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Cardiac Conduction Defects in Systemic Lupus Erythematosus

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Abstract

Systemic autoimmune conditions may cause morbidity and mortality. Systemic lupus erythematosus (SLE) is a prominent example of such diseases. It can result in conduction abnormalities due to accelerated atherosclerosis, vasculitis, or autoantibodies-induced myocarditis. Cardiac conduction abnormalities may produce sinus tachycardia, sinus bradycardia, prolonged QT intervals, atrial fibrillation, or atrioventricular (AV) nodal blocks. Neonatal lupus is sometimes associated with anti-Ro/SSA and anti-La/SSB antibodies, but their role remains a matter of controversy in adults.

Categories: Cardiology, Allergy/Immunology, Rheumatology
Keywords: cardiac lupus, anti-ro/ssa, anti-la/ssb

Introduction And Background

Among all the cardiac manifestations of systemic lupus erythematosus (SLE), the main ones are coronary artery disease, myocardial dysfunction, pericardial effusion, and mitral regurge [1-4]. Cardiac involvement is observed in 50% of the cases [5]. These abnormalities are not very well understood and, most often, are asymptomatic. Anti-Ro/SSA antibodies have relevance to neonatal lupus [6], but their role is undefined in adults. In most cases, the patients are asymptomatic at presentation, and electrocardiographic abnormalities are linked to an autoimmune condition. Sinus tachycardia might be the only SLE manifestation involving the conduction system, and it usually resolves following treatment with steroids [7]. In this review, we discuss the most commonly occurring cardiac manifestations in patients with SLE and explain if there is any relationship with antibodies present in both adult and neonatal populations.

Review

Conduction abnormalities in neonates

Neonatal lupus is a consequence of trans-placental migration of maternal immunoglobulin G (IgG) autoantibodies to SSA and/or SSB autoantigens. Autoantibodies identified are of the IgG subtype [6]. This induces serious, even fatal, heart blocks ranging from subclinical first-degree heart blocks to complete heart blocks [7].

Finding conduction defects in neonates without anatomical abnormalities of the heart suggests asymptomatic mothers having anti-SSA/Ro and anti-SSA/La antibodies [8]. Heart blocks in newborns are not related to such diseases in mothers. Congenital cardiac blocks are diagnosable in-utero or in the early neonatal period, and 80-90% of these are due to neonatal lupus [9]. Morbidity and mortality are considerable, at 60% and 30%, respectively, requiring lifelong cardiac pacing in the majority of cases [10]. It is important to detect congenital blocks as early as possible by fetal kinetocardiogram and/or echocardiogram to document atrioventricular (AV) conduction blocks as early as 14-24 weeks [11]. Mortality rates depend on gestational age at birth, with worse prognosis if born before 34 weeks, increasing to 52% vs. 9% if born later. Infants with first- or second-degree blocks at birth can progress to a complete heart block [8]. For patients with lower degrees of heart block, fluorinated steroids, dexamethasone, or betamethasone are the main therapies [12], despite potential adverse reactions to perinatal steroids during neurodevelopment. Steroids are not recommended to treat complete heart block cases and may not be curative [13]. There is a high rate of spontaneous recovery from sinus rhythm in those with transient first-degree congenital heart block [14]. A pacemaker is installed in the majority of the cases, immediately after birth [15]. However, heart failure develops even after pacemaker insertion in 5-11% of the patients [16]. The mechanism for the progression of conduction defects in neonatal lupus is not clear. Endocardial fibroelastosis, ventricular dilatation, and/or ventricular asynchrony can occur and lead to syncope, sudden cardiac death, and heart failure [16,17]. Nevertheless, in most cases, the prognosis is excellent beyond a few months [15]. Table *1* lays out all cardiac conduction defects that are observed in neonatal lupus.

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Abnormalities
1st degree AV block
2nd degree AV block
Complete heart block
Atrial and ventricular ectopic beats
Atrial flutter
Ventricular and Junctional tachycardia
Long QT syndrome
Sinus node dysfunction

TABLE 1: Cardiac conduction abnormalities observed in neonatal lupus*

*[18]

AV: atrioventricular

Conduction abnormalities in adults

1) Autoantibodies

Adults with SLE also can exhibit a variety of conductions. Tachyarrhythmia, bradyarrhythmias, AV nodal blocks (all types), and QT prolongation have been reported and described in the literature [19]. Anti-Ro/SSA antibodies are detected in numerous connective tissue disorders [20]; however, unlike in neonatal lupus, autoantibodies may have a less clear pathological role in adults. Normal people may carry these antibodies in a subclinical form in up to 3% of the general population [21]. There might be no relationship between these antibodies and conduction defects in mothers whose babies were born with neonatal lupus-induced congenital heart blocks [22]. Among patients with SLE having a correlation of anti-Ro antibodies to conduction defects, QT prolongations and non-specific ST-segment elevations are the most common ones [23,24]. QT prolongation is an important focus of attention since it can result in fatal arrhythmias, irrespective of autoimmunity [25]. Studies revealed a mortality association with subtle electrocardiographic changes when SLE patients were followed for 10 [26], 20 [27], and 30 [28] years. Sudden death was the fourth most common cause of death among SLE patients [27]. There is an association between anti-RO/SSA antibodies and QT prolongation as reported in an SLE patient population [29]. Antibodies act on L-type and T-type calcium channels and potassium channels that lead to congenital heart block, and age-related repolarization anomalies in adults are likely [30]. Table *2* depicts studies for and against an association between anti-Ro/SSA antibodies and repolarization anomalies.

Other than QT prolongation, heart blocks are rarely observed in adults with SLE. Some case reports of such patients are listed in Table *2*, including a variable AV nodal block in a patient, where a type I block progressed to a type II block [31].

Study/case report	Conduction defect (including repolarization)	Cause (autoantibodies/other)
Cardoso et al. [32]	Prolonged QTc calculated by Bazzet's formula	Indeterminate
Paradiso et al. [33]	Late excitation potentials	Indeterminate
Guzman et al. [34]	Sinus tachycardia	Indeterminate
Yavuz et al. [35]	Prolonged Qtc	Associated with anti-Ro/SSA antibodies
Pineau et al. [29]	Prolonged Qtc	Associated with anti-Ro/SSA antibodies
Kong et al. [36]	Ventricular ectopy, atrial fibrillation	Associated with myocarditis and pericarditis
Costedoat-C et al. [37]	Prolonged QT	No significant difference in mean QTc duration in association with the presence of antibodies
Gordon et al. [22]	Prolonged QT	No significant difference in mean QTc duration in association with the presence of antibodies
Maier et al. [38] (case report)	Third-degree AV block	Presence of anti-Ro/SSA antibodies in serum
Lim et al. [39] (case report)	Third-degree AV block	Presence of anti-Ro/SSA antibodies in serum
Arce-S et al. [40] (case report)	Third-degree AV block	Presence of anti-Ro/SSA antibodies in serum
Mevorach et al. [41] (case report)	Third-degree AV block	Presence of anti-Ro/SSA antibodies in serum
Edwards et al. [42]	Third-degree AV block	Presence of anti-Ro/SSA antibodies in serum
Martinez-C et al. [43]	Third-degree AV block	Presence of anti-Ro/SSA antibodies in the serum of one of the two subjects
Bilazarian et al. [44] (case report)	Third-degree AV block	Presence of nuclear RNP antibodies (anti-U1-RNP)

TABLE 2: Studies and case reports of systemic lupus erythematosus-related conduction system anomalies

AV: atrioventricular; RNP: ribonucleoprotein

2) Other Causes

SLE can affect many cardiac structures. Myocarditis is an asymptomatic manifestation of lupus, occurring in 8-25% of patients with SLE [45]. Cardiac conduction changes include sinus tachycardia and/or non-specific ST-T wave abnormalities [46,47]. Nevertheless, mortality is higher: 19% vs. 8% in clinical myocarditis vs. subclinical forms. Myocarditis with hemodynamic compromise is a major cause of mortality [48]. A chronic resting sinus tachycardia is associated with augmented lupus activity as depicted by an elevated higher SLE disease activity index [49].

Coronary insufficiency can lead to acute coronary syndromes and sudden death due to arrhythmogenesis [50]. SLE also leads to premature atherosclerosis due to inducing inflammation. Controlling these risk factors might mitigate the atherosclerosis process.

Discussion

SLE causes profound morbidity and mortality. Cardiac conduction defects occur in adults as they do in neonates, but the adult conduction defects are more complex. Repolarization anomalies and subclinical echocardiographic changes are the main manifestations of the disease conduction system [23,24]. It is also clear that autoantibodies are not sensitive to depict conduction anomalies nor vice-versa. It should be noted that the studies described above are low in statistical power. Observing a larger population for a research study is difficult since SLE affects the cardiac conduction system less than other organs; nevertheless, it may affect the myocardium, pericardium, valves, and cause coronary arteries conduction defects. Most patients

are prescribed steroids or hydroxychloroquine to suppress the disease before a conduction abnormality presents. A causal relationship to serum markers may or may not be discovered. Cardiac conduction defects occur among patients with SLE and range from sinus tachycardias to prolonged QT-induced ventricular arrhythmias. Larger studies are still needed to reach a conclusive understanding.

Conclusions

SLE with cardiac manifestations can be seen in 50% of cases. In neonates, various cardiac conduction anomalies are manifested; early detection and installation of a cardiac pacemaker are required in most cases for better prognosis. The most common adult cardiac manifestation of SLE are QT prolongation, non-specific ST-segment elevations, and myocarditis. Our review of the literature has shown the presence of anti-Ro/SSA antibodies and conduction defects.

Additional Information

Disclosures

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