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A case of cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) patient presenting with chorea

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Abstract

In cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), clinical presentation with movement disorders such as dystonia and progressive supranuclear palsy-phenotype are rarely reported. None of the CADASIL cases, to our knowledge, has been reported with chorea. Herein, we describe a Korean woman with CADASIL who had presented with chorea. ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) showed hypometabolism in the right basal ganglia. We found decreased FDG uptake of the right basal ganglia by SPM analysis.

INTRODUCTION

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a hereditary small vessel vasculopathy caused by mutations in the *NOTCH3* gene on chromosome 19.[1-2] In this disease, fibrosis and stenosis of penetrating arteries in the cerebral white matter lead to progressive cognitive decline and finally vascular dementia.[3] Recent reports have introduced new rare atypical clinical presentations such as dystonia and parkinsonism with progressive supranuclear palsy-phenotype.[4-5] However, none of the CADASIL cases, to our knowledge, has been reported with chorea symptoms. Herein, we describe a Korean woman with CADASIL who had presented with chorea. ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) showed hypometabolism in the right basal ganglia, especially the putamen.

CASE REPORT

This was a 58-year-old woman with a 3-year history of gradual onset and intermittent choreic movements of the left hand. She visited our outpatient clinic within 3 months of symptom onset with a history of progressively worsening involuntary movements. She also complained of migraine-like headaches since the age of 20 and insidious onset of cognitive decline recently. Past medical history was not remarkable for stroke risk factors such as hypertension, heart disease, or hyperlipidemia. There was no other apparent cause for chorea, such as a history of hyperglycemia, use of estrogen such as hormone replacement therapy or other drugs, or history of Sydenham chorea. In her family, her mother was diagnosed with dementia and a living younger sister complained of headaches but without a history of stroke, mood changes or dementia. There was no definite family history of chorea.

Neurological examination of the patient showed choreic movements affecting mostly the left hand and lip (Video 1). There were no motor, sensory or reflex abnormalities or cerebellar or parkinsonian signs. She scored 28 out of 30 on the mini-mental status examination and was found to have severely depressed mood as evidenced by a high score (26 out of 30) on the geriatric depression scale.

Laboratory findings included normal complete blood count, liver, renal and thyroid function tests, electrolytes, and caeruloplasmin. Peripheral blood smear did not show acanthocytosis. Brain magnetic resonance imaging (MRI) revealed diffuse ischemia of the posterior and lateral aspect of the putamen, and periventricular and subcortical white matter in the FLAIR image, without brain atrophy (Figure 1). Hypometabolism of right basal ganglia was revealed in the visual analysis of FDG-PET. Significantly decreased FDG uptake in the putamen was shown using statistical parametric mapping (SPM 2) (Figure 2). Skin biopsy was normal but she had a positive NOTCH3 mutation - c.899G>A (p.Cys300Tyr) (genomic DNA

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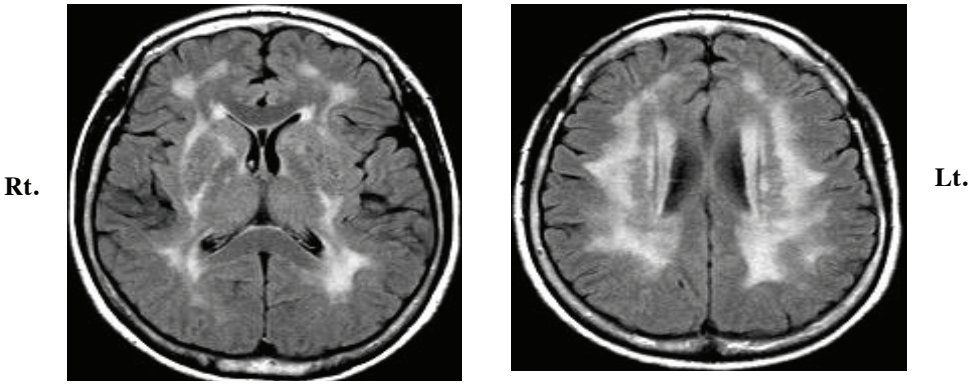
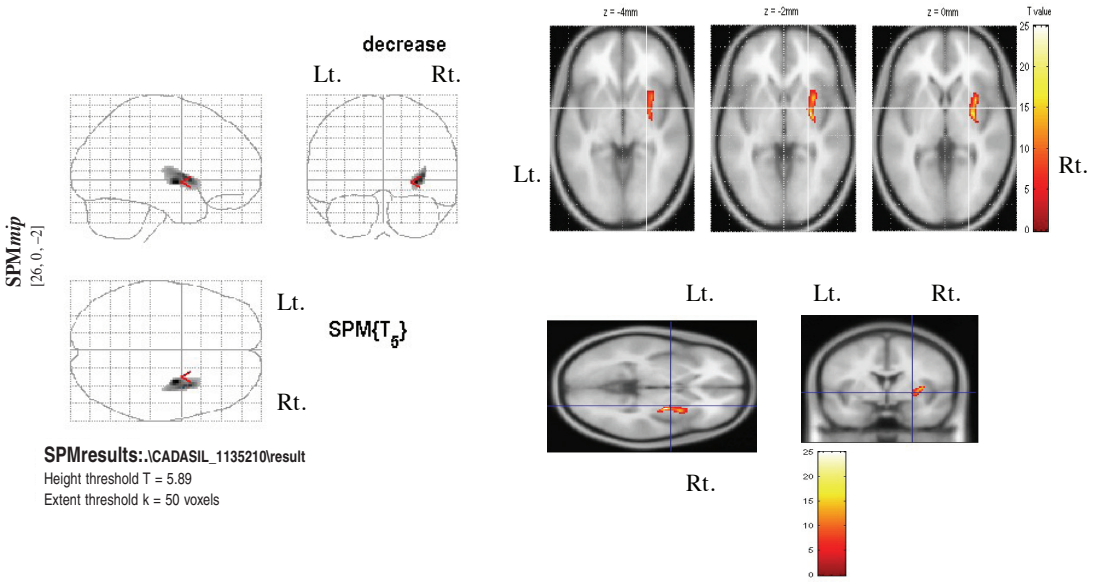


Figure 1. Axial FLAIR magnetic resonance imaging of brain shows extensive bilateral periventricular white matt ischemia in the patient. The ischemic changes of right lateral and posterior limb of putamen are more extensively involved than left side.

isolated from peripheral leukocytes). Molecular genetic studies for Huntington's disease, and spinocerebellar ataxias (SCAs) 1, 2, 3, 6, 7 and 8 were negative.

DISCUSSION

To our knowledge, this is the first reported case of CADASIL presenting with chorea. We further showed hypometabolism of the basal ganglia in this patient by FDG-PET. Left hand and lip chorea in our patient was undoubtedly associated with hypometabolism of right basal ganglia, especially putamen. We suggest that subcortical white matter ischemia caused by the NOTCH3 gene mutation



Statistics: ***volume summary (p-values corrected for entire volume)***

cluster-level			voxel-level				*x*, *y*, *z* {mm}		
$P_{corrected}$	k_E	$P_{uncorrected}$	$P_{corrected}$	T	($Z_=$)	$P_{uncorrected}$			
0.000	311	0.000	0.741	24.91	(4.76)	0.000	30	–4	–2
			0.886	19.65	(4.52)	0.000	34	8	0
			0.967	15.63	(4.27)	0.000	36	–2	6

Figure 2. ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) finding in patient showing a hypometabolism involving right BG, especially putamen (SPM 2 analysis).

affected the function of basal ganglia circuitry. As a result, right putaminal hypometabolism was associated with left-sided choreic movements in our patient. MRI also showed more widespread involvement in the region of the right basal ganglia compared to the left side. A previous report suggested that neuronal loss secondary to ischemia could explain hypometabolism in cortical and subcortical structures in CADASIL.[6] Stroke could induce delayed-onset dystonia due to lesions involving components of the cortico-thalamo-basal ganglia circuits, with most lesions involving the striatum or thalamus.[4,7]

We suggest that extrapyramidal involuntary movements occurring in the context of CADASIL may be related to dysfunction of basal ganglia circuitry by way of cortical-subcortical disconnection, caused by structural lesions of chronic white matter ischemia.

Legends to the Video

Video 1. http://www.neurology-asia.org/content/17/3/neuroasia-2012-17(3)-247-v1.avi
The video shows choreic movements predominantly involving the left hand and lip.

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