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VALVULAR HEART DISEASE

CASE REPORT: CLINICAL CASE

Systemic Lupus Erythematosus Causing Rapid Progression of Mitral Valve Disease

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ABSTRACT

A 33-year-old woman with systemic lupus erythematosus presented with rapid progression of mitral valve disease within a 5-year period, highlighting concerns regarding routine surveillance guidelines for mild to moderate valvular disease. (JACC Case Rep 2024;29:102429) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Systemic lupus erythematosus (SLE) is an autoimmune disease that commonly affects young women with clinical manifestations that may involve any organ system.[1] Cardiac manifestations of SLE are propagated by small- and medium-vessel vasculitis in up to 50% of patients, antiphospholipid antibody syndrome (APLS) in about 25% to 40% of patients, and premature atherosclerosis; however, exact rates for this manifestation are undefined. Thus, cardiovascular disease accounts for about one-third of deaths in SLE.[2-5] The clinical course of these conditions is quite variable and limitedly reported, especially as it pertains to echocardiographic progression.

LEARNING OBJECTIVES

- To understand the common manifestations of mitral valve disease associated with SLE.
- To understand the cardiac disease course and treatment options available for mitral valve disease in SLE which include medical management pending definitive surgical management (valve replacement strategies).
- To review limitations of echocardiographic methods to evaluate mitral valve area.

HISTORY OF PRESENTATION

A 33-year-old woman with a past medical history of SLE, APLS, and Libman-Sacks endocarditis initially presented to the clinic 6 years prior with a malar rash, serositis, and arthritis. She was treated in the clinic thereafter with hydroxychloroquine and steroids without concern for organ involvement on serial blood work. She initially underwent transthoracic echocardiogram (TTE) during an admission for a lupus flare in 2019 showing normal left ventricular (LV) systolic function and mild mitral valve regurgitation (MR) (**Figures 1 to 5**, Videos 1 to 8). A transesophageal study confirmed the findings of restricted posterior leaflet motion and mild MR (Videos 9 and 10). Due to a prior hospital admission for a pulmonary embolism in the setting of APLS (+antinuclear antibodies, +anti-double-stranded DNA antibodies, +anti-Ro, +anti-La, +APLS serologies [Lupus Anticoagulant Diluted Russell Viper Venom-Time 54.5 seconds, anticardiolipin immunoglobulin

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ABBREVIATIONS AND ACRONYMS

APLS = antiphospholipid antibody syndrome

LV = left ventricular

MR = mitral valve regurgitation

MS = mitral stenosis

MVA = mitral valve orifice area

NBTE = nonbacterial thrombotic endocarditis

P1/2t = pressure half-time

RHD = rheumatic heart disease

SLE = systemic lupus erythematosus

TTE = transthoracic echocardiogram

G >100 IgG phospholipid units-U/mL and anti-β2 glycoprotein I immunoglobulin G >100 U/mL]), the patient was advised anticoagulation with warfarin (Table 1). She was lost to follow-up and was nonadherent to disease-modifying medications during this time.

PAST MEDICAL HISTORY

The patient's past medical history was limited to what is listed in the history of presentation.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for this patient was SLE vs rheumatic heart disease (RHD), which may present in a similar manner but may be differentiated by clinical course.

INVESTIGATIONS

The patient presented to the outpatient clinic with joint pain and swelling involving her bilateral shoulders, elbows, and metacarpophalangeal/proximal interphalangeal joints with associated chest pain and respiratory distress (Table 1). Electrocardiogram increased voltage with nonspecific repolarization abnormalities (Figure 6). A repeated TTE showed preserved LV systolic function but an akinetic LV apex, anterior mitral leaflet doming with severe MR, mitral stenosis (MS) (mean gradient, 18.5 mm Hg; mitral valve area by planimetry, pressure half-time [P1/2t], and continuity = 1.4, 2.3, and 0.5 cm^2, respectively), and severe pulmonary hypertension (Figures 1 to 5, Videos 1 to 8). An electrocardiogram-gated contrast-enhanced cardiac computed tomography scan showed no evidence of obstructive coronary artery disease (Figure 7).

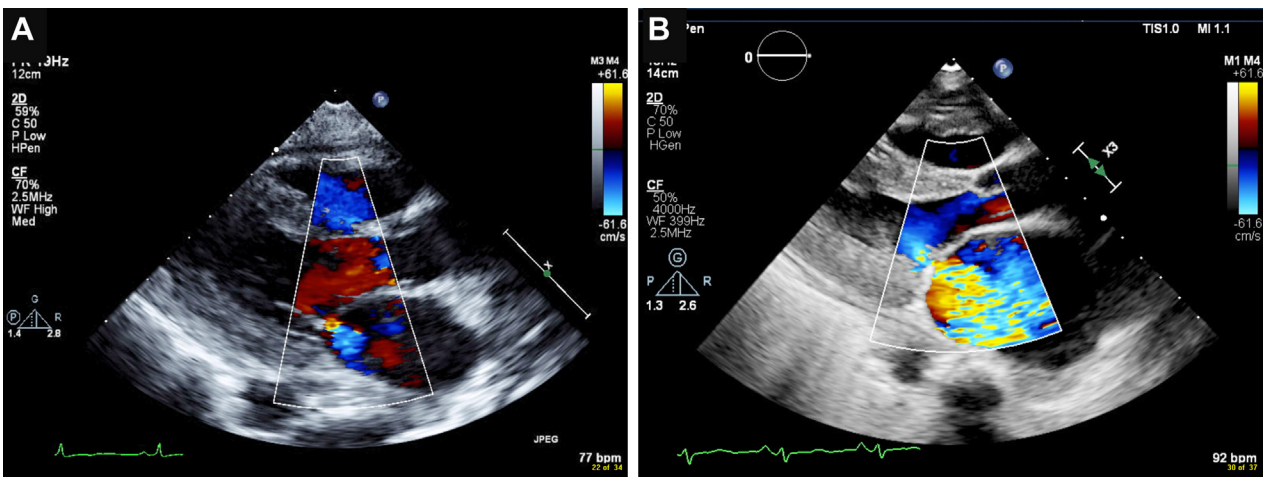
MANAGEMENT

From a treatment perspective, although diagnosed with severe MR, due to concomitant significant stenosis, mitral valve repair was not a viable option for this patient. Thus, she was medically managed with hydroxychloroquine, azathioprine, and intravenous steroids. She was started on therapeutic enoxaparin to be bridged to warfarin but was discharged on apixaban due to concerns regarding her adherence for follow-up testing and her preference for oral medications. She was started on metoprolol tartrate for mitral valve disease and lisinopril for proteinuria. While undergoing additional cardiac testing, the patient opted to leave against medical advice and follow-up in the outpatient setting to complete ischemic workup and consider valve replacement strategies.

DISCUSSION

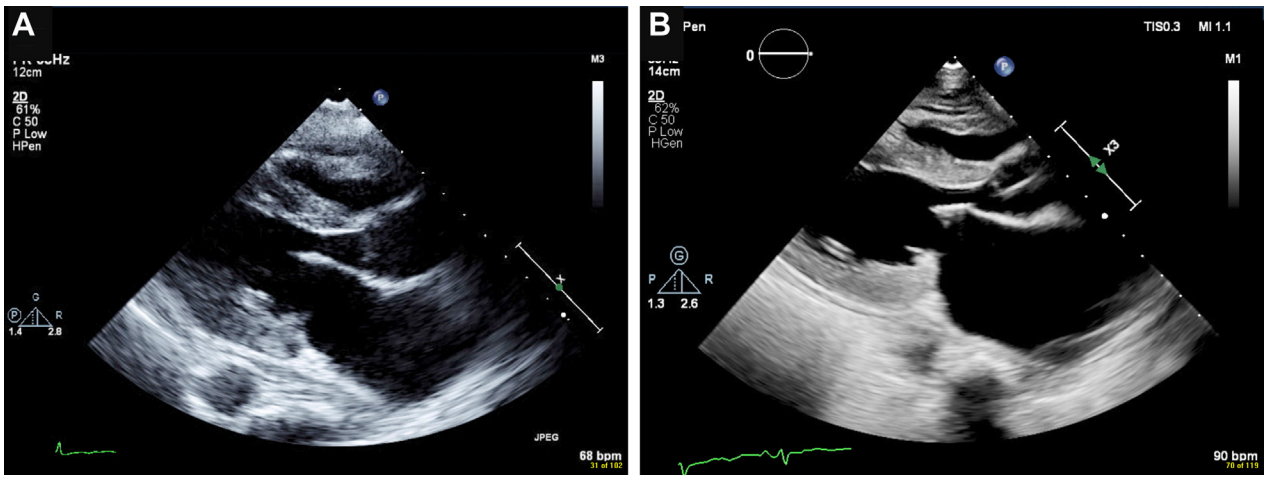
Prior studies have noted an increased risk of severe MS/MR in patients with SLE with a history of APLS.[1,6] An unfortunate complication of these autoimmune conditions is valvular disease and early onset heart failure. It is postulated that autoimmune pathways

FIGURE 1 Parasternal Long-Axis Images at End-Diastole Obtained at Baseline



Parasternal long-axis images at end-diastole obtained at baseline (A) demonstrating posterior leaflet restriction and mild leaflet thickening. At 5-year follow-up (B), there is now a reduction in anterior leaflet excursion with doming.

FIGURE 2 **Parasternal Color Doppler Short-Axis Images Obtained at Baseline**

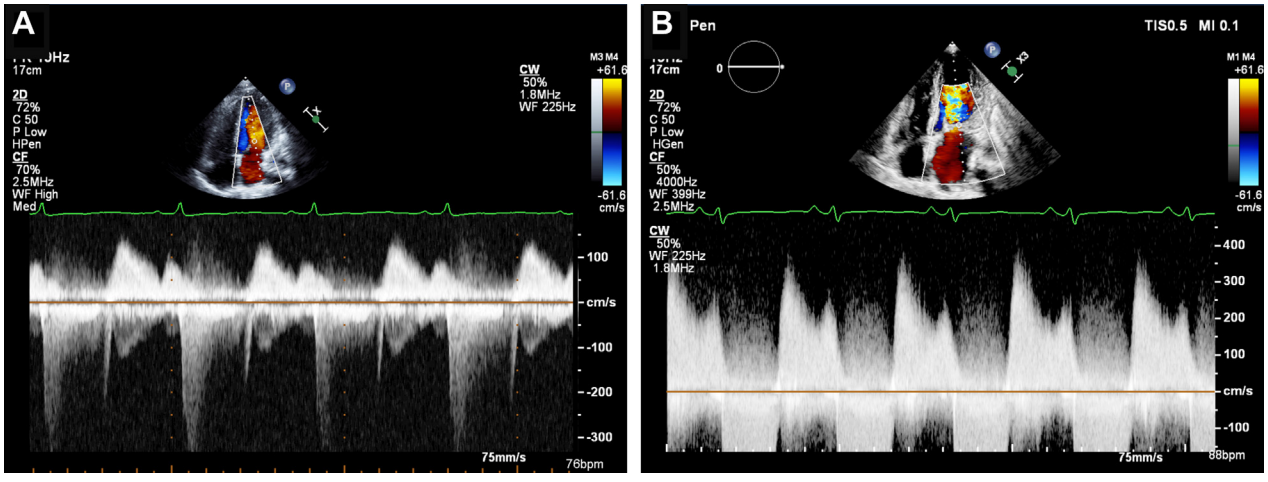


Parasternal color Doppler short-axis images obtained at baseline (A) showing mild mitral valve regurgitation and at 5-year follow-up (B) showing severe mitral valve regurgitation.

that lead to inflammatory cell infiltration and immune complex deposition lead to valvular disease in such cases, most commonly impacting the mitral valve. MS is interestingly the least common valvular manifestation in this patient group (<5% risk).[7] Thus, prior reports on MS and cardiac disease progression in such patients are limited. Although more common than MS, the prevalence of severe MR that progresses to the point of mitral valve replacement is rare; albeit, repair has been previously described.[8,9] Due to the wide array of presentations, first-line diagnostic tools include a TTE and an autoimmune panel, as was done in this patient.

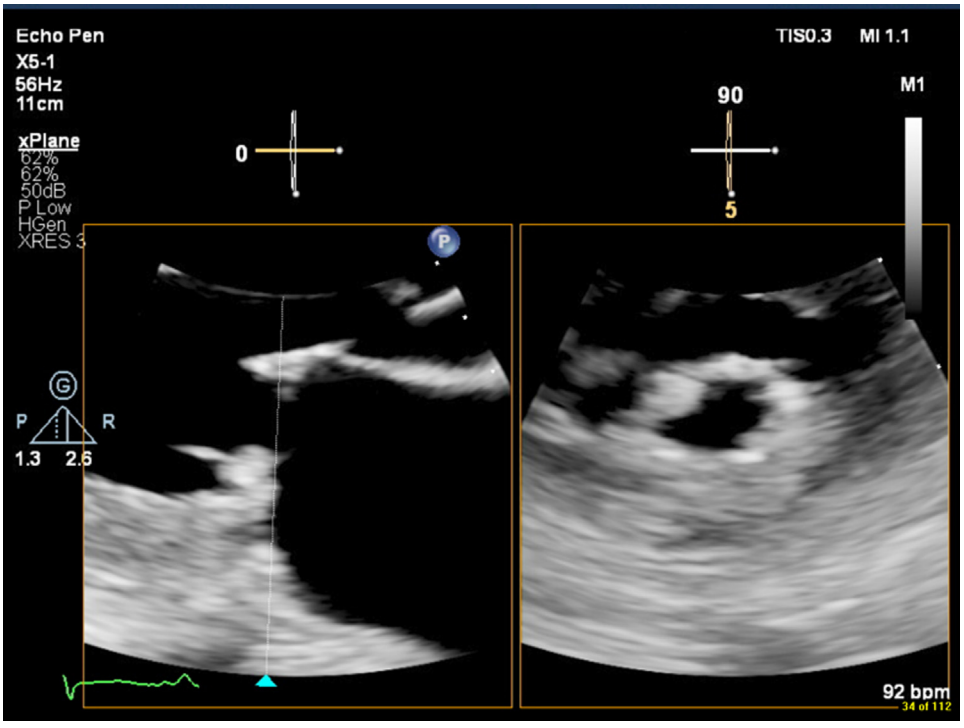
Current guidelines recommend routine surveillance (≥3 years) in patients presenting with mild MR without a change in clinical status or cardiac examination.[10] A unique aspect of this patient's case is the rapid progression of mitral valve disease leading to

FIGURE 3 **Continuous Wave Doppler Left Ventricular Inflow Recordings Obtained at Baseline**



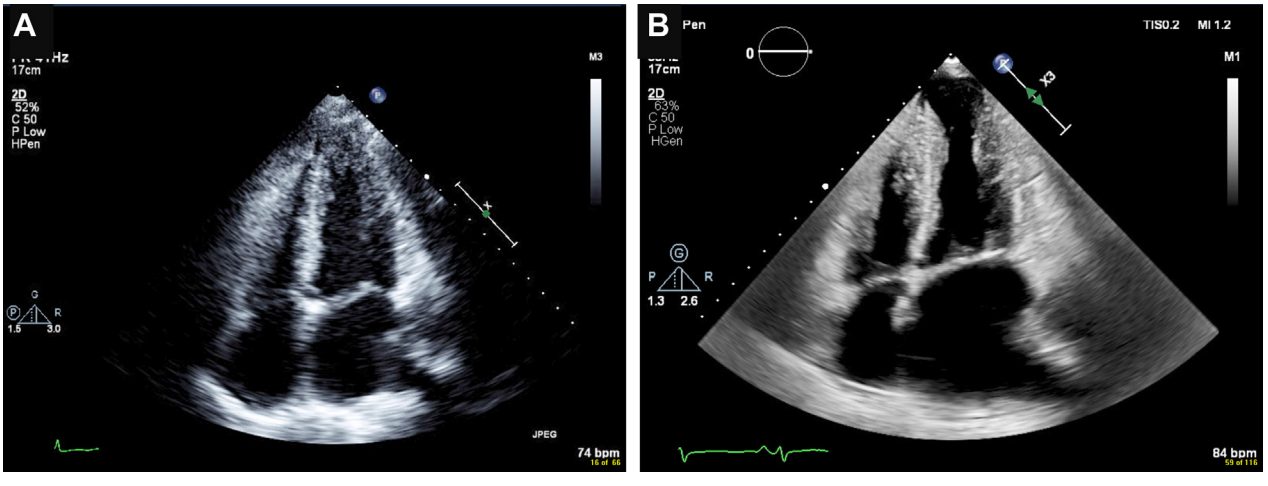
Continuous wave Doppler left ventricular inflow recordings obtained at baseline (A) showing mild transvalvular gradient and mild mitral valve regurgitation, and at 5-year follow-up showing severely elevated gradients with increase mitral valve regurgitation signal intensity (B).

FIGURE 4 Biplane Parasternal Images Obtained at 5-Year Follow-Up



Biplane parasternal images obtained at 5-year follow-up demonstrating mitral valve leaflet doming, commissural fusion, and reduced orifice area.

FIGURE 5 Apical 4-Chamber Images Obtained at Baseline



Apical 4-chamber images obtained at baseline (A) and at 5-year follow-up (B). Notice the new appearance of apical dyskinesis and left atrial enlargement.

TABLE 1 Laboratory Testing Results From 2019 and 2024

Test	2019	2024
Lupus anticoagulant (Diluted Russell Viper Venom Time), seconds	Positive, 66.1	Positive, 54.5
Anticardiolipin i immunoglobulin G, GPL-U/mL	>100	Negative
Anti-β2 glycoprotein immunoglobulin G, U/mL	>100	Negative
White blood cell count, K/uL	3.8	2.8
Hemoglobin, g/dL	10.8	8.3
Platelet count, K/uL	208	182
Sodium, mEq/L	136	138
Potassium, mEq/L	4.1	3.8
Chloride, mEq/L	100	104
Carbon dioxide, mEq/L	21	24
Anion gap, mEq/L	15	10
Blood urea nitrogen, mg/dL	8	12
Creatinine, mg/dL	0.50	0.63
GFR, mL/min/BSA	>120	119
Glucose, mg/dL	103	89
Magnesium, mg/dL	1.7	1.6
Alkaline phosphatase, U/L	89	88
Aspartate transaminase, U/L	24	20
Alanine transaminase, U/L	10	11
Albumin, g/dL	3.4	2.6
Total bilirubin, mg/dL	0.4	0.2
Direct bilirubin, mg/dL	<0.2	<0.2
Troponin I, ng/mL	0.01	0.01
Creatine kinase, U/L	61	79
Urine random protein, mg/dL	100	300
Urine glucose, mg/dL	Negative	Negative
Urine ketone, mg/dL	15	Negative

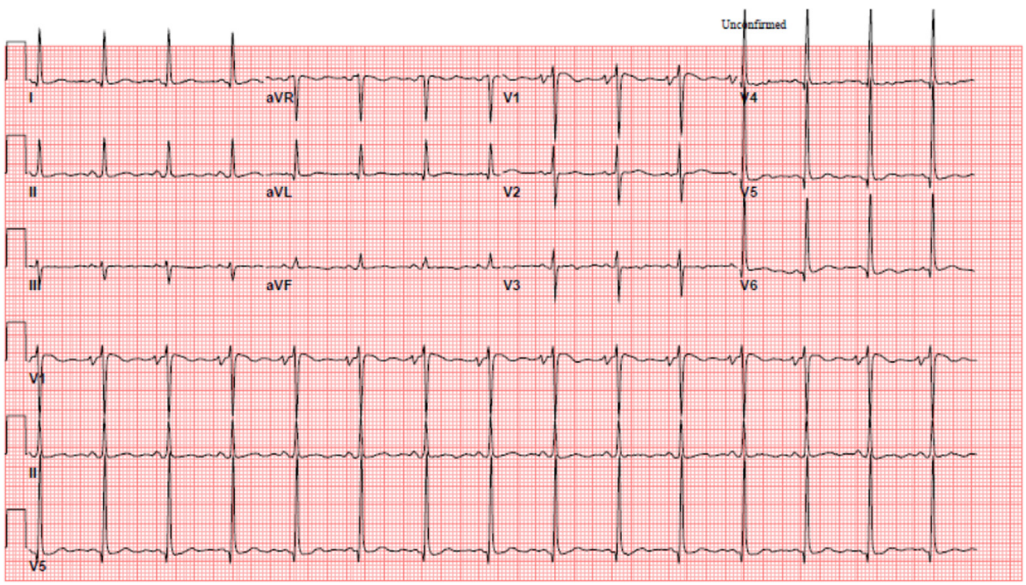
BSA = body surface area; GFR = glomerular filtration rate; GPLU = IgG phospholipid units.

moderate MS and severe MR over only a 5-year time course. The patient had initially presented with a near-normal TTE notable only for mild MR. The patient was lost to follow-up and discontinued therapy, returning 5 years later with dyspnea due to moderate MS, severe MR, and severe pulmonary hypertension. Furthermore, she was noted to have a dyskinetic LV apex which, in the setting of SLE, was concerning for an ischemic/embolic event. Although electrocardiogram did not show dynamic ischemic changes and cardiac markers returned negative, the patient left against medical before additional cardiac testing could be completed.

RHD is the primary cause of acquired heart disease in young adults and presents as a complication of rheumatic fever.[11] MS is most commonly associated with RHD and presents on TTE with anterior mitral valve leaflet thickening and chordal thickening resulting in restricted leaflet motion. This patient's TTE findings were quite similar to those seen in RHD.

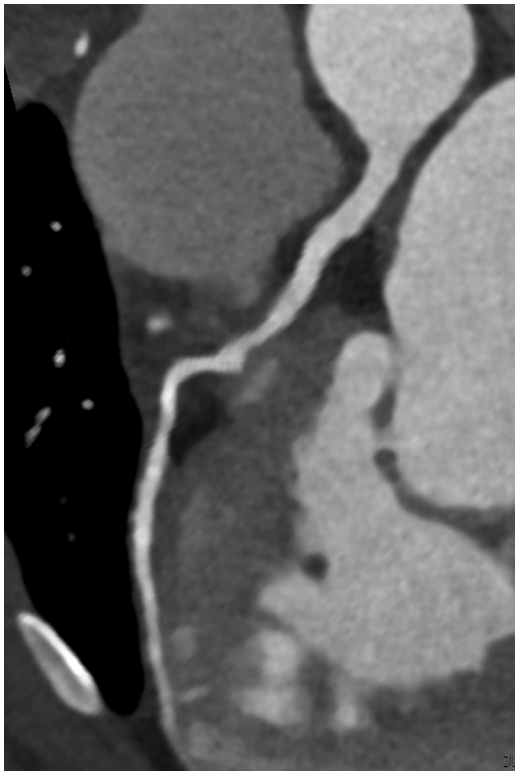
Nonbacterial thrombotic endocarditis (NBTE) may present similarly to SLE with APLS. There is a paucity of data regarding progression of this disease with some reports recommending that NBTE be surveilled with the most recent American College of Cardiology/American Heart Association valvular heart disease guidelines.[12] It is unclear whether the autoimmune nature of SLE or triple-positive APLS may progress at a more rapid rate than the

FIGURE 6 Electrocardiogram Obtained at 5-Year Follow-Up



Electrocardiogram obtained at 5-year follow-up showing increased voltage and non-specific ST-segment abnormalities.

FIGURE 7 Computed Tomographic Angiographic Image of the Left Anterior Descending Coronary Artery



Computed tomographic angiographic image of the left anterior descending coronary artery demonstrating no evidence of obstructive coronary artery disease.

hypercoagulable pathophysiology of NBTE because existing data are limited. Closer routine surveillance testing may be beneficial to diagnose both conditions early in their disease course.

Two important echocardiographic parameters used to quantify the severity of MS are mitral valve orifice area (MVA) and magnitude of the gradient across the mitral valve. P1/2t may be used to estimate MVA;[13] however, this method overestimates MVA in the presence of severe MR, when left atrial compliance is reduced. Conversely, the continuity method results in underestimation of MVA because flow across mitral valve orifice exceeds flow across LV outflow tract. Thus, in cases where P1/2t and continuity measurements are limited, planimetry is required.

From a rheumatologic perspective, APLS is commonly diagnosed clinically but confirmed using 3 common assays: lupus anticoagulant, anticardiolipin, and anti-β2 glycoprotein I antibodies. A subset of patients, similar to the present patient, present with a triple-positive profile of APLS denoted by the simultaneous presence of all 3 antibodies.[14] These patients represent a special high-risk patient population due to their greater risk of clotting and well-documented obstetric complications secondary to hypercoagulability.

FOLLOW-UP

The patient is being evaluated by the cardiothoracic surgery team at our institution for surgical valve replacement.

CONCLUSIONS

SLE with APLS is a risk factor for valvulopathy, specifically regarding the mitral valve. Closer routine surveillance may be required in patients with established valvular disease. SLE and RHD may present similarly on imaging; thus, patients should be diagnosed in the context of their clinical history. When faced with the limitations of continuity and P1/2t in MS with concomitant severe MR, planimetry offers valuable data when conducted by an experienced operator.

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REFERENCES

1. Alghareeb R, Hussain A, Maheshwari MV, Khalid N, Patel PD. Cardiovascular complications in systemic lupus erythematosus. *Cureus*. 2022;14(7):e26671.

2. Doria A, Iaccarino L, Sarzi-Puttini P, Atzeni F, Turriel M, Petri M. Cardiac involvement in systemic lupus erythematosus. *Lupus*. 2005;14(9):683-686.

3. Nor MA, Ogedegbe OJ, Barbarawi A, et al. Systemic lupus erythematosus and cardiovascular diseases: a systematic review. *Cureus*. 2023;15(5):e39284.

4. Leone P, Prete M, Malerba E, et al. Lupus vasculitis: an overview. *Biomedicines*. 2021;9(11):1626.

5. Yelnik CM, Xie X, Guerra MM, et al. Prevalence of clinically meaningful antiphospholipid antibodies in patients with systemic lupus erythematosus varies by race and ethnicity. *Ann Rheum Dis*. 2024;83(3):404-406.

6. Moyssakis I, Tektonidou MG, Vasilliou VA, Samarkos M, Votteas V, Moutsopoulos HM. Libman-Sacks endocarditis in systemic lupus erythematosus: prevalence, associations, and evolution. *Am J Med*. 2007;120(7):636-642.

7. Foroughi M, Hekmat M, Ghorbani M, Ghaderi H, Majidi M, Beheshti M. Mitral valve surgery in patients with systemic lupus erythematosus. *ScientificWorldJournal*. 2014;2014:216291.

8. Fernández-Dueñas J, López-Granados A, Mesa-Rubio D, Ariza-Cañete J, Gallo-Marín M, Concha-Ruiz M. Regurgitación mitral severa en endocarditis de Libman-Sacks. Cirugía reparadora [Severe mitral regurgitation in Libman-Sacks endocarditis. Conservative surgery]. *Rev Esp Cardiol*. 2005;58(9):1118-1120.

9. Ningyan W, Jappar IA, See Hooi E, Khung Keong Y. Severe mitral regurgitation from Libman–Sacks endocarditis treated with MitraClip: a case report. *Eur Heart J Case Rep*. 2021;5(10):ytab361.

10. Douglas PS, Garcia MJ, Haines DE, et al. ACCF/ASE/AHA/ASNC/HFSA/HRS/SCAI/SCCM/SCCT/SCMR 2011 Appropriate Use Criteria for Echocardiography: A Report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Society of Echocardiography, American Heart Association, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Critical Care Medicine, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance Endorsed by the American College of Chest Physicians. *J Am Coll Cardiol*. 2011;57(9):1126-1166.

11. Dass C, Kanmanthareddy A. Rheumatic heart disease. In: *StatPearls*. 2024. Treasure Island (FL): StatPearls Publishing.

12. Zmaili M, Alzubi J, Lo Presti Vega S, Ababneh E, Xu B. Non-bacterial thrombotic endocarditis: a state-of-the-art contemporary review. *Prog Cardiovasc Dis*. 2022;74:99-110.

13. Matshela MR. Prognostic value of the most important parameters during echocardiographic evaluation of mitral valve disease. *E-Journal of Cardiology Practice*. 2018;16(23).

14. Cottrell J, Al Sanani A, Ogu I, Chaffin D. Triple positive antiphospholipid antibody syndrome in pregnancy with high frequency plasma exchange: a case report. *Transfus Med Hemother*. 2023;50(2):154-158.

KEY WORDS antiphospholipid antibody syndrome, mitral regurgitation, mitral stenosis, systemic lupus erythematosus

APPENDIX For supplemental videos, please see the online version of this paper.