Annals of Nuclear Medicine Vol. 16, No. 1, 71–74, 2002

A case of general paresis showing marked treatment-associated improvement of cerebellar blood flow by quantitative imaging analysis

Masayuki MORIKAWA,* Jun KOSAKA,* Teruhiko IMAI,** Hiroyoshi OHSAWA,* Junzo IIDA* and Toshifumi KISHIMOTO*

*Departments of *Psychiatry and **Oncoradiology, Nara Medical University*

We describe a patient with general paresis who developed progressive dementia and a cerebellar syndrome including wide-based gait, slurred speech, and intention tremor. Quantitative analysis by means of a Patlak plot of single-photon emission computed tomography (SPECT) with ^{99m}Tc-ethyl cysteinate dimer showed generally low blood flow in the cerebrum and the cerebellum. After antisyphilitic therapy, blood flow in the brain, especially in the cerebellum, improved noticeably, as did the cognitive disorder and the cerebellar syndrome.

Key words: general paresis, cerebellar ataxia, cerebellar blood flow, single-photon emission computed tomography (SPECT), blood flow quantitation

INTRODUCTION

GENERAL PARESIS is the only syphilitic syndrome in which spirochetes can be demonstrated in the tissues of the brain; the pathology of general paresis is thought to result directly from their presence.[1,2] These pathologic changes affect the meninges and cerebral vasculature.[1] While general paresis is rare in Japan today, occasional cases are still reported, increasingly including descriptions of brain imaging findings. Computed tomography (CT) and magnetic resonance imaging (MRI) in patients with general paresis both show diffuse cerebral atrophy.[2] Single-photon emission computed tomography (SPECT) has been reported to show a significant bilateral reduction in cerebral blood flow, especially in the frontal and temporal cortices. In some of these cases, cerebral blood flow has been found to improve after antisyphilitic therapy coinciding with improvement in the mental disorder.[2]

The quantitation method of Matsuda et al.,[3–5] which uses a Gjedde-Patlak plot,[6] has proven useful for non-invasive SPECT measurement of cerebral blood flow with ^{99m}Tc-ethyl cysteinate dimer (^{99m}Tc-ECD); blood sampling is not required. We used this analytic method in a rare case where a reduction in cerebellar blood flow demonstrated by SPECT in a patient with general paresis improved noticeably after antisyphilitic therapy; clinical cerebellar symptoms also notably abated.

CASE REPORT

A 39-year-old man was admitted to our psychiatric ward in April 1998 because of progressive dementia and cerebellar ataxia. He was unmarried and had a history of many sexual partners during his twenties. In April 1997 he retired from the company where he had steadily worked. He then had several briefly held jobs. Beginning in December 1997 he remained alone at home. Early in January 1998 he developed an intention tremor of the hand and an equilibrium disorder that sometimes caused falls in flat, unobstructed areas. In addition, he lost interest in his surroundings and gradually became increasingly forgetful and slow in his movements.

On admission the patient was disoriented, and showed indifference and easy distractibility. Mental testing results were consistent with dementia without delusions or hallucinations. In the revised Wechsler adult intelligence scale (WAIS-R), the full-scale intelligence quotient (IQ)

Received February 8, 2001, revision accepted October 31, 2001.

For reprint contact: Masayuki Morikawa, M.D., Ph.D., Department of Psychiatry, Nara Medical University, Shijo-cho 840, Kashihara 634–8522, JAPAN.

E-mail: mmorikaw@naramed-u.ac.jp

was 53 (verbal IQ, 69; performance IQ, <46), indicating a discrepancy between verbal and performance scores. The Bender gestalt test (BGT) score was 68 points. These findings suggested an organic mental syndrome. Neurologic examinations disclosed an Argyll Robertson pupil and mildly increased deep tendon reflexes in the upper limbs. Romberg's test was negative. A degree of incoordination was present, including a wide-based gait, slurred speech, and intention tremor of the hands. The rhythm on repeated knee patting was irregular, and patting of a designated spot showed excessive variability, reflecting a cerebellar syndrome.

General physical examination and routine laboratory tests were normal, except that the serum Venereal Disease Research Laboratory (VDRL) test was positive (titer, 1: 64) and the Treponema pallidum hemagglutination assay (TPHA) test was positive (titer, 1: >20480). An enzyme-linked immunosorbent assay for human immunodeficiency virus (HIV) was negative. In cerebrospinal fluid (CSF), the VDRL test was positive with a 1:2 titer, and the TPHA test was positive with a 1: >20480 titer. The fluorescent treponemal antibody absorption (FTA-ABS) test was positive in both CSF and serum. CSF examination revealed a high cell count (9/mm^3) and a slightly increased protein content (60 mg/d*l*). The glucose content and the opening pressure were normal. CSF tests for viruses and nontreponemal bacteria were negative. Electrocardiogram and chest X-ray revealed normal. Chest CT did not reveal any aortic lesions, indicating cardiovascular syphilis. The Vista 1.5-tesla MR scanner was used to obtain T1- and T2-weighted spin-echo images (TR = 3000 msec, TE = 100 msec, NSA = 1). Brain MRI revealed mild, diffuse cerebral atrophy and dilation of the lateral ventricles. Small ischemic lesions were seen in both frontal lobes (Fig. 1). The electroencephalogram (EEG) was abnormal, showing low voltage and slowing of the basic rhythm, 6 to 7 Hz.

The patient was diagnosed with general paresis according to the criteria of Hooshmand et al.[7] on the basis of clinical and laboratory findings. He was treated intramuscularly with 1 million units of potassium benzyl penicillin, twice daily for 4 weeks. On the day after starting the therapy, a Herxheimer reaction occurred. Six weeks later VDRL and TPHA tests in CSF were unchanged, but the cell count in CSF had normalized (1/mm^3). Other CSF tests were normal. Antisyphilitic therapy improved the patient's coordination, as evident from decreased intention tremor, improved gait and speech patterns, and the knee patting test. Mental status gradually improved, although MRI findings in the brain were unchanged. The EEG showed improvement, including a normal alpha rhythm (9 to 10 Hz). By the WAIS-R, full-scale IQ was 84 (verbal, 106; performance, 61), and the BGT score was 31 points. About 1 year after treatment, the WAIS-R showed a full-scale IQ of 92 (verbal, 113; performance, 68).

SPECT, with ^{99m}Tc-ECD (600 MBq), was carried out by means of a gamma camera (MULTISPECT 3; Siemens, Erlangen, Germany) with parallel-type, low-energy, high-resolution collimators. SPECT performed immediately after the start of therapy demonstrated low blood flow in the cerebrum (mean cerebral blood flow [mCBF], 41.65 m*l*/100 g/min), the bilateral frontal lobes (33.9 m*l*/100 g/min), the bilateral temporal lobes (43.6 m*l*/100 g/min) and the cerebellum (63.1 m*l*/100 g/ min; Fig. 2a). When SPECT was repeated 6 months after the start of therapy, CBF had significantly improved (mCBF, 59.3 m*l*/100 g/min); flow had improved more strikingly in the cerebellum (82.6 m*l*/100 g/min; Fig. 2b). Blood flow in the bilateral frontal lobes (57.9 m*l*/100 g/min) and the bilateral temporal lobes (54.8 m*l*/100 g/min) had also improved. Improvement of cerebellar blood flow was associated with decreasing severity of manifestations of the cerebellar syndrome.

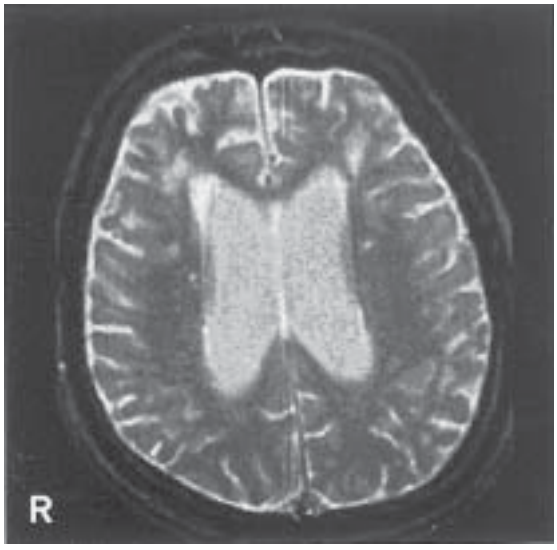

Fig. 1 Brain magnetic resonance imaging (T2-weighted image) at the level of the lateral ventricle reveals mild, diffuse cerebral atrophy and dilation of the lateral ventricles. Small ischemic lesions are seen in both frontal lobes.

DISCUSSION

We have described a patient with general paresis whose treatment was associated with noticeably improvement in cerebellar blood flow on SPECT. SPECT analysis employed a quantitative approach, the method of Matsuda et al.,[3–5] which is a useful means of non-invasive cerebral flow measurement with ^{99m}Tc-ECD that does not require blood sampling. This method enabled us to detect a change in cerebellar blood flow that could not be detected by the traditional method of relative comparison, and the method was reliable with repeated SPECT observation. After antisyphilitic therapy, brain MRI findings were unchanged; in contrast, the patient's cognitive disorder and cerebellar syndrome improved, EEG findings nor-

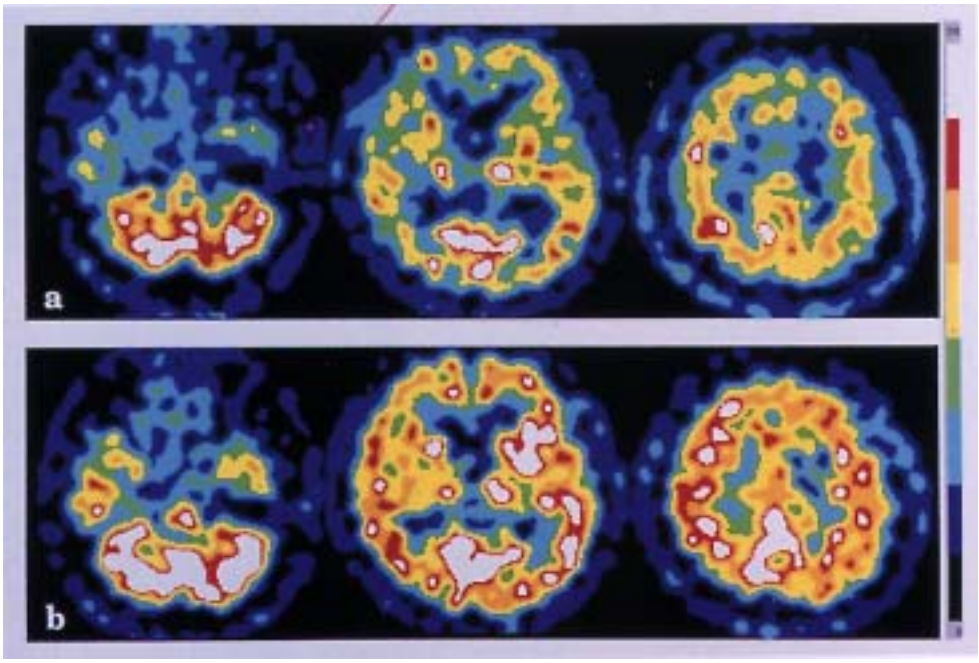

Fig. 2 Quantitative single-photon emission computed tomography (SPECT) images at the level of the cerebellum (left), basal ganglia (middle), and lateral ventricle (right). a: SPECT immediately after initiation of therapy reveals generally low blood flow in the cerebrum and the cerebellum (April 1998). b: Six months after initiation of therapy, blood flow shows significant improvement, which is especially marked in the cerebellum (October 1998).

malized, and SPECT revealed improvement in blood flow in the cerebrum and the cerebellum. These findings are plausible because lesions of the brain in general paresis are closely related to cerebral vessels,[1] and treatment improves the vascular pathology.

In the light of improvement on brain SPECT, the blood flow in the cerebrum and cerebellum might have reflected the improvement in the brain ischemia after antisyphilitic therapy. Brain function on the reversible part is considered to have gradually improved after the improvement in blood flow. The irreversible part might have left the sequelae, demonstrating the discrepancy between the WAIS-R verbal and performance IQ scores (verbal > performance IQ score). Concerning the details of improvement, it could be speculated that the improvement in cerebellar symptoms was in agreement with that in cerebellar blood. And remarkable improvement (more than 6 points in the scaled score [SS]) was shown in Digit Span, Arithmetic, Similarities and Picture Completion in 11 WAIS-R subtests. Digit Span, Arithmetic and Picture Completion imply improvement in concentration and memory in part, and Similarities implies improvement in grasping relationships, ability at conceptual formation and ability to judge. Moderate improvement (3–5 points in SS) was shown in Vocabulary and Comprehension, which imply the improvement in memory, organization and anticipation. On the other hand, Slight improvement (2 points in SS) was shown in Information and the 4 other performance subtests, and, generally, performance IQ includes visual organization-visual motor coordination.

Therefore, it was supposed that there was partial improvement in "failure to organize multiple memory items" which is caused by frontal lobe malfunction, caused by the treatment. Namely, the impairment is in the dementia symptoms due to the impairment of the association mechanism, and related to the impairment of the neuronal circuit under the cortex of the frontal lobe, which connects the subcortex with the cortex of the frontal lobe. And the improvement in dementia symptoms in this case might be due to the improvement in blood flow in the frontal lobe on SPECT, so that SPECT with quantitative analysis is a useful method for assessing brain dysfunction in general paresis.

REFERENCES

1. Lishman WA. *Organic Psychiatry: the Psychological Consequences of Cerebral Disorder*. (3rd ed) Blackwell, Oxford, England, 1998: 336–346.
2. Kawai N, Baba A, Mizukami K, Sakai T, Shiraishi H, Koizumi J. CT, MR, and SPECT findings in a general paresis. *Comput Med Imaging Graph* 1994; 18: 461–465.
3. Matsuda H, Tsuji S, Shuke N, Sumiya H, Tonami H, Hisada K. A quantitative approach to technetium-99m hexamethyl propylene amine oxime. *Eur J Nucl Med* 1992; 19: 195–200.

4. Matsuda H, Yagishita A, Tsuji S, Hisada K. A quantitative approach to technetium-99m ethyl cysteinate dimer: a comparison with technetium-99m hexamethyl propylene amine oxime. *Eur J Nucl Med* 1995; 22: 633–637.
5. Takeuchi R, Matsuda H, Yonekura Y, Sakahara H, Konishi J. Noninvasive quantitative measurements of regional cerebral blood flow using technetium-99m-L,L-ECD SPECT activated with acetazolamide: quantification analysis by equal-volume-split ^{99m}Tc-ECD consecutive SPECT method. *J Cereb Blood Flow Metab* 1997; 17: 1020–1032.
6. Patlak CS, Blasberg RG. Graphical evaluation of blood-to-brain transfer constants from multiple-time uptake data. Generalizations. *J Cereb Blood Flow Metab* 1985; 5: 584–590.
7. Hooshmand H, Escobar MR, Kopf SW. Neurosyphilis. A study of 241 patients. *JAMA* 1972; 219: 726–729.