

Cardiovascular Manifestations of Rheumatic Diseases

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Abstract: Autoimmune rheumatic diseases can affect the cardiac vasculature, valves, myocardium, pericardium, and conduction system. Although the high risk of cardiovascular pathology in patients with autoimmune inflammatory rheumatological diseases is not owing to atherosclerosis alone, this particular condition contributes substantially to cardiovascular morbidity and mortality.. Prompt recognition of cardiovascular abnormalities is needed for timely and appropriate management, and aggressive control of traditional risk factors remains imperative in patients with rheumatic diseases. Moreover, therapies directed towards inflammatory process are crucial to reduce cardiovascular disease morbidity and mortality.

Keywords: Rheumatic diseases, cardiovascular manifestations, rheumatoid arthritis, SLE, systemic sclerosis

1. Introduction

Systemic rheumatic diseases are autoimmune inflammatory conditions that involve several organs, frequently involving the blood vessels and the heart. Rheumatologic diseases can be considered as causes of myocardial, valvular, and pericardial and conduction system abnormalities. The prevalence and importance of cardiovascular disease in rheumatologic disorders have increased in the setting of therapeutic advances. One should consider chronic inflammation as a cause of cardiac diseases in people with and without chronic inflammatory joint disease. Treatments to suppress inflammation have potential benefit in reducing cardiovascular disease morbidity and improving musculoskeletal function. Cardiovascular morbidity and mortality rate is higher in association with many of the rheumatic conditions than normal conditions. In particular, coronary heart disease seems to be associated with inflammatory rheumatic conditions. It is likely that chronic systemic inflammation increases accelerated atherosclerosis in these patients. While classic and enthusiastic involvement of heart is devoted to acute rheumatic fever (ARF) (Owlia 2011), specific rheumatic diseases are commonly associated with heart involvement (Owlia 2006, Roman and Salmon 2007, Kitas et al. 2001; Guedes et al. 2001, Turesson et al. 2004, Voskuyl 2006).

2. Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a common chronic autoimmune disease. It is more common in women than in men (2 to 4 times) (Roman and Salmon 2007). Cardiovascular disorders are responsible for about half the death of patients with RA (Lebowitz 1963). It is an unknown cause of higher rates of

coronary disease in rheumatoid patients. The most mortality associated with RA is due to cardiovascular disease, especially because of ischemic heart disease (Turesson et al. 2004, Wällberg-Jonsson et al. 1997, Dolomon et al. 2003). One of the cardiac manifestations of RA is premature atherosclerosis, especially in the carotid. The prevalence of carotid atherosclerosis in RA is high (Gonzalez-Juanatey 2003, Roman and Salmon 2007). Cardiac involvements in RA include pericarditis, valvulitis, myocarditis, and an increased prevalence of atherosclerotic coronary heart disease. The pericardium is affected in approximately 40% of patients, with pericarditis being the most frequent cardiac manifestation in RA (Kitas et al. 2001, Owlia 2006). Pericarditis is more common in patients with rheumatoid nodules and a positive RF (Owlia 2006). Silent pericardial effusion is seen more frequently than acute symptomatic pericarditis in patients with RA (Sagrìstà-Sauleda et al. 1999). Constrictive pericarditis is not common but can occur (Nomeir et al. 1979). The risk of congestive heart failure is high in RA patients. Heart failure may be one of the main causes of increased cardiovascular mortality in RA, particularly in men (Wolfe and Michaud 2004, Crowson et al. 2005, Nicola et al. 2005). Diastolic LV dysfunction on Echo-Doppler was found more in RA patients than in the general population (Bhatia et al. 2006). Secondary amyloidosis in the past was found in the rheumatoid hearts but is now rare in rheumatoid disease, and can cause cardiomyopathy and AV block (Owlia 2006), though conduction abnormalities have been reported (Guedes et al 2001, Seferovic et al. 2006). Echocardiographic and autopsy studies show evidence of valvular disease in almost 30% of patients with RA.¹⁹ As compared to normal population, mitral regurgitation may be more common in RA patients. Aortic root abnormalities, including aortitis, have been

Volume 7 Issue 2, February 2018

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reported in association with RA, but are still rare (Guedes et al 2001, Roldan et al 2007). Coronary vasculitis is a rare complication of RA, but patients with RA have an increased risk of CAD and premature death from atherosclerotic disease (Guedes et al 2001). Villecco et al. described right bundle branch block in 35% of 60 patients with RA (Seferovic et al. 2006, Villecco et al 1983). It was discovered that AV block is rare in RA, but usually complete. Ahern et al. described congenital complete heart block (CHB) in 0.1% of the patients with RA, especially in females, and concluded that it is more common in patients with subcutaneous nodules (Ahern et al. 1983). According to one study, RA is associated with an increased risk of cardiovascular and/or cerebrovascular disease morbidity due to MI, CHF, and probably CVA, and may be an independent risk factor for these events Wolfe et al. 2003).

3. Systemic Lupus Erythematosus (SLE)

Cardiac involvement is a common and significant cause of morbidity and mortality in SLE patients. Its prevalence is more than 50%.²³ The cardiovascular manifestations of SLE are valvular heart diseases associated with Libman-Sacks lesions, serositis associated with pericardial disease, and venous and arterial thrombosis associated with antiphospholipid antibodies (Owlia 2006). In SLE, arterial stiffness is increased even without atherosclerosis; it is related to the duration of the disease, C-reactive protein levels, and interleukin-6 (Roman et al. 2005). Abnormalities of structure and function of LV have been seen in SLE patients (Cervera et al. 1992, Omdal et al. 2001). Myocarditis is a rare manifestation of SLE diagnosed clinically or detected at autopsy associated with the activity of the disease (Law et al 2005, Klareskog et al 2006). Even though valvular nodules have been observed in patients with SLE, the clinical manifestation of valvular heart disease is much less common in SLE (Owlia 2006). Echocardiographic studies showed different frequencies of vegetations or nodules detected on the mitral (7 to 15%) and aortic (3 to 19%) valves (Owlia 2006). Significant valvular heart disease included <20% of patients undergoing Doppler echocardiography (Perez-Villa et al. 2005). Large transthoracic echocardiographic studies show an association between high levels of anticardiolipin antibodies, valvular nodules, and regurgitation, especially those involving mitral valve (Khamashta et al. 1990, Nihoyannopoulos et al. 1990). Pericardial disease is the most common clinical cardiovascular manifestation of SLE. However, 20 to 50% of SLE patients in relatively large series had clinical manifestation of pericarditis with or without pericardial effusion (Crozier et al 1990, Nihoyannopoulos et al 1990, Cervera et al. 1992, Sturfelt et al. 1992). Pericardial effusion most commonly occurs in the severe level of the activity of the disease (flares), but may be asymptomatic (Cervera et al. 1992). Moderate to large pericardial effusions were reported in 7% of patients in one series (Cervera et al. 1992). Cardiac tamponade is rare without renal failure. The other rare cardiac manifestation of SLE is pericarditis constrictive (Owlia 2006). Myocarditis is uncommon in SLE that includes autopsy studies. Myocardial abnormalities are more common in echocardiography than clinical manifestations (Doria et al. 2005). Endocarditis is another cardiac manifestation of SLE that is more common in

echocardiography studies than clinical manifestations (Owlia 2006). Arrhythmias can occur in patients with SLE. The most common arrhythmia is sinus tachycardia. It can be seen in active disease, and can be resolved with treatment of SLE (Owlia 2006). The infants from mothers with anti-Ro or anti-La without diagnosis of SLE have an increased incidence of congenital complete atrioventricular (AV) block (Finkelstein et al. 1997). Coronary arthritis is another rare cardiac manifestation whose diagnosis is difficult (Vaarala et al. 1995). Aortitis can occur rarely in SLE (Ohara et al. 2000). Pulmonary artery hypertension is common but is usually mild. It may be without clinical manifestation which is diagnosed initially by echocardiography (Johnson et al. 2004). In a study conducted on echocardiography, variable valve diseases such as mitral valve thickening or vegetation, mitral valve prolapsed, and aortic valve vegetation; mitral, aortic, and tricuspid regurgitation; mitral stenosis are reported. The conclusion of this study was that valvular heart involvement is common in patients with SLE (Gabielli et al 1995). In another investigation, mitral annulus calcification and aortic valve calcification are common in young patients with SLE (Molad et al. 2006). Mitral prolapse is more prevalent in SLE patients (Kahan et al., 2009).

4. Systemic Sclerosis

Cardiac manifestations in SSc are different from silent involvement to overt clinical signs associated with increasing mortality and morbidity (Kahan et al. 2009). One of the cardiac manifestations of systemic sclerosis is myocardial abnormalities, including segmental wall motion abnormalities, and impaired coronary flow reserve in the absence of epicardial coronary artery disease, and coronary vascular diseases (Kahan et al 1986, Vacca et al. 2006). True myocardial abnormality is more common in SSc patients with diffuse disease and peripheral skeletal myositis. Abnormalities of right and/or left ventricular are observed for both of them (Follansbee et al. 1984). Microvascular abnormalities are base events in patients with systemic sclerosis. Recent studies also show the involvement of large arteries in patients. The stiffness of the microvascular and large arteries has been reported (Cheng et al. 2003). A large investigation of 106 patients with systemic sclerosis showed decreased aortic distensibility in comparison to the control group (Moysakakis et al 2005). In patients with systemic sclerosis, diffuse conduction abnormalities and arrhythmias are seen as detected by electro-cardiography (Kostis et al 1988). The most common arrhythmia in SSc patients is premature ventricular contraction. The risk of CHF and cardiac sudden death is increased in SSc patients with coexistent skeletal myositis. Primary valvular disease is uncommon in patients with systemic sclerosis (Kahan et al 2009). Pulmonary artery hypertension is a serious clinical manifestation in SSc patients (Chang et al 2006). Pericardial disease is detected in autopsy studies in patients with systemic sclerosis (Byers et al 1997). Clinical manifestations of systemic sclerosis are very rare (Roman and Salmon 2007). In large echocardiography studies, small pericardial effusion was reported in 14% of 77 patients with SSc (moysakakis et al 2005).

5. Ankylosing Spondylitis

One of the cardiac manifestations of ankylosing spondylitis is aortic disease, which includes aortic regurgitation and/or aortitis that is recognized even before ankylosing spondylitis was diagnosed. Mitral regurgitation was also reported in AS patients. The other aortic disease is thickening of aortic wall. Mild aortic root dilatation has been reported in patients with ankylosing spondylitis (Roman and Salmon 2007, Lautermann and Braun 2002). Another cardiac manifestation of ankylosing spondylitis is conduction abnormalities from 2 to 20% among patients (Lautermann and Braun 2002, Yildirim et al. 2002, Brunner et al., 2006). The most common conduction abnormality in patients with ankylosing spondylitis is first-degree atrioventricular block. Higher grade atrioventricular block and right and left bundle-branch block have also been seen in ankylosing spondylitis patients (Lautermann and Braun 2002, Roman and Salmon 2007). Atrial fibrillation was reported in AS, especially in patients with HLA-27 (Brunner et al. 2006). Myocardial dysfunction including diastolic filling abnormalities is another cardiac manifestation of ankylosing spondylitis (Lautermann and Braun 2002, Yildirim et al 2002, Roman and Salmon 2007). Myocardium and pericardium can rarely be affected, though pericarditis is rare in AS (Owlia 2006). Peripheral vascular disease and congestive heart failure are more common in ankylosing spondylitis patients than in the general population; this causes higher death rate in these patients than in the general population (Han et al. 2006, Roman and Salmon 2007). Another cardiac manifestation in AS that is detected in electrocardiography is QT dispersion (QTd) which is greater in ankylosing spondylitis patients than in the healthy population (Lautermann and Braun 2002).

6. Antiphospholipid Syndrome

Antiphospholipid syndrome (APS) is an autoimmune systemic disease that is associated with thrombotic arteries and veins and recurrent fetal loss (Kaplan et al. 1992). APS is the cause of different cardiac abnormalities. The most common cardiac involvement in APS is valvular disease (Amigo 2007, Soltész et al. 2007) with prevalence of 82% detected by transesophageal echocardiography (Soltész et al. 2007), including verrucous endocarditis which leads to valvular thickening, insufficiency (Kaplan et al. 1992) and vegetation (Soltész et al. 2007). APS can also cause coronary artery bypass graft occlusion and premature myocardial infarction (Kaplan et al 1992). APS causes accelerated atherosclerosis which leads to cardiac disease. Cardiovascular mortality is increased in patients with APS. Other cardiac manifestations of APS include ventricular dysfunction, intracardiac thrombi, myxomas, endocardial disease, myocardial involvement, microvascular thrombosis, and pulmonary hypertension (Tenedios et al. 2006, Amigo 2007, Soltész et al. 2007). A major clinical cardiac manifestation of APS is arterial thrombosis (Urbanus et al. 2009). In one study conducted on valvular involvements, the prevalence of valvular disease in patients with APS was 19%; the most common valvular involvement was mitral (91%), and the most common lesion was mitral insufficiency (Munoz-Rodriguez et al. 2002).

7. Takayasu Arteritis (TA)

Takayasu arteritis (TA) is an idiopathic disease that involves the large vessels. It is more common in Japan. Its prevalence has been reported as 1 in every 3000 autopsies (Hashimoto et al. 1996). It is more common in young women than men (Roman and Salmon 2007). Cardiac manifestations result from aortic involvement. This involvement is aortic aneurysm which leads to aortic regurgitation and inadequately treated hypertension. Left ventricular systolic dysfunction is another cardiac manifestation of TA that is seen in about 18% of patients with TA (Pfizenmaier et al 2004). TA can lead to vessel wall thickening, fibrosis, and stenosis. In unusual cases, it can mimic infective endocarditis (Alcelik et al. 2011). In one case report, coronary arteritis was reported as an unusual cardiac manifestation of TA (Ouali et al. 2011). In other studies, aortic valve regurgitation and heart failure were reported as cardiac involvements in TA patients (Weyn et al. 2009, Lee et al 2011). Aortic valve regurgitation can occur alone as a sole cardiac involvement of TA patients (Ravelli et al 1999).

8. Giant Cell Arteritis (GCA)

Giant cell arteritis (GCA) is more common in the older population whose age is more than 50 years. The mean age of patients is 74 years. GCA involves the large vessels. Its cardiac involvement is aortitis that can affect the primary branches of aorta. The other cardiac manifestations in GCA patients are thoracic aortic aneurysms which are 17 times more common than patients without GCA and abdominal aortic aneurysms that are 2.5 times more than patients without GCA. Another manifestation of GCA is thoracic aortic dissection which leads to increased mortality in GCA patients (Nuenninghoff et al 2003). Coronary artery disease, aortic valve insufficiency, and left ventricular dysfunction are other cardiac involvements (Elberhardt and Dhadly 2007, Niclauss et al. 2008). Myocardial infarction is rare in patients with giant cell arteritis (Lie et al 1995). In one case report, cardiogenic shock was reported as one of the manifestations of GCA (Niclauss et al. 2008).

9. Polyarteritis Nodosa (PAN)

Polyarteritis nodosa (PAN) is a disease that affects medium-size arteries (Jennette et al 1994, Owlia 2006). It is rare, and its prevalence is less than 1/100000 in a year. The predominance of men and women is the same. It can occur in different ranges of age, but its incidence peak is between 40 and 60 years. PAN has cardiac manifestations, the most common of which is hypertension. Other cardiac manifestations include angina, myocardial infarct, congestive heart failure, and left ventricular hypertrophy, though coronary arteritis may also occur (Owlia 2006). In one case report, aortic dissection was reported as one of the cardiac manifestations of PAN (Iino et al. 1992). Pericarditis is rare in patients with PAN (Owlia 2006).

10. Churg-Strauss Syndrome (CSS)

Churg-Strauss syndrome (CSS) is a rare disease that involves small vessels. Its prevalence is 2.4/1000000

annually. It involves all ages and genders. There is no predominance between male and female, and its age peak is 35 to 50 years old. The frequency of cardiac involvements in CSS is different, that is, from 15 to 55%. Cardiac involvement is a major cause of death in patients with CSS. It is a cause of mortality in half of CSS patients. Most common cardiac manifestations of CSS patients are pericarditis, myocarditis, and less common, coronary arthritis. Congestive heart failure may occur in 15 to 30% of patients with CSS. Myocardial and epicardial granuloma can be seen. In one case report, acute myocarditis and cardiogenic shock were reported as cardiac manifestations of Churg-Strauss syndrome (Courand et al. 2012). In another case report, myopericardial involvement was reported as a cardiac manifestation of Churg-Strauss syndrome (Courand et al. 2012)⁷⁴. In one study, supraventricular and ventricular arrhythmias were reported as cardiac manifestations of CSS which occurs frequently (Szczeplik et al. 2011). Left ventricular systolic dysfunction was also reported as a cardiac manifestation in CSS (Strube 1991, Neumann et al. 2009). In one study, pericardial effusion (41%) and mild to severe valvular insufficiency (73%) were reported as cardiac manifestations of patients with CSS (Neumann et al. 2009). In one case report, acute coronary syndrome was reported as a cardiac manifestation of CSS (Wagner et al. 2007).

11. Behcet's Disease (BD)

Cardiac manifestations, albeit rare, are among the most life-threatening complications in BD. Pericarditis, coronary artery stenosis and/or aneurysm, myocarditis, cardiomyopathy, congestive heart failure, valvular pathology, endocarditis, intracardiac thrombosis, and aneurysm of aorta or its branches are major problems in this regard (Owlia et al. 2012). Estimated incidence of cardiac involvement reported 1%–5% in a case series. Mortality is rather high (around 20%). Cardiac involvement in BD could be asymptomatic (Owlia et al. 2012). Pericarditis is the most common cardiac manifestation in BD. Acute pericarditis, tamponade, constrictive pericarditis have been reported (Owlia et al. 2012). Coronary artery disease is rare in BD. It is more common in males younger than 40 years of age. CAD can lead to clinical manifestation of myocardial infarction, silent ischemia, and stable or unstable angina. Aneurysm, stenosis, and occlusion of arteritis are the most common etiologies for CAD in BD (Owlia et al. 2012). Coronary aneurysms are more frequent than the stenosis and can present as acute coronary syndrome and myocardial infarction, but sometimes are symptomatic (Owlia et al. 2012). In young adults with myocardial infarction, BD should be considered as a nonatherosclerotic cause of CAD. Coronary arteritis may lead to myocardial infarction, but in some of patients with MI, coronary artery is normal. It seems that severe BD cases are to be more prone to AMI. It was shown that occlusion is developed as a result of thrombosis formation in CAD, consequently producing AMI (Owlia et al. 2012). A few cases with intracardiac thrombus which often precedes other manifestations of BD have been reported (Owlia et al. 2012). These thrombi are found mainly in the right ventricle and are often associated with pulmonary artery aneurysm (Owlia et al. 2012). It looks that endomyocardial fibrosis plays a role in the intracardiac thrombus development in some patients (Owlia et al. 2012),

Due to high specificity of right heart thrombus in BD, in any patient with this finding, diagnosis of BD should be considered (Owlia et al. 2012). Intracardiac thrombus is the major differential diagnosis when a young patient presents with an intracardiac mass (Owlia et al. 2012). This makes enormous diagnosis of cardiac myxoma in some instances (Owlia et al. 2012). It is especially common in young adults BD patients in the Middle East (Owlia et al. 2012). It is difficult to specify the mechanism of intracardiac thrombi formation. Good prognosis has been reported contrary to several recurrences of thrombosis (Owlia et al. 2012). Intracardiac thrombus can lead to superior vena cava syndrome (Owlia et al. 2012) and pulmonary embolism (Owlia et al. 2012). Endocardial involvement may present with mitral and aortic valve prolapse, mitral or aortic insufficiency, aneurysm of sinus Valsalva, and endocarditis mimicking bacterial endocarditis (Owlia et al. 2012). The fibrosis secondary to endocardial involvement in BD may predispose to intracardiac thrombus formation. It was reported that valvular prolapse including mitral valve prolapse can be related to vasculitis and tissue derangement. Most of the aneurysm of the sinus Valsalva has been found in right coronary sinus which project into the right atrium or ventricle. Usually the problem is diagnosed after rupture of aneurysm. A few cases of sinus Valsalva aneurysm in BD have been reported. Usually they occurred in active phase of BD and are enlarging. Heart failure due to ruptured aneurysm requires urgent surgical repair. Conductive abnormalities were also reported in several papers in the past that they could directly be attributable or even nonrelated to BD per se (Owlia et al. 2012).

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