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Mitral Annulus Disjunction and Arrhythmic Mitral Valve Prolapse: Emerging Role of Cardiac Magnetic Resonance Imaging in the Workup

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Abstract

Mitral valve prolapse is a commonly described entity with a highly variable and benign course. However, it is associated with ventricular arrhythmias and sudden cardiac death in a small subset of patients. Recent studies have yielded insight into myocardial mechanics and the causation of ventricular arrhythmias in these groups of patients.

Mitral annular disjunction (MAD) characterized by detachment of mitral annulus from left ventricular myocardium is associated with morphological and functional remodeling of the left ventricular myocardium. Resultant fibrosis acts as a substrate of ventricular arrhythmia and sudden cardiac death.

We present two such cases of arrhythmic mitral valve prolapse associated with MAD. Cardiac magnetic resonance imaging provides excellent morphological information and also helps in the assessment of fibrosis.

Keywords
- ► mitral regurgitation
- ► mitral valve prolapse
- ► mitral annulus disjunction
- ► cardiac MRI

Introduction

Mitral valve prolapse is classically defined as the superior displacement of the mitral valve leaflet for >2 mm during systole. It results from myxomatous degeneration of valve leaflets.[1] The adverse effects include mitral regurgitation, heart failure, infective endocarditis, cardiac arrhythmias, and rarely sudden cardiac death.[2] Various studies have been performed to identify those patients with a higher risk of fatal ventricular arrhythmias. Timely identification of these high-risk patients will help in the planning of preventive intervention.

Mitral annular disjunction (MAD) is a recently described entity that is frequently associated with mitral valve prolapse. It is a structural abnormality of the annulus, characterized by separation of mitral valve annulus from left ventricular (LV) myocardium. Resultant myocardial curling (posterobasal wall) and fibrosis act as an arrhythmic substrate. This can result in ventricular arrhythmia and hence the terminology of arrhythmic mitral valve prolapse is coined[3] (►**Fig. 1**).

Cardiac magnetic resonance imaging (CMR) provides a better assessment of leaflet morphology and mitral annular plane. Myocardial mechanics and function can also be assessed using cine images. Moreover, tissue characterization with late gadolinium enhancement (LGE) images helps in the identification of fibrosis. Thus, CMR provides valuable prognostic information in these patients.[3,4]

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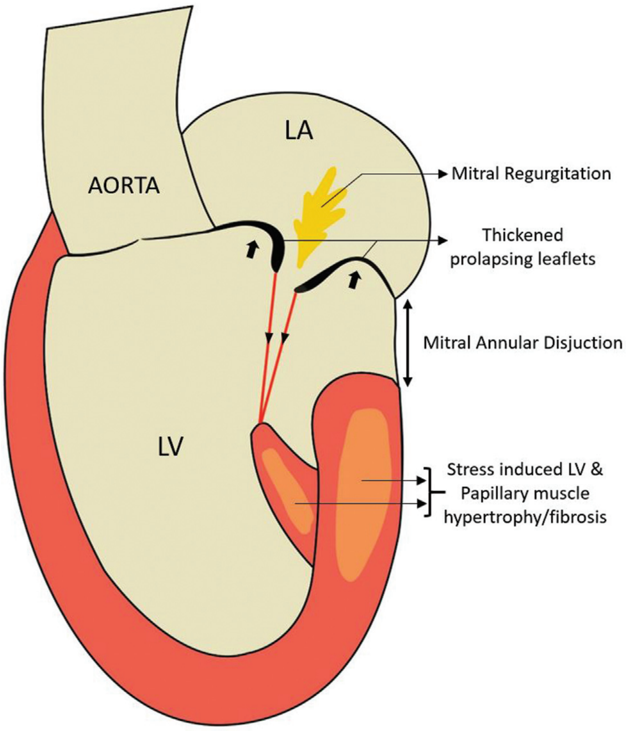

Fig. 1 Diagrammatic representation of pathophysiology of arrhythmic mitral valve prolapse. LA, left atrium; LV, left ventricle.

Case Report

Case 1

A 43-year-old male diagnosed with mitral valve prolapse presented with occasional palpitations and mild chest discomfort. Clinical examination revealed tachycardia with a midsystolic click. An invasive cardiac angiogram performed 2 years ago showed unobstructed coronary arteries. His troponins were negative and electrolytes were normal. Two-dimensional (2D) echocardiography showed normal wall motion and function. The mitral valve showed myxomatous morphology with bileaflet prolapse. The presence of spiked systolic lateral mitral annular velocities (Pickelhaube sign) was noted with moderate mitral regurgitation (►**Fig. 2**).

CMR confirmed mitral valve prolapse and moderate mitral regurgitation (regurgitant volume = 37 mL and regurgitant fraction = 31%). Cine images in the long axis reveal separation of LV myocardium from mitral valve annulus, suggesting annular disjunction (separation for 13 mm). Systolic curling of the posterobasal left ventricle was also evident. There was no significant late gadolinium enhancement, however. Mild reduction of global longitudinal strain (GLS; 18.5%) and increased T1 values (1,250 ms; normal values: 1,150 ± 50 ms) were observed. The left ventricular ejection fraction (LVEF) was normal 60% (►**Fig. 3**).

Case 2

A 40-year-old female with a history of mitral valve prolapse presented with two episodes of sustained ventricular tachycardia, reverted with adenosine. Clinical examination revealed a holosystolic murmur. 12-lead electrocardiogram (ECG) showed sinus rhythm without signs of ischemia. 2D echocardiography showed depressed LV systolic function, myxomatous mitral valve, bileaflet mitral valve prolapse (MVP), and severe mitral regurgitation. There was a separation of LV myocardium from mitral valve annulus, suggestive of mitral annulus disjunction. There was also the presence of ostium secundum atrial septal defect with left to right shunt (►**Fig. 4**).

CMR showed thickened myxomatous mitral valve leaflets and mitral valve prolapse with severe mitral regurgitation (regurgitant volume = 42 mL, regurgitant fraction = 40%). Cine images reveal separation of LV myocardium from mitral valve annulus suggesting annular disjunction (longitudinal distance: 9 mm). There is systolic curling of the posterobasal left ventricle. Bowing of interatrial septum toward right side noted with subtle defect and dephasing jet suggestive of ostium secundum atrial septal defect. No regional wall motion abnormality was seen. Focal late gadolinium enhancement was observed at the LV posterobasal wall. There was a reduction of GLS (20.6%) and increased T1 values (1,321 ms; normal values: 1,150 ± 50 ms). LVEF is mildly reduced 52% (►**Fig. 5**).

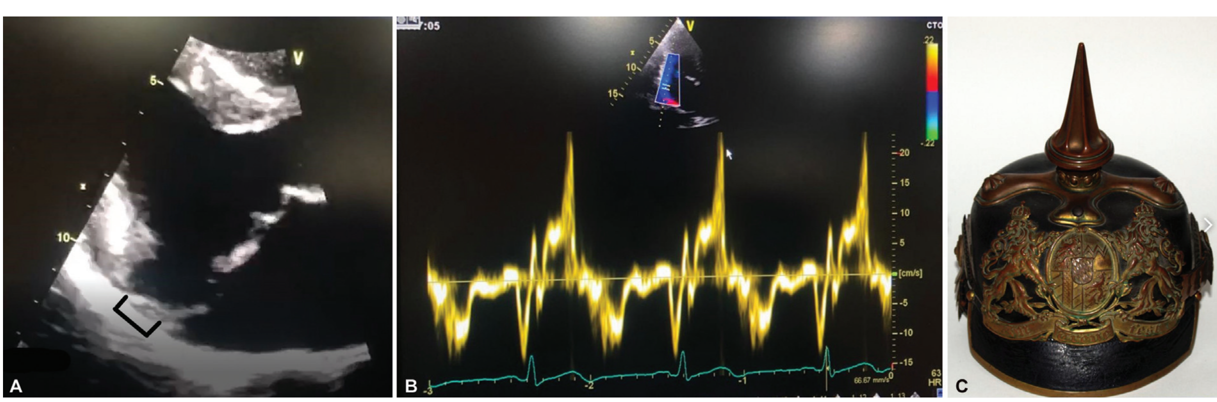

Fig. 2 Case1 echocardiography (**A**) Parasternal long-axis view showing mitral regurgitation with prolapse and annular disjunction. (**B**) Doppler tissue imaging showing spiked systolic lateral mitral annular velocities: Pickelhaube sign (**C**); a spiked helmet worn in the 19th and 20th centuries by Prussian and German military. (©Engelberger/Wikimedia Commons/CC-BY-SA-3.0/GFDL).

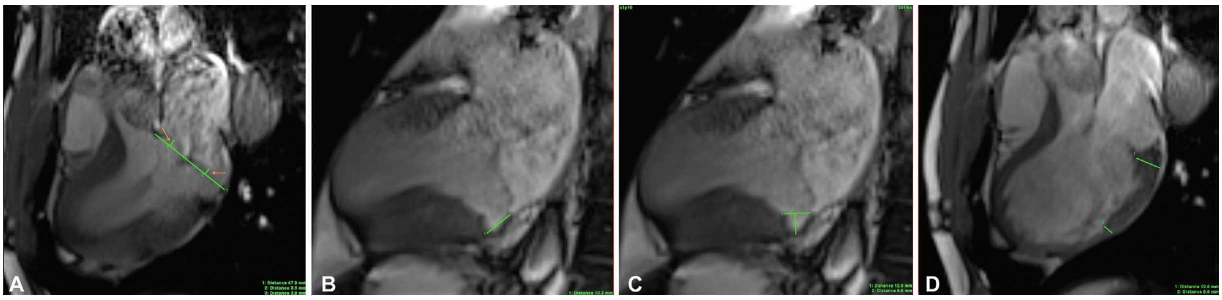

Fig. 3 Case 1 CMR (**A**) 3D Long axis view showing bileaflet prolapse. The prolapsed distance is measured as superior displacement of leaflet beyond mitral annulus (*orange arrows*) (**B**) Long-axis view, Longitudinal mitral annulus disjunction (MAD; *green line*) length is measured from the junction of left atrial (LA) wall–posterior MV leaflet to the top of the left ventricular (LV) inferobasal wall during end systole (**C**). Same image as in (**B**) showing measurement of curling distance by tracing a line between the LA wall–posterior MV leaflet junction and top of LV inferobasal wall, and from this line, a perpendicular line to the lower limit of the mitral annulus during end-systole. (**D**) LV basal hypertrophy. The LV thickness of basal and mid segments of the inferolateral wall is measured at diastole on long axis view. Base-to-mid ratio: 2.7. 3D, three-dimensional; CMR, cardiac magnetic resonance imaging; MV, mitral valve.

Methodology

Contrast-enhanced CMR was performed on 3-Tesla MRI scanner (Magnetom Verio; Siemens, Erlangen, Germany) with a phased-array body coil. ECG gated spin-echo and gradient-echo images were obtained with 25 phases of the cardiac cycle. Cine steady-state free precession pulse sequences were acquired in two-chamber, four-chamber, three-chamber, and parallel contiguous short-axis stack. Phase-contrast images of the aorta and main pulmonary artery were obtained.

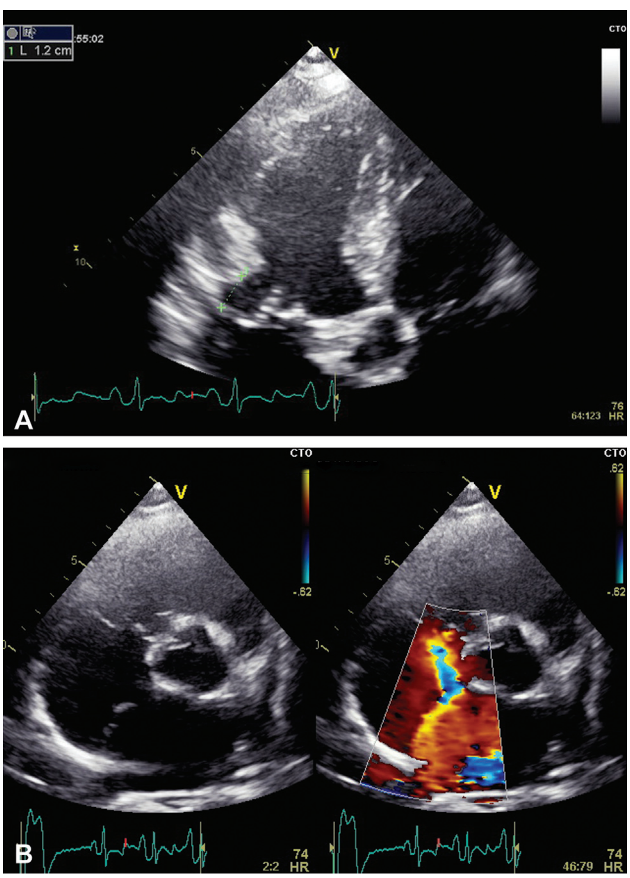

Fig. 4 Case 2 echocardiography. (**A**) Apical four-chamber view showing mitral regurgitation with prolapse and annular disjunction. (**B**) Jet in interatrial septum suggestive of ostium secundum atrial septal defect.

0.15 mmol/kg gadobutrol (Gadovist, Bayer Pharma AG, Leverkusen, Germany) was administered intravenously with acquisition of postcontrast perfusion. Delayed enhancement images were acquired at a 10-minute interval after administration of gadolinium. Data analysis and postprocessing was performed on dedicated CMR postprocessing software (suiteHEART; NeoSoft LLC, Wisconsin, United States).

Multiplanar capability, superior spatial resolution, accurate assessment of chamber size and function are few reasons why CMR is the preferred modality for workup in these groups of patients. More importantly, tissue characterization obtained with late gadolinium enhancement images is the gold standard for the evaluation of myocardial fibrosis. The following table (►**Table 1**) is a summary of MRI findings and an ideal view/sequence for the assessment of different pathological abnormalities.[3–8]

Mitral valve annulus is a three-dimensional (3D) structure; hence, assessment of the entire circumference is essential. High-quality images and multiple planes obtained during tailored MRI protocol will be essential for a complete assessment. Additional CMR sequences may be performed for detailed assessment of mitral valve, prolapse, regurgitation and circumferential MAD as shown in (►**Fig. 6**).[3,9] However, these could not be performed in our cases due to time constraints.

Discussion

The mitral annulus is a 3D saddle-shaped structure exhibiting dynamic changes during the cardiac cycle. The motion of the annulus is passive and determined by the contraction and relaxation of adjacent structures. Normally the annulus contracts during systole and moves downward and anteriorly. This is important for the balanced distribution of mechanical stresses.[10,11]

Mitral valve prolapse is estimated to affect approximately 2 to 3% of the general population. The clinical outcomes are highly variable and depend on factors like age, degree of

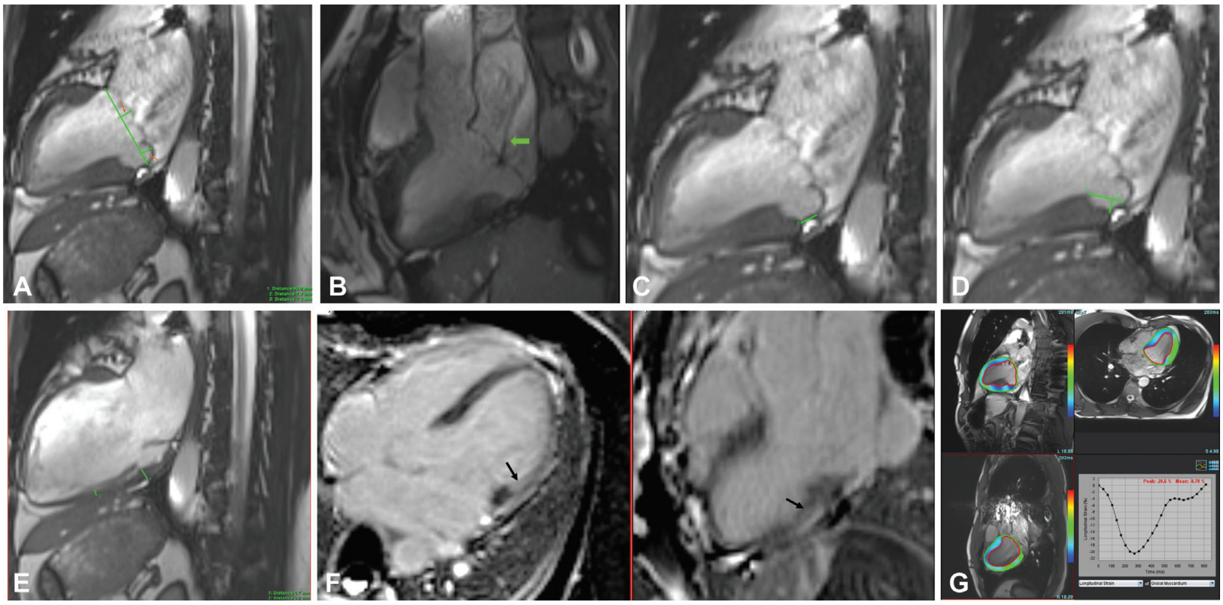

Fig. 5 Case 2 CMR. (**A**) Two-chamber view demonstrating bileaflet mitral valve prolapse with prolapse distance measurements (*orange arrows*). (**B**) Note regurgitant jet from mitral regurgitation (*green arrow*) (**C**) Note the separation of LV myocardium from mitral annulus (*green line*: MAD distance). (**D**) Curling of LV myocardium seen in two-chamber view with quantitative measurement of curling distance (*yellow arrow*). (**E**) LV basal hypertrophy Base: Mid LV thickness ratio of 2:1. (**F**) Focal LGE involving the posterobasal wall of LV myocardium. (**G**) Color coded feature tracking map in long axis views with global longitudinal strain curve depicting reduction in GLS. CMR, cardiac magnetic resonance imaging; GLS, global longitudinal strain; LV, left ventricle; MAD, mitral annulus disjunction.

Table 1 CMR workup[3–8]

Abnormality	CMR findings	CMR workup.	Implications
Prolapse	Superior displacement of valve leaflet >2 mm	2C, 4C, 3C cine (end systole)	
Classic/myxomatous	Leaflet thickening >5 mm	2C,4C, 3C cine	
Longitudinal distance for mitral annular disjunction	Distance between left atrial (LA) wall-posterior mitral valve (MV) leaflet junction to the top of the LV inferobasal wall during end-systole. (if >1 mm)	2C, 3C cine (end systole)	>8.5 mm increased risk of ventricular arrhythmias
Left ventricular (LV) basal to mid ventricular thickness	Ratio of LV thickness of basal and mid segments of the inferolateral wall	2C, 3C cine (end diastole)	≥1.5 indicates basal LV hypertrophy Locally increased stretch and myocardial function
Curling of myocardium	Line between the top of LV inferobasal wall and the LA wall–posterior MV leaflet junction, and from this line, a perpendicular line to the lower limit of the mitral annulus	2C, 3C cine (end systole)	≥3.5 mm severe curling
Paradoxical annulus expansion	Positive difference between end-systolic diameter and end-diastolic diameter	Cine images	Increased risk of failure of Mitral Valve repair
Fibrosis	LV wall or papillary muscle LGE	Delayed enhanced images	LV fibrosis acts as a substrate for electrical instability
Severity of MR	LV stroke volume—forward flow of aorta (for regurgitant volume/fraction)	Cine and phase-contrast images	
Global longitudinal strain	Deformation analysis	Feature tracking	
T1 mapping	Increased values with interstitial fibrosis	Parametric mapping (MOLLI/ShMOLLI)	

Abbreviations: C, chamber, CMR, cardiac magnetic resonance imaging; MOLLI, Modified Look-Locker inversion recovery; ShMOLLI, shortened MOLLI.

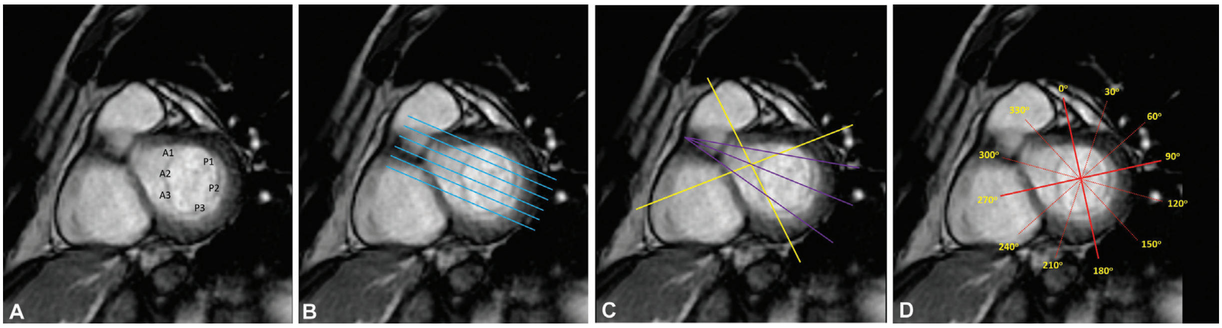

Fig. 6 CMR planning for assessment of mitral valve. (**A**) CMR short axis view at the level of mitral valve showing anatomy of mitral valve. A1, A2, and A3 scallops in the anterior leaflet. P1, P2, and P3 scallops in the posterior leaflet. (**B**) Modified left ventricular outflow tract view. Contiguous stack of cine images perpendicular to the mitral commissures transecting the principal line of coaptation to visualize and assess all the mitral scallops A1–P1, A2–P2, and A3–P3. (**C**) Additional/alternative slices perpendicular to the coaptation plane of the valve leaflets (*yellow and/or purple lines*) (**D**) For circumferential assessment of annular plane, six left ventricular long-axis cine slices are acquired at every 30 degrees. The first projection was aligned through the superior right ventricular free wall insertion into the septum, and was defined as 0° in the annular plane, followed by clockwise labeling of the long-axis slices. CMR, cardiac magnetic resonance imaging.

Table 2 Classification of mitral valve prolapse[13,14]

Clinical classification	
Primary/nonsyndromic	Isolated disease
Secondary/syndromic	Associated with connective tissue disorders such as Marfan's syndrome, Loeys–Dietz syndrome, Ehlers–Danlos syndrome, osteogenesis imperfecta, and pseudoxanthoma elasticum
Histological classification	
Barlow's Disease	Classic/myxomatous degeneration Diffusely thickened and redundant leaflets
Fibroelastic deficiency	Diffusely thinned leaflets with focal thickening

mitral regurgitation, LVEF, ventricular ectopy, and atrial diameters. High-risk populations may develop significant MR, heart failure, infective endocarditis, stroke, cardiac arrhythmias, and even sudden cardiac death.[12]

The classification of MVP is shown in the following table (►**Table 2**).[13,14]

MAD is defined as a wide separation between the left atrium-mitral valve junction and left ventricular free wall. In simpler words, it is the superior displacement/atrialization of the posterior leaflet base. It leads to paradoxical annular enlargement and flattening during systole with systolic curling of the LV, increasing stress on the leaflets and chordae which may accelerate the degenerative process. The mechanical traction on the papillary muscles and posterolateral LV wall can lead to morphological and functional remodeling including myocardial hypertrophy or fibrosis which could be the substrate of ventricular arrhythmias and sudden cardiac death. In fact, due to these underlying myocardial involvements, this condition is also known as "concealed cardiomyopathy."[4,15]

MAD can also occur "de novo," in normal individuals without mitral valve prolapse. However, an increased prevalence of arrhythmias is associated with this abnormality.[3]

Arrhythmic mitral valve prolapse is characterized by myxomatous degeneration, bileaflet prolapse, mitral annular disjunction, and papillary muscle fibrosis. A combination of mechanically triggered premature ventricular contractions (PVCs) from the mitral valve apparatus with the increased autonomic tone, predisposes for the development of sudden cardiac death in these high-risk individuals.[12]

Close surveillance monitoring and medications like β-blockers will provide first-line therapy in symptomatic individuals. Catheter ablation is reserved for cases where electrical triggers can be mapped. Defibrillator therapy and mitral valve surgery are other long-term options.[12]

Conclusion

Mitral annulus disjunction shows an increased prevalence of arrhythmic events. Hence timely diagnosis is crucial in patient management. Though it can be identified on 2D echocardiography/TEE, CMR undoubtedly adds value to diagnosis.

The mitral annular plane is a 3D structure; hence, assessment of the entire circumference can be archived with focused CMR study. Correct planning and tailored CMR protocol will provide diagnostic, as well prognostic information of this life-threatening condition.

Note

The study was undertaken by conforming to the Declaration of Helsinki.

Conflict of Interest

None declared.

Acknowledgments

All cardiac magnetic resonance imaging data postprocessing has been done using suiteHEART; NeoSoft LLC, Wisconsin, United States.

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