Rapid progression of coronary atherosclerosis after cardiac resynchronisation therapy: cause or coincidence?

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SUMMARY

An 85-year-old man with a diagnosis of idiopathic dilated cardiomyopathy presented with worsening breathlessness and reduced functional capacity. Previous angiography had demonstrated only mild, single-vessel coronary atherosclerosis. Owing to the occurrence of severe symptoms despite optimal medical therapy, cardiac resynchronisation therapy (CRT) was performed by means of biventricular pacemaker implantation. The patient was readmitted, 6 months later, with an acute ST-segment myocardial infarction. Urgent coronary angiography demonstrated severe multivessel atherosclerotic coronary artery disease, in the absence of any alteration in basal drug therapy or modifiable cardiovascular risk factor profile. Percutaneous coronary intervention was performed with good result. We postulate a potential causal association between CRT and accelerated coronary atherosclerosis, with alterations in blood flow dynamics and coagulation properties as potential mechanisms. There are no previous reports of this phenomenon in the published literature.

BACKGROUND

This case raises, for the first time, the possibility that cardiac resynchronisation therapy (CRT) for heart failure may lead to progression of coronary artery disease. The message of this case report is straightforward and clear, and we believe it will be of interest and practical relevance to clinicians. Coronary artery disease and heart failure are major health problems globally. CRT is being increasingly utilised for the treatment of heart failure, with recent European guidelines recommending this therapy for even relatively mild (New York Heart Association (NYHA) class 2) disease. Thus, we feel it is of importance to alert the scientific community to the possibility of such an association, such that clinicians might be vigilant to early signs of coronary disease progression after CRT. We also hope that it might stimulate other clinicians to report similar cases, as well as forming a potential avenue for future research.

CASE PRESENTATION

An 85-year-old man with an established diagnosis of idiopathic-dilated cardiomyopathy presented with worsening breathlessness and reduced functional capacity. His medical history was of dyslipidaemia, peptic ulcer disease and pernicious anaemia. Previous coronary angiography had shown no significant coronary artery disease.

During the current presentation, he described symptoms of NYHA class III heart failure despite

optimal medical therapy. The 12-lead electrocardiogram demonstrated significant prolongation of the QRS interval (140 ms). Transthoracic echocardiography revealed severe left ventricular systolic dysfunction (ejection fraction <20%) and significant interventricular mechanical delay. Repeat coronary angiography demonstrated only mild atheroma within the proximal left anterior descending artery (LAD) but no flow limiting stenoses within any of the major epicardial arteries (figure 1A,B). In accordance with current heart failure guidelines, the patient underwent cardiac resynchronisation therapy by means of biventricular pacemaker implantation. This resulted in improved NYHA functional status (class II) with a dramatic increase in left ventricular systolic function (ejection fraction 55%) after several months.

Six months after device implantation, the patient was re-admitted with an acute anterior ST-segment elevation myocardial infarction. Coronary angiography revealed a critical stenosis within the proximal LAD, as well as a severe lesion within the mid-portion of the right coronary artery (RCA) (figure 1C,D). The LAD lesion was distal to the ostium and persisted after intracoronary nitrate administration, and hence could not be attributed to catheter-induced dissection or spasm. The patient therefore underwent urgent percutaneous intervention to the LAD and RCA with excellent immediate results.

DIFFERENTIAL DIAGNOSIS

In this case, there appears to have been a close temporal relationship between the initiation of CRT and rapid progression of coronary disease. There had been no changes to background medical therapy, and modifiable cardiovascular risk factors remained well controlled throughout. Both angiographic studies were conducted in the same laboratory and image quality was good. It remains possible that the aetiology of this patient's left ventricular dysfunction was indeed ischaemic, and that the worsening of his previously mild coronary atherosclerosis was coincidental with respect to the initiation of CRT. However, the alarmingly rapid progression of his coronary disease, as well as its close temporal relationship with the initiation of CRT in a patient that had not developed any significant degree of coronary obstruction, during his previous 85 years of life, raises a potential causal association.

OUTCOME AND FOLLOW-UP

The patient remains well at follow-up and reports NYHA functional class II heart failure symptoms

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Figure 1 Coronary angiography before and after cardiac resynchronisation therapy (CRT). (A) Left coronary circulation immediately before CRT, showing minor atheroma within the proximal left anterior descending artery (LAD) and an unobstructed circumflex artery (LCx). (B) Right coronary artery (RCA) immediately before CRT. No significant stenoses are evident. (C) Left coronary circulation 6 months after CRT initiation. Right atrial (RA) and left ventricular (LV) pacing leads are labelled. A critical stenosis of the proximal LAD can be seen (arrowed). (D) RCA 6 months after CRT initiation. Right ventricular (RV) and RA pacing leads are labelled. A severe stenosis of the mid-RCA is apparent (arrowed).

with continuation of his CRT. He has reported no symptoms suggestive of ongoing coronary ischaemia.

DISCUSSION

This case demonstrates a potential causal association between cardiac resynchronisation therapy and accelerated coronary atherosclerosis. There have been no previous reports of such an association in the literature. We speculate that alterations in the haemodynamics of coronary blood flow or its coagulation profile might be responsible for this phenomenon.

CRT has been demonstrated to lead to an increase in coronary artery blood flow velocity.¹ Increased flow velocity and accelerated atherosclerosis have been reported in the ulnar artery after collection of the ipsilateral radial artery for bypass grafting.² It may therefore be the case that CRT leads to relatively abrupt alterations in the flow characteristics of chronically underperfused coronary vessels, which might in theory create a milieu for atherosclerotic disease progression. In addition, CRT-induced left ventricular reverse-remodelling is associated with decreased levels of Annexin-A5,³ a plasma protein that has been demonstrated to have powerful anti-atherothrombotic properties.⁴ Hitherto unrecognised haematological and neuroendocrine effects of CRT may therefore also play a role in creating a substrate for accelerated atherosclerosis.

Awareness of the existence of such an association should alert clinicians to symptoms such as angina developing in patients that have undergone CRT, and presents a potential avenue for future research.

Learning points

- Cardiac resynchronisation therapy (CRT) may be causally associated with rapid progression of coronary atherosclerotic disease.
- Clinicians should be vigilant to symptoms such as anginal chest pain after initiation of CRT, which may represent a manifestation of this phenomenon.
- Alterations in coronary haemodynamics, as well as reduced plasma levels of antiatherothrombotic proteins have been reported after CRT. These changes may be responsible for this effect, and present potential avenues for future research.

Competing interests None.

Patient consent Obtained.

REFERENCES

- 1 Flevari P, Theodorakis G, Paraskevaidis I, *et al.* Coronary and peripheral blood flow changes following biventricular pacing and their relation to heart failure improvement. *Europace* 2006;8:44–50.
- 2 Gaudino M, Serricchio M, Tondi P, *et al.* Chronic compensatory increase in ulnar flow and accelerated atherosclerosis after radial artery removal for coronary artery bypass. *J Thorac Cardiovasc Surg* 2005;130:9–12.
- 3 Ravassa S, García-Bolao I, Zudaire A, *et al.* Cardiac resynchronization therapy-induced left ventricular reverse remodelling is associated with reduced plasma annexin A5. *Cardiovasc Res* 2010;88:304–13.
- 4 Cederholm A, Frostegård J. Annexin A5 as a novel player in prevention of atherothrombosis in SLE and in the general population. *Ann NY Acad Sci* 2007;1108:96–103.

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