of right coronary artery (RCA) dilatation in a patient who experienced sudden death in 1812 (2). The term *ectasia* was first used by Bjork in 1966 to describe dilated coronary arteries (3). The literature prior to this date consisted of only postmortem reports. Coronary angiography and new diagnostic tools have enabled clinicians to discover more cases of ectasia. However, not all patients with ectasia are symptomatic and receive coronary angiography examination; hence, the real incidence is unknown. The reported incidence is between 0.3% and 4.9% at autopsy and during coronary angiography (4–6). Zeina et al determined that the prevalence of CAE in consecutive participants who underwent coronary multidetector computed tomography (MDCT) was 8% (7). Sharma et al found an incidence as high as 12% in an Indian population (8), which may have different demographic characteristics.

There is a male preponderance, with a male-to-female ratio of 3:1 (5,9,10). The proximal and middle parts of the RCA are most commonly affected by ectasia, although the reasons for this are not clear.

Involvement of the left anterior descending artery and left circumflex artery is variable. The left main coronary artery is less commonly involved. Most cases of CAE involve only a single vessel. Disturbance in blood flow filling and washout are major characteristics of CAE. Delayed antegrade filling, a segmental back flow phenomenon, and local deposition of dye (stasis) in the dilated coronary segment have been observed during imaging [11,12].

2. Definition and classification

There are various methods for defining CAE. Hartnell et al defined CAE as an arterial segment with a diameter at least 1.5 times the diameter of the adjacent normal coronary artery [6]. Markis et al provided the following classification of CAE based on the extent of coronary involvement: type I, diffuse ectasia of two or three vessels; type II, diffuse disease in one vessel and localized disease in another vessel; type III, diffuse ectasia of one vessel only; and type IV, localized or segmental ectasia [9]. This classification is used extensively. Plehn et al preferred to use the term *coronary artery aneurysm* for segmental ectasia, reserving the term *ectasia* for diffuse vessel involvement [13]. They classified aneurysms as small (<5 mm), medium (5–8 mm), or giant (≥8 mm). In addition, coronary artery aneurysm has been classified as the fusiform or saccular type based on the anatomic shape of the ecstatic segment. There is no general concept concerning the critical diameter required for the development of rupture.

To date, only a few reports have described the anatomic changes that occur in CAE over time. Plehn et al reported a patient who presented with ectatic lesions that rapidly progressed to aneurysmatic lesions within 3 years [13]. The patient was treated with aneurysm ligation and coronary artery bypass grafting (CABG). Periodic careful follow-up of patients with CAE is recommended.

3. Etiology and pathogenesis

More than 50% of CAE cases are reportedly caused by atherosclerosis [5,10,12]. Compensatory vessel enlargement in the presence of coronary atherosclerotic plaques is a common phenomenon that is viewed as positive remodeling [14]. Progressive overcompensation leading to ectasia may be caused by an inadequate extent of media atrophy and fracture of the internal elastic lamina, as well as atypical rearrangement of smooth muscle cells [15,16]. Virmani et al provided a detailed pathologic characterization of CAE, including lipid deposition with foam cells, fibrous caps and significant loss of musculoelastic vascular wall components as the main histological abnormalities [17]. The reason why stenosis develops in some individuals with atherosclerosis while dilatation occurs in others is unknown. Genetic susceptibility is likely to explain why certain individuals are at risk of developing CAE [18,19].

Many other clinical entities can cause dilation of the coronary arteries, such as syphilis, mycotic or bacterial infection, Kawasaki disease, trauma, congenital heart disease, inflammatory disorders, connective tissue disorders such as Marfan syndrome, scleroderma, systemic lupus, Ehlers-Danlos syndrome, periarteritis nodosa, Behcet's disease and congenital defects [12,20–22]. Prolonged exposure to herbicides such as 2,4,5-T (trichlorophenoxyacetic acid) and 2,4-D (dichlorophenoxyacetic acid) has been associated with CAE [23]. These herbicides, which contain acetylcholinesterase inhibitors, can increase the levels of acetylcholine and stimulate the production of nitric oxide. Nitric oxide can stimulate relaxation of the coronary artery. At present, it is not known whether or not chronic relaxation of the smooth muscle layer of the coronary artery causes CAE [24].

CAE can also be iatrogenic in origin, for example after percutaneous coronary intervention (PCI). Chiu et al reported a patient who developed coronary artery aneurysm after successful stent implantation for a chronic totally occluded lesion [25]. Interestingly, the aneurysm spontaneously regressed a few months later without further intervention. It was thought that the most likely mechanism for this was shear stress inducing vessel positive remodeling after an intervention procedure, with subsequent negative remodeling when the shear stress returned to baseline.

Lamblin et al found that patients with CAE had a higher percentage of the 5A/5A polymorphism of metalloproteinase-3 (MMP-3), which is actively involved in the proteolysis of extracellular matrix proteins [26]. The levels of inflammatory markers such as plasma interleukin-6, C-reactive protein, V-CAM, I-CAM and E-selectin are elevated in CAE patients [27–30]. This suggests a role for the inflammatory process in this setting.

Pinar et al determined that CAE was associated with the classical cardiovascular risk factors except for diabetes, which was rare in patients with isolated CAE [31]. This negative correlation between diabetes and CAE has also been reported by others. Williams et al found impaired nitric oxide-mediated vasodilatation in patients with non-insulin-dependent diabetes [32]. However, Zeina et al demonstrated that there was no apparent correlation between CAE and hypertension, hyperlipidemia, diabetes, smoking and a family history of coronary artery disease [7]. The actual relationship between CAE and traditional cardiovascular risk factors still needs to be clarified by further study.

Considering all of the above findings, Manginas and Cokkinos speculated that CAE occurs due to two

different mechanisms in two distinct patient groups: (1) commonly in patients with concomitant coronary artery disease due to severe and chronic arterial inflammation; and (2) rarely in subjects without coronary atherosclerosis as a result of exogenous interstitial nitric oxide vascular overestimation [12].

4. Clinical manifestations

Although it has been shown that more than half of patients with CAE have underlying coronary artery stenosis, the symptoms do not directly correlate with the degree of stenosis. Sayin et al postulated that CAE subjects patients to a higher risk of myocardial ischemia irrespective of the extent of stenosis [33]. On the contrary, the Coronary Artery Surgery Study database showed no difference in 5-year survival for patients with both CAE and coronary artery disease compared with those with only coronary artery disease [5].

Angina is the most common symptom in patients with CAE; ST-elevation myocardial infarction, non-ST-elevation myocardial infarction, heart failure, and severe arrhythmias such as ventricular tachycardia and fibrillation have also been reported. Bove and Vlietstra demonstrated that ectatic arteries are prone to spasm [34]. Suzuki et al used computer analysis to evaluate the effects of ergonovine- and acetylcholine-induced spasm [35]. They found that the actual narrowing induced by these agents usually occurred adjacent to the ectatic portion and less commonly within the ectatic area. Perlman and Ridgeway documented a large, left anterior descending artery thrombus in a patient with triple vessel coronary artery ectasia [36]. Huikuri et al reported a case of large spontaneous dissection of an ectatic right coronary artery in a patient with out-of-hospital cardiac death [37]. Tomaru et al described a patient who presented with sudden onset of shortness of breath followed by respiratory arrest, in whom coronary angiography showed type I CAE and two-vessel disease [21]. Gore et al reported a case of congenital coronary artery aneurysm in which the patient presented with dyspnea and syncope [38]. Tuzun et al found that stiffness parameters in the aorta are impaired in patients with CAE as well as in those with coronary artery disease [39]. The increased stiffness may be responsible for left ventricle diastolic dysfunction, which is very important because it might play a key role in the development of heart failure. CAE has been reported to be associated with aortic aneurysm and patients present with abdominal pain. In a retrospective study by Stajduhar et al, 20.8% of patients who underwent operations for abdominal aneurysm had CAE [40]. Some patients with CAE are asymptomatic and the disease is found incidentally during catheterization.

5. Diagnostic methods

Coronary angiography is now the criterion standard for diagnosing CAE. Coronary angiography offers a detailed definition of coronary anatomy, making it possible to characterize the distribution and size of coronary aneurysms and also to detect coronary stenosis. A treadmill exercise test and thallium-201 myocardial perfusion scan can be used to evaluate myocardial ischemia caused by CAE. Intravascular ultrasound can be used to assess the luminal size and condition of the arterial walls, and also to differentiate true from false aneurysms caused by plaque rupture [41]. Magnetic resonance imaging has been successfully used to assess coronary anatomy in patients with CAE. Greil et al reported a small series of adolescents and young adults with Kawasaki disease, who were diagnosed by coronary magnetic resonance angiography [42]. MDCT is one of the newest tools used to diagnose CAE, and it is not invasive like coronary angiography. Zeina et al found a high prevalence (8%) of CAE when using MDCT as a diagnostic tool [7]. The first congenital CAE diagnosed by MDCT was reported by Ayusawa et al in 2008 [43].

6. Treatment

CAE is not a benign coronary anomaly. Sorrel et al suggested treating CAE patients with: (1) anticoagulation therapy, utilizing chronic warfarin therapy to offset the risk of thrombus formation and to keep the international normalized ratio at around 2.0–2.5; (2) antiplatelet therapy, utilizing aspirin (80–360 mg/day) to minimize platelet aggregation; and (3) antispasm therapy, utilizing calcium-channel blockers [24]. Nitrates could also be used, but added care should be emphasized to provide a nitrate-free "holiday" and prevent chronic exposure to these agents.

Therapy should be tailored to each individual patient because of the serious bleeding complications associated with warfarin use. Tuncer et al reported two cases of CAE, one in a patient with myocardial infarction and one with unstable angina [44]. A large thrombus was seen in both patients and they were treated with aspirin, warfarin and metoprolol. One patient received MDCT after follow-up, which revealed that the thrombus had almost completely dissolved after 3 months. Warfarin was then discontinued in both cases and clopidogrel was given. But these treatment strategies have not been studied prospectively. Heparin and thrombolytic therapy have been successfully used for recanalization. For patients with coexisting obstructive lesions and refractory angina despite medical treatment, PCI can be performed. But there can be difficulties during stent deployment because the ectatic arteries are usually much larger than normal

arteries. Selection of a stent of adequate size and its expansion are very important, and can be determined by intravascular ultrasound. Rha et al reported a challenging case of implantation of two 3.5×18 sirolimus-eluting stents parallel to each other in a large ectatic coronary artery [45]. They suggested that in lesions which have a large reference diameter, the clinician can consider parallel stenting using drug-eluting stents as a new intervention strategy. CABG has been used for many years for the treatment of significant coronary artery disease coexisting with CAE, and the postoperative outcome is uniformly good.

In our opinion, treatment should be tailored according to clinical manifestations and the number and involvement of the coronary arteries. Medical therapy is recommended for patients with symptomatic nonobstructive CAE. Surgery (CABG, aneurysm ligation, or aneurysmorrhectomy) is a better choice for patients who are refractory to coronary medical therapy and not suited for PCI.

7. Prognosis

There are different opinions about the prognosis of CAE [9,46–48]. Markis et al reported an annual mortality rate of 15% during a mean follow-up period of 24 months [9]. Baman et al reported a significant adverse outcome among the 276 CAE patients they studied, with a 5-year mortality rate of 29.1% [47]. Recently, because the techniques and equipment for revascularization have significantly improved, the prognosis of CAE seems to be better. Valente et al reported that the prognosis of CAE was good with a low mortality rate (2%) [48], possibly because their patients with ST-elevated myocardial infarction and acute coronary syndrome all underwent PCI and the most severe cases with coexisting coronary stenosis underwent CABG.

8. Conclusion

CAE is worth closer study, as the different etiologies and complicated pathophysiology are still not completely understood. With the use of different modern treatment strategies, the prognosis seems to be improving gradually. But these therapeutic modalities need large-scale, randomized, controlled studies to prove their long-term effectiveness.

References

1. Morgagni JB. *De sedlbus, et causis morborum per anatomen indagatis*. Tomus primus, Liber II, Epist 27, Article 28, Venetiis, 1761.
2. Packard M, Weehsler HF. Aneurysm of the coronary arteries. *Arch Intern Med* 1929;43:1–14.
3. Bjork L. Ectasia of the coronary arteries. *Radiology* 1966;87:33–4.
4. Oliveros RA, Falsetti HL, Carroll RJ, Heinle RA, Ryan GF. Atherosclerotic coronary artery aneurysm: report of five cases and review of literature. *Arch Intern Med* 1974;134: 1072–6.
5. Swaye PS, Fisher LD, Litwin P, et al. Aneurysmal coronary artery disease. *Circulation* 1983;67:134–8.
6. Hartnell GG, Parnell BM, Pridie RB. Coronary artery ectasia. Its prevalence and clinical significance in 4993 patients. *Br Heart J* 1985;54:392–5.
7. Zeina AR, Sharif D, Blinder J, Rosenschein U, Barmeir E. Noninvasive assessment of coronary artery ectasia using multidetector computed tomography. *Coron Artery Dis* 2007;18:175–80.
8. Sharma SN, Kaul U, Sharma S, et al. Coronary arteriographic profile in young and old Indian patients with ischemic heart disease: a comparative study. *Indian Heart J* 1990;42: 365–9.
9. Markis JE, Joffe CD, Cohn PF, Feen DJ, Herman MV, Gorlin R. Clinical significance of coronary arterial ectasia. *Am J Cardiol* 1976;37:217–22.
10. Befeler B, Aranda MJ, Embi A, Mullin FL, El-Sherif N, Lazzara R. Coronary artery aneurysm: study of their etiology, clinical course and effect on left ventricular function and prognosis. *Am J Med* 1977;62:597–607.
11. Kruger D, Stierle U, Herrmann G, Simon R, Sheikhzadeh A. Exercise-induced myocardial ischemia in isolated coronary artery ectasias and aneurysms ("dilated coronopathy"). *J Am Coll Cardiol* 1999;34:1461–70.
12. Manginas A, Cokkinos DV. Coronary artery ectasias: imaging, functional assessment and clinical implications. *Eur Heart J* 2006;27:1026–31.
13. Plehn G, van Bracht M, Zuehlke C, et al. From atherosclerotic coronary ectasia to aneurysm: a case report and literature review. *Int J Cardiovasc Imaging* 2006;22:311–6.
14. Varnava A. Coronary artery remodeling. *Heart* 1998;79: 109–10.
15. Crawford T, Levene CI. Medial thinning in atheroma. *J Pathol Bacteriol* 1953;66:19–23.
16. Bendeck MP, Zempo N, Clowes AW, Galardy RE, Reidy MA. Smooth muscle cell migration and matrix metalloproteinase expression after arterial injury in the rat. *Circ Res* 1994;75:539–45.
17. Virmani R, Robinowitz M, Atkinson JB, Forman MB, Silver MD, McAllister HA. Acquired coronary arterial aneurysm: an autopsy study of 52 patients. *Hum Pathol* 1986;17:575–83.
18. Kajinami K, Kasashima S, Oda Y, Koizumi J, Katsuda S, Mabuchi H. Coronary ectasia in familial hypercholesterolemia: histopathological study regarding matrix metalloproteinases. *Mod Pathol* 1999;12:1174–80.
19. Akdemir R, Qzhan H, Gunduz H, et al. HLA-DR B1 and DQ B1 polymorphisms in patients with coronary artery ectasia. *Acta Cardiol* 2004;59:499–502.
20. Lam CS, Ho KT. Coronary artery ectasia: a ten-year experience in a tertiary hospital in Singapore. *Ann Acad Med Singapore* 2004;33:419–22.
21. Tomaru A, Takigawa K, Kagawa N, et al. Coronary artery ectasia—a case report and literature review. *Angiology* 1993;44:415–9.
22. Tatli E, Surucu H, Aktoz M, Buyuklu M. Coronary artery ectasia in a patient with Behcet's disease. *Saudi Med J* 2007;28:1281–2.
23. England JF. Herbicides and coronary ectasia. *Med J Aust* 1981;1:371.

24. Sorrel VL, Davis MJ, Bove AA. Current knowledge and significance of coronary artery ectasia: a chronologic review of the literature, recommendations for treatment, possible etiologies, and future considerations. *Clin Cardiol* 1998;21:157–60.
25. Chiu FC, Liu SC, Lin JW, Hwang JJ, Tseng CD. Development of a coronary artery aneurysm following stent implantation in a chronic, totally occluded lesion. *Acta Cardiol Sin* 2007;23:203–7.
26. Lamblin N, Bauters C, Hermant X, Lablanche JM, Helbecque N, Amouyel P. Polymorphisms in the promoter regions of MMP-2, MMP-3, MMP-9 and MMP-12 genes as determinants of aneurysmal coronary artery disease. *J Am Coll Cardiol* 2002;40:43–8.
27. Adiloglu AK, Can R, Nazli C, et al. Ectasia and severe atherosclerosis: relationships with *Chlamydia pneumoniae*, *Helicobacter pylori*, and inflammatory markers. *Tex Heart Inst J* 2005;32:21–7.
28. Turban H, Erbay AR, Yasar AS, Balci M, Bicer A, Yetkin E. Comparison of C-reactive protein levels in patients with coronary artery ectasia versus patients with obstructive coronary artery disease. *Am J Cardiol* 2004;94:1303–6.
29. Tokgozoglu L, Ergene O, Kinay O, Nazli C, Hascelik G, Hoscan Y. Plasma interleukin-6 levels are increased in coronary artery ectasia. *Acta Cardiol* 2004;59:515–9.
30. Turhan H, Erbay AR, Yasar AS, et al. Plasma soluble adhesion molecules; intercellular adhesion molecule-1, vascular cell adhesion molecule-1 and E-selectin levels in patients with isolated coronary artery ectasia. *Coron Artery Dis* 2005;16:45–50.
31. Pinar BE, Lopez Palop R, Lozano Martinez-Luengas I, et al. Coronary ectasia: prevalence, and clinical and angiographic characteristics. *Rev Esp Cardiol* 2003;56:473–9.
32. Williams SB, Cusco JA, Roddy MA, Johnstone MT, Creager MA. Impaired nitric oxide-mediated vasodilatation in patients with non-insulin-dependent diabetes mellitus. *J Am Coll Cardiol* 1996;27:567–74.
33. Sayin T, Doven O, Berkalp B, Akyurek O, Gulec S, Oral D. Exercise-induced myocardial ischemia in patients with coronary ectasia without obstructive coronary artery disease. *Int J Cardiol* 2001;78:143–9.
34. Bove AA, Vlietstra RE. Spasm in ectatic coronary arteries. *Mayo Clin Proc* 1985;60:822–6.
35. Suzuki H, Takeyama Y, Hamazaki Y, et al. Coronary spasm in patients with coronary ectasia. *Cathet Cardiovasc Diagn* 1994;32:1–7.
36. Perlman PE, Ridgeway NA. Thrombus and anticoagulation therapy in coronary ectasia. *Clin Cardiol* 1989;12:541–2.
37. Huikuri HV, Mallon SM, Myerburg RJ. Cardiac arrest due to spontaneous coronary artery dissection in a patient with coronary ectasia—a case report. *Angiology* 1991;42: 148–51.
38. Gore I, Smith J, Clancy R. Congenital aneurysms of the coronary arteries with report of a case. *Circulation* 1959; 19:221–7.
39. Tuzun N, Tanriverdi H, Evrengul H, Kuru DS, Ergene AO. Aortic elastic properties in patients with coronary artery ectasia. *Circ J* 2007;71:506–10.
40. Stajduhar KC, Laird JR, Rogan KM, Wortham DC. Coronary arterial ectasia: increased prevalence in patients with abdominal aortic aneurysm as compared to occlusive atherosclerotic peripheral vascular disease. *Am Heart J* 1993;125:86–92.
41. Garrand TJ, Mintz GS, Popma JJ, Lewis SA, Vaughn NA, Leon MB. Intravascular ultrasound diagnosis of a coronary artery pseudoaneurysm following percutaneous transluminal coronary angioplasty. *Am Heart J* 1993;125: 880–2.
42. Greil GF, Stuber M, Botnar RM, et al. Coronary magnetic resonance angiography in adolescents and young adults with Kawasaki disease. *Circulation* 2002;105:908–11.
43. Ayusawa M, Sato Y, Kanamaru H, et al. Multidetector-row computed tomographic depiction of congenital coronary artery aneurysms and ectasia. *Int J Cardiol* 2008;127: e172–4.
44. Tuncer C, Sokmen G, Sokmen A, Suner A. Diffuse coronary ectasia and intracoronary thrombus involving left circumflex coronary artery and presenting as acute coronary syndrome: report of two cases. *Int J Cardiol* 2008;128: e25–7.
45. Rha SW, Wani SP, Oh DJ. Parallel stenting using two sirolimus-eluting stents in an ectatic coronary artery stenosis. *Heart* 2007;93:976.
46. Ramappa P, Kottam A, Kuivanemi H, Thatai D. Coronary artery ectasia—is it time for a reappraisal? *Clin Cardiol* 2007;30:214–7.
47. Baman TS, Cole JH, Devireddy CM, Sperling LS. Risk factors and outcomes in patients with coronary artery aneurysms. *Am J Cardiol* 2004;93:1549–51.
48. Valente S, Lazzeri C, Giglioli C, et al. Clinical expression of coronary artery ectasia. *J Cardiovasc Med* 2007;8: 815–20.