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ORIGINAL ARTICLE

Relationship between primary restless legs syndrome and migraine with aura

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Abstract In this study, the prevalence and characteristics of definite migraine in primary restless legs syndrome (pRLS) patients and matched control patients (CPs) were investigated. We evaluated 63 consecutive adult pRLS patients and 141 age- and sex-matched controls in this case–control study. The diagnosis of migraine and its subtypes were defined based on *The International Classification of Headache Disorders-II*. Only those with "definite" migraine were included in the study. The mean age of 63 adult pRLS patients (15 men and 48 women) who participated in the study was 49.4 years. A total of 27 patients (42.9%) had definite migraine. Of these migraineurs, seven (11.1%) were without aura and 20 (31.8%) were with aura. The mean age of the 141 matched CPs was 48.7 years. A total of 32 CPs (22.7%) experienced migraine. Among these 32 migraineurs, 28 (19.9%) were without aura and four (2.8%) were with aura. Migraine and migraine with aura were significantly more common in pRLS patients than in CPs. pRLS patients with migraine were more anxious and experienced a shorter duration of RLS symptoms than pRLS patients without migraine. Migraineurs in the pRLS group tended to have high scores for severity of migraine headache by Visual Analog Scale score and high levels of disability by Migraine Disability Assessment

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grading than those in the control group. pRLS patients showed a positive association with definite migraine headaches. In contrast to results highlighted in recent studies, we found a strong link between migraine with aura and pRLS.

Introduction

Restless legs syndrome (RLS) is a prevalent sensory motor disturbance characterized by distressing deep sensations in the limbs, particularly the legs, associated with an urge to move, often during rest [1]. RLS affects approximately 4—29% of the general population, predominantly females (female-to-male ratio 2:1) [2]. In most cases, the etiopathogenesis of RLS is idiopathic, although some secondary etiologies such as iron deficiency, pregnancy, uremia, diabetes mellitus, polyneuropathy, rheumatoid arthritis, and spinal disorders may be present [3]. However, its pathophysiology remains unclear to date.

Migraine is a common primary headache disorder that affects approximately 10—20% of the general population, especially females (female-to-male ratio of 2—3:1) [2]. It has been reported that migraine may be complicated by a number of comorbidities, such as stroke, cardiovascular disease, anxiety and depressive disorders, epilepsy, irritable bowel syndrome, and pain disorders [2,4].

The similar prevalence, female-to-male ratio, pathophysiology (unclear in both), and complications and comorbidities of migraine and RLS have attracted increasing attention in clinical practice. An association between primary headaches, especially those of migraine and RLS in adult patients, has been reported. The prevalence of migraine was reported to be higher in pRLS patients than in general population [3,5]. It has also been confirmed that RLS is more common in patients with migraine than in those without migraine [6—10].

In the current study, our main objective was to compare the prevalence of subtypes of definite migraine (with or without aura) in primary RLS (pRLS) patients and matched control patients (CPs) to study the association between both diseases. The secondary objective was to determine whether or not family history, severity of diseases, the presence of anxiety and depressive disorders, or sleep quality exhibited any differences between pRLS patients and CPs. We also determined whether there were any differences in the severity of sleep disturbances, migraine headache, and anxiety or depression between migraineurs in the pRLS group and those in the control group.

Methods

Sample of patients and CPs

In this study, 340 consecutive patients (age >18 years) suffering from RLS symptoms followed at the outpatient clinic of the Department of Neurology at the Sakarya University (Sakarya, Turkey) between July 2014 and November 2015 were informed about the study.

Only patients with pRLS diagnosed according to the standard diagnostic criteria of International Restless Legs Syndrome Study Group (IRLSSG) [11] were examined in detail. Two patients declined participation; 170 patients with RLS symptoms did not participate in further investigations for eliminating the secondary causes of RLS. Secondary causes of RLS were detected in 40 patients (1 with chronic back pain after lumbar spinal instrumentation surgery; 1 with active patellofemoral osteoarthritis with elevated C-reactive protein level, erythrocyte sedimentation rate, and white blood cell count; 3 with venous insufficiency with ultrasonographic evidence; 8 with diabetes mellitus, which was clinically, laboratory, and/or electrophysiologically proven; and all others diagnosed with iron deficiency with or without anemia) and they were all excluded from the study.

We also excluded patients using any medication or receiving medical treatment or diagnosed with "probable" migraine or with "definite" migraine in addition to any other primary headaches. Only 63 pRLS patients (15 men and 48 women) with a mean age of 49.4 ± 11.7 years (22—85 years) who fulfilled all study criteria were thus eligible to participate in this study. Figure 1 shows the recruitment of patients to the pRLS group.

Age- and sex-matched CPs were selected. The physical and neurological examination results of all CPs were normal, and they did not have any clinical evidence of RLS and/or systemic disorders. Patients in the control group also went through the same laboratory and clinical assessments as the patients in the pRLS group. Patients were excluded according to the criteria specified for the pRLS group. Of the 240 CPs informed about the study, 141 CPs (44 men and 97 women) with a mean age of 48.7 ± 8.1 years (27—61 years) were eligible and included in the study. Figure 2 shows the recruitment of patients to the control group.

The Ethical Committee of Sakarya University School of Medicine provided ethical approval for this study. Informed written consent was obtained from each patient included in this study.

Data collection

Sociodemographic data, including age, sex, medical history of the patient, and his/her family medical history, were collected. Patients were asked about similar symptoms for RLS and migraine in their close relatives. Family history was considered positive if any first-degree relative was reported