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A Case of Nonelderly Progressive Subcortical Vascular Encephalopathy (PSVE) without Hypertension

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Abstract. The authors report a case of a young woman with progressive subcortical vascular encephalopathy without hypertension. She had no known risk factors for cerebrovascular disease. All known causes of progressive subcortical vascular encephalopathy in young patients without hypertension were eliminated by laboratory investigation. Magnetic resonance imaging revealed diffuse white matter injury, and single photon emission computed tomography showed a decrease in cerebral blood flow mainly in the white matter and temporal cortex bilaterally. In addition to recently described causes of subcortical ischemia in young and middle-aged individuals, other etiologies still remain to be identified.

Key word : CADASIL, CARASIL, risk factors, MRI

Introduction.

It is well known that hypertension is a major risk factor for the development of progressive subcortical vascular encephalopathy (PSVE)[1]. However, PSVE without hypertension has been reported. Among these young adult-onset PSVE without hypertension was included[2~25]. Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) and cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy (CARASIL) are types of PSVE without hypertension with characteristic clinical manifestations and patterns of heredity. The authors report a case of a nonelderly female patient with PSVE without hypertension, and without other known vascular risk factors, or familial history.

Case Report

A 54 year-old, previously healthy woman first noticed forgetfulness in the winter of 1994. She also suffered from intermittent claudication, especially in the left leg, in December 1994. Dysarthria appeared in April 1995, and the symptoms gradually progressed over subsequent months. She was first examined by physicians in February 1996. Family history was unremarkable. She had no history of earlier transient neurologic deficits, migraine headaches, menstrual abnormalities, coagulation abnormalities, or systemic symptoms that might suggest a vasculitic process. On admission, her height was 155cm, and her body weight was 58kg. The pulse rate was 60/min and the blood pressure was 130/76mm Hg. Her blood pressure had been normal throughout her life. Her score on the revised Hasegawa-Dementia Scale (HDS-R) was 23/

Table 1. Laboratory data.

items	values	normal range
sugar	89	65-110 mg/dl
cholesterol	165	130-220 mg/dl
triglycerides	98	46-130 mg/dl
HDL-cholesterol	45	42-92 mg/dl
lactate	1.30	0.44-1.33 mmol/1
pyruvate	24	45-113 μmol/1
T3	117	70-160 ng/ml
T4	8.9	4.7-9.6 μg/dl
TSH	1.40	0.4-4.95 μu/ml
protein S antigen	107	65-135 %
protein S	9.2	6.6-11.5 μg/dl
protein C antigen	92	70-150 %
protein C	87	55-140 %
antithrombin III	108.0	82.0-125.0 %

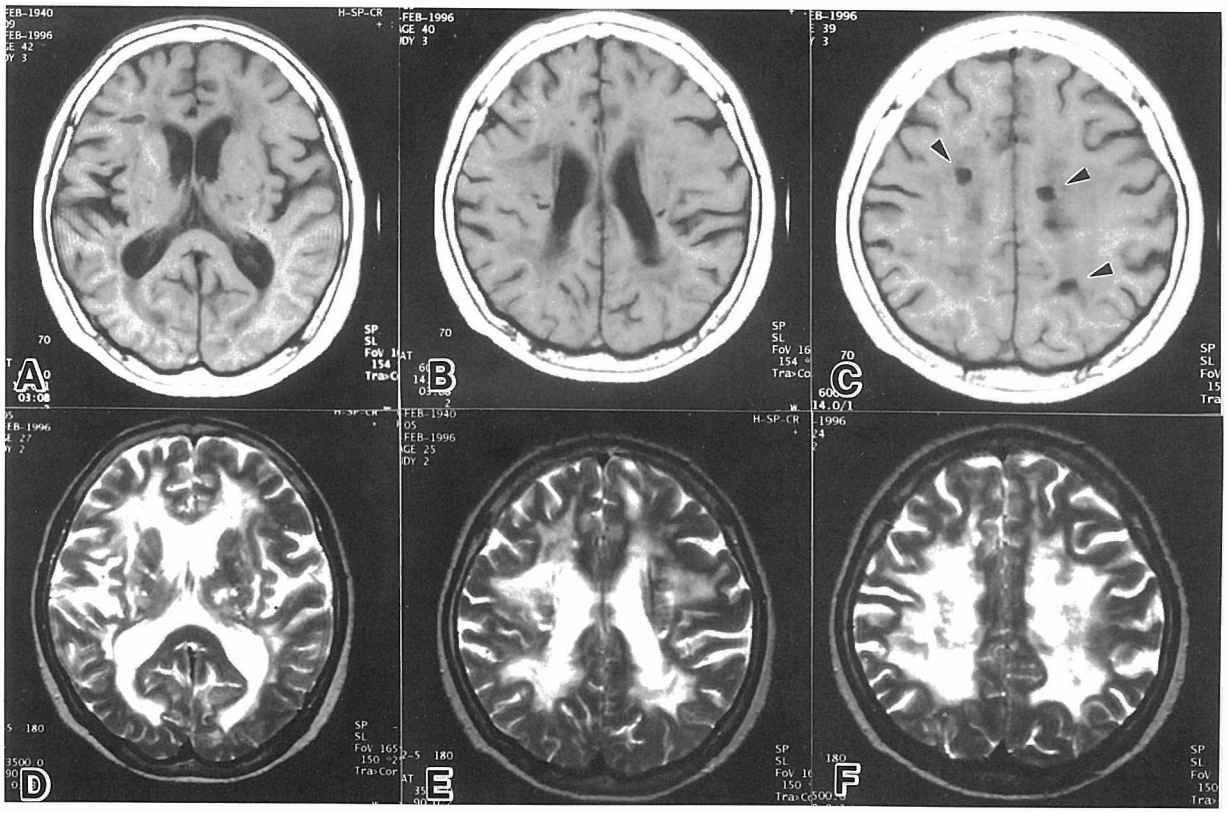

Fig 1. T1-weighted, axial spin-echo (SE) (TR 600/TE 14) images (A,B,C), and T2-weighted, axial SE (TR 3500/TE 90) images (D,E,F). T1-weighted images (A,B,C) show spotty abnormal hypo- intensity areas in the white matter and T2 weighted images (D,E,F) reveal diffuse abnormal hyper-intensity. T1-weighted images also show spotty low intensity areas in white matter consistent with old infarctions (arrowheads) (C).

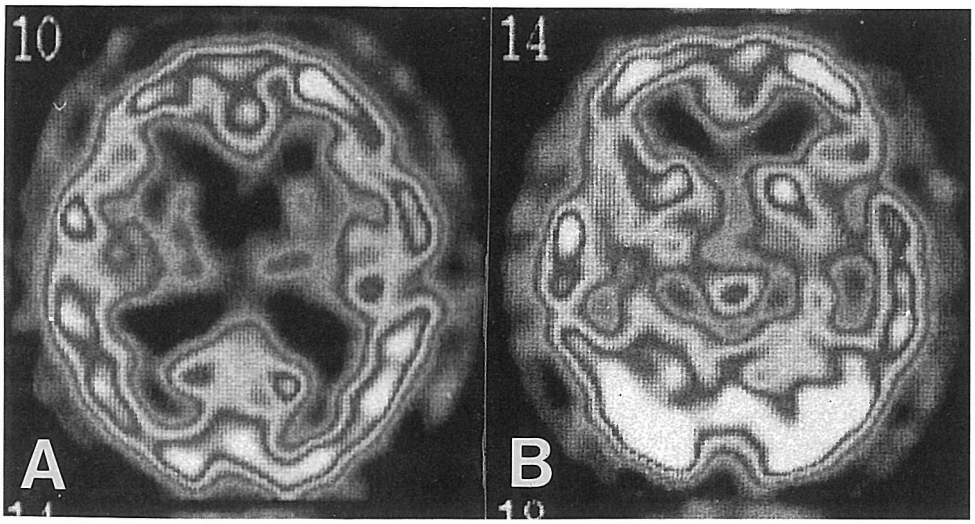

Fig 2. Single photon emission computed tomography (99mTc-HMPAO). Cerebral blood flow is decreased mainly in the white matter (A) and in the temporal cortex (B) bilaterally (arrows).

30. The neurologic examination revealed exaggerated tendon reflexes, snout reflex, jaw jerk, and bilateral Chaddock signs. Her speech was thick and slurred, and pseudobulbar palsy was noted. Her gait was slightly unstable but not ataxic. Her sensation was intact. Clumsiness of fingers was observed bilaterally. She smoked no tobacco and drank no alcohol. She was not diabetic. Peripheral blood examination yielded no abnormalities. The serum analysis showed normal range except for pyruvate 24 (45 to 113mol/l)(Table 1). Anticardiolipin antibody, lupus anticoagulant, antinuclear antibody (ANA), and rheumatoid factor were all negative. Her cerebrospinal fluid was normal, and the myelin basic protein and oligoclonal IgG bands were negative. Platelet agglutination, platelet adhesiveness, bleeding time, prothrombin time, partial thromboplastin time, and collagen were normal. A superconductive magnetic resonance (MR) imaging unit with a field strength of 1.5 tesla (Magnetom Vision, Siemens-Asahi Meditech, Tokyo, Japan) was used to image her brain. T1-weighted axial images showed diffuse abnormal hypo-intensity lesions (Fig.1-A,B) and T2-weighted images revealed hyper-intensity lesions in the white matter (Fig.1-D,E,F). There were also four small areas of abnormal hypo-intensity by T1-weighted MR imaging consistent with old infarction (Figs.1C). MR angiography revealed no stenosis or occlusion of the vertebral-basilar system or the internal carotid arteries (data not shown). Single photon emission computed tomography (SPECT) showed a decrease in cerebral blood flow mainly in the subcortical white matter and in the temporal cortex bilaterally (Fig.2).

Her intermittent claudication and dysarthria did not change significantly for 7 months after admission to our hospital in February, 1996. Her dementia slowly progressed, and her score on the HDS-R was 12/30 in September, 1996.

Discussion.

In general, hypertension is the primary known risk factor for PSVE[1]. However, PSVE without hypertension has been reported, including several reports of nonelderly PSVE without hypertension[2~20,23~25]. In our case, known risk factors such as hypertension, hypercholesteremia, diabetes mellitus, obesity, smoking, and drinking were not detected.

Mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes (MELAS), protein S deficiency, protein C deficiency, antithrombin III deficiency, and anti-phospholipid antibody syndrome are representative diseases which can cause nonel-

derly PSVE without the presence of other known risk factors. In our case, however, the presence of these causes was excluded by the laboratory data.

Recently, some types of nonelderly PSVE without hypertension have been reported using new nomenclature because of the characteristic clinical symptoms and patterns of inheritance. These include cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)[2~9] and cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy (CARASIL)[10~20]. CADASIL is characterized, by the absence of hypertension, recurrent subcortical ischemic strokes starting in early or middle adulthood, and leads to dementia in some patients[2~9]. Other manifestations include migraine and episodes of depression[4~6]. Some investigators have reported that CADASIL is related to hemiplegic migraine because both diseases have been mapped to chromosome 19[21,22], and migraine often accompanies CADASIL[4~6]. In contrast, CARASIL is a young adult-onset arteriosclerotic leukoencephalopathy associated with alopecia and spondylosis deformans without hypertension[10~20]. All reported cases have been Japanese, and almost all patients were male. Diffuse white matter disease has been observed using neuroimaging techniques in both CADASIL and CARASIL. In this case, some small old infarctions were revealed as hypo-intensity lesions on T1-weighted images, in addition to the diffuse white matter vascular injury (Figs.1C). Our patient was not diagnosed as suffering from either CADASIL nor CARASIL due to the absence of both characteristic heredity and symptoms. A few other nonelderly patients with PSVE but without hypertension, characteristic clinical or laboratory findings or heredity patterns indicating CADASIL or CARASIL have been reported[23~25]. We must investigate and not neglect these disease entities because there exists the possibility that new etiologies may be established in PSVE using modern pathologic or molecular biologic methods in the near future. These patients are of interest as they may represent examples of clinical entities yet to be described.

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