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Original Research

Pleckstrin homology-like domain family B member 1 rs498872 polymorphism and glioma risk in Chinese Han population

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Abstract: This case-control study aimed to investigate the association between PHLDB1 rs498872 polymorphism and the risk of glioma in a Chinese Han population. A total of 210 patients and 235 controls were enrolled in this study. The CT genotype and TT genotype were significantly associated with the risk of glioma (OR=1.48, 95%CI 1.00-2.19, *P*=0.05 and OR=2.40, 95%CI 1.06-4.10, *P*=0.03), respectively. In addition, T allele of PHLDB1 rs498872 polymorphism was significantly associated with an increased risk of glioma (OR=1.58, 95%CI 1.08-2.29, *P*=0.02). We also found that PHLDB1 rs498872 polymorphism was not associated with histology and tumor grade of glioma. In conclusion, this study found that PHLDB1 rs498872 polymorphism was significantly associated with glioma risk in Chinese Han population.

Key words: PHLDB1; Glioma; Polymorphism; Association.

Introduction

Glioma accounts for 80% of central nervous system tumors and is the most common primary malignant brain tumor in adults (1). Patients with aggressive forms of glioma have an average survival time of 15 months (2). Although chemotherapy, radiotherapy and microsurgery have previously been used to treat gliomas, the majority of patients succumb to the disease within two years of the diagnosis (3). Therefore, detailed investigation is required to establish the underlying mechanisms of glioma pathogenesis and identify novel therapeutic approaches to treat glioma.

Recently, many studies suggested that genetic factors played important roles in the pathogenesis of glioma. Walsh et al. indicated that eight SNPs in/near seven different genes (TERT, EGFR, CCDC26, CDKN2A, PHLDB1,RTEL1, TP53) were significantly associated with glioma risk (4). Sanson et al. showed that variation in 7p11.2 was a determinant of inherited glioma risk (5). Ghasimi et al. indicate that CDKN2A/B risk genotypes are associated with primary glioblastoma without IDH mutation (6). PHLDB1 contains a PH domain, a Forkhead-associated (FA) domain and a structural maintenance of chromosomes ATPase (SMC) domain (7). Chen et al. indicated that PHLDB1 rs498872 polymorphism was significantly associated with glioma risk (8). Therefore, we did a case-control study to confirm their results.

Materials and Methods

Study subjects

This study included Chinese Han glioma cases and controls from Jilin Province Cancer Hospital. A total of 210 patients and 235 controls were enrolled in this study. All of the glioma cases were newly diagnosed from 2013 to 2016. Glioma diagnosis was confirmed for all cases by MRI and histopathology. We received institutional review board approval and informed consent was obtained from subjects. Tumor types and stages were determined according to the World Health Organization classification.

Genotyping

Genomic DNA from blood and tissue was isolated using commercially available kits with standard protocol. Genotyping of the PHLDB1 rs498872 polymorphism was done with the Mass-ARRAY iPLEX platform (Sequenom, San Diego, California) through the use of an allele-specific matrix-assisted laser desorption/ionization time-of-flight mass spectrometry assay (8).

Statistical analysis

SNP was tested for deviation from the Hardy-Weinberg equilibrium (HWE) among controls by comparing the observed and expected genotype frequencies using the chi-square test. Demographic characteristics were compared between cases and controls by means of a chi-square test and Student's t test. Unconditional logistic regression was used to calculate the odds ratios (ORs) and 95% confidence intervals (CIs). All statistical analyses were performed by SPSS for Windows software (version 16.0 SPSS, Chicago, IL). All comparisons were two-sides, and $P < 0.05$ was regarded as statistically significant.

Results

There was no significant differences in the sex and

Table 1. Characteristics of the cases and controls.

Characteristics	Case (n)	Control (n)	*P* value
Total	210	235	
Age at diagnosis			
≤40	15	18	0.84
>40	195	217	
Sex			
Male	137	159	0.59
Female	73	76	
Histology			
Glioblastoma	72		
Non-glioblastoma	138		
Tumor grade			
High	137		
Low	73		

age distribution between the case and control groups (Table 1). Among 210 glioma patients, there were 72 glioblastoma patients and 138 non-glioblastoma patients. Most of the glioma patients were high grade patients. PHLDB1 rs498872 polymorphism was in line with the HWE in controls (P>0.05).

Association between PHLDB1 rs498872 polymorphism and the risk of glioma were analyzed using unconditional logistical regression analysis (Table 2). The CT genotype and TT genotype were significantly associated with the risk of glioma (OR=1.48, 95%CI 1.00-2.19, P=0.05 and OR=2.409, 95%CI 1.06-4.10, P=0.03), respectively. In addition, T allele of PHLDB1 rs498872 polymorphism was significantly associated with an increased risk of glioma (OR=1.58, 95%CI 1.08-2.29, P=0.02). Furthermore, we investigated the association between PHLDB1 rs498872 polymorphism and histology and tumor grade. The results are listed in Table 3. We found that PHLDB1 rs498872 polymorphism was not associated with histology and tumor grade of glioma.

Discussion

In this case-control study of a Chinese population, we found that CT genotype and TT genotype were significantly associated with the risk of glioma, respectively. In addition, T allele of PHLDB1 rs498872 polymorphism was significantly associated with an increased risk of glioma. Furthermore, we investigated the association between PHLDB1 rs498872 polymorphism and histology and tumor grade. We found that PHLDB1 rs498872 polymorphism was not associated with histology and tumor grade of glioma.

Liu et al. found that glioma susceptibility is associated with rs1799782 and rs25487 of X-ray repair complementing defective repair in Chinese hamster cells 1 (XRCC1), rs1805377 of XRCC4, rs1800067 of excision repair cross-complementing rodent repair deficiency complementation group 4 (ERCC4) and rs3212986 of ERCC1 in Asian population, and rs12917 of O-6-methylguanine-DNA methyltransferase (MGMT) and rs1136410 of poly(ADP-ribose) polymerase 1 (PARP1) in Caucasian population (9). Zhang et al. suggested that demonstrates that the RTEL1 rs2297440 polymorphism plays a moderate, but significant role in the risk of glioma (10). Jia et al. suggested that ERCC2 rs13181 was associated with a higher susceptibility to glioma in the Chinese population (11). Lu et al. suggested that the rs4295627 SNP is associated with an increased risk of glioma (12). Cao et al. indicated that the TERT genetic polymorphism rs2853676 is associated with increased risk of glioma (13). Pooyan et al. indicated that PAI-1 4G/5G polymorphisms with increasing glioblastoma cancer risk in Iranian patients (14). Wang et al. suggests that XRCC1 Arg399Gln polymorphism contribute to increased risk of glioma (15).

Some limitations should be addressed. First, more studies with large sample sizes are needed to further identify the result. Second, other SNPs in PHLDB1 should be assessed in the future studies. Third, potential gene-gene interaction and gene-environment interaction were evaluated. Finally, a lack of sufficient eligible studies limited the stratified analysis.

In conclusion, this study found that PHLDB1 rs498872 polymorphism was significantly associated with glioma risk in Chinese Han population.

Conflicts of interest

None

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Table 2. Distribution of genotypes in cases and controls.

Genotype	Case (%)	Control (%)	OR	95%CI	*P* value
CC	88 (41.9%)	125 (53.2%)	1.00	Reference	
CT	97 (46.2%)	93 (39.6%)	1.48	1.00-2.19	0.05
TT	25 (11.9%)	17 (7.2%)	2.09	1.06-4.10	0.03
TT+CT vs. CC	122 (58.1%)	110 (46.8%)	1.58	1.08-2.29	0.02

Table 3. Relation of PHLDB1 rs498872 polymorphism and histology and tumor grade.

Characteristics	TT+CT	CC	OR	95%CI	*P* value
Histology					
Glioblastoma	39	33	1.00	Reference	
Non-glioblastoma	83	55	1.28	0.72-2.27	0.41
Tumor grade					
High	79	58	1.00	Reference	
Low	43	30	1.05	0.59-1.87	0.86

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