Restless legs syndrome in patients with multiple sclerosis: epidemiology and genetics

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Objectives

The restless legs syndrome (RLS) is a frequent neurological disorder and it presents as both idiopathic and secondary forms. Idopathic RLS is associated with common genetic variants in *MEIS1, BTBD9*, *PTPRD* and *MAP2K5/LBXCOR1*. Recently, multiple sclerosis (MS) was indentified as a common cause for secondary RLS, the prevalence of RLS in MS patients ranges from 13.3 to 37.5.%. The aim of our study was to evaluate the prevalence of RLS among Czech patients with MS and to further analyze the impact of known genetic determinants for RLS in patients with MS.

Methods

Epidemiological study: We enrolled consecutively Czech patients with multiple sclerosis coming to our center. Each patient underwent a semi-structured interview. A patient was considered to be affected by RLS if he/she met all four standard criteria with a life-long interval.

Genetic study: In the genetic association study, 642 subjects were included, 203 MS patients with RLS were compared to 438 MS patients without RLS. In total 13 single nucleotide polymorphisms within the four genomic regions were genotyped according to the results of previous genome-wide association scans using mass spectrometry.

Results

Epidemiological study: A total of 765 subjects (553 females, 211 males, mean age 36.54, ±SD 9.5) with multiple sclerosis were included in the study. The diagnosis of RLS was confirmed in 245 subjects (32.1%, 95% CI 28.7-35.4%) with MS. Patients suffering from both MS and RLS were significantly older (38.6 vs. 35.6 years), had longer durations of MS symptoms (11.0 vs. 8.2 years) and had higher EDSS score (2.9 vs. 2.3).

Genetic study: No significant association with *MEIS 1*, *BTBD9* and *PTPRD* was found in 203 patients with MS, despite sufficient statistical power for first two loci. There was a trend for association with *MAP2K5/LBXCOR1* - the best model for the risk allele was the recessive model (p nominal = 0.0029, p corrected for four loci and allelic + recessive model = 0.023, odds ratio = 1.60 - 95% CI, 1.17 – 2.18).

Conclusion

We confirmed the findings of previous studies that life-long RLS prevalence is high in patients with multiple sclerosis. MS should be considered among the causes of secondary RLS forms. The genetic risk variants *MEIS 1* and *BTBD9* for idiopathic RLS do not increase the risk for secondary RLS in MS, *LBXCOR 1* can partially contribute to the phenotype. In patients with MS, RLS may be the consequence of specific lesion of central nervous system pathways involved in the aetiology RLS.