Atrial Flutter with Atrial Alternans in a Patient with Cardiac Amyloidosis

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Abstract

Mechanical cardiac alternans is usually associated with left ventricular dysfunction. Atrial alternans has been described on invasive assessment of atrial action potentials, however cannot be detected clinically. Herein we report a patient who had transthyretin type cardiac amyloidosis with prior history of recurrent atrial fibrillation requiring ablations as well as ablation for atrial flutter and a recent history of cardioversion for atrial flutter. The patient presented with diastolic heart failure and recurrent atrial flutter and was referred for a TEE guided cardioversion. Mechanical left and right atrial alternans was seen on Doppler interrogation of both atrial appendages with velocities corresponding to the flutter P wave on the ultrasound ECG monitor. The patient was successfully cardioverted with the TEE probe in situ. Post cardioversion TEE showed resumption of normal albeit reduced mechanical atrial function in the left atrium and preserved right atrial function in tissue Doppler imaging. Our case demonstrates the mechanical phenomenon of atrial alternans in both atria on TEE with disappearance of atrial alternans during sinus rhythm suggesting rate related atrial alternans likely related to atrial stiffness from amyloid infiltration and as well as possibly scar formation from prior ablations.

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DATA AVAILABILITY STATEMENT

All relevant data has been presented in the manuscript.

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Abstract

Mechanical cardiac alternans is usually associated with left ventricular dysfunction. Atrial alternans has been described on invasive assessment of atrial action potentials, however cannot be detected clinically. Herein we report a patient who had transthyretin type cardiac amyloidosis with prior history of recurrent atrial fibrillation requiring ablations as well as ablation for atrial flutter and a recent history of cardioversion for atrial flutter. The patient presented with diastolic heart failure and recurrent atrial flutter and was referred for a TEE guided cardioversion. Mechanical left and right atrial alternans was seen on Doppler interrogation of both atrial appendages with velocities corresponding to the flutter P wave on the ultrasound ECG monitor. The patient was successfully cardioverted with the TEE probe in situ. Post cardioversion TEE showed resumption of normal albeit reduced mechanical atrial function in the left atrium and preserved right atrial function in tissue Doppler imaging. Our case demonstrates the mechanical phenomenon of atrial alternans in both atria on TEE with disappearance of atrial alternans during sinus rhythm suggesting rate related atrial alternans likely related to atrial stiffness from amyloid infiltration and as well as possibly scar formation from prior ablations.

Key words: Atrial alternans, transesophageal echocardiography, Doppler ultrasound, cardiac amyloid, atrial flutter

Case History

A 78-year-old Caucasian male with a past medical history significant for chronic diastolic heart failure with preserved ejection fraction (HfpEF), atrial fibrillation status post pulmonary vein isolation 8 years ago and extensive circumferential ablation for recurrent atrial fibrillation 6 years ago, as well as cavo-isthmus ablation with bidirectional block for atypical atrial flutter with recurrence of atrial flutter 5 years ago presented with increasing dyspnea and palpitations. Flecainide and Diltiazem had been discontinued due to side effects and renal impairment.

There was discordance between QRS voltage on ECG and the degree of left ventricular (LV) wall thickness on echocardiogram (Figure 1B, 1C, 1D), leading to suspicion for. infiltrative cardiomyopathy, subsequently confirmed as Transthyretin type type cardiac amyloidosis and confirmed on two-dimensional speckle-tracking echocardiography (2D-STE) and cardiac magnetic resonance imaging (MRI). Serum light chains were both slightly elevated but with normal ratio. STE revealed abnormal global averaged LV longitudinal peak systolic strain of -8 % (normal = more negative than -18%, Figure 2A), and prominent apical sparing pattern suggestive of cardiac amyloidosis (Figure 2B). MRI showed significantly increased left ventricular wall thickness, diffuse subendocardial, predominantly late, gadolinium enhancement and preserved LV function, ejection fraction of 59% and normal LV volumes. Right ventricular (RV) volumes were preserved with mild systolic dysfunction and RV ejection fraction of 41%. Late gadolinium enhanced sequences demonstrated global predominantly subendocardial but some areas of transmural late gadolinium enhancement Enhancement also extended to the atrial walls, left greater than right, with mild thickening of the interatrial septum (Figure 2C). Pre-contrast T1 mapping value was significantly elevated at greater than 1300 ms (normal 1020 ms, Figure 2D). Findings were consistent with cardiac amyloidosis. Patient was started on Tafamadis, underwent transesophageal echocardiography (TEE) guided cardioversion and was discharged.

Two months later patient was admitted for recurrent progressive exertional dyspnea and palpitations with ECG similar to prior admission 2 months ago showing atypical slow atrial flutter with 2:1 block and left bundle branch block (Figure 1A). Heart rate was 90 beats/minute and blood pressure was 120/86 mm Hg. Chest x-ray did not show any acute cardiopulmonary process. INR was 2.0, serum potassium was 5.3 mEq/L, serum creatinine was 1.76 mg/dL, serum magnesium was 2.4 mg/dL, and NT-Pro BNP was 4335 pg/mL (normal [?] 77). Medications included apixaban 5 mg bid, spironolactone 25 mg qd, tafamidis 61 mg qd and tramadol 50 mg qd. He was initiated on amiodarone 100 mg bid and furosemide diuresis and referred for TEE-guided cardioversion. TEE identified no left or right atrial appendage thrombus, mild MR and trace TR. TEE probe was left in situ during cardioversion to assess left atrial (LA) appendage post cardioversion, due to post cardioversion atrial stunning, and higher risk of thrombus formation in cardiac amyloid. Patient was successfully cardioverted at first attempt with return to normal sinus rhythm (Figure 3). TEE demonstrated LVEF of 38% prior to, and 41% following cardioversion. Pre-cardioversion TEE pulsed

wave PW Doppler (PW) of the right atrial appendage showed regular Doppler velocities corresponding to each flutter wave on the ECG but with reduced amplitude of every alternate appendage velocity (Figure 4A). Doppler velocity returned to normal pattern post-cardioversion (Figure 4B). RA appendage velocities were normal in amplitude post cardioversion. LA appendage flow velocities showed similar pattern with alternate smaller amplitude PW Doppler velocities corresponding to every alternate flutter wave (Figure 4C), with return to normal pattern but with reduced velocities post-cardioversion (Figure 4D). Mitral inflow PW Doppler showed a single early filling wave with an indiscernible A wave pre cardioversion (Figure 4E). which reverted to E and A fusion pattern post cardioversion due to the presence of first-degree AV block (Figure 4F). Tricuspid annular tissue Doppler imaging pre cardioversion showed two additional velocities, one with smaller amplitude preceding and one with larger amplitude following annular e' wave, both immediately following the flutter P wave on the ECG prior to cardioversion (Figure 5A). These waves disappeared during sinus rhythm with good amplitude tissue Doppler a' wave suggesting good right atrial function after cardioversion (Figure 5B). These velocities were almost unrecognizable on mitral inferolateral annular Doppler pre cardioversion (Figure 5C) and normal tissue Doppler mitral annular pattern emergent post cardioversion (Figure 5D).

Other pre cardioversion TEE findings included restrictive appearing mitral inflow pattern (Figure 5E) and increased TR peak velocity at 3.1 m/sec corresponding to a pressure gradient of 38 mm Hg and consistent with LV diastolic dysfunction and pulmonary venous hypertension. He remained in normal sinus rhythm and discharged the following day. Five months later, the patient underwent dual-chamber biventricular pacemaker implantation with the coronary sinus lead placed into a lateral branch of the coronary sinus. He underwent AV nodal ablation three months after the implantation of the pacemaker. ECG post AV nodal ablation showed biventricular pacing at 70 bpm with underlying slow atrial flutter (Figure 6).

Discussion:

To our knowledge, ours is the first case report demonstrating the mechanical phenomenon of atrial alternans by TEE Doppler echocardiography in both atria in a patient with atrial flutter. An earlier study in ten patients with mechanical pulsus alternans suggested an atrial mechanism in two patients evidenced by lack of an "a" preceding each strong beat on apexcardiogram and echo M mode (1) and in an animal model of rapid atrial pacing (2). Clinical data on atrial alternans is sparse since atrial repolarization occurs during electrical activity of ventricles in the conventional ECG and hence measurements of atrial repolarization require invasive methods. Atrial alternans manifested by beat to beat alterations of atrial action potentials has been proposed as a precursor of atrial fibrillation (3).

In clinical practice, mechanical cardiac alternans is due to ventricular alternans and mechanisms of its development have been well studied along with its role in development of ventricular arrhythmias, however, alternans in atrial tissue remains much less investigated. Excitation-contraction coupling and intracellular Ca^{2+} regulation in ventricular and atrial tissue vary suggesting differences in alternans generation and regulation (4).

Cardiac involvement in light chain amyloidosis is associated with a high burden of cardiac arrhythmia including atrial fibrillation. In a small thick ventricle in cardiac amyloid, atrial contraction causes a significant contribution to diastolic filling, since early diastolic filling period is short due to rapid rise in LV filling pressure. Occurrence of atrial fibrillation or flutter in cardiac amyloid therefore reduces LV diastolic filling, reduces cardiac output and increases LA filling pressure which leads to new or worsening heart failure as in our patient who had diffuse cardiac amyloid infiltration and had slow atrial flutter with fixed 2:1 block. LA mechanical function was poor during atrial flutter, however LV diastolic filling improved post cardioversion from mechanical atrial contraction as shown on mitral inflow Doppler. Right atrial function improved significantly post cardioversion. LA appendage Doppler velocities however did not improve significantly post cardioversion likely due to post cardioversion left atrial appendage stunning. We have described this phenomenon of differential atrial stunning, left greater than right earlier (5), which in another patient led to a new LA appendage thrombus formation (6).

Our patient had undergone ablation procedures for atrial fibrillation as well as for atrial flutter in the past.

In addition, our patient had cardiac amyloidosis confirmed by MRI with delayed gadolinium enhancement of both the ventricles as well as both the atria. Atrial fibrillation and atrial flutter have been traditionally associated with left atrial enlargement, however, our patient had normal left atrial volumes on cardiac MRI. The atria were likely stiff and non compliant due to amyloid infiltration. Both scar related abnormality from prior ablations as well as significant extracellular atrial amyloid infiltration with increased atrial stiffness and progressive loss of atrial function may have contributed to atrial alternans (7). Resolution of alternans during sinus rhythm suggests that increased atrial contraction rate in impaired atria in our patient likely caused the atrial alternans due to variable repolarization after alternate beat as has been shown in an animal model of atrial pacing.[2] One MRI study found that atrial reservoir function was significantly worse in patients with TTR compared to light chain cardiac amyloid, despite similar maximum left atrial volume and sphericity index, indicating worse left atrial function in TTR compared to light chain amyloid (8).

Heart failure can induce atrial remodeling, including electrical remodeling atrial fibrosis, stretch and dilatation, that may contribute to atrial action potential alternans and mechanical atrial alternans (9). Our patient had normal LA volumes and did not have significant mitral or tricuspid regurgitation to cause atrial stretch but marked LV diastolic dysfunction from amyloid infiltration caused elevated LA pressure and likely caused atrial stretch. Mechanical stretch, and hypertrophy have been shown to be associated with arrhythmogenic atrial alternans (10,11).

Evaluation of right atrial appendage along with LA appendage, as well as the tissue Doppler imaging of mitral and tricuspid annuli pre cardioversion and in situ TEE during cardioversion allowed us to evaluate LV, atrial and appendage function post cardioversion in our patient and diagnose atrial alternans. This approach has many advantages as reported in our earlier studies (5,6,12,13).

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Figure Legends:

Figure 1

A) Baseline twelve lead ECG showing atrial flutter with 2:1 block, occasional premature ventricular contraction and LBBB prior to cardioversion. Black arrows show atrial flutter waves on ECG rhythm strip II. ECG is of low voltage. Diffuse increase in LV wall thickness is seen in parasternal long axis (B), short axis (C) and apical 4 chamber views (D). TTE LV wall thickness - ECG voltage paradox is present.

Figure 2

Two dimensional echocardiographic speckle tracking LV longitudinal strain imaging curves are shown in apical 4 chamber, 2 chamber and long axis views along with bull's eye map in A. Magnified bulls eye map is shown in B. Global averaged LV longitudinal peak systolic strain is abnormal at -8 % (normal = more negative than -18%) along with prominent apical sparing pattern highly suggestive of cardiac amyloidosis. Cardiac magnetic resonance image with gadolinium contrast (C) shows diffuse predominantly subendocardial late gadolinium enhancement of left and right ventricles. LV ejection fraction was 59% with preserved left ventricular volumes. Right ventricular volumes were preserved with mild diffuse systolic dysfunction, right ventricular ejection fraction of 41%. Left greater than right biatrial delayed gadolinium endocardial enhancement is also seen with normal left atrial volume. There is mild thickening of the interatrial septum. Pre-contrast T1 mapping value was significantly elevated at greater than 1300 ms (normal 1020 ms) (D) due to alteration in myocardial structure from amyloid deposition.

Figure 3

Post-cardioversion twelve lead ECG showing sinus rhythm with 1st degree AV block. Sinus p waves are shown with black arrows.

Figure 4

Pulsed wave (PW) Doppler images of the right atrial appendage pre (A) and post cardioversion (B) and left atrial appendage pre (C) and post cardioversion (D). Alternating amplitudes of Doppler velocities (white arrows) corresponding to mechanical atrial contraction following atrial flutter waves (yellow arrows) are shown pre cardioversion in right (A) and left atrial appendage (C). Doppler velocity amplitudes (white arrows) corresponding to mechanical atrial contraction following electrical atrial P wave (yellow arrows) returned to normal post cardioversion in both right (B) and left atrial appendage (D). Mitral inflow PW Doppler showing minimal atrial mechanical contraction velocities (white arrows) following flutter waves preceding each QRS complex (yellow arrows) pre cardioversion (E) F) Mitral inflow PW Doppler post cardioversion showing presence of mechanical atrial contraction (white arrows) following atrial P waves (yellow arrows), however there is E and A approximation due to first degree AV block and relative increased heart rate of 80 bpm.

Figure 5

Tricuspid annular tissue Doppler imaging pre cardioversion showing two extra velocities, one with smaller amplitude preceding and one with larger amplitude following annular e' wave, both immediately following the flutter P wave on the ECG prior to cardioversion (A). These waves disappeared during sinus rhythm after cardioversion (B). These velocities were almost unrecognizable on mitral inferolateral annular Doppler pre cardioversion (C) and normal tissue Doppler mitral annular pattern emergent post cardioversion (D). Restrictive appearing mitral inflow pattern (E) and increased TR peak velocity of3.1 m/sec corresponding

to a pressure gradient of 38 mm Hg is shown (F). Due to Doppler beam insonation angle of 60 degrees with the tricuspid annulus there is Doppler signal noise most marked in A.

Figure 6

Twelve lead ECG showing atrial flutter waves (black arrows) with biventricular pacing at 70 beats per minute following the implantation of biventricular pacemaker and AV nodal ablation.