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Are ECG findings overlooked in Lyme disease, which is the cause of AV complete block?

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Abstract

Objective: Lyme disease-associated carditis and conduction disturbances are well known, but there is insufficient data in the literature on the effects of Lyme disease on global electrocardiography (ECG) morphology. This study aims to evaluate the effects of Lyme disease on ECG morphology.

Method: The study included 48 consecutive patients who were hospitalised in our centre with a diagnosis of AV complete block between 01 January 2020 and 01 August 2023. Patients were divided into two groups as Lyme positive (Group 1) and negative (Group 2). Afterwards, demographic and laboratory data of the patients were recorded. All ECG data including ventricular rate, atrial rate, QRS duration, P wave dispersion (Pd), QTc dispersion (QTcd), and fragmented QRS were analysed from routine electrocardiograms obtained using standard extremity and chest leads at 25 mm/s and 10 mm/mV. The data obtained were compared between the groups.

Results: The mean age was 72.5(51.7-82.2) in group 1 and 74(68-79.7) in group 2, respectively. There was no significant difference between them (P= 0.593). In the study population, the ratio of males and females was similar between the groups. In ECG evaluation of the study population, no significant difference was found between atrial rate, ventricular rate, QRS duration, QTc duration and frequency of fragmented QRS ($p<0.05$). QTcd and Pd were significantly higher in Lyme + (Group 1). (75(56-84.5) vs 52(45-64.5), p=0.002; 58(50-62) vs 42.5(39-45.5), $p<0.001$, respectively).

Conclusion: When the results of our study are evaluated; Lyme disease causes an increase in Pd and QTcd in addition to affecting the AV node as known in the literature. These findings suggest that cardiac involvement of Lyme disease affects the cardiac conduction system more than thought.

Key Words: Lyme disease, Electrocardiography, AV complete block

AV tam blok nedeni olan Lyme hastalığında EKG bulguları gözden kaçıyor mu?

Özet

Amaç: Lyme hastalığına bağlı kardit ve ileti bozuklukları iyi bilinmektedir ancak Lyme hastalığının global elektrokardiyografi (EKG) morfolojisi üzerine etkileri konusunda literatürde yeterli veri bulunmamaktadır. Bu çalışma Lyme hastalığının EKG morfolojisi üzerindeki etkilerini değerlendirmeyi amaçlamaktadır.

Yöntem: Çalışmaya 01 Ocak 2020 ile 01 Ağustos 2023 tarihleri arasında AV tam blok tanısıyla merkezimizde yatan 48 ardışık hasta dahil edildi. Hastalar Lyme pozitif (Grup 1) ve negatif (Grup 2) olmak üzere iki gruba ayrıldı. Daha sonra hastaların demografik ve laboratuvar verileri kaydedildi. Ventriküler hız, atriyal hız, QRS süresi, P dalga dispersiyonu (Pd), QTc dispersiyonu (QTcd) ve fragmente QRS dahil tüm EKG verileri, 25 mm/s ve 10 mm/s hızlarında standart ekstremite ve göğüs derivasyonları kullanılarak elde edilen rutin elektrokardiyogramlardan analiz edildi. Elde edilen veriler gruplar arasında karşılaştırıldı.

Bulgular: Grup 1'de yaş ortalaması sırasıyla 72,5(51,7-82,2), grup 2'de 74(68-79,7) idi. Aralarında anlamlı bir fark yoktu (P= 0.593). Çalışma popülasyonunda gruplar arasında erkek ve kadın oranı benzerdi. Çalışma grubunun EKG değerlendirmesinde atriyal hız, ventriküler hız, QRS süresi, QTc süresi ve fragmante QRS sıklığı arasında anlamlı fark saptanmadı ($p<0,05$). QTcd ve Pd Lyme+'da (Grup 1) anlamlı derecede yüksekti. (sırasıyla 75(56-84,5) vs 52(45-64,5), p=0,002; 58(50-62) vs 42,5(39-45,5), $p<0,001$).

Sonuç: Çalışmamızın sonuçları değerlendirildiğinde; Lyme hastalığı, literatürde bilindiği gibi AV düğümünü etkilemeye ek olarak, Pd ve QTcd'de artışa neden olmaktadır. Bu bulgular Lyme hastalığının kardiyak tutulumununda, kardiyak ileti sistemini sanıldığından daha fazla etkilediğini düşündürmektedir.

Anahtar kelimeler: Lyme hastalığı, Elektrokardiyografi, AV tam blok

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INTRODUCTION

Lyme disease is a multisystemic inflammatory disease caused by spirochetes of the genus Borrelia and occurs in temperate regions of the northern hemisphere (1). It is transmitted by ticks of the species Ixodes spp. and is the most common tick-borne zoonosis in the appropriate regions of North America, Asia and Europe (2). Generally, involves skin, joints, heart and central nervous system (1). It is the most common vector-borne infectious disease in the USA, with approximately 30,000 new cases recorded annually (3). Carditis develops in 4 to 10 % of untreated patients in the United States (4). Lyme carditis is most commonly associated with other manifestations of the disease (arthritis, erythema migrans or neurological disease), but can also occur independently (5). The spectrum of carditis is highly variable; some patients may be completely asymptomatic, while the main manifestations of Lyme carditis may be transient high-grade conduction disturbances (5).

Although Lyme disease-associated carditis and conduction disturbances are well known, there is insufficient data in the literature on the effects of Lyme disease on global electrocardiography (ECG) morphology. This study aims to evaluate the effects of Lyme disease on ECG morphology.

METHODS

The study included 48 consecutive patients who were hospitalized in our centre with a diagnosis of AV complete block between 01 January 2020 and 01 August 2023. All patients were subjected to the two-step test recommended by the American Centre for Disease Control for the serological diagnosis of Lyme disease. In the first step, antibody determination was performed by ELISA method, and in the second step, the diagnosis was confirmed by Western blot test in order to confirm the positive results. Patients were divided into two groups as Lyme positive (Group 1) and negative (Group 2). Afterwards, demographic and laboratory data of the patients were recorded. All ECG data including ventricular rate, atrial rate, QRS duration, P wave dispersion (Pd), QTc dispersion (QTcd), and fragmented QRS were analyzed from routine electrocardiograms obtained using standard extremity and chest leads at 25 mm/s and 10

mm/mV. The obtained data were compared between the groups.

P wave dispersion measurement

To determine P wave dispersion, the mean value of no less than three P wave lengths was computed for each lead. The commencement of the P wave was regarded as the initial discernible ascent from the isoelectric baseline in positive waveforms and the primary observable descent from the isoelectric baseline in negative waveforms. The return to the isoelectric line was acknowledged as the termination of the P wave. The maximum conduction time was determined by utilizing the Pmax value obtained from any derivation. The disparity between the maximum value (Pmax) and the minimum value (Pmin) was computed and designated as Pd. The measurements were conducted using manual means. The utilization of a magnifying glass and compass served to enhance the level of sensitivity. The Pd values obtained from Group 1 and Group 2 were subjected to a comparative analysis.

QT Dispersion Measurement

The QT interval in milliseconds was determined by measuring the distance between the commencement of the Q wave to the point where the T wave returns to the isoelectric line. In electrocardiograms (ECGs) exhibiting U waves, the nadir between the T and U waves has traditionally been regarded as the termination point of the T wave. The Bazett formula (QTc) was utilized to compute the corrected QT interval, taking into account the heart rate (QT/_R-R). The QTc interval of each derivation was determined by calculating the mean corrected QT interval of three consecutive beats. The measurement of QTc dispersion (QTcd) involved the computation of the discrepancy between the highest QTc interval (QTc maximum) and the shortest QT interval (QTc minimum). All measurements were conducted by hand. The utilization of a magnifying glass and compass served to enhance the level of sensitivity. The QTcd values obtained from Group1 and Group2 were subjected to a comparative analysis.

Statistical Analysis

The data were inputted into the SPSS (Statistical Package for Social Sciences) 22.0 statistical software program (IBM Corp., Armonk, NY, USA). The continuous variables were represented using either the mean ± standard deviation or the median with the interquartile range (median, 25th-75th percentiles), depending on the distribution of the data. The categorical variables were represented using frequency and percentage. The normality of the data was assessed using the Kolmogorov-Smirnov test and distribution graphs. The distinction between the groups was assessed using the Student's t-test (for data that followed a normal distribution) or the Mann-Whitney U test (for data that did not follow a normal distribution). The Chi-square

test was utilized to compare categorical data. The accepted level of statistical significance was determined to be $p<0.05$.

RESULTS

The study comprised a cohort of 48 individuals diagnosed with AV full block, divided into two groups: Group 1, consisting of 16 patients with Lyme disease, and Group 2, consisting of 32 patients without Lyme disease. The average age in group 1 was 72.5 years (with a range of 51.7 to 82.2 years), whereas in group 2 it was 74 years (with a range of 68 to 79.7 years). There was no statistically significant difference seen between the two groups, as shown by a p-value of 0.593. Within the research cohort, there was a comparable distribution of males and females across the various categories. There was no statistically significant disparity observed among the groups in relation to hypertension, diabetes, coronary artery disease, and smoking history ($p>0.05$). During the regular transthoracic echocardiogram, it was seen that the left ventricular ejection fractions were comparable between the two groups. The ejection fractions were measured to be 55 (with a range of 50-60) in one group and 55 (with a range of 50-55) in the other group. The statistical analysis indicated that there was no significant difference between the groups, with a p-value of 0.221. The demographic and baseline laboratory characteristics of the research population are shown in Table 1.

Table 1. Demographic information and basic blood parameters of the groups

Variables	Lyme + Group 1 (n=16)	Lyme – Group 2 (n=32)	P value
Age (years)	72.5(51.7-82.2)	74(68-79.7)	0.593
Gender (n%female)	6(37.5)	17(53.1)	0.262
HT n(%)	10(62.5)	27(84.4)	0.134
DM n(%)	4(25)	15(46.9)	0.194
Smoking n(%)	3(18.8)	8(25)	0.514
CAD n(%)	4(25)	11(34.4)	0.515
LV EF	55(50-60)	55(50-55)	0.221
Creatinine (mg/dl)	0.88±0.29	0.83±0.23	0.245
Haemoglobin (g/dl)	14.10±1,29	13,65±1,14	0.185
Haematocrit	42.30±4,18	42.39±4.25	0.321
White blood cell (10^3/mL)	8.3±2.5	8.5±2.9	0.456
Sodium (mEq/L)	138 ± 3.5	139 ± 2.4	0.395
Potassium (mEq/L)	4.3 ± 0.2	4.4 ± 0.3	0.186

Table 2. Comparison of ECG parameters of the groups

Variables	Lyme + Group 1 (n=16)	Lyme – Group 2 (n=32)	P value
Ventricle rate *bpm*	41(35-44,75)	44(40-45)	0.067
P wave rate *bpm*	70(60-84)	70(60-76,25)	0.78
QRS time *msec*	100(93,5-142)	110(90-139,5)	0.868
QTc interval *msec*	394(382-457,5)	389(378-442)	0.221
QTc dispersion	75(56-84,5)	52(45-64,5)	**0.002**
P dispersion	58(50-62)	42,5(39-45,5)	**<0.001**
Fragmented QRS n(%)	9(56.3)	10(31.3)	0.102

In the assessment of the study population's electrocardiogram (ECG), there was no statistically significant disparity seen in terms of atrial rate, ventricular rate, QRS duration, QTc length, and frequency of fragmented QRS. The study found that there was a statistically significant increase in QTc dispersion and P wave dispersion in individuals with Lyme disease (Group 1). The comparison between the two groups yielded the following results: 75 (56-84.5) vs 52 (45-64.5), with a p-value of 0.002; and 58 (50-62) versus 42.5 (39-45.5), with a p-value less than 0.001, respectively. The ECG parameters of the groups are presented in a comprehensive manner in Table 2.

DISCUSSION

The evaluation of the research cohort's electrocardiogram (ECG) revealed no statistically significant differences in atrial rate, ventricular rate, QRS duration, QTc interval, and frequency of fragmented QRS complexes. The research investigation revealed a statistically significant elevation in QTc dispersion and P wave dispersion among people diagnosed with Lyme disease (Group 1). The findings of the comparison between the two groups are as follows: Group A had a median value of 75 (range: 56-84.5), while Group B had a median value of 52 (range: 45-64.5), with a statistically significant p-value of 0.002. Similarly, Group A had a median value of 58 (range: 50-62), while Group B had a median value of 42.5 (range: 39-45.5), with a p-value less than 0.001, indicating a significant difference between the two groups. Table 2 provides a complete presentation of the ECG parameters for the respective groups.

Lyme disease is a zoonotic illness that is characterized by systemic manifestations and has the potential to induce acute atrioventricular (AV) blockages of varied severity. The incidence of cardiac involvement in the progression of Lyme disease is rather infrequent. In general, the prognosis of Lyme carditis is favorable (6). It is advisable to consider hospitalization for patients who exhibit a high level of clinical suspicion for Lyme disease, together with instances of syncope or the presence of second or third degree atrioventricular block (7). Around 35% of those diagnosed with Lyme carditis may experience the advancement of atrioventricular block, necessitating the temporary insertion of a cardiac pacemaker (8, 9). Nevertheless, it has been observed that individuals diagnosed with high-grade AV block often experience recovery over a span of around one week, whereas those with less severe conduction problems tend to recover within a timeframe of approximately six weeks (10, 11). Due to the notable incidence of remission, it is advised against expeditiously proceeding with the permanent installation of a cardiac pacemaker (8).

The most prevalent symptom of Lyme carditis, as determined by a research assessing patients with this condition, was identified to be temporary

atrioventricular block. The observed distribution of maximal atrioventricular block in all patients was found to be 49% for third degree, 16% for second degree, and 12% for first degree. The electrophysiological findings indicate that the engagement of the cardiac conduction system might exhibit either localized or extensive characteristics (8). Nevertheless, the findings of our study indicate that there is a resemblance in QRS shape between individuals who tested positive for Lyme disease and those who tested negative. This implies that the atrioventricular (AV) node may exhibit heightened sensitivity to Lyme illness. Although antibiotic therapy is administered, the occurrence of permanent pacemaker installation for Lyme carditis is infrequent (12, 13).

Lyme disease is often categorized into three distinct phases. The initial phase of infection in a specific area (stage 1) often manifests within a timeframe of 2 to 30 days following the bite of a tick. This stage is marked by symptoms like those of influenza, as well as the presence of erythema migrans. The second stage of early disseminated illness is generally distinguished by the presence of neurological problems and musculoskeletal abnormalities. Cardiac anomalies are typically observed during this period. The late stage of infection (stage 3) often manifests from months to years following the first erythema migrans and is distinguished by the presence of monoarthritis or oligoarthritis, primarily affecting the larger joints, alongside neurological symptoms.

Lyme disease has been seen to impact all layers of the heart in a pathological manner (14). The presence of vasculitis affecting intramyocardial vessels may also be seen. The occurrence of valvular dysfunction as a result of Lyme carditis is infrequent, as indicated by a study with a sample size of 15. Lyme carditis is characterized by the presence of myocardial involvement. Diffuse ST-T wave alterations are indicative of cardiac involvement. In the majority of instances, myocardial dysfunction tends to be of a mild kind and has a limited duration (16, 17). The observed elevation in QTcd in patients with Lyme disease in our study can be interpreted as indicative of cardiac involvement.

The occurrence of myocardial involvement resulting in echocardiographic left ventricular dysfunction or clinical congestive heart failure is estimated to be between 10 to 15% in individuals (8). The left ventricular ejection fraction (LVEF) of the patients included in our study had comparable values in both groups. This finding implies that myocardial involvement is less commonly detected in individuals with Lyme disease, especially in cases when the atrioventricular (AV) node is impacted.

There have been reports indicating that early use of antibiotics for Lyme disease can effectively avoid the occurrence of subsequent problems. Nevertheless, the efficacy of antibiotic therapy in

expediting the resolution of cardiac symptoms associated with Lyme disease lacks clinical substantiation (1). The observed rise in Pd and QTcd within our study indicates that cardiac involvement extends beyond the AV node, encompassing both atrial and ventricular regions. Hence, it would be advantageous to devise independent prospective research to assess the impact of antibiotic therapy on electrocardiogram (ECG) outcomes.

QTcd is recognized as a marker of regional heterogeneity in cardiac repolarization. Furthermore, an elevated QTcd is regarded as a non-invasive indicator that signifies the potential for ventricular arrhythmia (18). Hence, it is our contention that heightened QTcd in individuals diagnosed with Lyme disease warrants more vigilance in monitoring.

The Pd waveform is a straightforward electrocardiogram (ECG) observation that is employed to evaluate the durations of intra- and inter-atrial conduction, as well as the transmission of irregular sinus impulses in atria that are prone to atrial fibrillation (19, 20). There is evidence suggesting that extended Pd durations can be linked to the presence of stable angina pectoris (21) and acute coronary syndrome (22). Additionally, such durations have been found in individuals who have undergone coronary artery bypass surgery (23). Hence, exercising caution about atrial arrhythmia in individuals with Lyme disease might prove to be beneficial.

CONCLUSION

In summary, based on the findings of our investigation, it can be inferred that Lyme disease has the potential to induce high-grade AV blocks through its impact on the AV node. Furthermore, it appears to have detrimental effects on several phases of the conduction system in both the atria and ventricles.

Study Limitations

The most important limitation of our study is undoubtedly the small number of Lyme positive patients. However, the fact that cardiac involvement is not very common in Lyme disease seems to be the most important reason for this. Nevertheless, the number of cases related to Lyme endocarditis seems to be acceptable when compared with the studies in the literature. In addition, the fact that it was a retrospective and single-centre study can be said as an additional study limitation.

Ethics Committee Approval: Our study is a retrospective study and institutional permission was obtained to access the retrospective data of the patients after the permission of the clinical research ethics committee (03.02.2023-KAEK-3/36) was obtained. The principles of patient privacy and confidentiality were observed, and data were collected in accordance with the Declaration of Helsinki.

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