Original article

Measurement of Decreased Cerebellar Blood Flow of Machado-Joseph Disease by Brain Perfusion SPECT.

Kikuo MACHIDA, Nornari HONDA, Makoto HOSONO, Takeo TAKAHASHI, Akio KASHIMADA, Yuhji SHIMIZU, Hisato OSADA, Wataru WATANABE, Masahide O' MICHI, Nobuyuki OHTAWA, Mikihito HONDO, Takemichi OKADA, Nobutaka USUI, Keiichiro NISHIMURA and Masanobu KINOSHITA*

Department of Radiological Science and *4thDepartment of Internal Medicine, Saitama Medical Center, Saitama Medical School

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Abstract

Machado-Joseph disease (MJD) is an autosomal dominant spinocerebellar degenerative disease first described among the Portuguese and their descendants in New England and California. Subsequently, MJD has been found in families from many countries including Japan.
The locus for MJD has been assigned to 14q24.3-q32 by genetic linkage. Recent development of brain perfusion SPECT is remarkable and has allowed us to measure blood flow quantitatively using non-traumatic Patlak' s method. In this paper, we report a 63 year-old female of MJD in whom we were able to demonstrate remarkable decrease of cerebellar blood flow compared to cerebral cortex. Her MRI revealed a moderate atrophy of cerebellum. And we would like to suggest that a marked decrease of the cerebellar blood flow by SPECT is one of the useful findings to diagnose MJD.

Introduction

Machado-Joseph disease (MJD)/SCA3 is an autosomal dominant spinocerebellar degenerative disease first described among the Portuguese and their descendants in New England and California. Subsequently, MJD has been found in families from many countries including Japan. The locus for MJD has been assigned to 14q24.3-q32 by genetic linkage [1].

Using PET and SPECT, several investigators reported the changes of cerebellar blood flow in patients with spinocerebellar degenerative disease[2-5] . Since Matsuda et al [6] reported noninvasive measurements of regional cerebral blood flow using Tc-99m hexamethylpropylene amine oxime in 1993, development of brain perfusion SPECT is remarkable and has allowed us to measure blood flow quantitatively using non-traumatic Patlak' s method. In this paper, we report a 63 year-old female of MJD in whom we were able to demonstrate remarkable decrease of cerebellar blood flow compared to cerebral cortex. Her MRI revealed slight atrophy of cerebellum. And we would like to suggest that a marked decrease of cerebellar blood flow by SPECT is one of the useful findings to dingnose MJD.

Case Report

A 63 year-old man was referred to our hospital with chief complaint of ataxia from the other hospital due to the moving. About 7 years ago, she noticed progressive gait disturbance and ataxia. MRI revealed a slight cerebellar atrophy.
She was diagnosed MJD and was confirmed with genetic analysis [7].
Family history revealed her elder brother had MJD and her younger sister died when child. Her

Contact address of the principal author :
1981 Kamoda, Kawagoe City, Saitama Pref. Japan 350-8550 (postal code), Kikuo MACHIDA
Tel +81-492-28-3516, Fax +81-492-26-5284.

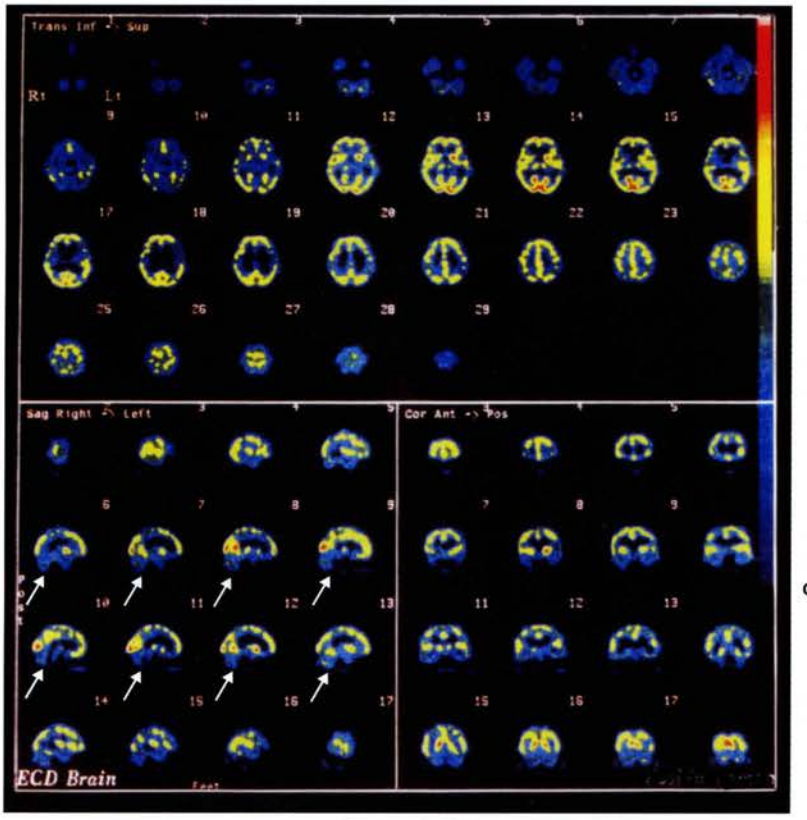

Figure 1 (a)

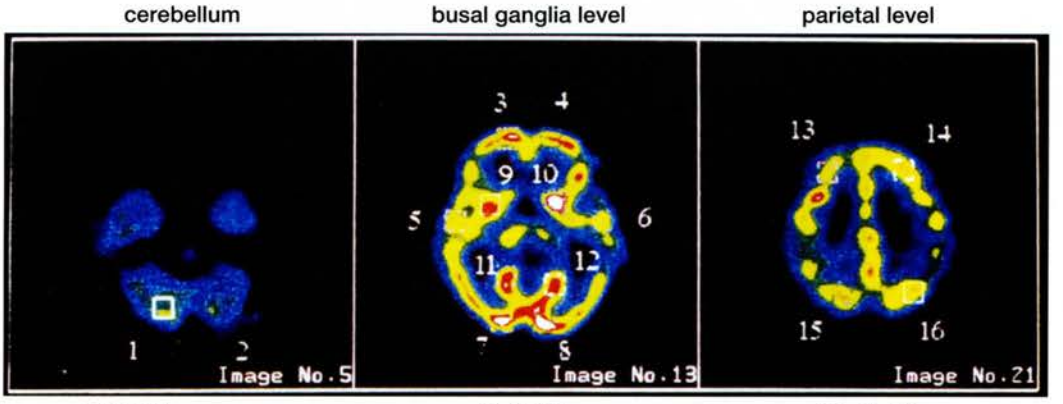

Figure 1 (b)

Figure 1

(a) Tc-99m ECD SPECT images are shown (axial, sagittal and coronal). Note decreased cerebellar blood flow, blue in color in sagittal images (arrows).

(b) Measured values of blood flow are shown. Blood flow in cerebellum is smaller than that in cerebrum, although in normal cases cerebellar blood flow is l0-15 ml/100g/min higher than cerebral blood flow.

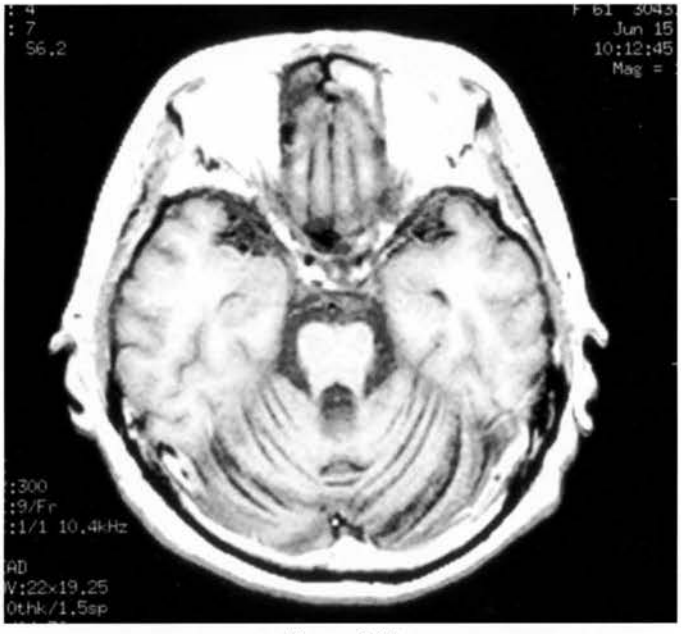

Figure 2 (a)

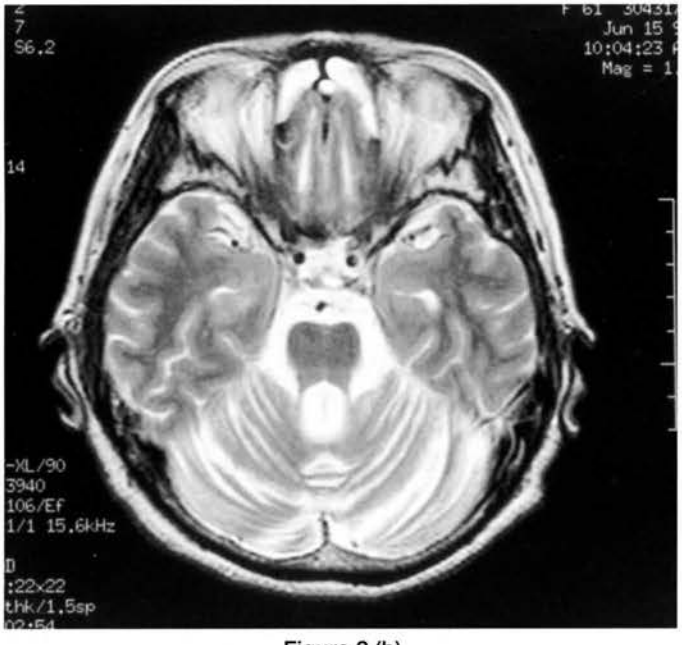

Figure 2 (b)

Figure 2
(a) MRI, TI and T2 weighted images. Only slight atrophy is revealed in cerebellum and pons in spite of remarkable decrease of blood flow.

two cousins also suffered from MJD.

On admission to our hospital, she showed disturbance of eyeball movement, horizontal nystagmus, dysarthria, pyramidal tract sign (stronger in right than in left), atrophy of extremity muscel, ataxia, dysesthesia, generalized hyperreflexion without rigidity.

Laboratory data included following: leucocyte count 5,400/mm^3, red cell count $441x10^4/mm^3$, hemoglobin concentration 13.3g/dl, TP 7.1 g/dl, A/G 1.96, GOT 19 IU/l, GPT 16 IU/l, LDH 375 IU/l, CPK 107 IU/l, gamma GTP 11 IU/l, Na 145 mEq/l, K 4.2 mEq/l, Cl 106 mEq/l, BUN 13 mg/dl, creatinine 0.5 mg/dl, uric acid 5.0 mg/dl, Ca 9.4 mg/dl, P 4.5 mg/dl, total cholesterol 247 mg/dl, CRP 0.1 mg/dl, blood sugar 100 mg/dl, triglyceride 103 ml/dl, beta lipoprotein 404 mg/dl. Urinalysis was not remarkable.

After intravenous bolus administration of 740 MBq of Tc-99m ethyl cysteinate dimer (Tc-99m ECD), using Matsuda's method we measured mean cerebral blood flow and regional cerebral and cerebellar blood flow non-invasively in this patient. Brain SPECT was performed using a three-head gamma camera equipped with low-energy high-resolution fan-beam collimators (Prism 3000, Picker, Cleveland, OH). The projection data were obtained in a 128× 128 format for 24 angles in a 120 degrees arc for each detector with 30 sec per angle. Butterworth-Wiener (order 8, cutoff of 1 cycle/cm) and Ramp filters were used for prefiltering and reconstruction, respectively. The reconstructed images were corrected for attenuation with Chang's first-order method, using an attenuation coefficient equal to 0.09.

Perfusion SPECT images are shown in **Figure 1 (a, b)**. Note decreased cerebellar blood flow in **Figure 1 (a)**, which is blue in color, indicated by the arrows in sagittal images. In **Figure 1 (b)**, the measured blood flow in regions of interest is shown. In cerebellar areas, flow is 37.97 ml/100g/min in the right and 35.42 in the left. However, blood flow in cerebral cortical area is between 41.14 and 60.17, and higher than cerebellar blood flow. Usually it is well known that cerebellar blood flow is 10-15 ml/100g/min higher than cerebral cortex.

MRI, T1- and T2-weighted images, are shown in **Figure 2 (a, b)**, and both images revealed slight atrophy of cerebellum and pons.

Discussion

Machado-Joseph disease (MJD) is an autosomal dominant spinocerebellar degenerative disease first described among the Portuguese and their descendants in New England and California. Subsequently, MJD has been found in families from many countries including Japan.

In brain perfusion images, using Patlak's method, it is quite easy, safe and nontraumatic to measure blood flow of each region of interest in cerebral cortex and cerebellum [7]. Until recently only PET study and other SPECT methods allowed us to measure cerebral blood flow, but both methods necessitate to withdraw arterial blood continuously. Previous investigators reported decreased blood cerebellar flow in patients with spinocellebellar degenerative diseases[2-5]. In MJD report on measurement of brain blood flow rare.

And we would like to point out that in this patient decrease of cerebellar blood flow is remarkable, although MRI images revealed only slight atrophy of cerebellum and pons. Therefore, measurement of brain perfusion and the detection of decrease of cerebellar blood flow might be useful in the diagnosis, evaluating and follow up of MJD.

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