

Case Report

Spontaneous Coronary Artery Dissection and Acute Myocardial Infarction During Pregnancy

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Spontaneous coronary artery dissection is a rare cause of infarction in the general population, but a common cause of myocardial infarction during pregnancy, and even nowadays carries a high risk of mortality. We describe the case of a 31-year-old primigravida who presented during the 34th week of pregnancy with the chief complaint of chest pain and was found to suffer from myocardial infarction. She was otherwise healthy and had no known risk factors for coronary artery disease. The patient was treated conservatively with nitrates, aspirin, heparin and beta-blockers, eventually sustained a large myocardial infarction and, after an initial period of instability, remained asymptomatic. A week later she delivered 3 healthy babies. A coronary angiogram performed 3 months after the initial event revealed an extensive obstructive dissection of the circumflex coronary artery. The decision whether to pursue percutaneous coronary intervention, surgical revascularisation or appropriate medical therapy, is based on clinical presentation, the extent of the dissection, and the amount of ischaemic myocardium at risk. Cardiologists must be aware of this rare entity during pregnancy or postpartum, since early diagnosis and treatment are crucial for the survival of the mother and the foetus.

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Pregnancy is accompanied by natural changes in the cardiovascular system and coagulation mechanisms that increase the risk of myocardial ischaemia,^{1,2} but the incidence of acute myocardial infarction is remarkably low. In a large recent study in the USA the rate recorded was 6.2 cases per 100,000 deliveries and the mortality was 5.1%.³

The pathogenetic mechanisms implicated in the occurrence of acute coronary events during pregnancy are mainly the presence of atheromatous plaque in the coronary vessels and, less frequently, coronary artery dissection and various hypercoagulable states.^{4,5} Spontaneous coronary artery dissection is a rare cause of myocardial infarction in the general population.⁶ Most of the cases described refer to women, either during pregnancy or,

more commonly, during the three months after delivery, with the dissection usually being located in the anterior descending coronary artery.^{7,8} Only a small number of cases have been described so far in the international literature.⁹

We report the case of a young, pregnant woman, who was gestating three embryos (after *in vitro* fertilisation) and who in the third trimester suffered an acute myocardial infarction. She was treated conservatively and on a later coronary angiographic examination was found to have extensive dissection of the circumflex artery.

Case presentation

A 31-year-old primigravida, in the 34th week of a pregnancy resulting from suc-

cessful *in vitro* fertilisation (triplets), was brought by relatives to the emergency room because of retrosternal constrictive pain. The pain had started 30 minutes earlier, showed a steady increase in intensity with no radiation, and was accompanied by heavy perspiration, nausea, and dizziness. The patient had no history of any episodes of pain either at rest or on effort, nor any risk factors for coronary artery disease. Her home medications included calcium, iron, and folic acid supplements.

The patient was in distress with a good level of consciousness. Her temperature was 36.8°C, blood pressure was 70/50 mmHg in both arms, pulse 75 beats per minute, respiratory rate 24 breaths per minute, and oxygen saturation 98% while she was breathing room air. The breath sounds were normal bilaterally. The jugular veins were distended (an expected finding during pregnancy). The cardiac examination revealed a 2-3/6 mid-systolic murmur, best heard at the 3rd to 4th left intercostal space, but no diastolic murmur or pericardial rub.

The electrocardiogram (ECG) revealed normal sinus rhythm, ST-segment elevation <1 mm in leads III and aVF, with deep ST-segment depression in leads I and aVL and V₁-V₆, and incomplete right bundle branch block (Figure 1). On the right and posterior chest ECG leads there was ST-segment

elevation. The emergency transthoracic echocardiographic examination showed akinesis of the inferior and posterior left ventricular wall (Figure 2), with estimated overall left ventricular ejection fraction of 45%, and no dilatation or evidence of dissection of the proximal part of the aorta.

The patient was treated with crystalloid solutions, unfractionated heparin, aspirin, and morphine for pain relief. Within a short time, her clinical condition stabilised, with an increase in her blood pressure, pain remission, and improvement of the ECG changes. A decision was taken not to institute any thrombolytic therapy. Intravenous nitrates and oral metoprolol were added to the treatment regimen and were initially well tolerated.

Two hours later, the patient showed signs of acute heart failure, with reappearance of the ischaemic ECG findings, but this time with a good blood pressure. She was treated with diuretics, morphine, and a higher dose of nitrates, and again rapidly improved. The patient had elevation of cardiac enzymes (creatin kinase 3581 IU/L, creatine kinase-MB 593 IU/L) and ECG evolution indicative of acute inferior myocardial infarction (QS waves in leads III and aVF).

After stabilisation, the patient was transferred to a tertiary centre, where one week later she underwent induced normal labour without complications

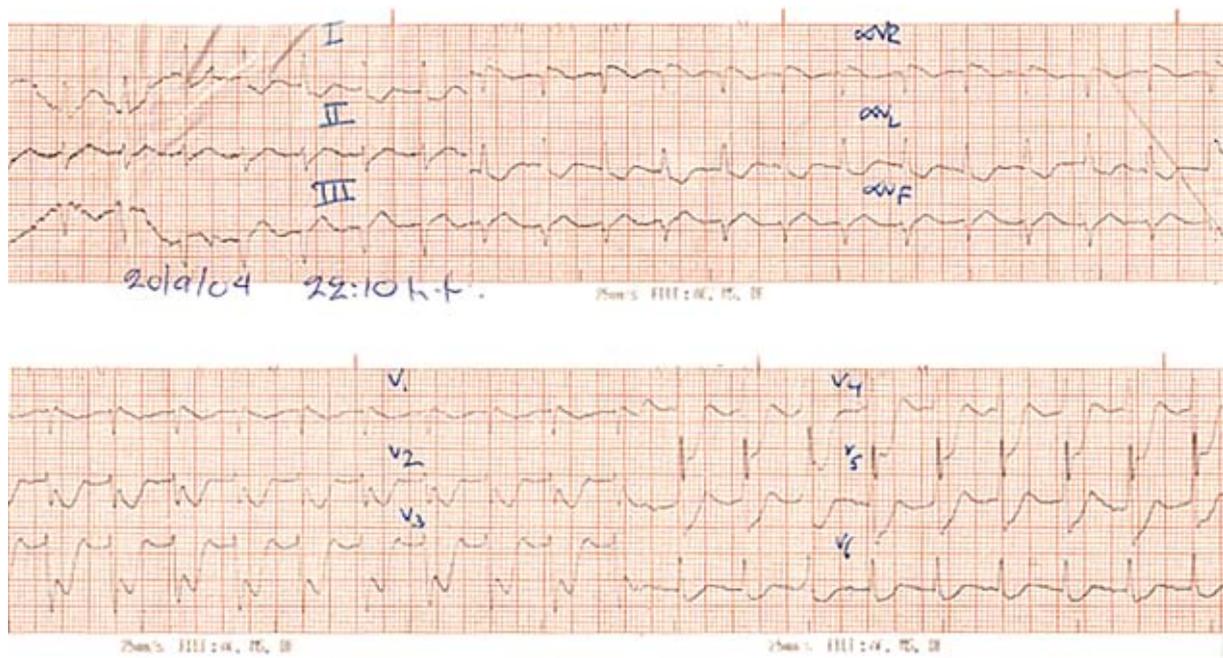


Figure 1. Twelve-lead ECG on admission, showing borderline ST-segment elevation in leads III and aVF, accompanied by large ST-segment depression in leads V₂-V₅.

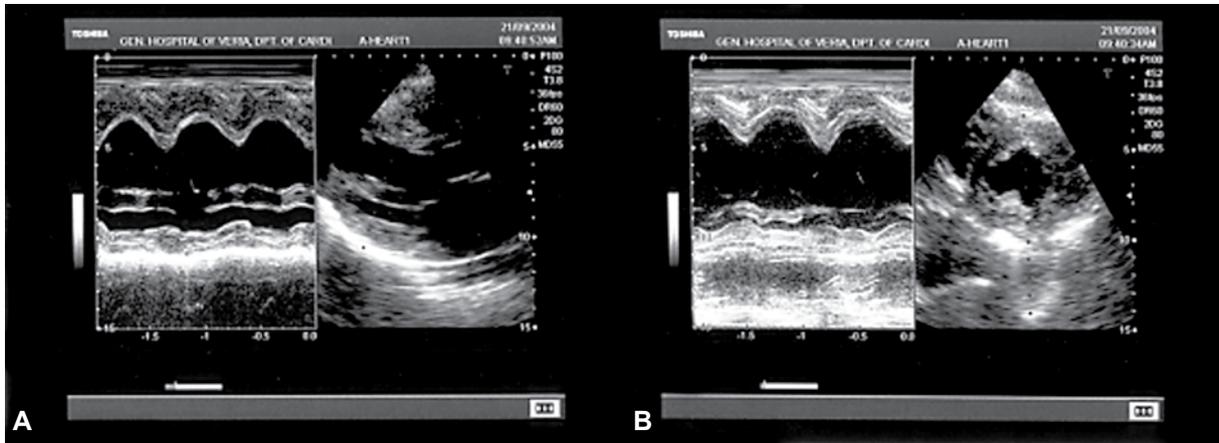


Figure 2. Two-dimensional and M-mode echocardiography on admission in long-axis (A) and short-axis (B) views, showing hypokinesis of the inferior wall and compensatory hyperkinesis of the interventricular septum. There is no right ventricular dilation.

and gave birth to three healthy babies. The patient remained asymptomatic and three months later she underwent a coronary angiographic examination. The angiogram demonstrated coronary vessels with smooth margins, without stenoses, but revealed an extensive dissection of a dominant circumflex artery (Figures 3-5). The right coronary artery was small and

supplied only the right ventricle. The left ventricle was dilated, with akinesis of the lateral and inferior wall, as well as hypokinesis of the anterior wall. The global ejection fraction was measured at 35% and there was no mitral regurgitation.

Thallium-201 scintigraphy under dipyridamole drug challenge showed an inferolateral severe perfu-

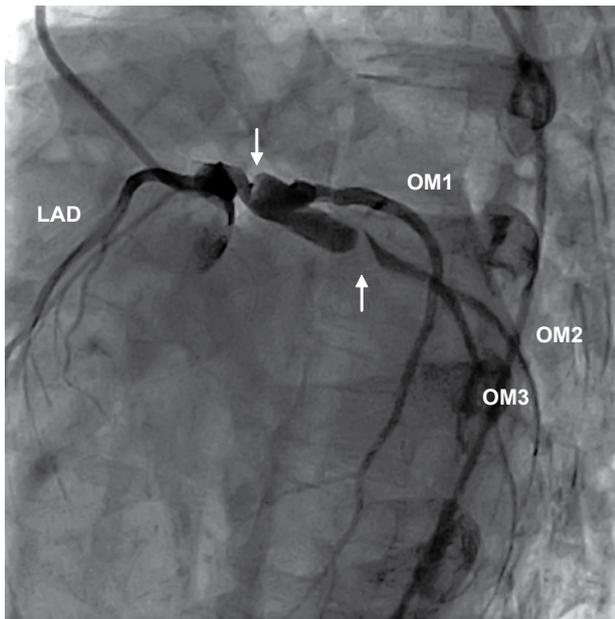


Figure 3. The left anterior oblique projection shows the dissection in the circumflex artery, which starts at the ostium of the vessel and extends to the atrioventricular continuation of the artery, with a severe degree of compression of the lumen (arrows). The extension to the first marginal branch (OM1) is clearly seen in a different projection (Figure 5).

LAD – anterior descending branch; OM1/2/3 – first/second/third marginal branch

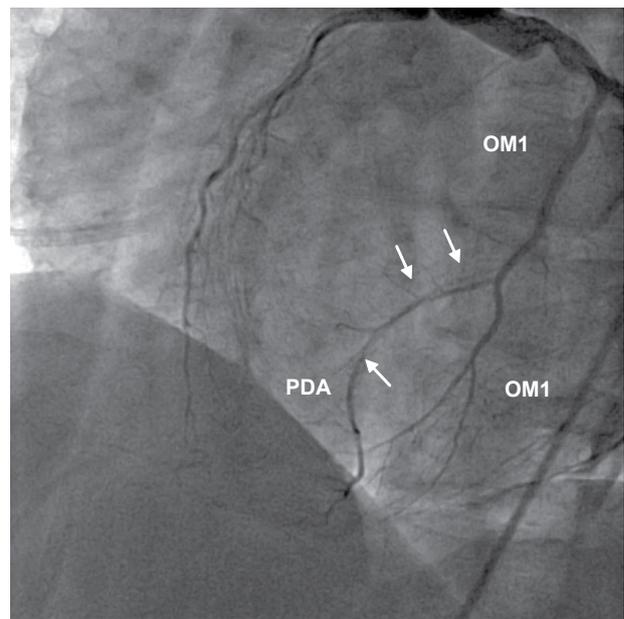


Figure 4. In the same projection as in Figure 3, at the end of the contrast injection, the continuation of the circumflex artery can be seen filling late (arrows) ending in the posterior descending artery (PDA), which is part of a left dominant system. Filling of the PDA is mainly from collaterals. A comparison of Figures 3 and 4 allows the discrimination of overlapping vessels.

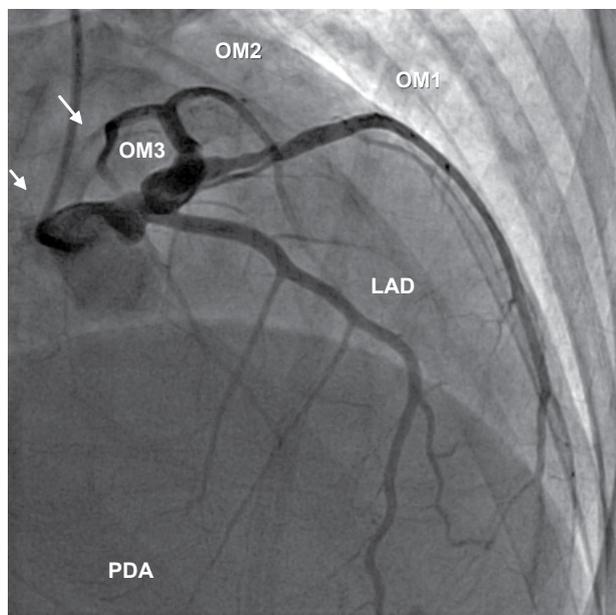


Figure 5. Right anterior oblique projection with cranial tilt, showing the extension of the dissection to the first marginal branch (OM1). The arrows point to the just discernible continuation of the circumflex artery beyond the ostium of the third marginal branch (OM3) and the posterior descending artery (PDA), which is filled mainly via collaterals.

sion defect and thallium-201 readministration for the evaluation of viable myocardium showed minimal enhancement of thallium-201 uptake. Based on the coronary angiographic findings, safe revascularisation was considered feasible only with aortocoronary bypass and not with coronary angioplasty, considering the large diameter of the false lumen. However, taking into account the small amount of viable myocardium on the myocardial scintigram and the patient's symptom-free condition, it was decided to continue with the conservative management. The patient did very well with no problems over a follow up of two years.

Discussion

The incidence of acute myocardial infarction (AMI) during pregnancy and puerperium reported by various studies ranges from 2.8-10 cases per 100,000 deliveries.^{3,4,10} In a recent report by James et al,³ concerning pregnant women in the USA, the incidence of AMI for the period 2000-2002 was calculated to be 6.2 cases per 100,000 deliveries. In the same study, the mortality rate for pregnant patients with AMI was found to be 5.1%,³ substantially lower than in older

studies (7.3% to 37%),^{4,10-12} probably because of improvement in the diagnosis and treatment of these patients. In general terms it appears that pregnant women are at 3 to 4 times greater risk of AMI than non-pregnant women, although the incidence in absolute terms is very small.³ Independent predisposing factors that have been associated with an increased risk of infarction in pregnant women are age over 30 years, the third trimester of pregnancy, multiparity, hypertension, eclampsia and pre-eclampsia, diabetes, smoking, thrombophilia, need for blood transfusion, and appearance of infection following delivery.^{3,4}

In a study by Roth et al, which analysed 125 cases of myocardial infarction in pregnant women, the main cause was found to be atheromatous coronary artery disease. Coronary angiography performed in 68 of the patients found coronary atheromatosis in 43%, coronary artery dissection in 16%, thrombus without atheromatous lesions in 21%, and normal coronary arteries in 29% of patients.⁴

Spontaneous coronary artery dissection is an unusual cause of myocardial infarction and in the majority of cases (80% of the total) it is encountered in young women during pregnancy or immediately after, as well as in women who are taking contraceptives.^{6,13,14} In the largest analysis to date, which included 58 cases of spontaneous coronary artery dissection related to pregnancy, Koul et al⁸ found that the majority (78%) occurred during the period after delivery and usually within the first two weeks. The patients tended to be older (mean age 33 years), multiparous, and only 30% of them had risk factors for coronary artery disease. Of course, the high mean age does not rule out the occurrence of dissection in much younger patients.⁹ The main vessel affected (78% of patients) was the anterior descending branch, followed by the circumflex artery (29%) and the right coronary artery (26%). It is noteworthy that in 24% of patients the dissection included the main stem of the left coronary artery, while in 40% of patients there were dissections in more than one vessel.⁸

In our own case the patient was relatively old and had no risk factors for coronary artery disease; however, she was not multiparous. In addition, this is one of the rare cases where the dissection occurred during gestation and not after delivery, while on the subsequent coronary angiogram the only vessel showing dissection was the circumflex artery, a finding that is rare in the literature. Indeed, although the circumflex artery is often involved in the dissection of other arteries in pregnant women, its isolated dissec-

tion is an extremely rare phenomenon. There are very few reports of isolated dissection of the circumflex coronary artery in the international literature¹⁵⁻¹⁷ and in only one did the dissection occur during pregnancy, as in our case.¹⁷ Of course, one cannot rule out the possibility of healed dissections at other sites, given that the coronary angiographic examination in our patient was performed three months after the acute infarction.

The pathogenesis of coronary artery dissection related to pregnancy has not been fully elucidated, but haemodynamic changes and, to a greater degree, changes in the connective tissue of the vascular wall are the two probable basic pathophysiological mechanisms. The dissection usually starts 2 cm from the coronary artery ostium and extends distally, although a retrograde progression may occur in rare cases. The level of the dissection is located in the outer third of the media, or between the media and the adventitia, and the hematoma that forms compresses true lumen of the vessel, thus impeding free blood flow.^{8,14,15}

The arterial wall undergoes certain changes during pregnancy that make it more vulnerable to dissection, such as breakdown of collagen and elastin and a reduction in proteoglycans, probably as a result of an increased expression of metalloproteinases, and hypertrophy and hyperplasia of smooth muscle fibres.^{8,18,19} These changes are attributable to the special hormonal environment of pregnancy, and in particular to the increase in oestrogen and relaxin levels, while there are indications that these return to normal three months after delivery.^{8,19-21} In some cases of dissection there is infiltration of the coronary artery adventitia by eosinophil granulocytes, but their pathological significance in weakening the media^{22,23} has not been accepted by everyone.²⁴ Apart from these morphological changes, the increase in cardiac output (up to 50% in the third trimester and up to 80% during delivery) produces forces that may cause rupture and haemorrhage in the vascular wall.^{8,9}

The diagnosis of spontaneous dissection can be made by coronary angiography, which is the examination of choice. However, in our patient this was not possible, nor could she be transferred immediately to a centre with a catheterisation laboratory. The prospect of exposing the foetus to radiation and the possible consequences are a cause for concern when a pregnant patient undergoes coronary angiography and/or percutaneous coronary angioplasty. Lead covers can protect the patient's pelvic region from radiation, and access via the radial rather than the femoral

artery usually limits the foetal exposure to less than 5 rad (50 mGy), an exposure level that is considered the threshold for termination of the pregnancy.^{4,25,26}

The indicated therapeutic approach to these patients is not well defined because of the small number of cases. Thrombolytic therapy, though used during pregnancy in the past,⁴ is relatively contraindicated because of the increased risk of haemorrhage for both mother and foetus, as well as because of the risk of extending the dissection.^{27,28} A coronary angiogram performed as emergency is good not only in demonstrating a dissection but also other causes of coronary obstruction, leading to the appropriate management plan.^{4,26}

The prognosis of patients with coronary artery dissection seems to have improved in recent years. In 1993, in a retrospective study by Engelman et al, the overall mortality was 66%.²⁹ In the analysis by Koul et al in 2001 the mortality was lower (38%). The same report stressed that, following the deaths on arrival and during the first hours, management of the surviving 36 patients after diagnosis, with medications in 47% of cases, aortocoronary bypass in 30%, angioplasty in 11%, and transplantation in 8% (using the raw data of the paper), was associated with zero mortality, suggesting the importance of prompt diagnosis for these patients' favourable clinical course.⁸ Whether an earlier diagnosis and appropriate treatment could have improved the survival is not clear. Treatment with antiplatelet medication and beta-blockers is recommended in patients with single-vessel dissection without compromise of the coronary circulation, since approximately 50% of these patients show spontaneous healing of the dissection, while an even greater percentage are asymptomatic.⁹ In young patients who have an isolated dissection in the proximal part of a coronary artery that supplies a large region of viable myocardium, without a good collateral circulation, the best choice is probably percutaneous angioplasty without or preferably with stenting, aiming to eliminate the false lumen and the obstruction.^{9,14,30,31} The possibility of extending the intramural haematoma proximally and distally by the stent compression should be a consideration.³² In our patient the dissection was extensive, with the diameter of the false lumen being too large for effective sealing by a stent, and it is probable that even if a coronary angiogram had been obtained on presentation little could have been offered by angioplasty. Aortocoronary bypass for the treatment of coronary artery dissection is indicated if the dissection is in

the main stem, if there is dissection in multiple vessels, or if other invasive methods are unsuccessful and there is refractory, recurring ischaemia.^{5,9,14} In cases of severe heart failure following dissection heart transplantation has been tried successfully.³³ In our case the decision to follow a conservative approach was made 3 months after delivery and was based on the fact that the patient was asymptomatic, with only a small amount of viable myocardium, while a less invasive approach (coronary angioplasty) seemed to be limited by the extent and size of the dissection.

Two important points relevant to the management of patients with AMI during pregnancy are the timing of the delivery and drug treatment. Our patient's delivery took place one week after the AMI, since the patient had no new episodes of pain or dyspnoea and was haemodynamically stable. It has been suggested that delivery following AMI should be postponed for 2-3 weeks, so as to achieve complete healing of the infarcted region, but there are no studies showing that such a delay improves the result. It should be noted that, of the two delivery methods (vaginal or caesarean section), neither is clearly superior to the other in such a patient and the decision should be made on a case-by-case basis.⁴ In our patient we chose the vaginal delivery method with good results and without complications. Of the drugs usually used in the treatment of acute coronary events, unfractionated or low molecular heparin, aspirin, beta-blockers, and nitrates, as well as morphine and furosemide, may be administered with relative safety during pregnancy. In contrast, angiotensin converting enzyme inhibitors and angiotensin II antagonists are contraindicated, because of the risk they pose to foetal development and survival throughout pregnancy.^{4,34} The latter drugs were not given to our patient initially, but were added to her treatment after delivery. As regards clopidogrel and platelet IIb/IIIa inhibitors, there is no reason not to use them if there are strong indications.³⁴ We chose not to administer antiplatelets other than aspirin because of the risk of haemorrhage, should urgent intervention be needed to remove the embryos.

Conclusions

Spontaneous coronary artery dissection is a rare entity in the general population. In contrast, it is a relatively common cause of AMI in pregnant women. The treating physician should consider the possibility of dissection in any woman who complains of chest pain

during pregnancy or puerperium. Prompt diagnosis of this severe condition contributes to a significant improvement in the prognosis of both mother and foetus.

References

1. Chesnutt AN. Physiology of normal pregnancy. *Crit Care Clin.* 2004; 20: 609-615.
2. Gabbe SG, Niebyl JR, Simpson JL. *Obstetrics: Normal and Problem Pregnancies.* 4th ed. New York: Churchill Livingstone; 2001.
3. James AH, Jamison MG, Biswas MS, Brancazio LR, Swamy GK, Myers ER. Acute myocardial infarction in pregnancy: a United States population-based study. *Circulation.* 2006; 113: 1564-1571.
4. Roth A, Elkayam U. Acute myocardial infarction associated with pregnancy. *Ann Intern Med.* 1996; 125: 751-762.
5. Frey BW, Grant RJ. Pregnancy-associated coronary artery dissection: a case report. *J Emerg Med.* 2006; 30: 307-310.
6. Celik SK, Sagcan A, Altintig A, Yuksel M, Akin M, Kultursay H. Primary spontaneous coronary artery dissections in atherosclerotic patients. Report of nine cases with review of the pertinent literature. *Eur J Cardiothorac Surg.* 2001; 20: 573-576.
7. Dhawan R, Singh G, Fesniak H. Spontaneous coronary artery dissection: the clinical spectrum. *Angiology.* 2002; 53: 89-93.
8. Koul AK, Hollander G, Moskovits N, Frankel R, Herrera L, Shani J. Coronary artery dissection during pregnancy and the postpartum period: two case reports and review of literature. *Catheter Cardiovasc Interv.* 2001; 52: 88-94.
9. Maeder M, Ammann P, Drack G, Rickli H. Pregnancy-associated spontaneous coronary artery dissection: impact of medical treatment. Case report and systematic review. *Z Kardiol.* 2005; 94: 829-835.
10. Ladner HE, Danielsen B, Gilbert WM. Acute myocardial infarction in pregnancy and the puerperium: a population-based study. *Obstet Gynecol.* 2005; 105: 480-484.
11. Hankins GD, Wendel GD, Leveno KJ, Stoneham J. Myocardial infarction during pregnancy: a review. *Obstet Gynecol.* 1985; 65: 139-146.
12. Badui E, Enciso R. Acute myocardial infarction during pregnancy and puerperium: a review. *Angiology.* 1996; 47: 739-756.
13. Karabinos IK, Salahas A, Tavernarakis A. Acute coronary syndrome with ST-segment elevation in a patient with spontaneous dissection of the anterior descending coronary artery branch: case report and review of the literature. *Hellenic J Cardiol.* 2004; 45: 408-414.
14. Almeda FQ, Barkatullah S, Kavinsky CJ. Spontaneous coronary artery dissection. *Clin Cardiol.* 2004; 27: 377-380.
15. Sage MD, Koelmeyer TD, Smeeton WM. Fatal postpartum coronary artery dissection. A light- and electron-microscope study. *Am J Forensic Med Pathol.* 1986; 7: 107-111.
16. Bertrand E, Seka R, Adoh M, et al. Spontaneous coronary artery dissection: apropos of a case with associated spasm and regression of the dissection. *Arch Mal Coeur Vaiss.* 1993; 86: 249-253.
17. Bucciarelli E, Fratini D, Gilardi G, Affronti G. Spontaneous dissecting aneurysm of coronary artery in a pregnant woman at term. *Pathol Res Pract.* 1998; 194: 137-139.

18. Manalo-Estrella P, Barker AE. Histopathologic findings in human aortic media associated with pregnancy. *Arch Pathol.* 1967; 83: 336-341.
19. Wingrove CS, Garr E, Godsland IF, Stevenson JC. 17 β -oestradiol enhances release of matrix metalloproteinase-2 from human vascular smooth muscle cells. *Biochem Biophys Acta* 1998; 1406: 169-74.
20. Qin X, Chua PK, Ohira RH, Bryant-Greenwood GD. An autocrine/paracrine role of human decidual relaxin. II. Stromelysin-1 (MMP-3) and tissue inhibitor of matrix metalloproteinase-1 (TIMP-1). *Biol Reprod.* 1997; 56: 812-820.
21. Williams EJ, Benyon RC, Trim N, et al. Relaxin inhibits effective collagen deposition by cultured hepatic stellate cells and decreases rat liver fibrosis in vivo. *Gut.* 2001; 49: 577-583.
22. Robinowitz M, Virmani R. Spontaneous coronary artery dissection and eosinophilic inflammation: a cause and effect relationship? *Am J Med.* 1982; 72: 923-928.
23. 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: 527-532.
24. Dowling GP, Buja LM. Spontaneous coronary artery dissection occurs with and without periadventitial inflammation. *Arch Pathol Lab Med.* 1987; 111: 470-472.
25. Sharma GL, Loubeyre C, Morice MC. Safety and feasibility of the radial approach for primary angioplasty in acute myocardial infarction during pregnancy. *J Invasive Cardiol.* 2002; 14: 359-362.
26. Sullebarger JT, Fontanet HL, Matar FA, Singh SS. Percutaneous coronary intervention for myocardial infarction during pregnancy: a new trend? *J Invasive Cardiol.* 2003; 15: 725-728.
27. Antman EM, Anbe DT, Armstrong PW, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction; A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of patients with acute myocardial infarction). *J Am Coll Cardiol* 2004; 44: E1-E211.
28. Buys EM, Suttorp MJ, Morshuis WJ, Plokker HW. Extension of a spontaneous coronary artery dissection due to thrombolytic therapy. *Cathet Cardiovasc Diagn.* 1994; 33: 157-160.
29. Engelman DT, Thayer J, Derossi J, Scheinerman J, Brown L. Pregnancy related coronary artery dissection: a case report and collective review. *Conn Med.* 1993; 57: 135-139.
30. Gonzalez JI, Hill JA, Conti CR. Spontaneous coronary artery dissection treated with percutaneous transluminal angioplasty. *Am J Cardiol.* 1989; 63: 885-886.
31. Schiff JH, Gries A, Ehehalt R, Elsaesser M, Katus HA, Meyer FJ. A pregnant woman with acute myocardial infarction due to coronary artery dissection: pre-hospital and in-hospital management. *Resuscitation.* 2007; 73: 467-474.
32. Chue CD., Routledge HC, Townend JN. Spontaneous coronary artery dissection and the role for percutaneous coronary intervention: to treat or not to treat? *J Invasive Cardiol* 2009; 21: E44-E47
33. Curiel P, Spinelli G, Petrella A, et al. Postpartum coronary artery dissection followed by heart transplantation. *Am J Obstet Gynecol.* 1990; 163: 538-539.
34. Wilson AM, Boyle AJ, Fox P. Management of ischaemic heart disease in women of child-bearing age. *Intern Med J.* 2004; 34: 694-697.