Case reports

Amyloidosis of epicardial and intramural coronary arteries as an unusual cause of myocardial infarction and refractory angina pectoris

Daniela Miani, Maurizio Rocco*, Ezio Alberti**, Leonardo Spedicato, Paolo Maria Fioretti

*Department of Cardiovascular Sciences, *Department of Pathology, S. Maria della Misericordia Hospital, Udine, **Department of Cardiology, Hospital of Tolmezzo (UD), Italy*

Key words:
Amyloid; Angina; Myocardial infarction.

The present case report refers to a 65-year-old male patient with subocclusion of the right coronary artery who had an inferior myocardial infarction that was treated with coronary angioplasty. The patient subsequently developed intractable angina pectoris in the absence of critical coronary stenosis at serial coronary angiography. Doppler wire velocity demonstrated an impaired coronary flow reserve. The patient died of cardiogenic shock. *Postmortem* examination revealed amyloid involvement of the media of the epicardial coronary arteries and severe amyloid deposition in the media and adventitia with obstruction of the lumen of the intramyocardial coronary arteries. Widespread ischemic areas were present in the myocardium with only slight amyloid deposition. In this patient myocardial infarction and unstable angina were a rare initial manifestation of primary amyloidosis.

(Ital Heart J 2002; 3 (8): 479-482)

Received February 26, 2002; revision received July 5, 2002; accepted July 10, 2002.

Address:

Dr.ssa Daniela Miani

Dipartimento di Scienze Cardiovascolari A.O. S. Maria della Misericordia Piazzale S. Maria della Misericordia, 15 33100 Udine E-mail: miani.daniela@aoud.sanita.fvg.it

Introduction

Primary amyloidosis (AL) is a rare systemic disease characterized by extracellular deposition of amyloid fibrils derived from the immunoglobulin light chains of monoclonal plasma cells[1].

Congestive heart failure is the most common initial manifestation of this disease and occurs in 80% of patients[1]. Angina pectoris as a first symptom of amyloidosis has rarely been described[2]. Usually angina is not attributable to the involvement of the epicardial coronary arteries, but to intramural coronary obstruction. We describe the case of a male patient with AL amyloidosis, which manifested for the first time with myocardial infarction and unstable angina pectoris consequent to epicardial right coronary stenosis and intramyocardial coronary artery obstruction.

Case report

A 65-year-old male patient in previously good health was admitted in July 1999 at a county hospital with an acute inferior myocardial infarction complicated by transient third degree atrioventricular block. His only risk factors were a history of hypercholesterolemia and past smoking. He was treated with intravenous streptokinase with complete rapid resolution of symptoms. The peak total creatinine phosphokinase serum level was 720 U/l. After a few days he developed unstable angina with paroxysmal atrioventricular block. The ECG showed a downsloping ST-segment depression in the lateral leads. An echocardiogram showed a normal left ventricle with trivial mitral and tricuspid insufficiency. Coronary angiography was performed showing 90% stenosis of the right coronary artery (Fig. 1) which was successfully treated with angioplasty and stenting.

Subsequently the patient felt well and 3 months later a stress test at low workload was negative for angina and ischemia (rate-pressure product 14 600 b/min·mmHg). Shortly afterwards, however, he developed effort angina and another stress test at a similar workload was positive for induced ischemia. Symptoms were accompanied and

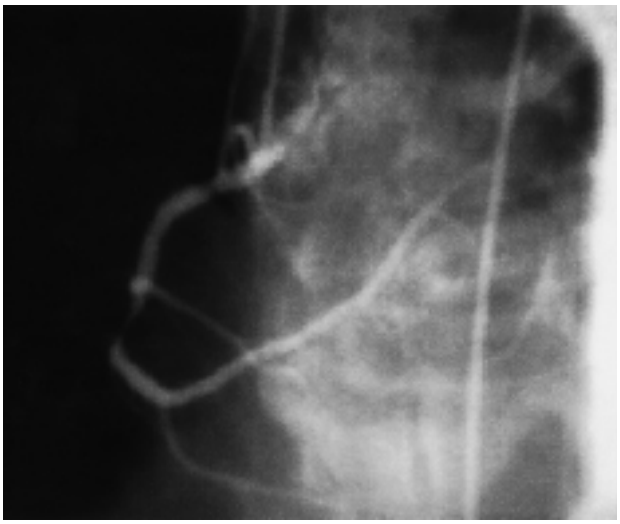

Figure 1. *Critical stenosis (90%) of the main right coronary artery at coronary angiography.*

worsened by supraventricular tachycardia associated with dyspnea. A new coronary angiography was performed and revealed a non-critical intrastent restenosis of the right coronary artery. A stress myocardial scintigraphy showed severe hypoperfusion at numerous sites. At rest the perfusion of the inferior wall and apex was significantly improved. After 2 months, due to persistent severe angina with mild effort and cold in spite of therapy with beta-blockers, aspirin, nitrates and statins, the patient underwent a new coronary angiography that showed an unchanged subcritical intrastent stenosis of the right coronary artery, confirmed at intravascular ultrasound. However, Doppler wire velocity revealed pathological pre and post-stenosis flow velocity; the coronary flow reserve was impaired even after intracoronary adenosine; the flow velocity ratio was > 1.7 m/s. He was treated with a new angioplasty intrastent. Doppler wire velocity confirmed the normalization of the coronary flow reserve. On admission, the patient was found to have a fourth degree tone and a murmur due to mitral insufficiency, but not heart failure. His blood pressure was 120/80 mmHg. The ECG showed sinus rhythm at 80 b/min, left axis deviation, a low voltage in the peripheral leads, a previous inferior myocardial infarction and an incomplete left bundle branch block. All laboratory tests were normal with the exception of electrophoresis: albumin 59%, α_1 1.4%, α_2 5.5%, beta 6.3%, gamma 25%. A diagnosis of monoclonal gammopathy was made. Urinalysis was normal without proteinuria.

In spite of angioplasty, the patient's symptoms did not improve and he continued to complain of severe effort angina and dyspnea. In July 2000 he was admitted again after an episode of prolonged chest pain with dyspnea and sweating. He was in cardiogenic shock with a blood pressure of 80/60 mmHg and a heart rate of 100 b/min. The ECG was unchanged with low voltages in the peripheral leads, previous inferior infarction and incomplete left bundle branch block. An emergency coronary angiography was performed revealing normal coronary arteries but a severe decrease in the systolic ventricular function with a left ventricular ejection fraction of 23%. Right heart catheterization showed pulmonary artery pressures of 53 mmHg systolic, 30 mmHg diastolic, mean 45 mmHg; the wedge pressure was 46 mmHg with a pronounced V wave; the cardiac index was 1.6 l/min/m^2. An intra-aortic balloon pump was inserted and the patient's hemodynamic status improved significantly: the cardiac index rose to 3.6 l/min/m^2, the arterial pressure to 109/89 mmHg, and the wedge pressure decreased to 26 mmHg. The patient was placed on a treatment regimen including dobutamine, a nitrate drip and intravenous furosemide. Serial echocardiography showed a transiently decreased hypokinesia of the lateral wall and interventricular septum followed by a worsening left ventricular function with a decrease in the ejection fraction from 33 to 20%. The left ventricle was hypertrophied; the right ventricular function was also impaired. Biatrial enlargement and severe mitral and tricuspid insufficiency were noted. The pulmonary artery pressure was 54 mmHg. On the basis of a suspect of fulminant myocarditis, all antiviral tests were performed but yielded negative results. The patient, on a therapeutic regimen consisting of dobutamine, nitrate infusion and heparin, remained relatively stable for 6 days. Paroxysmal atrial fibrillation, which caused chest pain associated with ST changes in the lateral leads and dyspnea, was treated with amiodarone; this therapy was however stopped after few days owing to episodes of torsade de pointes. Magnesium sulphate was started together with ACE-inhibitors. A brief attempt at weaning from dobutamine resulted in a quick increase in pulmonary pressures and a fall in the cardiac index. Two days later the patient developed asystole and all cardiac resuscitation attempts were useless.

Necropsy findings. *Postmortem* examination revealed cardiomegaly with biventricular enlargement. The heart weighed 740 g. The pericardial cavity contained about 500 ml of clear fluid. The myocardium showed focal patchy fibrosis. The myocardial tissue was translucent and thickened, measuring 2 cm in the left ventricular wall and septum with foci of fibrosis. The epicardial coronary arteries showed widespread non-critical, atherosclerotic changes. Histological examination revealed extensive amyloid deposition in the media and adventitia of the intramural coronary arteries and vasa vasorum whose lumen was narrowed (Figs. 2-4). On the other hand, there was involvement of the media without significant stenosis in the epicardial coronary arteries (Fig. 5). Amyloid deposition in the interstitium was limited.

There were no significant changes in the lungs, liver and pancreas, whereas amyloid deposits were found in the spleen vessels at the subendothelial level.

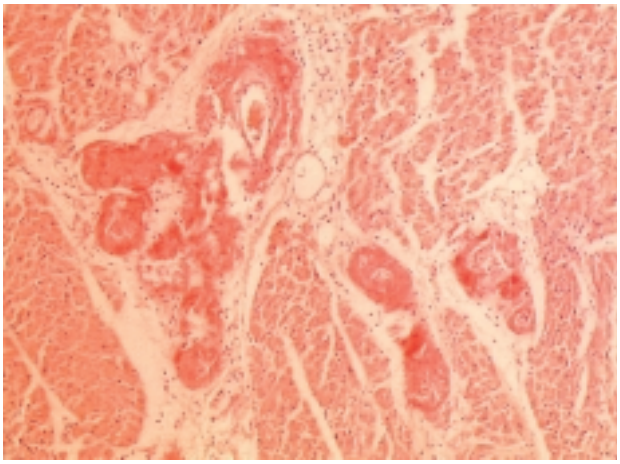

Figure 2. *Intramural coronary arteries with amyloid deposits on the wall (Congo red stain 10×).*

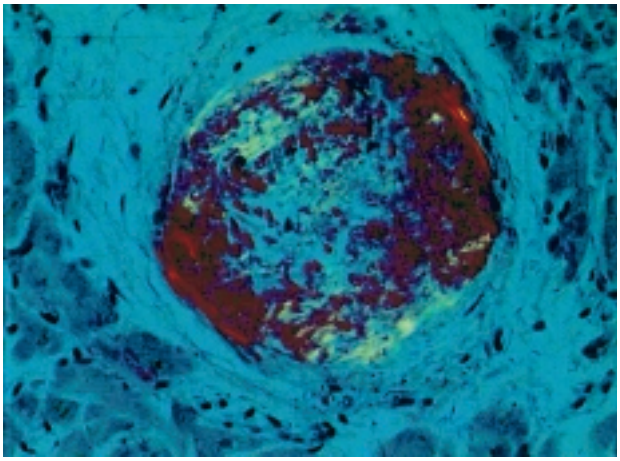

Figure 3. *Amyloid deposition with typical green birefringence (polarizing filter 10×).*

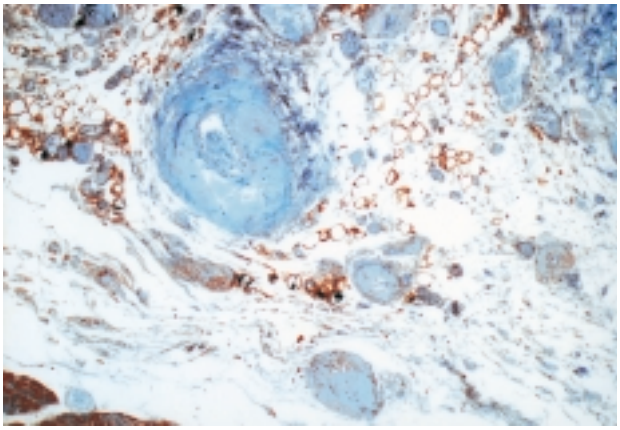

Figure 4. *Immunohistochemical demonstration of P amyloid deposition in the media of the coronary artery wall (10×).*

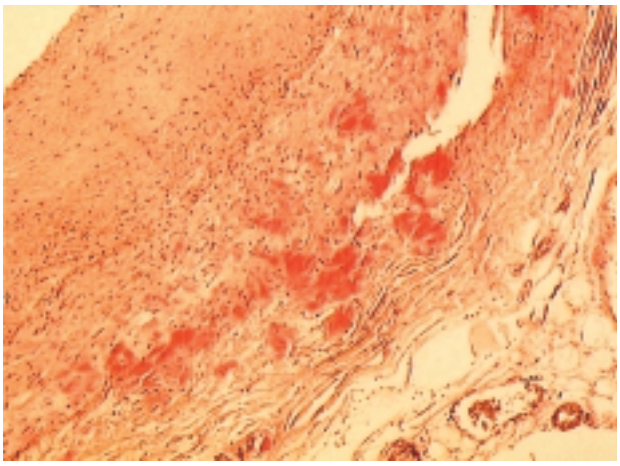

Figure 5. *Section of an epicardial coronary artery wall showing deposits of amyloid substance (Congo red stain 20×).*

Discussion

Amyloidosis is a disorder characterized by extracellular deposition of amyloid fibrils that are immunoglobulin-light-chain-related in AL amyloidosis[3].

Cardiac involvement is found in 80-100% of AL amyloidosis[4] and is due to parenchymal or vascular deposition.

Congestive heart failure is the most common presentation and typical angina pectoris is seldom described[2]. In an autoptic study of 108 patients, only 5 (4.6%) had severe amyloid deposition in the intramyocardial arteries[4]. The pathogenesis of angina is the deposition of amyloid that usually begins in the vascular media and later spreads to the adventitia and intima, with obliteration of the intramyocardial arteries[5] and impairment of the coronary flow reserve. As described by Mueller et al.[2], in these cases heart failure is the result of extensive chronic ischemic changes of the myocardium. Myocardial infarction and angina pectoris were our patient's first symptoms. Echocardiography was not suggestive of myocardial involvement in the early stages of the disease. In this case, however, the epicardial segment of the right coronary artery was also involved. For this reason, the patient was submitted to coronary angioplasty and stenting. In our case, normalization of the coronary flow reserve after the second angioplasty could be explained both by the characteristics of the epicardial coronary lesion as well as by the paucity of the involvement of the interstitial myocardium. The latter possibly allowed for a residual increase in the coronary flow reserve after maximal vasodilation induced by drugs, in spite of the fact that the literature suggests that there should be no variation in the coronary flow reserve since amyloidosis is exclusively a small vessel disease. To our knowledge, only one case of amyloidosis with coronary epicardial involvement has been described in the literature[6]; our patient, however, had only minimal myocardial interstitial infiltration, but massive intramural coronary artery obliteration. In the series discussed by Suwaidi et al.[5], amyloid infiltration of the intramural coronary arteries was the cause of angina in 5 out 153 patients with normal

coronary arteries at angiography. In their study, the intracoronary Doppler wire showed impairment of both the endothelium-dependent and endothelium-independent coronary flow reserves. According to these authors, this combination may represent an intrinsic disease of the vascular wall that could suggest a diagnosis of amyloidosis. As far as we know, this is the first time that in a patient a common pathogenesis involving the intramural coronary arteries, the epicardial artery and the vasa vasorum and leading to ischemic heart disease is described.

In conclusion, this case suggests that in the presence of a monoclonal gammopathy, intractable angina pectoris, subsequent to myocardial infarction successfully treated and an impaired coronary blood flow reserve, one should consider intramural vessel amyloidosis as a possible cause.

References

1. Buja LM, Khoi NB, Roberts WC. Clinically significant cardiac amyloidosis. Clinicopathologic findings in 15 patients. Am J Cardiol 1970; 26: 394-405.
2. Mueller PS, Edwards WD, Gertz MA. Symptomatic ischemic heart disease resulting from obstructive intramural coronary amyloidosis. Am J Med 2000; 109: 181-8.
3. Falk RH, Comenzo RL, Skinner M. The systemic amyloidoses. N Engl J Med 1997; 337: 898-909.
4. Smith RRL, Hutchins GM. Ischemic heart disease secondary to amyloidosis of intramyocardial arteries. Am J Cardiol 1979; 44: 413-7.
5. Suwaidi JA, Velianou JL, Gertz MA, et al. Systemic amyloidosis presenting with angina pectoris. Ann Intern Med 1999; 131: 838-41.
6. Saltissi S, Kertes PJ, Julian DG. Primary cardiac amyloidosis in a young man presenting with angina pectoris. Br Heart J 1984; 52: 233-6.