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CASE REPORT
Cardiovascular imaging

Torrential mitral regurgitation following right ventricular apical pacing in rheumatic mitral valve disease: a case report

Joseph Okafor *, Ali Vazir, Shouvik Haldar, and Rajdeep Khattar

Royal Brompton Hospital and National Heart and Lung Institute, Imperial College London, Guy Scadding Building, Dovehouse St, London, SW3 6LY London, UK

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Background Mitral regurgitation may develop or worsen following right ventricular apical pacing due to dyssynchronous left ventricular contraction. Pre-existing secondary mitral annular dilation is a well-recognized and important contributing factor. This description of pacing-induced torrential mitral regurgitation in the setting of rheumatic mitral valve disease is a rare case in which a primary mitral valve lesion was the antecedent mechanism.

Case summary A 60-year-old man was admitted with dizziness and pre-syncope. Twelve-lead electrocardiogram showed complete heart block. A dual-chamber pacemaker was implanted and programmed in DDD mode. Transthoracic echocardiography performed a day later demonstrated a left ventricular ejection fraction (LVEF) of 63% and moderate mitral regurgitation. The patient presented 4 months later with breathlessness and orthopnoea. Pacemaker interrogation demonstrated a 98% right ventricular pacing burden. Echocardiography revealed torrential mitral regurgitation secondary to left ventricular dyssynchrony and complete loss of leaflet coaptation with preserved systolic function. Post-capillary pulmonary hypertension was diagnosed following right heart catheterization. The patient underwent metallic mitral valve replacement, tricuspid annuloplasty, and left internal mammary artery grafting to the left anterior descending artery for a severe proximal stenosis. On inspection, the native mitral valve was notably rheumatic in appearance, and this was confirmed histologically.

Discussion It is important to closely monitor the progression of mitral regurgitation in those with primary mitral valve disease undergoing right ventricular pacing. Early follow-up may prevent the adverse haemodynamic consequences of worsening mitral regurgitation, with a greater chance of recovery of left ventricular function following surgery.

Keywords Pacemaker • Mitral regurgitation • Rheumatic • Echocardiography • Case report

ESC curriculum 2.1 Imaging modalities • 2.2 Echocardiography • 4.3 Mitral regurgitation • 5.9 Pacemakers • 6.2 Heart failure with reduced ejection fraction

Learning points

- Right ventricular apical pacing can induce or worsen mitral regurgitation by introducing dyssynchronous left ventricular contraction.
- Pre-existent secondary mitral annular dilatation is a recognized contributing factor, but the presence of antecedent rheumatic mitral valve disease is rare.
- It is important to closely monitor the progression of mitral regurgitation in those with primary mitral valve disease who undergo pacing.

* Corresponding author. Tel: +44 7960500695, Email: joseph.okafor@nhs.net
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Introduction

Mitral regurgitation (MR) may develop or worsen following right ventricular (RV) apical pacing. Studies report an incidence of 7% of new moderate MR after permanent pacemaker (PPM) implantation for atrioventricular (AV) block.[1] Severe regurgitation necessitating mitral valve replacement or repair (MVR) is rare (2%).[2] Dyssynchronous left ventricular (LV) contraction results in abnormal papillary muscle function, delayed end-diastolic mitral valve (MV) closure, and early systolic MR. Often the pre-existence of an abnormal MV is an important factor,[3] and the initiation of RV apical pacing may increase the severity of MR. Pre-existing secondary mitral annular dilation is well recognized, but the demonstration of a primary MV lesion as the antecedent mechanism of MR is less common.

We present a rare case of RV apical pacing-induced torrential MR with rheumatic MV disease as the underlying pathology.

Summary figure

Time	Events
Index presentation	The patient was admitted to hospital due to pre-syncope and undergoes dual chamber pacemaker implantation for complete heart block
Day 1	Transthoracic echocardiogram reveals moderate mitral regurgitation with anterior mitral leaflet doming and thickening, posterior leaflet restriction and mild annular dilatation.
12 weeks	Increasing breathlessness and orthopnoea. Admission for intravenous diuresis. Pacing check reveals 98% RV pacing burden.
12 weeks	Echocardiography now shows LV dyssynchrony and loss of leaflet coaptation with resultant torrential mitral regurgitation.
13 weeks	Patient undergoes metallic mitral valve replacement, tricuspid annuloplasty and left internal mammary artery grafting to the LAD artery. Native valve appearances consistent with rheumatic mitral valve disease.
14 weeks	Post-operative echocardiogram shows residual severe biventricular dysfunction. Patient discharged on optimal heart failure therapy.
12 months	LV function remains severely impaired while RV function improves. Patient listed for upgrade to cardiac resynchronisation therapy.

Case presentation

A 60-year-old man with no past medical history was admitted with subacute onset of dizziness and pre-syncope. The initial assessment revealed a profound bradycardia with a blood pressure of 167/92 mmHg. On auscultation, a pan-systolic murmur was audible. There were no clinical signs of pulmonary or peripheral oedema. Twelve-lead electrocardiogram demonstrated complete heart block (CHB) with a narrow QRS escape rhythm at 30 b.p.m. Immediate focused bedside echocardiography revealed preserved biventricular systolic function with no regional wall motion abnormalities and mild-to-moderate MR. Blood tests including full blood count, urea and electrolytes, bone profile, and thyroid function tests were unremarkable. High-sensitivity Troponin-I was 6.4 ng/L (<19.8), and C-reactive protein was 2 mg/L (0–10).

The patient underwent urgent dual-chamber PPM implantation. The right atrial lead was actively fixed to the right atrial appendage and the RV lead to the mid-apical septum. The device was programmed to DDD mode at a basic rate of 60 b.p.m. Detailed transthoracic echocardiography (TTE) performed 1 day post-pacing revealed normal LV volumes, mild septal dyssynchrony consistent with RV pacing, and LV ejection fraction (LVEF) of 63%. There was minor focal posterior mitral annular calcification with slight doming and thickening of the anterior MV leaflet and a mildly restricted posterior leaflet. The mean MV gradient was 1 mmHg. Colour flow imaging revealed a central jet of moderate MR with an effective regurgitant orifice area of 0.31 cm^2 (*Figure 1*; see Supplementary material online, *Video S1*). The nature of MR was unclear but was considered due to dual aetiology from posterior leaflet restriction and a primary MV lesion. The early-diastolic mitral annular diameter was 3.0 cm, and the left atrium was moderately dilated. RV size and function were normal. Overall right heart parameters suggested a low probability of pulmonary hypertension.

At 4 months follow-up, the patient complained of worsening breathlessness on exertion and orthopnoea, which began in the weeks following PPM implantation. Pacemaker interrogation revealed underlying CHB with atrial-sensed, ventricular-paced device function. The RV pacing burden was 98%. Twelve-lead electrocardiogram confirmed a paced left bundle branch abnormality pattern with the QRS duration of 145 ms. Repeat TTE revealed worsening cardiac structural and functional abnormalities such that the LV had remodelled into a moderately dilated, volume-loaded cavity with mildly dyssynchronous septal motion. The LVEF was 57%, and the global longitudinal strain was reduced at −14.3%. There was torrential MR due to marked posterior leaflet restriction and tethering of the anterior leaflet resulting in complete absence of coaptation with a 5 mm gap between the leaflet tips (*Figure 2*; see Supplementary material online, *Video S2*). A comparison of the quantitative echocardiographic data from day 1 post-pacing to 4 months follow-up is given in *Table 1*. The mean MV gradient was elevated at 7 mmHg in the context of severe MR and borderline tachycardia. However, the MV area equated by pressure half time was 2.89 cm^2, suggesting no concomitant mitral stenosis. The RV was dilated with severe systolic impairment with a fractional area change of 17% and three-dimensional RVEF of 33%. Colour flow revealed a broad jet of moderate-severe tricuspid regurgitation (TR) with a dense, triangular continuous wave Doppler profile and the proximal isovelocity surface area radius of 0.7 cm. The estimated pulmonary artery systolic pressure was elevated at 55–60 mmHg. Transoesophageal echocardiography confirmed absence of MV leaflet coaptation (*Figure 3*; see Supplementary material online, *Video S3*).

Following treatment with intravenous diuretics, coronary angiography revealed a co-dominant system with severe stenosis of the proximal left anterior descending (LAD) artery and two diagonal branches. Right heart catheterization revealed mild pulmonary hypertension secondary to left-sided heart disease with a mean pulmonary artery pressure of 30 mmHg, pulmonary capillary wedge pressure of 22 mmHg, and pulmonary vascular resistance of 1.95 WU.

The patient underwent successful mechanical MVR, tricuspid annuloplasty, left internal mammary artery grafting to the LAD artery, and excision of the left atrial appendage. On inspection, the native MV was notably rheumatic in appearance, and this was confirmed histologically. Post-operative imaging demonstrated a well-functioning MV prosthesis with no transvalvular regurgitation, but severe residual biventricular dysfunction. Oral heart failure treatment was optimized to include bisoprolol 5 mg, ramipril 2.5 mg, eplerenone 25 mg, and furosemide 80 mg daily. He was commenced on warfarin with target international normalized ration 2.5–3.5. He remained well at 12 months follow-up with New York Heart Association Class I–II symptoms. LV systolic function, however, remained severely impaired (LVEF 34%), but RV systolic impairment was mild. His pacemaker will be upgraded to include cardiac resynchronization therapy in light of the severe LV systolic dysfunction and pacing dependency.

Discussion

Pacemaker-induced MR is on a spectrum of adverse effects from RV apical pacing collectively termed Pacemaker Syndrome. Manifestations range from breathlessness and exercise intolerance due to loss of physiological AV synchrony to pacemaker-induced cardiomyopathy.[4]

The effect of pacing on AV valvular regurgitation is well recognized. Worsening TR may occur due to interaction between the pacing lead

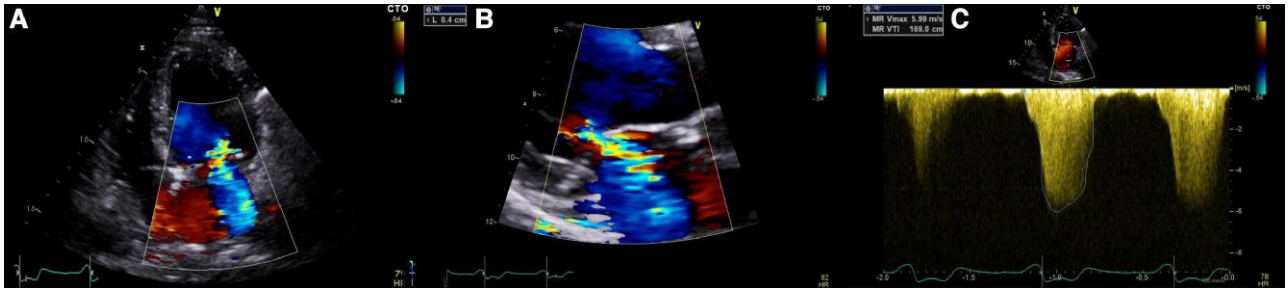

Figure 1 Transthoracic echocardiography performed on day 1 following permanent pacemaker implantation. Colour flow Doppler imaging in the (*A*) apical four-chamber and (*B*) parasternal long-axis views with vena contracta width of 0.4 cm. (*C*) Continuous wave Doppler profile of holosystolic mitral regurgitant jet but with a slightly incomplete Doppler envelope. Quantification by stroke volume method-confirmed moderate mitral regurgitation.

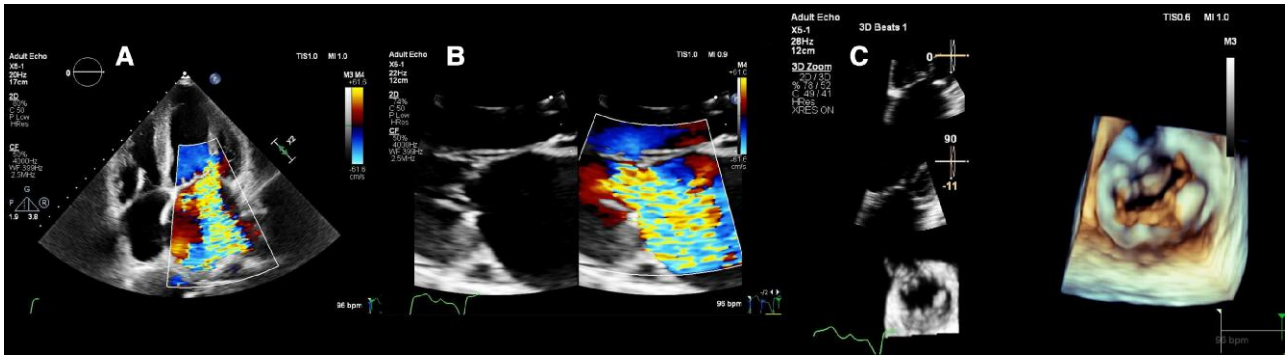

Figure 2 Transthoracic echocardiography 4 months following permanent pacemaker implantation with colour flow Doppler imaging in the (*A*) apical four-chamber and (*B*) parasternal long-axis view demonstrating progression to torrential mitral regurgitation. (*C*) Note the three-dimensional transthoracic echocardiography of the mitral valve from the left ventricular aspect demonstrating complete loss of leaflet coaptation in early systole.

Table 1 Serial echocardiographic parameters after right ventricular apical pacing with mitral valve quantification via stroke volume method

Parameter	Day 1 of RV apical pacing	4 months after RV apical pacing	1-week post-MVR
LV ejection fraction, %	63	57	32
LVIDd, cm	5.1	6.1	5.2
LVEDV, mL	67	145	98
LV GLS[a], %	−19.3	−14.8	N/A
Peak opposing wall delay[a], ms	137	339	N/A
MV annular diameter (A-P), mm	30	34	N/A
Regurgitant volume, mL/beat	53	106	N/A
Regurgitant fraction, %	51	69	N/A
EROA, cm^2	0.31	1.00	N/A
Vena contracta width, cm	0.40	0.76	N/A
Mean MV gradient, mmHg (heart rate)	1 (74 b.p.m.)	7 (97 b.p.m.)	3 (89 b.p.m.)
PASP, mmHg	—	55–60	37

A-P, anterior-posterior; EROA, effective regurgitant orifice area; GLS, global longitudinal strain; LV, left ventricle; LVEDV, left ventricular end-diastolic volume; LVIDd, left ventricular end-diastolic diameter; MR, mitral regurgitation; MV, mitral valve; MVR, mitral valve replacement; N/A = not assessed; PASP, pulmonary artery systolic pressure; PISA, proximal isovelocity surface area; RV, right ventricular.

[a]LV strain analysis by TomTec Imaging System, 2D Cardiac Performance Analysis software. Strain analysis not performed post-MVR. Endocardial strain values taken at peak systole.

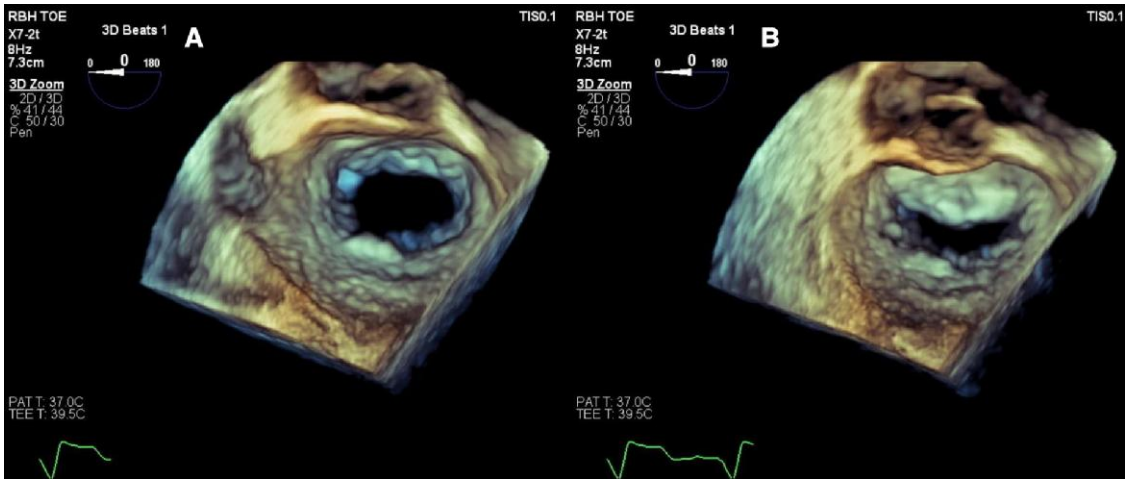

Figure 3 (*A*) Three-dimensional transoesophageal echocardiography in the mitral valve (MV) 'surgeon's view' highlighting loss of leaflet coaptation with frames frozen at (*A*) end-diastole and (*B*) end-systole. The posterior mitral valve leaflet is relatively fixed and immobile. Note the bulky thickening of the whole anterior mitral valve leaflet.

and tricuspid valve leaflets. Fibrous tissue formation also causes lead adherence and associated leaflet restriction.[5] Worsening MR after pacing is less common and usually functional in nature. Alizadeh *et al.*[1] studied 115 patients over 4 years following PPM implantation. Twenty were re-classified from no or trivial MR to mild MR, and 7 from no, trivial or mild MR to moderate MR. The mean LVEF decreased from 55 to 51%. However, no patients developed severe MR to warrant MV surgery. Proposed mechanisms include: (i) inverted ventricular depolarization sequence leading to dyssynchronous contraction and change in LV geometry,[2] (ii) altered papillary muscle function worsening pre-existing MR, and (iii) reduction in both the physiological forward motion of the mitral annulus and loss of the 59% decrease in MR orifice area normally seen during systole.[6]

Spartera *et al.*[7] studied the role of mechanical dyssynchrony in precipitating functional MR. A combination of decreased myocardial closing forces, MV apparatus distortion from increased tethering forces and mitral annular dysfunction from basal LV dyssynchrony is felt to be contributory. Improper timing of AV relaxation cycles during diastole also creates a positive pressure gradient through the MV with subsequent diastolic MR.

Severe MR after pacing requiring MV surgery is rare. Anguera *et al.*[8] reported 14 patients who deteriorated with acute pulmonary oedema following AV nodal ablation and PPM implantation. Four patients required MV surgery, all of whom had worsening MR due to dilatation of the MV annulus rather than a primary MV lesion. Miranda *et al.*[9] reported a case of acute pulmonary oedema secondary to severe MR immediately after RV apical pacing. The patient had no organic MV disease, and MR was secondary to LV dyssynchrony causing leaflet malcoaptation. This resolved on re-programming the device to VVI at 30 b.p.m to minimize pacing and repositioning the lead to the RV outflow tract. Other methods to reduce severity of functional MR include converting VVI to atrial pacing to promote intrinsic ventricular contraction or re-synchronization therapy.[2]

Le Tourneau *et al.*[10] reported two cases of primary MR in whom pacing in VVIR and DDD mode following AV nodal ablation resulted in acute severe MR. Both required emergency MV replacement. One patient had pre-existing posterior leaflet restriction with moderate MR. The other had moderate MR with a rheumatic MV, as in our case. To our knowledge, no other cases of worsening MR due to primary MV disease have been reported. In our case, there was striking clinical deterioration in the weeks following pacing. The mechanism was pre-existing rheumatic MV disease worsened by clear LV dyssynchrony and gross MV leaflet malcoaptation. Correction by MVR was required due to the torrential nature of MR, deteriorating LV function, and secondary pulmonary hypertension.

Conclusion

RV apical pacing is an important cause of MR progression in those with primary MV disease.

Our case highlights the need to closely monitor the evolution of MR in this group of patients following PPM implantation with serial echocardiography. Earlier follow-up may have prevented the adverse haemodynamic consequences of the progressively worsening MR with a greater chance of recovery of LV function following surgery.

Lead author biography

Dr Joseph Okafor is a researcher and Cardiology Specialty Registrar at Imperial College London and North West Thames Deanery, London. He holds a special interest in the use of multimodality imaging in structural heart disease diagnosis and interventions.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports*.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

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Data availability

The data underlying this article are available in the article and in its online supplementary material.

References

1. Alizadeh A, Sanati HR, Haji-Karimi M, Yazdi AH, Rad MA, Haghjoo M, *et al.* Induction and aggravation of atrioventricular valve regurgitation in the course of chronic right ventricular apical pacing. *Europace* 2011;**13**:1587–1590.
2. Barold SS, Ovsyshcher IE. Pacemaker-induced mitral regurgitation. *Pacing Clin Electrophysiol* 2005;**28**:357–360.
3. Sassone B, De Simone N, Parlangeli G, Tortorici R, Biancoli S, Di Pasquale G. Pacemaker-induced mitral regurgitation: prominent role of abnormal ventricular activation sequence versus altered atrioventricular synchrony. *Ital Heart J* 2001;**2**: 441–448.
4. Fanari Z, Hammami S, Hammami MB, Hammami S, Shuraih M. The effects of right ventricular apical pacing with transvenous pacemaker and implantable cardioverter defibrillator on mitral and tricuspid regurgitation. *J Electrocardiol* 2015;**48**:791–797.
5. Kim JB, Spevack DM, Tunick PA, Bullinga JR, Kronzon I, Chinitz LA, *et al.* The effect of transvenous pacemaker and implantable cardioverter defibrillator lead placement on tricuspid valve function: an observational study. *J Am Soc Echocardiogr* 2008;**21**:284–287.
6. Borgenhagen DM, Serur JR, Gorlin R, Adams D, Sonnenblick EH. The effects of left ventricular load and contractility on mitral regurgitant orifice size and flow in the dog. *Circulation* 1977;**56**:106–113.
7. Spartera M, Galderisi M, Mele D, Cameli M, D'Andrea A, Rossi A, *et al.* Role of cardiac dyssynchrony and resynchronization therapy in functional mitral regurgitation. *Eur Heart J Cardiovasc Imaging* 2016;**17**:471–480.
8. Anguera I, Brugada J, Brugada P, Mont L, Valentino M, Aguinaga L, *et al.* Hemodynamic deterioration in patients submitted to ablation of the atrioventricular node. *Rev Esp Cardiol* 1998;**51**:307–313.
9. Miranda R, Almeida S, Brandao L, Alvarenga C, Ribeiro L, Almeida AR, *et al.* Acute severe mitral regurgitation as an early complication of pacemaker implantation. *Europace* 2010;**12**:1791–1792.
10. Le Tourneau T, Klug D, Lacroix D. Mitral valve replacement for pacing-induced severe mitral regurgitation after radiofrequency ablation of the atrioventricular junction. *Heart* 1996;**76**:457.