Risk of Atrial Fibrillation in Pemphigus Vulgaris

Sir,

Mortality rate among pemphigus vulgaris (PV) patients is higher than general population. Coronary heart disease and cardiac arrhythmia have a statistically significant association with mortality in PV patients.[1] P-wave duration and P-wave dispersion (PWD) are important electrocardiogram (ECG) markers used to evaluate the risk of atrial arrhythmias. Some studies have shown that PWD has a predictive value for atrial fibrillation (AF) in patients with inflammatory conditions such as rheumatoid arthritis, scleroderma, and inflammatory bowel disease.[2-4] We performed a case–control study to investigate the risk of AF in PV patients through ECG markers.

Forty-five PV patients and 45 healthy age- and sex-matched controls were included in the study. The patients fulfilled the currently accepted criteria for PV, defined as the presence of typical mucocutaneous lesions confirmed by pathology and direct immunofluorescence (Shohada-e-Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran, 2014–2016).

Patients and control subjects with cardiopulmonary diseases, obesity (body mass index ≥30 kg/m^2), hypertension, hyperlipidemia, and diabetes mellitus were excluded from the study. Cardiopulmonary dysfunction was excluded by echocardiography. Biochemical variables such as fasting glucose levels and lipid panel were analyzed. All provided written informed consent for inclusion in the study. The Institutional Ethics Committee approved the protocol of the study according to the Declaration of Helsinki. All data analyses were performed using the statistical software JMP, Version 7, SAS Institute Inc., Cary, NC, 1989–2007. P values <0.05 were considered statistically significant.

In the supine position, 12-lead ECG of all subjects was recorded. The P-wave durations (P-max, P-min) were calculated in all 12 ECG leads. The difference between P-max and P-min was defined as PWD.

Baseline demographics and laboratory findings of the study groups are presented in Table 1. Dose of oral corticosteroid was 0–30 mg/day at the time of the study. Half of the patients were taking adjuvant drugs (Azathioprine or Mycophenolate mofetil).

PV patients had significantly higher abdominal obesity ($P < 0.05$). According to the NCEP ATP III definition, there was no significant difference regarding the prevalence of metabolic syndrome in PV patients compared with controls (40% in PV vs. 36% in controls, $P = 0.1$).

Patients with PV had significantly longer P-max duration than healthy controls [$P < 0.0001$, Figure 1]. However, two groups were similar in the P-min durations [$P = 0.07$, Figure 2]. Compared to control group, patients had significantly greater PWD [$P < 0.0001$, Figure 3]. No association was observed between PWD with regards

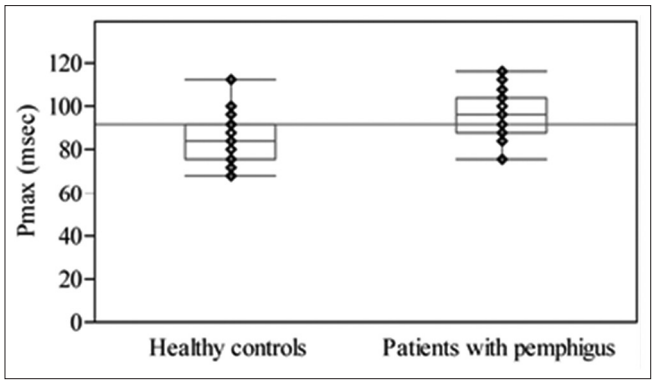

Figure 1: Pmax (msec) in patients with pemphigus and healthy controls. Middle point: median; Box: interquartile range (25-75 percentiles); Whisker: range (excluding outliers)

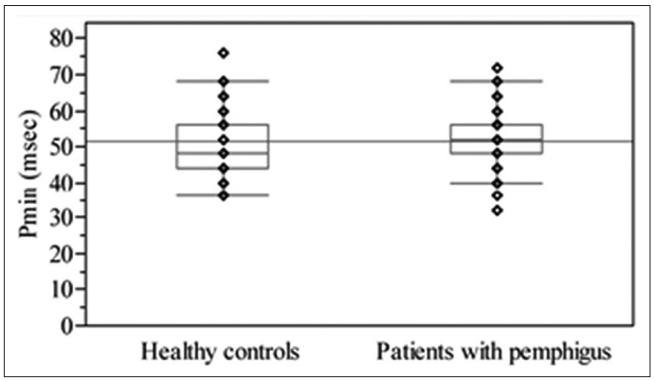

Figure 2: Pmin (msec) in patients with pemphigus and healthy controls. Middle point: median; Box: interquartile range (25-75 percentiles); Whisker: range (excluding outliers)

Table 1: Demographics and laboratory findings of patients with pemphigus vulgaris and healthy controls

Characteristic	Patients with pemphigus (45) vulgaris (*n*=45)	Healthy controls (45) (*n*=45)	*P*
Gender			
Female	14 (31.1%)	14 (31.1%)	
Male	31 (68.9%)	31 (68.9%)	
Age, years	49 (27-75); (35-58)	48 (28-71); (35-56.5)	0.92
BMI	29 (21.9-33); (26-29)	27 (22.9-31.2); (24.2-26)	0.03
Systolic BP, mmHg	125 (90-145); (105-130)	110 (100-135); (110-120)	0.48
Diastolic BP, mmHg	75 (60-80); (70-80)	70 (60-80); (70-80)	0.27
Triglyceride, mg/dL	150 (110-282); (134-228.5)	129 (87-184); (108-148)	0.01
Total cholesterol, mg/dL	170 (125-207); (153.5-197.5)	160 (110-203); (139-180.5)	0.049
Low-density lipoprotein, mg/dL	110 (64-150); (92-114)	94 (69-131); (86.5-109.5)	0.01
High-density lipoprotein, mg/dL	35 (22-47); (32-39)	39 (23-54); (35.5-40)	0.24
Fasting blood sugar, mg/dL	98 (75-105); (86.5-98)	88 (75-102); (84.5-91.5)	0.01

Phenotype, *n* (%), Mucosal, 14 (31.1%), Mucocutaneous, 30 (66.6%), Cutaneous, 1 (2%), Values are expressed as median (range); interquartile range, unless otherwise noted. BMI, Body mass index (calculated as weight in kilograms divided by height in meters squared); IQR: Interquartile range (25-75th percentile)

to disease duration, disease phenotype (cutaneous or mucocutaneous), dose of oral corticosteroid, and adjuvant drug ($P > 0.05$).

Increased risk of atrial arrhythmia in PV patients could be multifactorial. Drug-induced arrhythmia could be a potential mechanism of AF. Long-term use of oral glucocorticoids is associated with ischemic heart disease and heart failure which are triggers for AF development.

Although the risk of arrhythmia is greater with intravenous infusion of corticosteroids due to electrolyte shifts, there are reports of AF development following oral low-dose corticosteroid treatment.[5] Other drugs that have been reported to have arrhythmogenic effect and have widespread use in PV patients are Azathioprine and Bisphosphonates.[6,7]

Recent studies have indicated that inflammation might play a significant role in the initiation, maintenance, and preservation of AF. Some inflammatory cytokines, such as tumor necrosis factor-α, interleukin-6, and macrophage migration inhibitory factor, have been shown to be involved in the pathogenesis of PV, atherosclerosis, coronary heart disease, AF, stroke, and mortality.[8-10]

A major limitation of our study was low sample size. Because there was a high prevalence of components

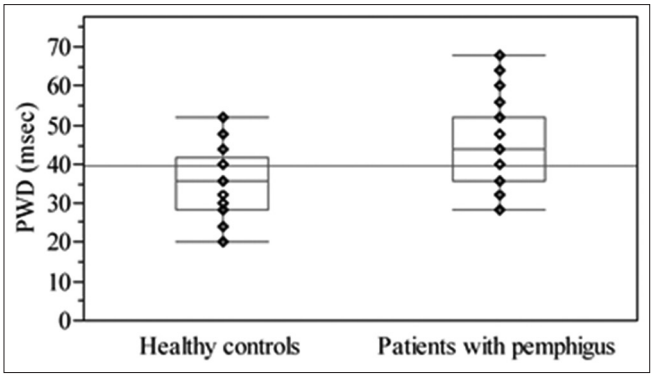

Figure 3: PWD (msec) in patients with pemphigus and healthy controls. Middle point: median; Box: interquartile range (25-75 percentiles); Whisker: range (excluding outliers)

of metabolic syndrome, it could be considered as a confounding factor. Further studies with more structural and functional assessment of cardiac parameters are recommended.

In conclusion, we found that PWD, P-max values were significantly higher than controls. Our result has shown that PV patients are at risk of developing AF.

Acknowledgement

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Source of Support

Nil.

Conflicts of Interest

There are no conflicts of interest.

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