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

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Spontaneous coronary artery dissection as a cause of acute coronary syndrome is a rare disease entity with extremely high mortality. The aetiology of spontaneous coronary artery dissection is to a large extent undetermined and it probably arises from a variety of causes involving multiple contributing factors. It is most frequently encountered in young women during pregnancy or post partum, after cocaine use, after aerobic exercise, in eosinophilic infiltration of the coronary vessel wall, in Ehlers Danlos syndrome, etcetera. The aetiology of spontaneous dissection in patients with coronary atherosclerosis is of different origin and it is likely that the following factors may be implicated: intramural haematoma, extensive rupture of an atheromatous plaque, increased apoptosis of smooth muscle fibres, increased wall stress on the intimaluminal surface of atheromata, and spasm. Prompt diagnosis is vitally important for the patient’s prognosis and is based on coronary angiography, while intracoronary ultrasound may also be of assistance in some cases. Treatment is usually invasive, through performing aortocoronary bypass surgery or percutaneous coronary angioplasty with stent implantation, although in some cases a conservative strategy may be more appropriate. We present the case of an acute coronary syndrome with ST-segment elevation, treated successfully with thrombolysis, in which coronary angiography revealed extensive type C dissection of the anterior descending coronary artery branch, starting in the first third and terminating in the vessel’s periphery, with satisfactory flow.

A man aged 48 years with no prior cardiological history came to our hospital’s Emergency Department complaining of acute retrosternal pain, reflected in the back, which had started an hour before. The patient was under treatment for hypertension, a smoker, and had a family history of coronary artery disease, since his sister had undergone coronary bypass surgery at a younger age than his own for the treatment of coronary artery disease. The ECG showed ST-segment elevation on leads V₂-V₅ (Figure 1). The patient was considered to be suffering from an acute coronary syndrome with ST-segment elevation and thrombolysis was judged to be the most suitable means of reperfusion. Indeed, thrombolysis with reteplase was effective, since the ST-segment elevation disappeared and the patient’s pain had stopped by the time the treatment was completed. The patient remained haemodynamically stable, free of complications and with no post-infarction angina during the next few days.
On the fourth post-infarction day the patient was brought to the Haemodynamic Laboratory for a coronary angiogram. Access was via the right femoral artery using a 4F diameter sheath. Selective left coronary catheterisation was performed using a Left Judkins 4 catheter and the right coronary artery was catheterised using a right Modified Amplatz. Left ventriculography was performed using a Pigtail 4F catheter.

The first projection (Figure 2) showed dissection of the anterior descending branch, starting proximally and ending in the distal third, also including the second diagonal branch. Non-significant stenosis (<50%) was seen immediately after the origin of the 1st. diagonal, while the flow in the peripheral part of the anterior descending was slightly reduced (<TIMI 3). In another projection of the left system (Figure 3) the dissection was seen to include peripherally both the second diagonal and the continuation of the anterior descending. A further projection (Figure 4) showed persistence of the contrast medium in the
vessel wall after its draining from the artery (type C dissection). The right coronary artery was free of lesions, while the ventriculography showed hypokinesia of the apex with a left ventricular ejection fraction of 40-45%.

In view of the patient’s haemodynamic stability, the good vascular flow (slightly reduced to <TIMI 3), the absence of significant angiographic stenosis and the extent of the dissection, it was decided that conservative management would be in the patient’s best interest at that time. We considered that the patient should undergo myocardial scintigraphy for the detection of ischaemia and probably a new angiographic examination at a later time.

Discussion

The case described here is one of acute coronary syndrome with ST-segment elevation, without significant coronary stenosis but with extensive dissection of the anterior descending coronary artery branch. Although it cannot be established whether the spontaneous coronary artery dissection was present to some degree before the onset of the acute coronary syndrome or whether it appeared subsequently, it does appear to have been the most significant pathophysiological event in the patient in question. We present this case because, although it is impossible to provide absolute proof of a causal relationship between the vessel dissection and the acute coronary syndrome, that nevertheless seems to be by far the most likely interpretation. Cases of acute coronary syndrome that are attributable to or related with spontaneous dissection of a coronary vessel are exceedingly rare. Furthermore, this case is of particular interest for two reasons: first, the haemodynamic flow target after the acute coronary syndrome had already been achieved through thrombolysis (slightly reduced flow, <TIMI 3) without there being any significant angiographic stenosis; second, the dissection was extremely extensive, which limited the invasive options.

The pathologoanatomical definition of coronary artery dissection describes blood accumulation in the media, with or without an entry portal from the intima. This creates conditions of obstruction of the true lumen of varying degree, leading to myocardial ischaemia and/or myocardial infarction. Coronary artery dissections are classified as either primary, or spontaneous dissection or secondary dissection. Secondary dissection is usually the consequence of a discrete and clear pathological mechanism, such as extension of an aortic dissection (in cystic medial necrosis of the aorta, Marfan syndrome, etc.) to the coronary vessels, or of traumatic aetiology following an invasive procedure involving the artery in question, such as coronary angiography, angioplasty or aortocoronary bypass surgery. In contrast, however,
primary or spontaneous coronary artery dissection involves an isolated section of a coronary vessel or vessels, with no obvious triggering factor, and is an extremely rare disease entity.

Spontaneous dissection was first described in 1931 in a post mortem examination of a 42-year-old woman who died suddenly following an episode of chest pain. Since then more than 150 cases have been described in the international literature. The real incidence of the disease, however, is not precisely known, since even in post mortem studies it can be underestimated because thrombus formation within the false lumen may be perceived as thrombosis of atheromatous vessel plaque. A study by Celik et al found 9 cases of spontaneous coronary artery dissection in a total of 3750 patients with findings suggestive of coronary artery disease during angiography, giving an incidence of 0.24%. It is estimated that 69% of cases are diagnosed during post mortem studies, while 80% involve women, mean age 40 years, of whom 25% are in pregnancy or post partum. Spontaneous dissection of the right coronary artery is more common in men, while dissection of the anterior descending is seen most often in women. Out of all the coronary vessels the anterior descending is affected most frequently (52.5%), followed by the right coronary artery (24%) and the main stem (13.5%). Spontaneous dissection of all three coronary vessels has been described and indeed with silent symptomatology, the clinical expression of the syndrome usually depends on the degree of vessel obstruction, from simple ischaemia and acute myocardial infarction to sudden death, which is also the most common manifestation.

Spontaneous coronary artery dissection is usually described in young women, during either pregnancy or post partum. Hormonal changes during this period, when the oestrogen-progesterone balance is disturbed, are believed to create conditions favourable for dissection. Similarly, cases of dissection have been described following the taking of contraceptive drugs. Cystic medial necrosis of coronary vessels and angiomatosis have also been considered as causes of spontaneous dissection. It is indicative that spontaneous dissection has been seen after intensive exercise, after cocaine use, and in type IV Ehlers Danlos syndrome. In some cases of spontaneous coronary artery dissection post mortem studies revealed the existence of eosinophilic infiltration in the boundary between the adventitia and the media. Some have considered periartheritis to be a cause of dissection as a result of the lytic action of eosinophil-produced proteases on the vessel wall, while others question the active pathophysiological role of eosinophiles and consider the infiltration to be simply an epiphenomenon. Hypertension does not appear to be related with spontaneous coronary artery dissection, since it is usually absent. However, spontaneous dissection of the right coronary artery has been described during a dobutamine stress echocardiographic examination during which there was a large increase in blood pressure.

In recent years cases of spontaneous dissection have been described in patients with atherosclerosis of the coronary vessels, with or without significant stenosis, as in the case we describe here. For this reason, spontaneous dissection may be categorised according to the presence or absence of coronary atherosclerosis. In this spirit, Chen and Duan proposed a different classification, as follows: a) with coexistent atherosclerotic coronary artery disease; b) in the period immediately after birth or during post partum; c) of undetermined aetiology.

The coronary vessels differ from the aorta in that they are resistance vessels, while the aorta is a capacitance vessel. The histological difference between them lies in the significant amount of elastic connective tissue present in the aorta, in contrast to the coronary vessels, because of the functional need for greater distensibility. The aorta consists of around 30 layers of elastic connective tissue (elastin and proteoglycans) that compensate for the increase in wall stress during systole arising from the need to accommodate the entire stroke volume within a very short space of time. These layers include smooth muscle fibres. The coherence of the entire substrate is maintained by the microfibrils, which are polymers of a 350kD protein, fibrillin, that connect the elastic tissues to each other and to the smooth muscle fibres. Pathological changes and inhomogeneity in the substrate can cause an uneven distribution in wall stress. In coronary atherosclerosis, the formation of intramural atheromata, which are soft in texture and lack elastic properties, firstly disturbs the geometry of the lumen and secondly promotes such inhomogeneity, leading to a non-uniform distribution of wall stress and creating conditions favourable for dissection. In fact, the wall stress in atheromatous plaques was evaluated in an earlier study using an experimental model. Similar pathophysiological changes can be induced by the formation of intramural haematomas.
In addition, increased apoptosis of smooth muscle fibres has been found to promote aortic dissection, either via an increased expression of the angiotensin II receptor AT2R23 or the nuclear receptor PPAR-γ,24 or through an increased expression of metalloproteinases25 MMP1, MMP2, MMP3 and MMP9. It is likely that similar mechanisms may play a part in spontaneous coronary artery dissection, especially in cases with coronary atherosclerosis, since increased apoptosis of smooth muscle fibres is known to be implicated as a mechanism that renders an atheromatous plaque vulnerable.

The role of the vasa vasorum in the pathogenesis of spontaneous coronary artery dissection is controversial. The question is to what extent a spontaneous coronary artery dissection arises from lysis of the intima proceeding towards the media, or from intramural haemorrhage from the vasa vasorum into the media,26 which proceeds towards the intima and usually causes lysis conditions in its continuation. An older study27 established the existence of an increased density of newly formed vasa vasorum in regions with atherosclerotic lesions, which are more fragile and are foci for intramural haemorrhage, thus promoting an uneven distribution of wall stress and conditions for vessel dissection.

Coronary artery spasm and rupture of an atherosclerotic plaque have also been described as a cause of spontaneous dissection,28 especially in cases with angiographically non-significant coronary atherosclerosis.

In the case described here, the patient had non-significant coronary atherosclerosis, as shown by coronary angiography, which revealed the presence of atheromatous plaque in the anterior descending branch immediately below the diagonal, causing <50% obstruction of the lumen. The mechanism causing the spontaneous dissection in this case, as in all cases with coexistent coronary artery disease, is not known. It is likely that the starting point of the spontaneous dissection was the above atheromatous plaque, with extension of the dissection both retrogradely towards the centre, as far as the proximal third of the vessel, and anterogradely, as far as the second diagonal artery and the distal third of the vessel. It could have been due to vessel rupture or spasm in the region in question, because of endothelial dysfunction or the formation of an intramural haematoma due to the fragile neovascularure of the atheromatous plaque. In the latter case, of course, the thrombolysis probably promoted the extension of the dissection along its entire length. It is possible, however, that the entry point of the dissection was in another part of the vessel without significant atheroma where the prevailing conditions included increased apoptosis of smooth muscle fibres. In conclusion, it appears that spontaneous dissection in cases with coronary atherosclerosis may have a variety of causes and a number of different mechanisms may contribute to a greater or lesser degree.

The prognosis in spontaneous coronary artery dissection, according to older published series, is generally poor. In a review by Cocco et al.6 50% of patients with spontaneous coronary artery dissection suffered sudden cardiac death, while 18-20% died during the first few hours. Similarly, in a series reported by Bernham et al.,29 the incidence of sudden death was high, touching 67%. Cases of acute coronary syndrome as a consequence of spontaneous coronary artery dissection are very rare, but such diagnoses are on the increase since more and more patients with acute coronary syndrome undergo coronary angiography during their hospitalisation. Owing to the very high mortality rate, there is usually not time for the physician to get involved in the diagnostic and therapeutic approach to spontaneous coronary artery dissection. For this reason, prompt diagnosis30 is of paramount importance in cases of patients with spontaneous dissection who survive long enough to reach hospital and has a significant effect on the prognosis. It should not be forgotten that although spontaneous dissection is an exceedingly rare cause of acute coronary syndrome in the population as a whole, it should be suspected at once in young men or women, usually without risk factors, who come to hospital with acute myocardial infarction or unstable angina.31 From this point of view, in young patients or middle-aged women without risk factors for coronary artery disease, who are admitted for acute coronary syndrome with or without ST-segment elevation, perhaps invasive management should be preferred, with referral for coronary angiography as soon as possible, thus guiding treatment in the patient’s best interests and preventing sudden death.

Diagnosis of the disease is made using coronary angiography, during which the false and the true lumen are visualised and may be distinguished by the radiotransparent zone of the intimal flap. Coronary vessel dissections are classified based on their morphology,32 which also determines the prognosis. In the case described here the dissection in the anterior
descending branch was of type C. Coronary intravascular ultrasound (IVUS) can help in the discovery of a small coronary artery dissection in cases with acute coronary syndrome and physiological or almost physiological coronary vessels. In addition, IVUS can reveal the boundaries of the dissection and can guide the therapeutic approach, while in other cases it can help in the differential diagnosis between dissection and the longitudinal rupture of a long atheromatous plaque. However, in cases with extensive dissections, as in the one reported here, the use of IVUS may be questionable, since it can delay rapid treatment, extend the dissection or cause blockage or rupture of the vessel as the transducer is introduced to the false lumen.

The therapeutic approach to spontaneous dissections can be divided into the pharmaceutical and the invasive. Nitrates, β-blockers and aspirin seem to have a place in all cases. As a therapeutic choice for the treatment of spontaneous dissections, thrombolysis appears to have been effective in some cases. Some researchers maintain that thrombolysis can extend the dissection, while others believe that lysis of the thrombus in the false lumen can restore flow in the true lumen. The invasive treatment of spontaneous dissections includes aortocoronary bypass and angioplasty with stent implantation. Although there are no randomised studies comparing thrombolysis with invasive treatment, it appears from an older, retrospective study that coronary bypass is particularly effective if the patient survives the first hours of dissection and is diagnosed promptly. In the present era, coronary bypass stood out as the basic invasive treatment of automatic dissections. However, even then De Maio et al suggested that coronary bypass should only be used in cases with spontaneous dissection of the main stem, three-vessel disease, or a significant degree of drug-refractory ischaemia. Despite the fact that coronary bypass surgery is extremely effective in the treatment of spontaneous coronary artery dissection as far as survival is concerned, these cases present significant technical difficulty in finding a healthy section of vessel for the peripheral anastomosis. Today, in the age of stents, invasive cardiology offers the fastest method of diagnosis and effective treatment of this disease entity, which has very high mortality and demands as rapid a therapeutic response as possible. The stent should be implanted at the point of the dissection’s entry portal. Of course, as in a case described by Himbert et al, there is the possibility of progressive angiographic recovery of a spontaneous dissection without any invasive treatment. In recent years the question has been raised as to whether stents should be implanted in coronary vessels with spontaneous dissection when the flow is good (or even slightly reduced <TIMI 3), or whether more conservative management is indicated.

The case described here tends to support the latter view. The patient was stabilised and asymptomatic, with a slightly reduced flow (<TIMI 3) that could have been disrupted by any intervention at that time. In addition, the extent of the dissection was such that any stent implantation would have had to include most of the length of the vessel, which would be far from easy in practice. As regards the bypass surgery alternative, the peripheral extent of the dissection and its unclear termination, along with its extension into an important diagonal branch, did not permit us to recommend the procedure without reservation. We considered that a scintigraphic evaluation of the degree of myocardial ischaemia and a further coronary angiography at a later time, along with drug treatment, offered the best strategy for the management of this patient.

References