Electrocardiographic Findings in Psoriatic Arthritis: A Case-Controlled Study

JOY FELD, GIORA WEISS, ITZHAK ROSNER, MICHAEL ROZENBAUM, ARIE LAOR, DORON RIMAR, LIHI EDER, HAIM BITTERMAN, and DEVY ZISMAN

ABSTRACT. ***Objective.*** We assessed cardiac conduction properties in patients with psoriatic arthritis (PsA).

Methods. Electrocardiogram (ECG) scans of 92 patients with PsA were compared to 92 age and sex matched nonpsoriatic, nonarthritic patients from general practice serving as controls.

Results. PR interval was found to be significantly longer in the PsA group compared to controls, 159.6 ± 21 ms versus 151.3 ± 26 ms, respectively ($p = 0.021$). No statistical difference was found with respect to the QRS interval or other atrial or ventricular conduction disturbances studied. No correlation was found between the PR interval and disease duration or PsA subtype. The use of nonsteroidal antiinflammatory drugs did not affect the PR interval. Methotrexate was not found to influence the PR interval, compared to other disease modifying antirheumatic drugs. Two PsA patients (2.1%) had a PR interval > 0.2 ms. Their prolonged PR interval could not be explained by medication use. The abnormal prolongation of the PR interval was asymptomatic, requiring no additional intervention. No patient had complete heart block.

Conclusion. Our study may suggest subtle involvement of the atrioventricular node in patients with PsA. (First Release Oct 1 2008; J Rheumatol 2008;35:2379–82; doi:10.3899/jrheum.080314)

Key Indexing Terms:
PSORIASIS ARTHRITIS CARDIAC CONDUCTION ELECTROCARDIOGRAPH

Psoriatic arthritis (PsA) is included as one of the spondyloarthropathies (SpA), a heterogeneous group of diseases characterized by arthritis, typically with oligoarticular and spinal involvement, enthesopathy, shared extraarticular features such as inflammatory eye disease, gastrointestinal/gynecourological inflammation and aortic valve disease[1,2], with overlapping mucocutaneous features and prominent familial aggregation, all occurring in the absence of serum rheumatoid factor. This group of diseases includes ankylosing spondylitis (AS), reactive arthritis, arthritis associated with inflammatory bowel disease, juvenile SpA, and nonspecific SpA.

From the Department of Rheumatology, Bnai Zion Medical Center, Haifa, Israel; Center for Interventional Vascular Therapy, Columbia University Medical Center, New York, NY, USA; and Department of Internal Medicine, Carmel Medical Center, Haifa, Israel.

J. Feld, MD, Department of Rheumatology, Bnai Zion Medical Center, Lin Clinic, Clalit Health Services, Haifa; G. Weiss, MD, Center for Interventional Vascular Therapy, Columbia University Medical Center, and Cardiovascular Research Foundation, New York, NY; I. Rosner, MD, Department of Rheumatology, Bnai Zion Medical Center, Associate Professor, Rappaport Faculty of Medicine, Haifa; M. Rozenbaum, MD, Department of Rheumatology, Bnai Zion Medical Center, Senior Clinical Lecturer, Rappaport Faculty of Medicine; A. Laor, MD, Department of Internal Medicine, Carmel Medical Center, Clinical Lecturer, Rappaport Faculty of Medicine; D. Rimar, MD; L. Eder, MD, Department of Internal Medicine, Carmel Medical Center; H. Bitterman, MD, Department of Internal Medicine, Carmel Medical Center, Associate Professor, Rappaport Faculty of Medicine; D. Zisman, MD, Department of Internal Medicine, Carmel Medical Center, Rheumatology Department, Lin Clinic, Clalit Health Services.

Address reprint requests to Dr. D. Zisman, Department of Internal Medicine, Carmel Medical Center, 7 Michal Street, Haifa, Israel. E-mail: devyzi@clalit.org.il

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Patients with PsA have increased HLA-B locus antigens, including Bw38, B17, B27, and possibly Bw39, with the presence of HLA-B27 correlating best with axial arthritis involvement[3]. The cardiac manifestations of the prototypical B27-positive arthropathy, AS, are foremost those of aortic valve involvement — with aortitis, conduction system disorders, and cardiomyopathy. Conduction system abnormalities may occur in up to 33% of patients with AS[4], with complete heart block found in 1%–9% of them[5-10]. Good, *et al* also described atrioventricular (AV) blocks in 6% of 164 patients with reactive arthritis[11].

In surveying the literature, scant data were found regarding cardiac arrhythmias in PsA patients, and we investigated this subject using the electrocardiogram (ECG), a bedside tool.

MATERIALS AND METHODS

We conducted a case-control study comparing the ECG findings of PsA patients with matched nonpsoriatic, nonarthritic patients in the same location. The study protocol was approved by the local institutional ethics committees of Clalit Health Services and the Bnai Zion Medical Center in accord with the Declaration of Helsinki.

Study population. Between January 2002 and December 2003, two groups of patients were recruited: (1) study group – consecutive patients fulfilling the Moll and Wright criteria[12] for PsA followed at the rheumatology clinics of Clalit Health Services and Bnai Zion Medical Center, Haifa; (2) control group – Individuals with neither psoriasis nor clinical arthritis of any type followed at the Clalit Health Services' Sapir outpatient community clinic.

Each patient in the study group was matched by sex and age to an individual in the control group. Informed consent was obtained from all participants prior to enrollment.

Patients' medical information was abstracted from their medical records. Data were gathered regarding demographics, medications, and concomitant diseases. Ischemic heart disease (IHD) is defined as a history of cardiac infarction and/or a history of angina pectoris. Repeated measurements of a patient's blood pressure > 140/90 mm Hg diagnosed hypertension[13]. Characteristic abnormalities observed on an echocardiogram were used to categorize subjects with congestive heart failure or cardiac valvular disease. Diabetes mellitus was diagnosed after repeated measurements of elevated glucose levels, fasting plasma glucose levels > 126 mg/dl, or a level of glucose > 200 mg/dl 2 h after a glucose challenge test[14]. For patients with PsA, a detailed data form was completed regarding the subtype of PsA, duration of the arthritis, nail and ocular involvement, and current treatment regimen including disease modifying antirheumatic drugs (DMARD), nonsteroidal antiinflammatory drugs (NSAID) and corticosteroids. It is important to note that the study was performed before biologic drugs were introduced into routine treatment of PsA in Israel.

An ECG strip was recorded by a physician or a trained nurse for all patients included in the study. All ECG strips were analyzed by a cardiologist blinded to the patients' diagnoses including psoriasis. The following cardiac conduction properties were assessed on the ECG recordings: rhythm and conduction properties of the atriums, AV node, and ventricles[15].

Statistical analysis. Statistical analysis was done using Sigmastat software version 3.5. Possible differences between the control and study groups in the cardiac conduction properties as estimated by PR and QRS intervals from the patients' ECG recordings were evaluated using T tests and the Mann-Whitney rank-sum test when the normality test failed. These tests were also used to evaluate the effect of treatment with methotrexate and NSAID on the PR interval compared to other prescribed DMARD. We tabulated and compared the prevalence of the different conduction abnormalities — sinus rhythm, atrial fibrillation, left and right ventricle hypertrophy, left and right atrial enlargement, right and left bundle-branch block, left anterior and posterior hemiblock, and ventricular and atrial premature beats — in the 2 populations using Fisher's exact test. Correlation between the duration of PsA and the PR interval was assessed using polynomial regression. Correlation between PsA subtype and PR interval was calculated using the Kruskal-Wallis one-way analysis of variance on ranks test. Results were considered statistically significant if $p < 0.05$.

RESULTS

Patient characteristics. Ninety-two patients participated in each study group. Table 1 presents data for patients' sex, age, and concomitant diseases that might affect the cardiac conduction properties, including IHD, hypertension, diabetes mellitus, valvular heart disease, and cardiomyopathy. Arthritis and AV node-modifier medications of the study and control groups are recorded in Table 2.

In the PsA group, 98.9% had psoriatic skin involvement, 58.7% had psoriatic nail involvement, and only 5.4% had psoriasis-associated ocular manifestations.

Table 1. Baseline characteristics of patients and controls.

Characteristics	PsA, n = 92	Control, n = 92	p
Age, yrs	53.8 ± 15	55 ± 15	0.37
Male (%)	39 (42)	39 (42)	1
Arthritis duration, yrs	7.6		
Ischemic heart disease (%)	8 (9)	9 (10)	1
Congestive heart failure	0	0	1
Valvular heart disease (%)	2 (2)	0	0.5
Hypertension (%)	26 (28)	28 (30)	0.87
Diabetes mellitus (%)	6 (7)	6 (7)	1

The average duration of the articular disease was 7.6 years. Diverse PsA subtypes were represented: 40.2% of patients had asymmetrical oligoarthritis; an additional 38% had symmetrical rheumatoid arthritis (RA)-like arthritis; 18.5% had axial involvement; 2.1% had a mutilans form of arthritis; and 2.1% had involvement of the distal interphalangeal (DIP) joints alone (Table 3).

Comparing the prevalence of IHD, hypertension, congestive heart failure, valvular heart disease, and diabetes mellitus, no significant statistical differences were found between the 2 groups (Table 1). Patients with PsA were treated less often with drugs from the beta-blocker group, 9.8% compared to 18.4% (Table 2), presumably due to the negative effect of these drugs on the skin manifestations of psoriasis[16]. There was no difference between the groups with respect to treatment with digoxin or calcium-channel antagonists.

Cardiac conduction system measurements. Table 4 presents details of the cardiac conduction properties that were measured. The PR interval was found to be significantly longer in the PsA group compared to controls, 159.6 ± 21 ms versus 151.3 ± 26 ms, respectively ($p = 0.021$), an elongation of 5.5% of the PR interval in the PsA group. Two patients of the PsA group (1.9%) had a pathologic PR interval > 0.2 ms, consistent with a first-degree AV block, compared to only one such patient in the control group. These 2 PsA patients had a RA-like type of arthritis, with no evidence of axial involvement. Their prolonged PR intervals could not be explained by medication use. The abnormal prolongation of the PR interval was asymptomatic, requiring no additional intervention. No subject had complete heart block.

No correlation was found between the duration of articular disease and the prolongation of the PR and QRS intervals. Similarly, no correlation was observed between prolongation of PR interval and the 3 PsA subtypes: asymmetric oligoarticular arthritis, RA-like symmetric polyarthritis, or spondyloarthritis. With respect to arthritis mutilans and arthritis with DIP joint involvement, the sample was too small to assess correlations. In addition, the relative infrequency of ocular involvement in the study group did not permit assessment of correlations.

No relationship was found between the antirheumatic drugs used, specifically methotrexate and NSAID, and the PR interval or other conduction parameters we examined.

DISCUSSION

The major finding of our study is a statistically significantly longer PR interval in the patients with PsA compared to individuals without psoriasis or arthritis. The PsA patients' mean PR interval was found to be 8.3 ms, 5.5% longer compared to the controls. Although the clinical relevance of this finding is questionable since the absolute difference was

Table 2. Antirheumatic and AV node-modifier medications.

Medications	PsA, no. of Patients (%) (n = 92)	Control, no. of Patients (%) (n = 92)
Nonsteroidal antiinflammatory drugs	74 (80)	0
Prednisone	7 (8)	0
Disease modifying antirheumatic drugs		
Methotrexate	54 (59)	0
Sulfasalazine	8 (9)	1 (1)
Azathioprine	7 (8)	0
Cyclosporine	3 (3)	0
Colchicine	4 (4)	0
Leflunomide	2 (2)	0
Hydroxychloroquine	3 (3)	0
Gold	1 (1)	0
AV node-modifiers		
Digitalis	0	0
Ca^{++} channel-blockers	11 (12)	11 (12)
Beta-blockers	9 (10)	17 (18)

Table 3. Distribution of psoriatic arthritis subtypes.

Subtype	Percentage of Patients
Asymmetrical oligoarthritis	40.2
Symmetrical rheumatoid arthritis-like arthritis	38
Axial involvement	18.5
Mutilans arthritis	2.1
Involvement of distal interphalangeal joints	2.1

Table 4. Cardiac conduction properties estimated by ECG recordings.

Conduction characteristics	PsA	Control	p
Rhythm			
Sinus rhythm*	92	90	0.5
Atrial fibrillation*	0	2	0.5
Atrial conduction			
Atrial premature beats*	3	0	0.25
AV conduction			
PR interval, ms	159.6 ± 21	151.2 ± 26	**0.021**
Ventricular conduction			
QRS interval, ms	83 ± 16	79.8 ± 16	0.096
Left ventricle hypertrophy*	4	3	1
Right ventricle hypertrophy*	0	0	1
Left atrial enlargement*	1	0	1
Right atrial enlargement*	0	0	1
Right bundle-branch block	4	2	1
Left bundle-branch block	2	2	1
Left anterior hemiblock*	1	5	0.21
Left posterior hemiblock*	0	0	1
Ventricular premature beats*	4	2	0.68

* No. of patients.

small, the importance of the observation is the implication of AV node involvement in the PsA systemic disease.

We could find only 2 previous studies in the literature addressing the issue of cardiac conduction in psoriasis/PsA. Carvalho, *et al*, in their study of 22 PsA patients, found a higher prevalence of premature atrial systoles, sinus bradycardia, and sinus tachycardia, with one patient found to have an AV block. They did not find a higher frequency of cardiac conduction disturbances than in a healthy control group[17]. Markuszeski, *et al* found a faster heart rate and supraventricular tachycardia in their small study of 32 psoriatic, not necessarily arthritic, patients[18]. In our study, similar differences with respect to rate and rhythm disturbances were not noted. As well, no other ventricular conduction disturbances were found.

Evidence of AV conduction disturbance has been sought in other spondyloarthropathies[4-11]. In these reports, varying degrees of AV block have been noted as occurring intermittently, suggesting a possible effect of the fluctuating inflammatory process. Some have postulated that the HLA-B27 antigen itself may be pathogenic in the development of conduction system abnormalities, with complete heart block reported in B27 antigen-positive individuals in the absence of spondylitis. In support of this assertion, the frequency of HLA-B27 is increased in male patients with pacemakers. In those patients with severe conduction system abnormalities and aortic insufficiency, the incidence of HLA-B27 positivity reportedly approaches 85%[4]. Due to the well known association between the presence of HLA-B27 and axial involvement[19], we addressed the correlation between PR prolongation and clinical axial involvement; no such correlation was found. Unfortunately, the genetic profile of subjects, especially the presence of HLA-B27, was not tested in our study.

Recently, Brunner, *et al*[20] reported altogether different results. They studied the rate of cardiac pathologies in male patients with longstanding AS (> 15 yrs) compared to a healthy population. Their major finding (without reaching statistical significance) was a trend toward an increased rate for mild to moderate aortic and mitral regurgitation compared to the healthy population. The frequency of conduc-

tion disorders in longstanding AS was comparable to the healthy population in their study[20].

Recently the issue of the increased risk of accelerated atherosclerotic cardiovascular disease in patients with rheumatic diseases, including PsA, has been addressed[21]. Cardiac conduction disturbances can be caused indirectly by atherosclerotic lesions if the branches of the coronary tree responsible for the blood supply to the conduction system are compromised[22]. This may be one explanation for the cardiac conduction disturbances found in our study, although there was no difference in the prevalence of clinical IHD between the 2 study groups.

Although a high proportion of the PsA patients were treated with NSAID and methotrexate, there was no apparent effect of this treatment on the cardiac conduction properties examined. It should be emphasized that effects of the newer biological treatments were not assessed in this study, as it was performed prior to their clinical use.

Compared to other cohorts, patients with PsA described here had similar characteristics with respect to the distribution of arthritis subtypes; however, our study population was 10 years older than most other published series[23-26]. The average duration of the articular disease in our study group was 7.6 years. Perhaps a longer followup period would have revealed additional significant findings, especially since cardiac manifestations of SpA are frequently identified only after many years of disease[1].

Our study has several limitations. It is not clear whether the longer PR interval found was related to the psoriasis or the associated arthritis, since the study population was not compared to psoriatic, nonarthritic patients. We have no extended followup data and thus the longterm clinical significance of the difference of PR interval is not known. Inflammation indices were not measured and thus no correlation with disease activity can be imputed. Finally, the severity of the arthritis at the time of ECG was not assessed, so a correlation between severity of disease and the conduction properties cannot be addressed.

Despite these limitations, our study identified subtle involvement of the AV node as observed by prolonged PR interval. The low prevalence of these ECG abnormalities does not allow full clinical interpretation. A prospective study with prolonged followup is warranted to elucidate the clinical significance of our observed conduction abnormalities.

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