Spontaneous coronary dissection of all three coronary arteries: a case description with medium-term angiographic follow-up

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Spontaneous coronary artery dissection is a rare cause of ischemic heart disease, often related with a poor prognosis. We report the case of a 38-year-old woman without cardiovascular risk factors, admitted to our coronary care unit for unstable angina with ECG findings of inferior ischemia. The day after, an acute anterior myocardial infarction occurred and was treated with intravenous thrombolysis. Again, there were ECG signs of transient inferior ischemia. Coronary angiography showed widespread spontaneous coronary dissection involving the terminal left main stem, both the left anterior descending and circumflex artery, and the right coronary artery even peripherally, rendering any type of revascularization procedure inappropriate. The patient was placed on beta-blockers, acetylsalicylic acid and nitrates and her symptoms resolved; the 17-month angiographic follow-up showed almost complete healing of spontaneous coronary artery dissection. The peculiarities of the case are discussed and a review of the literature is provided.

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Introduction

Spontaneous coronary artery dissection (SCAD) is a rare cause of ischemic heart disease. It occurs predominantly in young and otherwise healthy women. Its prognosis is often poor and its real incidence is largely unknown and probably underestimated[1-5]. Reports of SCAD simultaneously involving all three coronary arteries are even more exceptional and limited to 6 cases including ours[6-10]. In the majority of cases the diagnosis is made *post-mortem* and angiographic evidence of SCAD is very limited. The usual clinical presentation is sudden death or an acute myocardial infarction followed by death in a short time. In a minority of cases, the diagnosis is established angiographically during or after an episode of chest pain and a clinical diagnosis of acute myocardial infarction. Dissection can be associated with atherosclerotic coronary artery disease, it may be spontaneous or secondary to blunt chest trauma or else associated with aortic root dissection or Marfan's syndrome[1,11-13]. In case of spontaneous dissection, different pathologic situations may be taken into consideration. During pregnancy, pathologic alterations of the arterial wall may arise due to fragmentation of the reticulum fibers, hypertrophy of the smooth muscle cells and changes in the mucopolysaccharide content and protein composition of the media, leading to a weakening of the latter and ultimately to dissection during labor, delivery and also after parturition[1,7,10,14]. There has been documentation of impaired collagen synthesis in cultures of skin fibroblasts sampled from a woman who presented with SCAD following delivery[15]. Azam et al.[16] described a case of a young woman with SCAD associated with oral contraceptive use possibly with the same etiopathogenetic features of *post-partum* SCAD. Robinowitz et al.[17] observed the occurrence of eosinophilic infiltrates in the adventitia of patients who died of SCAD; this finding can be the cause of the dissection or an inflammatory reaction secondary to SCAD. A rare cause of coronary dissection is cystic medial necrosis that was reported in a few cases of SCAD[4,9]. Typical patterns of this abnormality are focal fragmentation of the elastic fibers and loss of smooth muscle cells from the media accompanied by deposits of acid mucopolysaccharides. These lesions are present in the media of the ascending aorta of patients with Marfan's syndrome and predispose them to aortic dissection. Other rare causes of SCAD are cocaine abuse[18], intense physical exercise[19], the impaired ability to form collagen (reduced type III procollagen synthesis) in the type IV Ehlers-Danlos syndrome characterized by skin ab-

normalities and vessel ruptures. A case of a 37-year-old woman with Ehlers-Danlos syndrome and SCAD was reported by Eltchaninoff et al.[20] in 1995.

Alternatively, primary hemorrhage from fragile vasa vasorum in the deep media may be responsible in selected cases.

We report the case of a woman with recurrent episodes of myocardial infarction and angiographically documented SCAD of all three major coronary arteries together with the medium-term clinical and angiographic follow-up.

Case report

The patient, P.B., is a 38-year-old woman. She was hospitalized in December 1999 because of intense chest pain developing during mild exercise and lasting for 30 min. ECG recorded during chest pain showed significant inferior ST segment elevation together with antero-lateral ST segment depression. Both chest pain and ST alterations spontaneously resolved after a few minutes. She had no known cardiovascular risk factors, had previously delivered 3 healthy children but was already admitted to another hospital in 1993 for a crushing chest pain. On that occasion, a non-Q wave inferior myocardial infarction was diagnosed. She was studied angiographically and an apparently long "stenosis" of the circumflex coronary artery in its second obtuse marginal branch together with limited distal dissection was documented. Subsequently she was placed on aspirin and beta-blockers, had her third child without any problem in 1996, and did well until this last episode of myocardial ischemia. Interestingly, 2 months before beta-blocker therapy (atenolol) was discontinued because of mild bronchospasm. After admission to the coronary care unit she was placed on intravenous nitrates, intravenous unfractionated heparin and oral aspirin. During the first 24 hours, ECG was stable and only a minimal release of the creatine kinase (CK)-MB isoenzyme was documented (7 ng/ml). The day after, the patient again presented with moderate chest pain accompanied by ST segment elevation in the anterior leads (V_2-V_4) with no response to conventional therapy. Thrombolytic treatment using intravenous tissue-type plasminogen activator was initiated with immediate accentuation of the chest pain and widespread anterior ST segment elevation (V_2-V_6, DI and aVL) and concomitant inferior ST segment depression (DII, DIII and aVF) (Fig. 1). Sixty min following the beginning of fibrinolytic therapy, the anterior ST segment elevation was no longer apparent and inferior ST segment elevation appeared (DII, DIII and aVF) with ST segment depression in leads V_2-V_4 (Fig. 2). After another 30 min there were signs of reperfusion with accelerated idioventricular rhythm and waning of pain. ECG was completely normal after another 30 min. Significant CK-MB release (peak value of 100 ng/ml) was registered. The subsequent course was uneventful and a coronary angiography was performed 4 days later. The coronary angiogram revealed extensive SCAD of all three coronary vessels with extension to the left main stem from the circumflex coronary artery (dissected from origin to distally) (Fig. 3). The left anterior descending coronary artery showed dissection mainly in its midsegment, and the right coronary artery from its midsegment to the posterior descending artery. Left ventriculography showed a normal global systolic function (ejection fraction 65%) with localized hypoakinetic inferior wall segments. The patient did well during the last few days of her hospital stay. A therapeutic regimen including aspirin (160 mg), oral nitrates (isosorbide dinitrate 20 mg tid) and beta-blockers (metoprolol 100 mg bid) was prescribed. All biohumoral assays performed in order to assess the inflammatory risk and coagulation abnormalities (complement, lupus anticoagulant, antinuclear antibodies, antimitochondrial antibodies, C-reactive protein, homocysteine, platelet count, partial thromboplastin time, international normalized ratio, S protein) were found to be within normal limits.

After hospital discharge the patient remained completely asymptomatic and other non-invasive diagnostic examinations followed. An echocardiogram con-

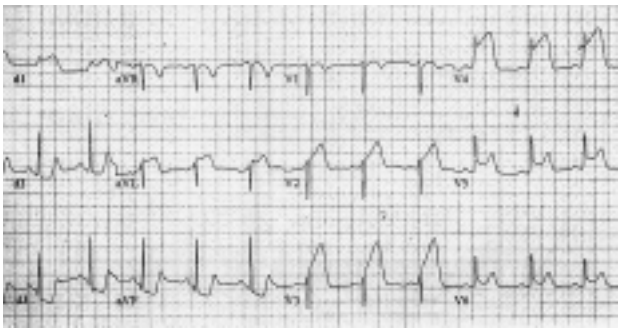

Figure 1. *Accentuation of chest pain with ST segment elevation in leads V_2-V_6, DI and aVL and ST segment depression in leads DII, DIII and aVF shortly after initiation of thrombolysis with tissue-type plasminogen activator.*

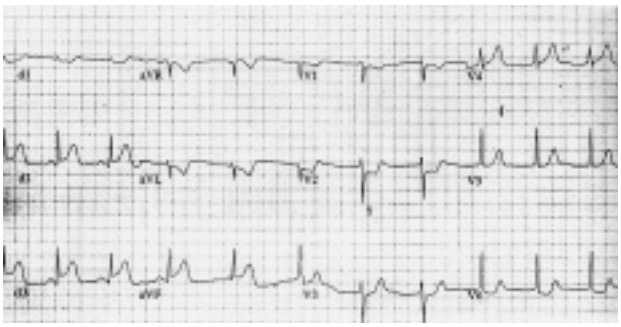

Figure 2. *Changes in the pattern of ischemia with ST segment elevation in leads DII, DIII and aVF and ST segment depression in leads DI, aVL, V_1-V_3 60 min following the initiation of tissue-type plasminogen activator therapy.*

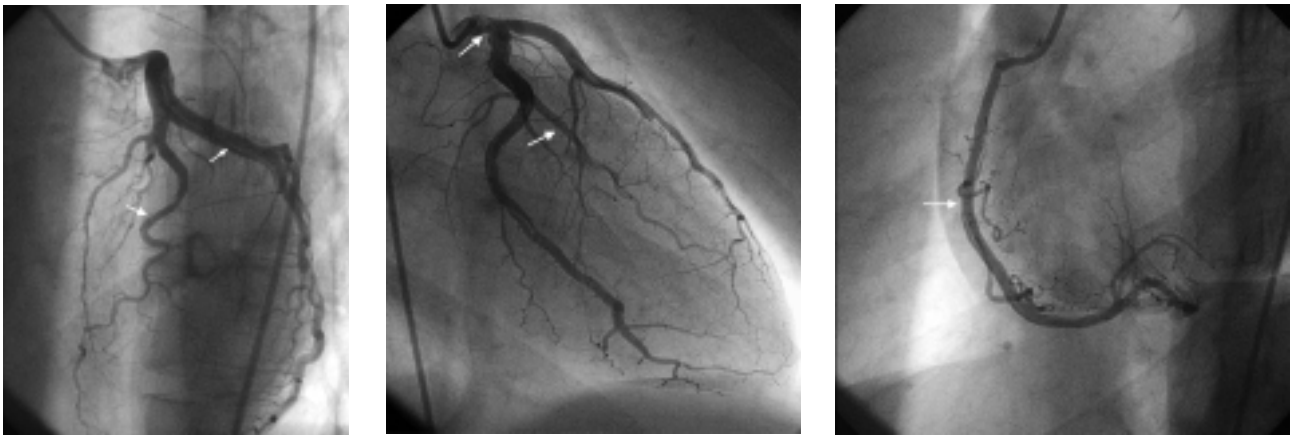

Figure 3. *Multiple views of the coronary angiogram performed 4 days after thrombolysis.* A: *left anterior oblique view of the left coronary artery (*arrows *pointing at dissections in the left anterior descending and circumflex coronary arteries).* B: *right anterior oblique view of the left coronary artery (dissection extending from the left main stem to the obtuse marginal branches indicated by* arrows*).* C: *left anterior oblique view of the right coronary artery showing dissection from the midsegment* (arrow) *to the posterior descending artery.*

firmed the presence of mild mitral valve prolapse with mild regurgitation. Echo-Doppler evaluation of the cerebral afferent, renal, mesenteric and lower limb arterial vessels was completely normal in all cases.

Thoracic and abdominal computed tomographic scan did not reveal any vascular abnormalities. Angiographic magnetic resonance imaging of the lower abdomen and pelvis showed only mild ectasia of the left common iliac artery (1.2 cm in diameter).

A skin biopsy was also taken to investigate collagen synthesis by fibroblasts. *In vitro* culture revealed a mildly abnormal type III collagen synthesis (type III/type I collagen 0.078, with normal values between 0.09 and 0.15) while type V collagen was normal and type V/type I collagen ratio in the range of normality. Besides, electrophoresis revealed that the migration of type I and III collagen chains was normal and there was no intracellular accumulation of collagen. On the basis of these findings, the diagnosis of Ehlers-Danlos syndrome was excluded.

All biohumoral assays for the presence of any coagulation defects were repeated and found to be within normal limits. All autoimmune antibody tests were normal.

At 1 year of follow-up the patient was completely asymptomatic and still on aspirin, metoprolol and oral nitrates. She was again admitted to hospital for a previously planned control coronary angiography.

Physical examination was normal except for a mild murmur due to mitral regurgitation. ECG and all biohumoral tests were normal.

Repeat coronary angiography, carried out 17 months after the previous, revealed the almost complete healing of SCAD especially in the left anterior descending coronary artery and the main stem together with a light enlargement of the arteries even in the right coronary artery (Figs. 4A-C). There was only persistence of an angiographically compatible image of dissection on the principal obtuse marginal branch (Fig. 4D), which was the same vessel that was found to be dissected at the very first angiography in 1993. This time, the dissection was very limited in length (approximately 5 mm). Again, the left ventricular ejection fraction was normal (70%). She was again discharged from the hospital on acetylsalicylic acid and beta-blockers.

Discussion

To date, various cases of SCAD have been reported in the literature but the total number of patients is limited more or less to 150[1,5]. Cases of spontaneous dissection of all three coronary vessels are exceptional. Being a rare and severe form of myocardial ischemia, often with a dramatic clinical presentation, the diagnosis is mainly *post-mortem*. Such an outcome is frequently due to the involvement of the left main stem[5]. Thus, the short-term prognosis is usually severe; however, if the acute phase is dominated, subsequent events are rare[1,21,22]. The case described here bears several peculiar aspects. Firstly, there was a widespread pattern of SCAD involving the terminal left main stem and both the proximal left anterior descending and circumflex coronary arteries; besides, the right coronary artery was widely dissected right up to the origin of the posterior descending artery. Secondly, this was the second episode of true and documented myocardial infarction with angiographic documentation of SCAD in the same patient. While the first coronary angiography after the first non-Q wave inferior myocardial infarction in 1993 documented a limited SCAD (confined to the circumflex coronary artery) the second showed the picture described above. Thirdly, angiography performed after 17 months documented the spontaneous and almost total healing of the dissection, together with an uneventful follow-up.

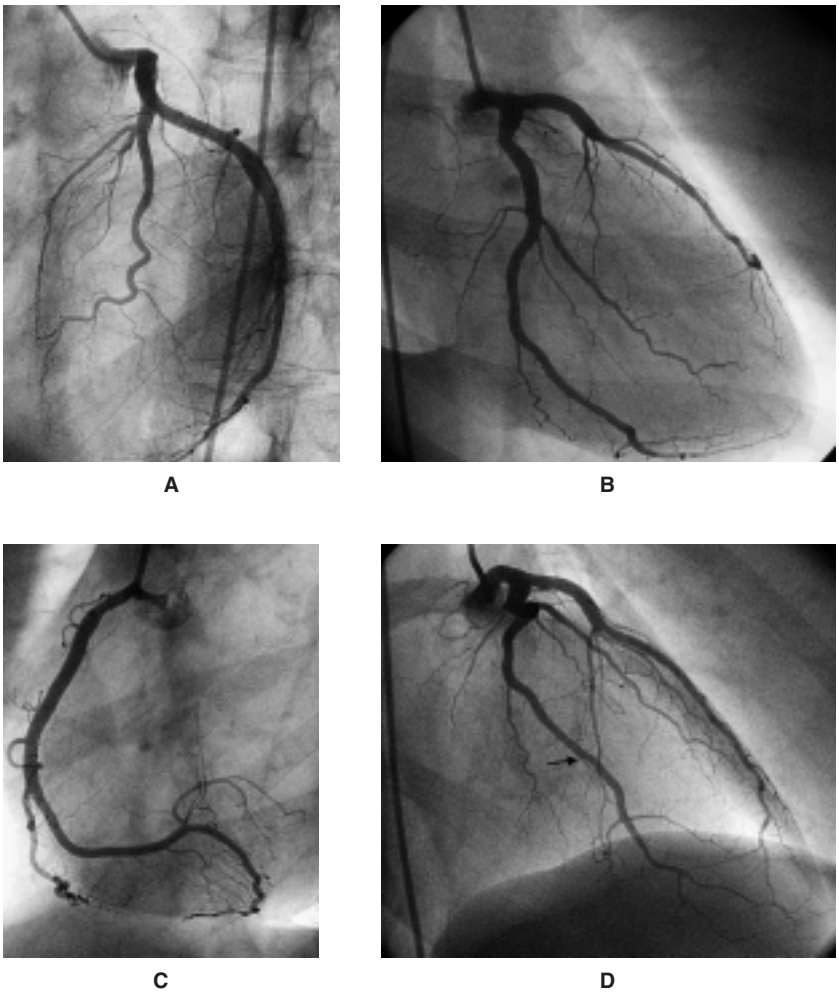

Figure 4. *Multiple views of the coronary angiogram performed at 17 months of follow-up.* A: *left anterior oblique view of the left coronary artery with no residual signs of dissection.* B: *right anterior oblique view of the left coronary artery without dissection.* C: *left anterior oblique view of the right coronary artery showing a normal lumen.* D: *cranial right anterior oblique view of the left coronary artery with minimal signs of residual dissection in the obtuse marginal branch of the left circumflex coronary artery* (arrow).

This case offers the chance to discuss the indication to thrombolytic treatment in this particular setting. The clinical result of tissue-type plasminogen activator administered in view of transmural anterior ischemia not responsive to conventional treatment was very satisfactory even though just before the appearance of reperfusion there was a shift towards inferior wall transmural ischemia. This poses the question about the possible role of fibrinolysis in reopening the left anterior descending coronary artery and, at the same time, favoring the occurrence and extension of dissection in the right coronary one. There has been a report in the literature[23] of one case of extension of SCAD due to thrombolytic therapy but most authors have described good results with medical management, including thrombolysis, of patients presenting with signs and symptoms of acute myocardial infarction and angiographically documented SCAD[2,8,24,25]. If the mechanism of complete obliteration of the lumen were due to enlargement of an intramural hematoma, fibrinolytic therapy may cause regression of the mass by degrading fibrin and thus leading to the reopening of the vessel. However, it is also possible that such treatment may impair healing of the dissection and even cause its further extension.

Further treatment of SCAD consists in coronary revascularization. There have been several reports of coronary artery bypass grafting for these patients, in particular for those with involvement of the left main stem or with multivessel dissections[5,26,27]. However, it is important to note that the literature suggests that coronary artery bypass grafting in the setting of SCAD may be hazardous because of the chance of progression of dissection in the venous and arterial conduits or into the distal part of the grafted vessels. Many reports recommend that this type of revascularization should be reserved to patients in whom aggressive medical treatment fails.

Several recent studies have reported stent placement for SCAD[28,29]. Results seem very good also with a reportedly low rate of restenosis. However, this treatment should be reserved to localized dissections and it could represent an easy solution in case of localized involve-

ment of the left main artery. However, this particular case has peculiar characteristics. Because of the widespread nature of the dissection, both coronary artery bypass grafting and the positioning of coronary stents were excluded. Covering the dissections by means of multiple stenting was not thinkable, even in view of the involvement of distal part of arteries < 2 mm in diameter. For the same reason, coronary artery bypass grafting was ruled out. At the same time the patient was stable with no signs and symptoms of residual ischemia after a small acute myocardial infarction and so there was no functional indication to coronary revascularization.

In this case we also have the interesting and quite rarely reported documentation of almost complete healing of dissection at an angiographic follow-up of more than 1 year. Three cases of spontaneous healing[7,10,21] of SCAD, all manifesting during or immediately after pregnancy, have been reported in the literature. The first was a left main stem dissection and the others, analogous to the present case, three-vessel SCAD. No hypothesis regarding the mechanisms of spontaneous healing has been made, in spite of the fact that in one study two vessels showed complete healing at angiographic follow-up, while the third developed an aneurysm[10]. We may only speculate that the cessation of the initiating noxa together with the interplay of flow direction towards or away from the intimal flaps may determine complete or almost complete healing or the formation of aneurysms. The case of P.B., however, poses great uncertainty about her future, since no causes were found, and the episodes of myocardial ischemia were two with a long intermediate period of complete absence of symptoms.

References

1. De Maio SJ, Kinsella SH, Silverman ME. Clinical course and long-term prognosis of spontaneous coronary artery dissection. Am J Cardiol 1989; 64: 471-4.
2. Ramamurti S, Maherer PR, Magnusson P, Bowyer J, Sasse L, Shaperman M. Idiopathic coronary artery dissection: rare in vivo diagnosis. Clin Cardiol 1985; 8: 57-60.
3. Nishikawa H, Nakanishi S, Nishiyama S, Nishimura S, Seki A, Yamaguchi H. Primary coronary artery dissection observed at coronary angiography. Am J Cardiol 1988; 61: 645-8.
4. Basso C, Morgagni GL, Thiene G. Spontaneous coronary artery dissection: a neglected cause of acute myocardial ischaemia and sudden death. Heart 1996; 75: 451-4.
5. Caddeo A, Delogu G, Cadeddu M, et al. Dissezione spontanea del tronco comune della coronaria sinistra: un caso clinico e revisione della letteratura. Ital Heart J Suppl 2001; 2: 413-7.
6. Antoniucci D, Diligenti M. Spontaneous dissection of three major coronary arteries. Eur Heart J 1990; 11: 1130-4.
7. Bac DJ, Lotgering FK, Verkaaik APK, Deckers JW. Spontaneous coronary artery dissection during pregnancy and post partum. Eur Heart J 1995; 16: 136-8.
8. Almahmeed WA, Haykowski M, Boone J, et al. Spontaneous coronary artery dissection in young women. Cathet Cardiovasc Diagn 1996; 37: 201-5.
9. Conraads VM, Vorlat A, Colpaert CG, et al. Spontaneous dissection of three major coronary arteries subsequent to cystic medial necrosis. Chest 1999; 116: 1473-5.
10. Rensing BJ, Kofflard M, Van den Brand MJBM, Foley DP. Spontaneous dissection of all three coronary arteries in a 33-week-pregnant woman. Cathet Cardiovasc Diagn 1999; 48: 207-10.
11. Boland J, Limet R, Trotteur G, Legrand V, Kulbertus H. Left main coronary dissection after mild chest trauma. Favorable evolution with fibrinolytic and surgical therapies. Chest 1988; 93: 213-4.
12. Kohli S, Saperia GM, Waksmonski CA, Pezzella S, Singh JB. Coronary artery dissection secondary to blunt chest trauma. Cathet Cardiovasc Diagn 1988; 15: 179-83.
13. Di Bartolomeo R, Pacini D, Nicolini F, Giancola R, Pierangeli A. Spontaneous dissection of coronary artery in a patient with ascending aortic aneurysm and aortic valve regurgitation. J Cardiovasc Surg 1999; 40: 531-3.
14. Borczuk AC, 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: 527-32.
15. Bonnet J, Aumailley M, Thomas D, Grosgogeat Y, Broustet J, Bricand H. Spontaneous coronary artery dissection: case report and evidence for a defect in collagen metabolism. Eur Heart J 1986; 7: 904-9.
16. Azam MN, Roberts DH, Logan WFWE. Spontaneous coronary artery dissection associated with oral contraceptive use. Int J Cardiol 1995; 48: 195-8.
17. Robinowitz M, Virmani R, McAllister HA Jr. Spontaneous coronary artery dissection and eosinophilic inflammation: a cause and effect relationship? Am J Med 1982; 72: 923-8.
18. Jaffe D, Broderick TM, Leier CV. Cocaine-induced coronary artery dissection. N Engl J Med 1994; 330: 510-1.
19. Sherrid MV, Mieres J, Mogtader A. Onset during exercise of spontaneous coronary artery dissection and sudden death. Occurrence in a trained athlete: case report and review of prior cases. Chest 1995; 108: 284-7.
20. Eltchaninoff H, Cribier A, Letac B. Multiple spontaneous coronary artery dissections in young women. Lancet 1995; 346: 310-1.
21. Himbert D, Makowski S, Laperche T, Steg G, Juliard JM, Gourgon R. Left main coronary spontaneous dissection: progressive healing without coronary surgery. Am Heart J 1991; 122: 1757-9.
22. Zampieri P, Aggio S, Roncon L, et al. Follow-up after spontaneous coronary artery dissection: a report of five cases. Heart 1996; 75: 206-9.
23. Buys EM, Suttorp MJ, Morshuis WJ, Plokker HWT. Extension of a spontaneous coronary artery dissection due to thrombolytic therapy. Cathet Cardiovasc Diagn 1994; 33: 157-60.
24. Behnam R, Tillinghast S. Thrombolytic therapy in spontaneous coronary artery dissection. Clin Cardiol 1991; 14: 611-4.
25. Leclercq F, Messner-Pellenc P, Carabasse D. Successful thrombolysis treatment of a spontaneous left main coronary artery dissection without subsequent surgery. Eur Heart J 1996; 17: 320-1.
26. Vicari R, Eybel C, Monson D. Survival following spontaneous coronary artery dissection. Surgical repair by extrusion of intramural hematoma. Am Heart J 1986; 111: 593-4.
27. Atay Y, Yagdi T, Turkoglu C. Spontaneous dissection of the left main coronary artery: a case report and review of the literature. J Card Surg 1996; 11: 371-5.
28. Hong MK, Satler LF, Mintz GS, et al. Treatment of spontaneous coronary artery dissection with intracoronary stenting. Am Heart J 1996; 132: 200-2.
29. Vale PR, Baron DW. Coronary artery stenting for spontaneous coronary artery dissection: a case report and review of the literature. Cathet Cardiovasc Diagn 1998; 45: 280-6.