Obstructive Sleep Apnea as the First Presentation of Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy

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Introduction: Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a rare hereditary disease caused by mutations in the *NOTCH3* gene on chromosome (19p13.2–p13.1). It is a systemic angiopathy characterized by recurrent transient ischemic attacks and strokes. However, which symptom is the first presentation that can be detected earlier by the patient or family is of interest and not well known.

Case presentation: A 43-year-old man was born to a family with a history of CADASIL, and a native of Taoyuan, Taiwan. He visited the out-patient department of family medicine for excessive daytime sleepiness and obvious episodes of breathing cessation during sleep. Complete physical examination, laboratory tests, and imaging studies were performed. Obstructive sleep apnea (OSA) was diagnosed by polysomnography on the basis of apnea-hypopnea index measured 12. Two years later, he presented with progressive cognitive decline, generalized slow response, and forgetfulness. Neuropsychological examinations were carried out by a neurologist and psychologist. Brain magnetic resonance imaging (MRI) revealed severe leukoencephalopathy. There were multiple small circumscribed hyperintense foci up to 0.9cm in size over the brain stem, bilateral basal ganglia and cerebral white matter on T2 weighted images (T2W1), suggestive of chronic lacunar infarctions. The clinical manifestations and MRI findings were highly suggestive of CADASIL, so genetic testing for *NOTCH3* mutations was performed. A heterogeneous mutation was detected that produced an arginine to cysteine substitution in exon 6 of chromosome 19p13.12 (p.Arg332Cys) (c.994C>T). The diagnosis of CADASIL was confirmed and daily Aspirin (Bokey®) 100mg plus Atorvastatin (Lipitor®) 20mg were prescribed. The patient was admitted to a nursing home due to disability one year later.

Discussion: OSA can be the first disorder of CADASIL. Recognition of an easily detected manifestation by the patient himself and families is important. Early identification and suitable management can prevent rapid deterioration and serious complications of such hereditary diseases.

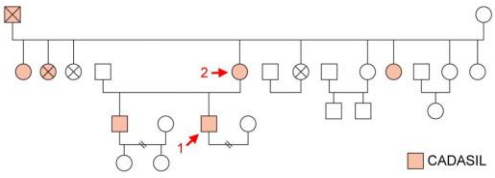

Figure: Genogram. The patient and his mother were indicated by arrowheads and labeled as Cases 1 and 2, respectively.

中文題目：阻塞型睡眠呼吸中止症為體顯性腦動脈血管病變合併皮質下腦梗塞及腦白質病變的第一個表徵

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