Cardiac Involvement in Systemic and Local Vasculitides: The Value of Noninvasive Multimodality Imaging

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Abstract: Despite significant advances in managing systemic vasculitides, cardiovascular morbidity, and mortality are still of primary concern. Advances in noninvasive imaging have broadened our understanding of the clinical heterogeneity of cardiac involvement in vasculitides. Common cardiovascular complications in primary or secondary vasculitides are; coronary artery aneurysms, acute coronary syndromes, myocarditis, pericarditis, endocarditis, and valvular dysfunction. Echocardiography, cardiac magnetic resonance , positron emission tomography, and computed tomography angiography are essential in identifying cardiac involvement and guiding treatment. Here, we present our experiences of cardiac involvement in systemic vasculitides,

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covering most aspects of common cardiac complications based on a multi-modality approach to challenging (real-world) cases. As many cardiac manifestations are clinically silent, heart function should be systemically assessed by a multimodality imaging-based approach, including ECG, serial echocardiograms with strain imaging and 3D, and cardiac magnetic resonance to detect early signs of cardiac manifestations. This enables timely intervention and optimal medical treatment, which is essential for a better prognosis. There is a need for better and closer collaboration in clinical practice and research fields between cardiologists and rheumatologists. (Curr Probl Cardiol 2023;48:101718.)

Introduction

Cardiovascular involvement is common in a wide range of autoimmune and inflammatory rheumatic diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), antiphospholipid syndrome (APS), systemic sclerosis (SSc), Behçet disease, idiopathic inflammatory myopathies (polymyositis and dermatomyositis), and systemic vasculitides.[1-6] Several of these disorders may directly affect the heart as part of their phenotype (eg, SLE, RA, and SSc). An indirect mechanism may also be involved, such as accelerated atherosclerosis and myocardial remodeling secondary to systemic and/or local inflammation, genetic predisposition, pharmacological therapy, and pulmonary involvement with the development of pulmonary hypertension may all contribute to the increased risk of cardiovascular disease (CVD).[7] Amyloidosis, most often secondary to persistent inflammation as seen in some of these rheumatic disorders, may also affect the myocardium, but has become much less common in recent years with better and more targeted immunosuppressive treatment modalities.

Besides myocardial inflammation that subsequently is replaced by fibrosis and the development of cardiomyopathy and heart failure (HF), the vasculitides may also cause myocardial ischemia, mainly if the epicardial or transmural coronary arteries or the aorta are involved. Pericarditis is another frequent complication that often leads to distressing symptoms with a higher recurrence rate. The 2015 European Society of Cardiology (ESC) guidelines on the diagnosis and management of pericardial disease highlight the fact that pericardial involvement is common in SLE, primary Sjögren's syndrome, RA and SSc, but may also be present in systemic vasculitides (eosinophilic granulomatosis with

polyangiitis [EGPA]), and Takayasu disease, Behçet disease, sarcoidosis, and inflammatory bowel diseases as well as familial Mediterranean fever and related genetic and of nongenetic auto-inflammatory diseases.[8]

There is a higher incidence of subclinical and clinical myocardial dysfunction and coronary artery disease in patients with SLE,[9] which is associated with poor prognosis.[10-13] Myocarditis is a rare cardiac manifestation in SLE and is often asymptomatic. In the early stages, it is difficult to detect by echocardiography or nuclear imaging modalities but can be reliably assessed by cardiac magnetic resonance (CMR).[14] Aortic and mitral valve thickening and progressive stenosis may also occur (Fig 1), regardless of the presence or absence of traditional risk factors for atherosclerotic CVD.

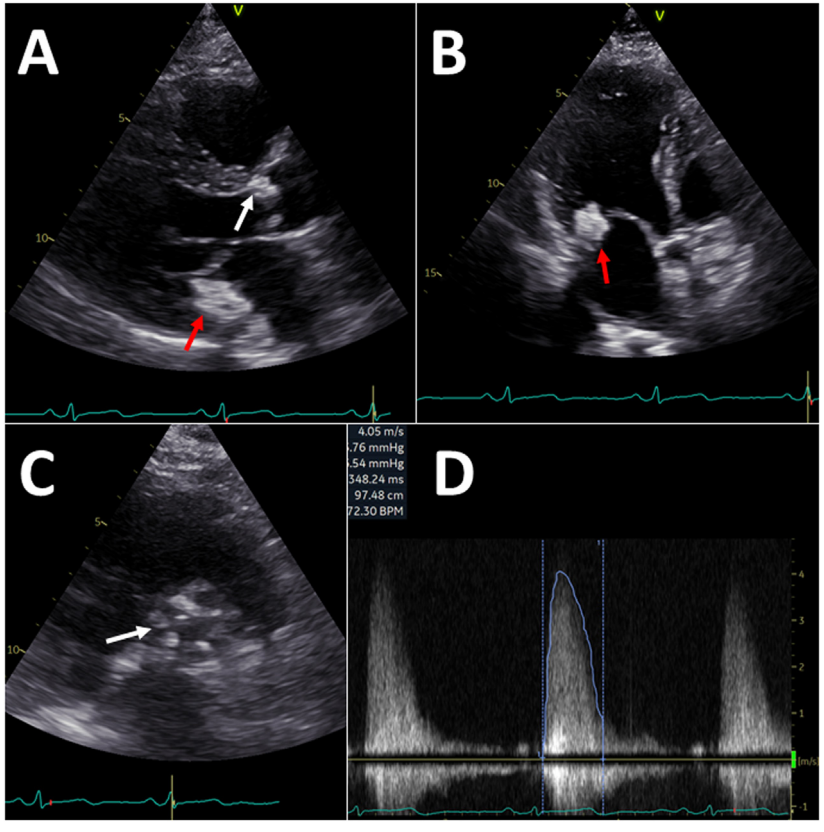

FIG 1. Echocardiographic images of a 65-year-old woman with autoimmune thyroiditis, Sjögren's syndrome and systemic lupus erythematosus (SLE) who have been under surveillance for aortic stenosis for 8 years. (A) parasternal long-axis and (B) apical 3-chamber views showing hugely calcified posterior mitral valve leaflet (arrows). (C) is parasternal short-axis view demonstrating a calcified/degenerative tricuspid aortic valve with a peak aortic jet velocity of 4 m/s measured with a stand-alone probe (D). (Color version of figure is available online.)

The association between RA and CVD is also well-known. Compared to the general population, patients with inflammatory joint diseases are at higher risk of developing CVD,[15] probably due to a combination of the increased burden of underlying traditional cardiovascular risk factors and the direct impact of inflammation which is a known risk factor and mediator of atherosclerosis and related diseases.[16,17]

SSc is a multi-organ, progressive disorder hallmarked by immune system dysregulation, vasculopathy, and organ fibrosis.[18-21] The heart is frequently affected in SSc and is, together with lung involvement, reported to account for most disease-related deaths. Common cardiovascular manifestations include subclinical and clinical right and left ventricular (LV) dysfunction, clinical HF, conduction system abnormalities and arrhythmias, coronary and pericardial disease, pulmonary arterial hypertension, most often secondary to pulmonary involvement, and atherosclerosis.[23-25] In SSc cardiovascular involvement is associated with poor prognosis.[21,22] It is commonly assumed that cardiac fibrosis is related to repeated focal ischemia leading to irreversible damage and/or myocarditis in these patients. Diastolic dysfunction is not uncommon either and has prognostic implications. In a large, unselected cohort of SSc from Norway, Tennøe et al.[26] showed that diastolic dysfunction was frequent in patients with SSc and associated with increased mortality.

Thus as outlined above, whereas several forms of autoimmune and inflammatory disorders may affect the heart both primarily and secondary, the present review article will focus on various forms of vasculitides.

In the recent issues of the journal *Current Problems in Cardiology*, Lin et al.[5] and Firouzi et al.[6] reviewed current evidence in the diagnosis and management of coronary arteritis presenting as an acute coronary syndrome in large- medium and small vessel vasculitis, particularly Takayasu's arteritis (Firouzi et al.), which is a chronic vasculitis of unknown etiology. In their clinical reviews, however, the focus was on the coronary arteries. The role of noninvasive imaging of other common cardiac complications in systemic vasculitides, such as myocarditis, pericarditis, and sterile/ nonbacterial endocarditis and valvular dysfunction, was not discussed. Furthermore, most reviews on cardiac involvement in vasculitides are focused on the etiologies, epidemiological and clinical characteristics, and pathogenesis. Imaging plays an essential role in diagnosing cardiac involvement in vasculitides, particularly in the early preclinical stages, and this will be discussed more thoroughly in this review.

Regarding noninvasive imaging in vasculitides, there are some position papers and recommendations for using CMR in autoimmune rheumatic diseases.[1,27] However, there are no established international

guidelines on using echocardiography in systemic vasculitides. Here, we present our experiences of cardiac involvement in systemic vasculitides, covering most aspects of cardiac complications based upon a multimodality approach of real-world challenging cases in a multicentre collaboration. The main focus is directed toward echocardiography and CMR. Primary vasculitis of the central nervous system does not involve the heart and will not be discussed here. Similarly, the etiologies of vasculitides and available pharmacological therapies are not the focus of this review.

Methods

Between January and February 2023, the database PubMed was searched with the following keywords: "Systemic vasculitis," "ANCA-associated vasculitis," "Eosinophilic granulomatosis with polyangiitis," "Churg-Strauss syndrome," "Echocardiography," "Cardiac magnetic resonance," yielding a total of 60 relevant articles. The literature review was mainly restricted to the original articles and review articles in English – published in paper or in electronic format. Although case reports often provide interesting and clinically relevant information, here, we only quote case reports directly relevant to our work where original data on the topic is lacking. The focus was mainly directed to the literature published between 2000 and 2023, though some important reports from the 1980s were included.

Cardiac Involvement in Systemic Vasculitides

Systemic vasculitides are complex clinical syndromes characterized by inflammation and fibrinoid necrosis associated with vascular remodeling and endothelial cell activation of the blood vessels that can affect any organ with heterogeneous clinical manifestations.[9] This process often leads to a narrowing and occlusion of the vessels but, in some cases, also dilation and aneurysm development**.** The incidence and prevalence of systemic vasculitides have risen over the past decade. Increased awareness and use of vascular imaging in clinical practice may partly explain this. Vasculitides can involve large arteries (aorta and its major branches) like in giant cell arteritis and Takayasu arteritis, medium-sized vessels, as in polyarteritis nodosa and Kawasaki disease. The anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitides (AAV) are associated with vasculitis in small-to-medium sized vessels. AAV include granulomatosis with polyangiitis (GPA) (previously known as Wegener's

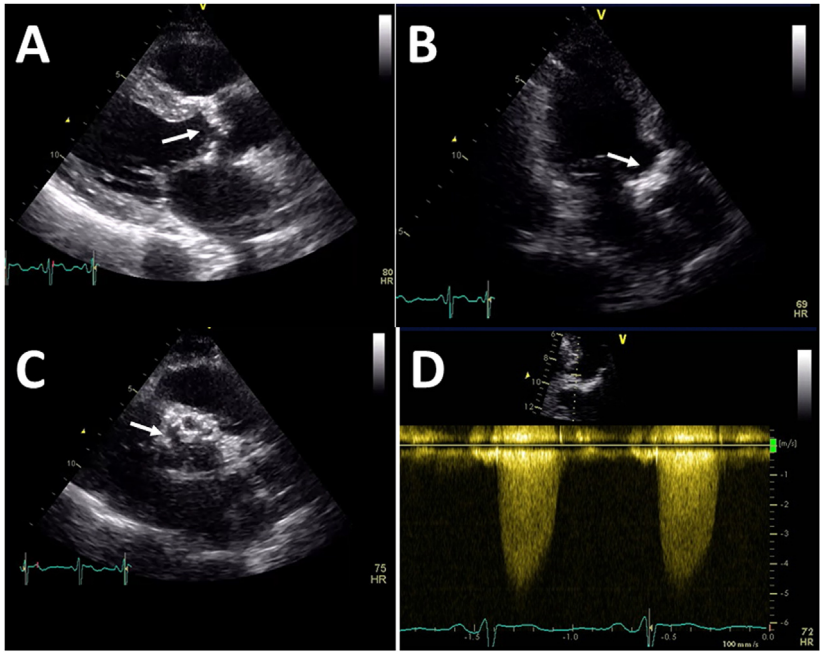

FIG 2. Echocardiographic images of a 76-year-old male patient with granulomatosis with polyangiitis (GPA), and kidney and lung involvement. His first presentation to Cardiology Department was symptoms related to aortic stenosis, which was not previously known. (A) parasternal long-axis, (B) apical 3-chamber and (C) parasternal short-axis views showing calcified aortic valve (arrow). (D) is CW-Doppler showing a peak aortic jet velocity of 4.5 m/s, consistent with severe aortic stenosis. (Color version of figure is available online.)

granulomatosis) (Fig 2), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA) - formerly known as Churg-Strauss syndrome (Figs 3–6, Table).[28-31]

Cardiac involvement is often an overlooked feature of systemic vasculitides. Diagnosing cardiac involvement is challenging, especially at the early subclinical stages of systemic vasculitides. The symptoms of myocardial involvement are often nonspecific, such as chronic fatigue, or may even be absent despite being clinically significant and sometimes life-threatening. Table

The prevalence of cardiac involvement in vasculitides varies across the studies, depending on the imaging modality used, duration of follow-up and the severity of the underlying vasculitis. Nilsen et al.[32] from Norway showed that the incidence and prevalence rates of ANCA-associated vasculitides were increasing, emphasizing the importance of a thorough screening for cardiac complications in these patients. Among the various

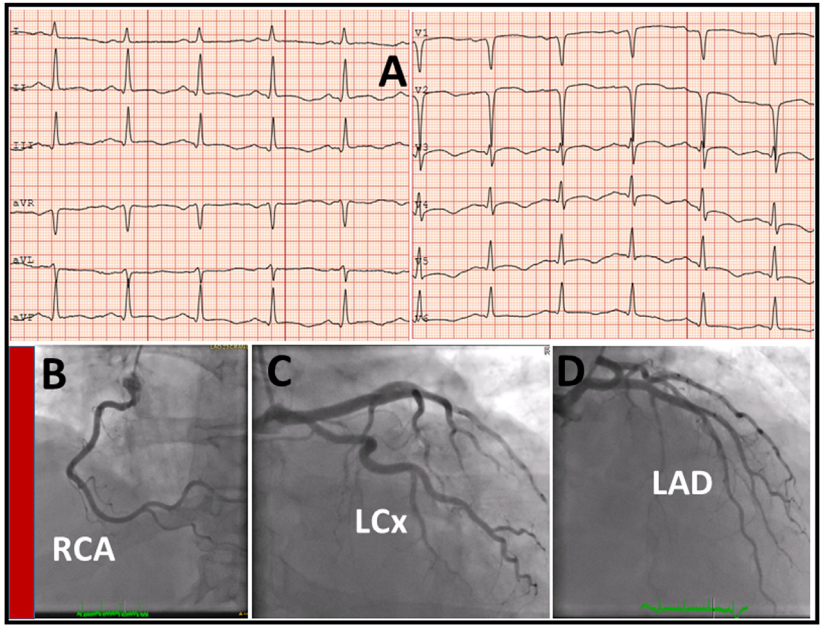

FIG 3. Electrocardiogram (A) and coronary angiography (B-D) images of a 63-year-old woman who presented with acute chest pain and elevated troponin T (1460 ng/L; ref. <15 ng/L). ECG shows sinus tachycardia (115 bpm), loss of R wave in V1-V2, prolonged QTc duration (533 ms), and widespread T-wave inversion. Coronary angiography demonstrates normal coronary arteries. After a meticulous investigation, she was diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA). LAD, left anterior descending; LCx, left circumflex; RCA, right coronary artery. (Color version of figure is available online.)

forms of vasculitides, EGPA is more frequently associated with cardiac complications (Figs 3–6). The incidence of EPGA is estimated to be 13/10,00,000 with an average age at diagnosis of 40 years. Although the clinical diagnosis of EGPA requires a triad of asthma, eosinophilia, and vasculitis, in broader terms, the disease can be characterized by asthma, nasal polyposis, rhinosinusitis, hypereosinophilia with organ infiltration, typically in the lungs, heart, and gastrointestinal tract, or in advanced stages also the peripheral nervous system, kidneys, and the skin.[31,33-34] Cardiac involvement can be found in 25-45% of patients with EGPA[4,35] and remain the leading cause of death.[36] Cardiac involvement is commonly seen in ANCA-negative individuals.[37] In EGPA, cardiac manifestations include ECG abnormalities, myocarditis, HF with reduced LV ejection fraction (EF), pericarditis (Figs 3–6), pericardial effusion, ventricular arrhythmias, pulmonary hypertension, intraventricular thrombi, elevated troponins, and valvular stenosis or regurgitation.[4,34,38] Among

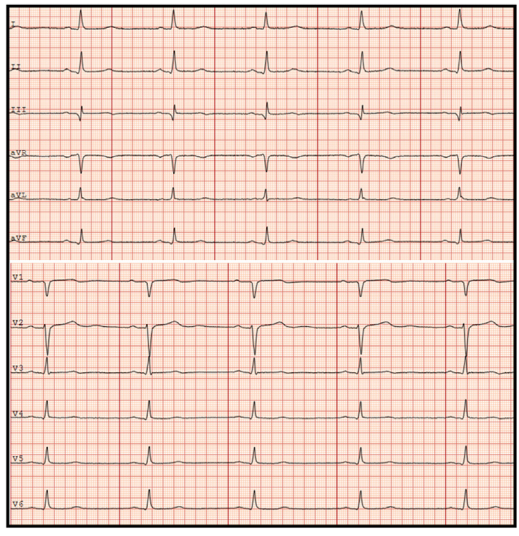

FIG 4. A repeated electrocardiogram after 4-week steroid treatment in the same patient as in *Figure 3* demonstrates sinus rhythm, HR of 64 bpm, poor R-wave progression in precordial leads, but normalization of QTc (398 ms), and T-waves. (Color version of figure is available online.)

these, endomyocarditis represent the more severe cardiac manifestation with a dismal outcome.[38]

Most severe forms of endomyocarditis in EGPA are characterized by vast eosinophilic infiltration. When these cells degranulate, it can cause massive myocardial damage due to the release of reactive oxygen radicals, cytokines, and matrix-degrading enzymes. In severe cases, EGPA-related myocardial involvement may mimic myocardial infarction (MI). In the Northern Norwegian Vasculitis Registry which included 140 cases (88 classified as GPA, 37 as MPA, and 15 as EGPA), the prevalence of cardiac involvement was 9%.[32] By contrast, in a retrospective study of 383 EGPA patients included in the French Vasculitis Study Group cohort, cardiovascular manifestations were diagnosed in 27.4% based on clinical findings combined with echocardiogram and electrocardiogram results. However, only 16.4% had cardiomyopathy, and 15.1% had pericarditis.[39]

In a case-control study, nearly two-thirds of patients with EGPA had abnormalities on CMR, while most were asymptomatic.[40] Notably, the absence of symptoms or ECG abnormalities could not exclude cardiac involvement because abnormal findings on echocardiography or CMR could still be detected in a significant proportion (38%) of patients. Similarly, Garcia-Vives et al.[35] showed that 45% of asymptomatic patients

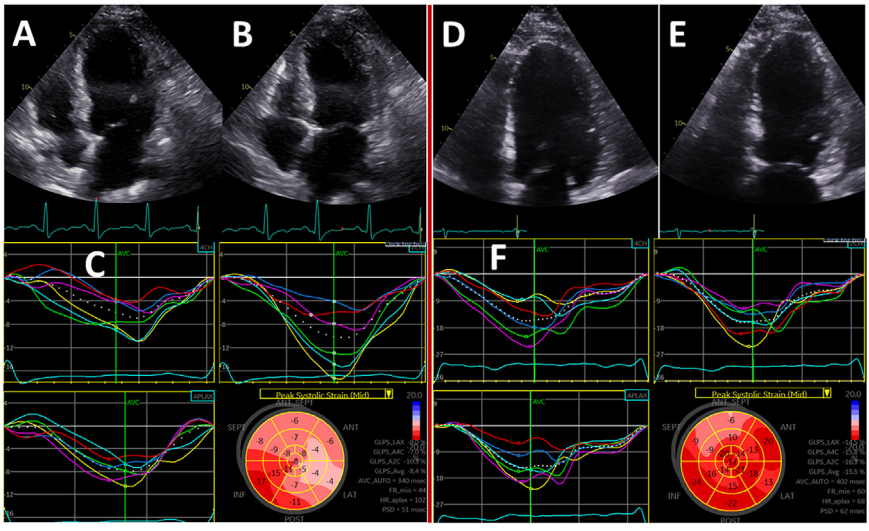

FIG 5. Echocardiography images of the same patient as in *Figure 3 and 4*. A (diastolic) and B (systolic) frames on apical 4-chamber views displaying global hypokinesia, especially the distal/apical septum and lateral wall, confirmed by impaired strain on Bulls eye plot (C). The ejection fraction was 32%, and the global longitudinal strain was -8.2% (C). 4-weeks later, there was still some residual hypokinesia in the apical septum (less systolic reduction in diameter) (D-E), but ejection fraction had improved to 50% and GLS to -16% (F). (Color version of figure is available online.)

with EGPA had an abnormal baseline cardiac evaluation. This allowed an earlier diagnosis of cardiac involvement, which is essential for a better outcome. Therefore, meticulous cardiac screening is recommended in all patients with EGPA, regardless of the presence or absence of cardiac symptoms.

The development of cardiovascular comorbidities such as hypertension and diabetes mellitus within 6 months from diagnosis was equally evident in large cohorts of large vessel disease, including giant cell arteritis and small-vessel (AAV) vasculitides.[41] The link between systemic vasculitis and CVD may be 2-fold: 1) Direct cardiac involvement either by the disease *per se* or due to therapy mainly use of glucocorticoids; or 2) Driven by inflammation and endothelial dysfunction.[42]

Concerning inflammation in the myocardium and small vessels, this may contribute to cardiac ischemia and myocardium remodeling involving several inflammatory cytokines with documented effects on the myocardium such as interleukin (IL)-6, IL-17, and tumor necrosis factor (TNF).[43] Furthermore, in other variable-vessel vasculitides, such as Behçet' s disease, a chronic inflammatory disorder of unknown etiology, vasculitis in the coronary arteries may also result in coronary thrombosis

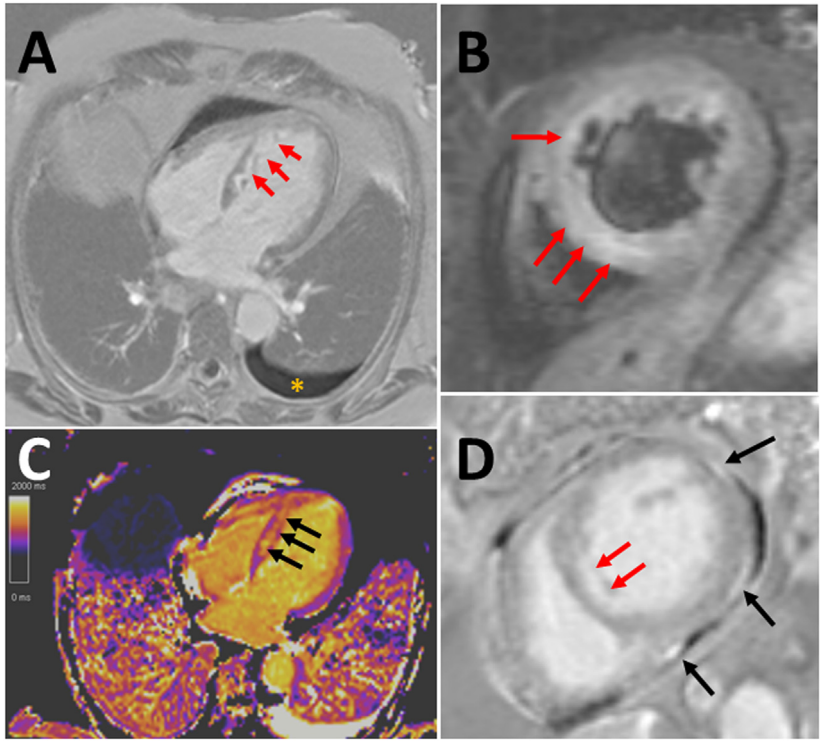

FIG 6. (A-D) CMR images of the same patient as in Figs 3–5. (A) 4-chamber view reveals subendocardial late gadolinium enhancement (LGE) in the septum (red arrows), suggesting myocarditis. (B) short-axis STIR (short T1 inversion recovery) sequence demonstrates edema in the septum. (C) 4-chamber view mapping showing the region of interest, interventricular septum with elevated T1 values of 1558 and basolateral 1060 (normal range: 1181-1371, 3 Tesla). (D) is another short-axis view of LGA sequence showing subendocardial LGE in mid-septum (red arrows) and pericardial involvement (black arrows). (Color version of figure is available online.)

and aneurysm.[44-46] Focal fibrinoid deposition and fibroblast proliferation in the small coronary arteries may be responsible for microvascular dysfunction, myocardial ischemia, and subsequent endomyocardial fibrosis. In addition, myocarditis, coronary arteritis, and valvular dysfunction may also occur in patients with vasculitis, leading to clinical HF and increased mortality.

Sterile (nonbacterial) vegetations, also called Libman–Sacks endocarditis or marantic endocarditis, are associated with inflammatory or autoimmune disorders (eg, SLE/secondary antiphospholipid syndrome), cancer, and other hypercoagulable states.[47] Structurally, these are a consequence of the deposition of sterile fibrin and platelets (platelet-fibrin vegetations of 1-4 mm size), that in addition to their role in coagulation, also play an

TABLE. Cardiovascular manifestations in common autoimmune and inflammatory rheumatic diseases, including systemic vasculitides.

Connective tissue diseases and vasculitides			Cardiovascular manifestations
Systemic lupus erythematosus			Subclinical and clinical myocardial dysfunction, myocarditis, pericarditis, CAD, valvular thickening and vegetations (Libman–Sacks endocarditis).
Rheumatoid arthritis			Subclinical and clinical HF, fibrosis, impaired global longitudinal strain, pericarditis, pericardial effusion, myocarditis, CAD, atrial fibrillation.
Systemic sclerosis			Clinical and subclinical right and LV dysfunction, HF, diastolic dysfunction (HFpEF), myocarditis, fibrosis, microvascular dysfunction, conduction abnormalities, arrhythmias, CAD, pericardial disease, pulmonary arterial hypertension.
Systemic vasculitides	**Variable vessel vasculitis**	Behcet's disease	Intracardiac thrombus, nonbacterial thrombotic endocarditis, myocarditis and pericarditis, systolic and diastolic LV dysfunction, reduced global longitudinal strain, dilated cardiomyopathy, endomyocardial fibrosis, conduction abnormalities, microvascular dysfunction, coronary arteritis, stenosis and aneurysms, aortic aneurysms or pseudoaneurysms, venous occlusion of the superior and/or inferior vena cava and/or pulmonary embolism.
	Large arteries	*Giant cell arteritis* *Takayasu arteritis*	Aortic aneurysm, dissection, or insufficiency, coronary stenosis, hypertension, CAD Aortic aneurysm, aortic incompetence, coronary arteritis, acute coronary syndromes, HF, myocarditis, hypertension, pulmonary arteritis.
	Medium-sized arteries	*Polyarteritis Nodosa* *Kawasaki disease*	Acute coronary arteritis, coronary artery dissection, myocardial infarction, LV dysfunction, new-onset hypertension. Coronary artery aneurysms and acute coronary syndromes.

(*continued on next page*)

TABLE. (*continued*)

Connective tissue diseases and vasculitides		Cardiovascular manifestations
Small-to-medium size vessels	Anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitides (AAV): *GPA, MPA, and EGPA*	ECG abnormalities, myocarditis, HF with reduced LV EF, pericarditis, pericardial effusion, ventricular arrhythmias, pulmonary hypertension, intraventricular thrombi, coronary arteritis, coronary artery vasospasm, microvascular dysfunction, and valvular dysfunction. EGPA: Eosinophilic infiltrate

CAD, coronary artery disease (either secondary to inflammation or coronary vasculitis); EF, ejection fraction; EGPA, eosinophilic granulomatosis with polyangiitis; GPA, Granulomatosis with polyangiitis; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; LV, left ventricular; MPA, microscopic polyangiitis.

essential role in inflammation on the surface of normal heart valve leaflets, commonly left-sided heart valves (Figs 7–8). Over time, this can result in serious complications like systemic embolization and progressive valvular dysfunction, for which high-risk valve surgery is required. It is essential to differentiate true nonbacterial thrombotic endocarditis from culture-negative infective endocarditis due to previous antibiotic therapy. Negative blood cultures and the lack of other Duke criteria often raise the suspicion of nonbacterial endocarditis. Although echocardiography (transthoracic or transesophageal) is the first-hand imaging modality for diagnosing vegetation, it may be difficult to differentiate sterile from infective/bacterial vegetation. However, when the diagnosis is established, serial echocardiograms are essential to assess vegetation size, regression or progression of valvular dysfunction, and evaluate heart function.

Finally, *Loeffler's* endocarditis (eosinophilic endomyocarditis) is a sporadic disease characterized by eosinophilic infiltration in the heart in idiopathic hypereosinophilic syndrome (HES) or associated with EGPA (among others), predominantly affecting the endocardium and leading to fibrosis and massive intracardiac (most often LV) thrombus formation (Fig 9). The natural history of *Loeffler's* cardiomyopathy includes a 3-phase process, that is, acute myocardial inflammation/necrosis, fibrin deposition with or without thrombus formation, and endomyocardial fibrosis with subsequent restrictive cardiomyopathy.[48-50] The condition is often underdiagnosed, can be confused with other causes of HF, and has a poor prognosis.[51]

Echocardiography is often the first-hand imaging modality to assess LV dysfunction, LV apical thrombus or cavity obliteration, endomyocardial fibrosis, or chronic restrictive cardiomyopathy. CMR and cardiac CT are other useful imaging modalities, although endomyocardial biopsy can establish the final diagnosis.[52]

Overall, in autoimmune and inflammatory rheumatic diseases such as RA, SLE (Fig 1), antiphospholipid syndrome and subtypes of systemic vasculitides (Fig 2), valvular sclerosis and/or stenosis (mitral and aortic) has received little attention. However, some previous reports have confirmed an association.[53,54] There is a need for large prospective studies to understand better the pathophysiological link between autoimmune/inflammatory rheumatic disease and aortic stenosis independent of the traditional cardiovascular risk factors-related degenerative process of the aortic valve.

Finally, during the recent years much focus has been directed towards HF with preserved EF (HFpEF), and importantly, this condition is strongly associated with systemic inflammation, autoimmune and inflammatory comorbidities.[55-57] Many systemic inflammatory rheumatic diseases are accompanied by an increased risk of HF, which begins at the

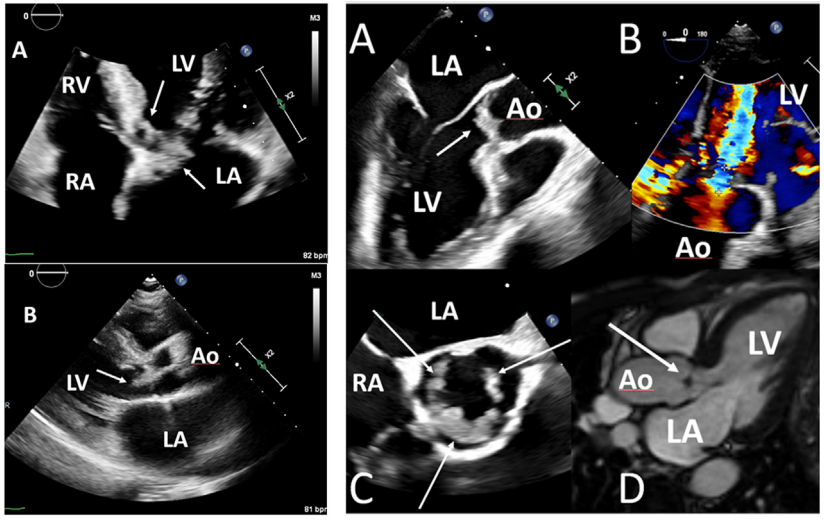

FIG 7. Transthoracic (TTE) (A-B left panel), transesophageal echocardiography (TEE) (A-C right panel) and cardiac magnetic resonance (CMR) (D) images of a 54-years old male patient with known palliative pancreas carcinoma presenting with chest pain and elevated troponin - showing large Libman-Sacks vegetations in the LV outflow tract with typical verrucous, nodular thickening (arrows in A and B in the left panel and A and C in right panel TEE images). (B) in the right panel is color imaging on transgastric view and demonstrating significant aortic regurgitation. (C) Short axis-view on TEE displaying the protruding vegetations circular at the tips of the aortic leaflets (arrows). (D) is a 3-chamber view from a CMR cine imaging with aforementioned vegetations (arrow).Ao, Aorta; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle. (Color version of figure is available online.)

onset of diagnosis and increases in proportion to the clinical severity and duration of the systemic inflammatory process. It seems that the myocardial involvement in systemic autoimmune and inflammatory disorders, including systemic vasculitides is not only the result of accelerated atherosclerosis and ischemic myocardial injury but could also be related to myocardial inflammation, coronary microvascular dysfunction, and fibrosis leading to HFpEF. Proinflammatory mediators characteristic of systemic inflammatory states (eg, classical inflammatory cytokines along with leptin, aldosterone and neprilysin) can cause development of HFpEF through a cascade of events ranging from systemic inflammation to myocardial fibrosis. However, the role of HFpEF in systemic vasculitides is far from clear, and there is a need for prospective studies that also include the assessment of diastolic dysfunction.

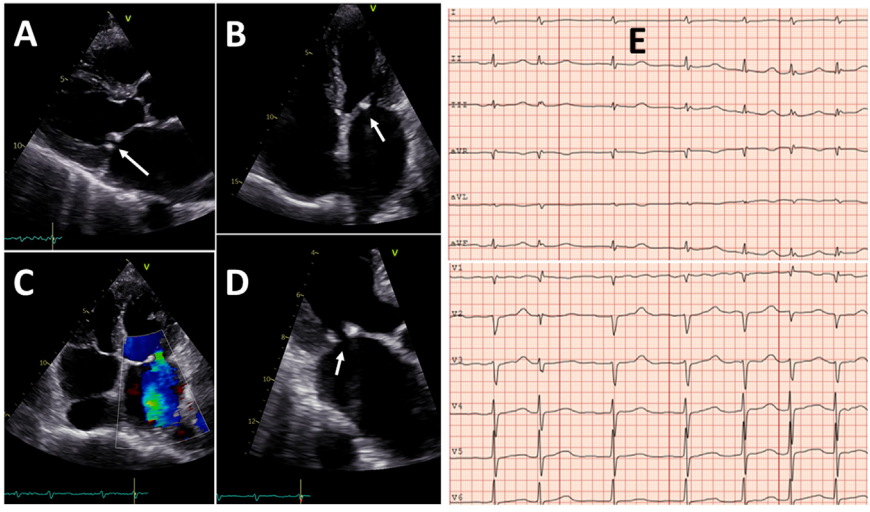

FIG 8. Echocardiography (A-D) images of a 70-year-female patient with systemic lupus erythematosus (SLE) and Raynaud's phenomenon displays thickened tips of mitral valve leaflet and Libman-Sacks vegetation on atrial side of anterior mitral valve leaflet (arrow) with associated moderate-to-severe mitral regurgitation (C). The ECG of the same patient (E) shows atrial fibrillation, low voltage QRS in the limb leads, and poor R-progression in V1-V3. (Color version of figure is available online.)

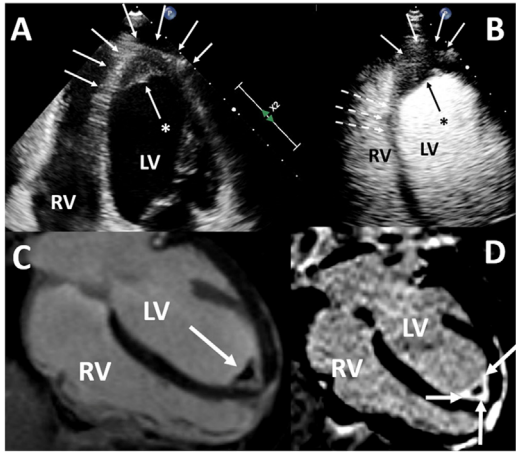

FIG 9. Loeffler Endocarditis: (A) Apical 4-chamber transthoracic echocardiography in a 33-year-old woman presenting with a stroke, demonstrating LV with apical thickening of the wall (arrow with asterisk). (B) Echo contrast showing septal myocardium with normal perfusion (dotted arrows) and apical myocardium without perfusion (multiple white arrows) and thrombus in the apex (black arrow with asterisk). (C) 4-chamber cardiac magnetic resonance (CMR) with early-gadolinium enhancement with LV thrombus (arrow) and (D) late-gadolinium enhancement (LGE) with hyperenhancement of the endomyocardial border depicting endomyocardial fibrosis (multiple arrows). T1- and T2 mapping showed normal values (not shown in the images). LV, left ventricle; RV, right ventricle. (Color version of figure is available online.)

Diagnosis

Diagnosing cardiac involvement in vasculitides can be challenging, particularly in complex multiorgan diseases, when cardiac symptoms are vague or absent. Evaluation of the patient with vasculitis should include a joint clinical and immunological assessment which constitutes careful history taking, laboratory assessment including cardiac-specific biomarkers (NT-proBNP, troponins), multimodality imaging including ECG, echocardiography, CMR, PET- CT, coronary CT and conventional coronary angiography, and in severe cases endomyocardial biopsy could be required. Patients with myocarditis may present with dyspnea or orthopnea, chest pain, palpitations, effort intolerance, or HF.[4] Myocarditis, at least in the early stage, may be difficult to detect by echocardiography or nuclear imaging modalities. In the absence of abnormal loading conditions (hypertension or aortic stenosis) or hypertrophic cardiomyopathy, a thickened myocardium on echocardiography and CMR in patients with EGPA is likely to represent myocarditis-induced myocardial edema and not necessarily LV hypertrophy, as shown in a patient with

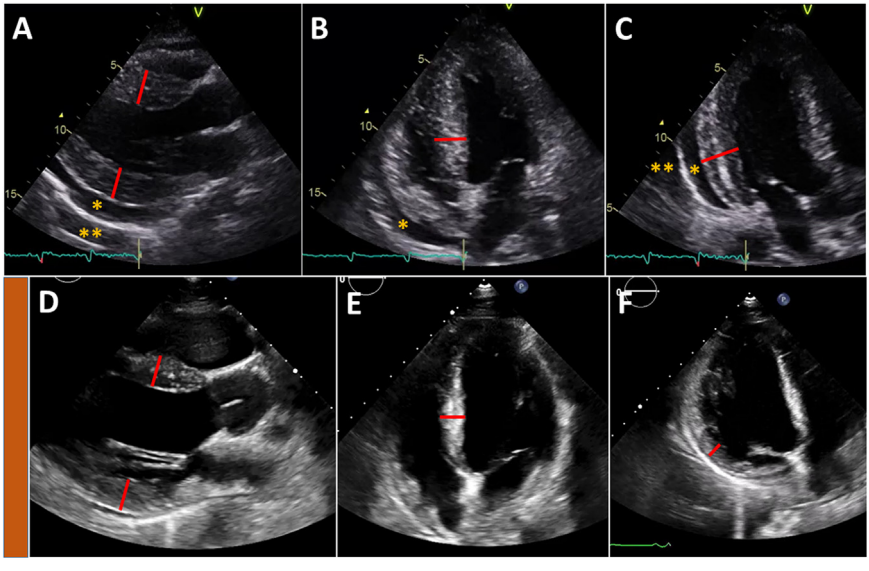

FIG 10. Echocardiographic images of a 31-year-old male patient with biopsy-verified eosinophilic myocarditis who was admitted with cardiogenic shock, severely reduced left ventricular ejection fraction, and generalized thickened left ventricular (LV) walls representing myocardial edema (red lines, A-C) and mild pericardial effusion (single asterisk) and pleural effusion (double asterisks). A repeated echocardiogram after 3 months showed a significant reduction in LV wall thickness (red lines, D-F). (Color version of figure is available online.)

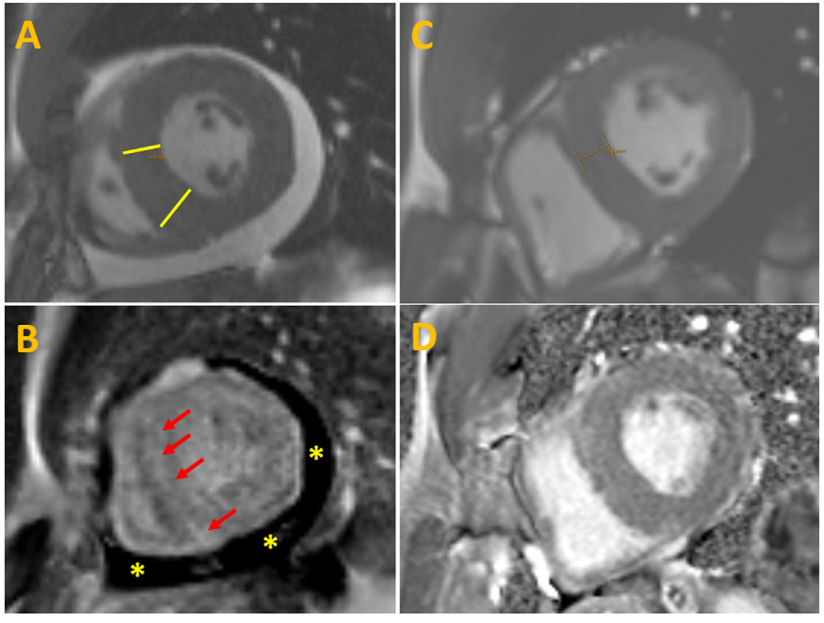

FIG 11. (A-D), cardiac magnetic resonance (CMR) images (short-axis views) of the same patient as in *Figure 10*, representing myocardial edema at baseline examination (A, mid-septum thickness of 1.7 cm, and 2 cm in posterior insertion point, yellow lines), late gadolinium enhancement (LGE) in the almost entire septum (B, red arrows) and pericardial effusion (asterisks). At the 3-month follow-up, there was marked regression in myocardial thickening/edema (mid-septum thickness of 1.1 cm) (C) and almost no signs of LGE or pericardial effusion (D). (Color version of figure is available online.)

eosinophilic myocarditis (Figs 10 and 11). This may reverse quickly after initiating high-dose corticosteroid treatment.[58] PET scan can reveal hypermetabolic mediastinal and hilar lymph nodes differentiating autoimmune diseases with cardiac involvement, such as cardiac sarcoidosis.[59] CMR (edema, inflammation, and fibrosis imaging) can detect cardiac involvement in early phases and thus avoid cardiovascular complications.[60] CMR with LGE images can visualize fibrosis, typically subendocardial fibrosis,[38,61] while increased T1 and T2 values can detect myocardial fibrosis and edema. However, more extensive CMR studies should be conducted to further investigate the prognostic value of fibrosis (LGE) on CMR in myocarditis-related autoimmune rheumatic diseases and systemic vasculitides. Endomyocardial biopsy may show inflammation, fibrosis, necrosis, and eosinophilic infiltrate.[38,61]

In Takayasu arteritis, the involvement of large vessels and coronary arterial abnormalities are relatively common. These result in aortic incompetence, myocarditis, or coronary heart disease. Therefore, cardiac

CT angiography is widely used as one of the main diagnostic imaging modalities.[62] Takayasu arteritis is more common in Asians than other racial groups and in younger women.[63,64] Kawasaki's disease is a medium-vessel vasculitis that affects the heart, with coronary artery aneurysms being the most common manifestation. Coronary angiography or CT of patients with Kawasaki often show dilatation/aneurysm of the coronary arteries. The patients with Kawasaki disease are commonly young children, and cardiac CT angiography is not the modality of choice, especially for serial evaluation, due to exposure to radiation and nephrotoxic contrast agents.

Statement of Ethics

The presented cardiac images were obtained as part of routine medical care in several cardiac centers in Europe. Ethical approval for the use of these samples for research purposes was not required in accordance with local guidelines. Written informed consent was obtained from all patients presented in this article.

Authors Contribution

SS: Conceptualization and design, drafting of the manuscript, editing and final approval; AMA, HYY, TF, THL, PA and RG: Writing, reviewing, editing, and final approval.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Not applicable.

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