

Brain perfusion SPECT in neuro-Behçet's disease: Discordance between Tc-99m-HMPAO and Tc-99m-ECD

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A patient with neuro-Behçet's disease was studied with both Tc-99m-HMPAO and Tc-99m-ECD brain perfusion SPECT during the same time period. In Tc-99m-HMPAO SPECT, focal high uptake was observed in the left basal ganglia where MRI depicted abnormal signal intensity. Conversely, Tc-99m-ECD SPECT did not show corresponding high uptake, but demonstrated rather low uptake in contrast to the Tc-99m-HMPAO SPECT. This case suggests that Tc-99m-HMPAO and Tc-99m-ECD may show discordant distribution in inflammatory brain disease such as neuro-Behçet's disease.

Key words: neuro-Behçet's disease, brain perfusion SPECT, Tc-99m-ECD, Tc-99m-HMPAO

INTRODUCTION

BEHÇET'S DISEASE is a chronic systemic inflammatory disease characterized by aphthous ulcers in oral and genital regions, skin eruptions, and ocular involvement such as iridocyclitis with hypopyon.^{1,2} Excepting these main lesions, Behçet's disease may involve many other organs, showing various clinical manifestations. Among these manifestations, a neurological one related to the involvement of the central nervous system is called neuro-Behçet's disease, which is important for the prognosis of this disease.³⁻⁵ In evaluating the involvement of the central nervous system, magnetic resonance imaging (MRI) has been playing a main role because of its high sensitivity in detecting the lesions involved.^{6,7} As for single photon emission computed tomography (SPECT) of brain perfusion, Tc-99m-hexamethyl propyleneamine oxime (Tc-99m-HMPAO) SPECT has been reported to be useful. It could depict perfusion abnormality associated with neuro-Behçet's disease, which could not be demonstrated on MRI.⁸ Since histopathological findings in neuro-Behçet's disease such as perivascular cell infiltration, gliosis, de-

myelination, and venous thrombosis were thought to originate chiefly in vasculitis,^{3,5,6,9} regional cerebral blood flow could be altered by neuro-Behçet's disease. In this respect, brain perfusion SPECT could be an examination of choice, providing valuable information regarding regional cerebral blood flow.

In this paper, a case of neuro-Behçet's disease is described, in which cerebral perfusion was evaluated with both Tc-99m-HMPAO and Tc-99m-ethyl cysteinate dimer (Tc-99m-ECD) SPECT. Although these SPECT examinations were carried out during the same time period, SPECT findings for the two tracers conflicted with each other. This case suggests that these tracers may show different distribution in inflammatory brain disease such as neuro-Behçet's disease.

CASE REPORT

A 40-year-old female admitted to the hospital for progressive gait and speech disturbances deteriorated over one month. Since nine years ago, she had been treated as having Behçet's disease in the complete form with three chief manifestations, iridocyclitis with hypopyon, skin eruption like erythema nodosum, and recurrent oral and genital aphthous ulcers. On admission, right hemiplegia and dysarthria were observed neurologically. In blood-analysis, positive C-reactive protein was revealed,

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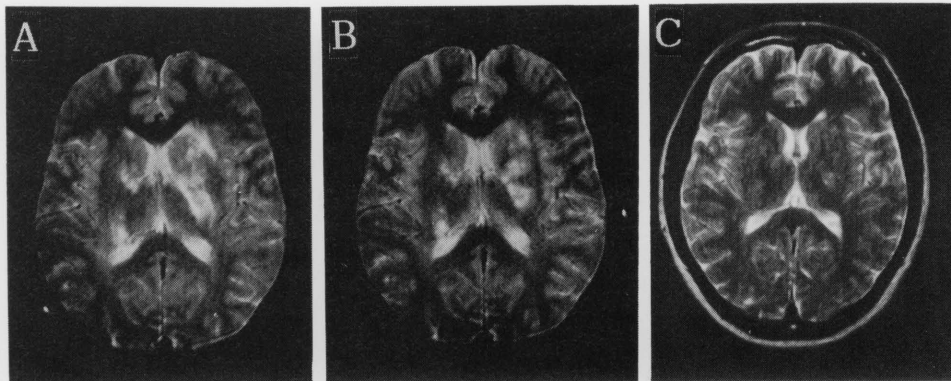


Fig. 1 Serial T2 weighted MRI images (TR = 2000 msec/TE = 90 msec for A and B, TR = 3500 msec/TE = 100 msec for C). On the first hospital day, disseminated abnormal high intensity lesions were demonstrated especially in the left basal ganglia, internal capsule, and corona radiata (A). These abnormal intensity lesions were still observed on the eighth hospital day (B). After prednisolone therapy, follow-up MRI performed 5 months later revealed marked improvement (C).

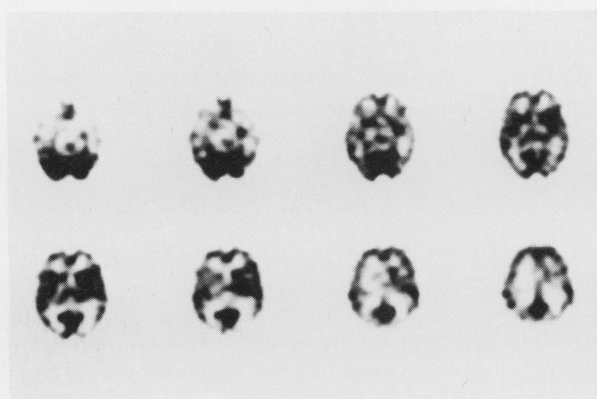


Fig. 2 Tc-99m-HMPAO SPECT performed on the first hospital day showed high uptake in the left basal ganglia extending to the left frontal cortex.



Fig. 3 Tc-99m-ECD SPECT performed on the fifth hospital day did not show corresponding high uptake in the left basal ganglia, but showed rather low uptake in contrast to the Tc-99m-HMPAO SPECT.

indicating the existence of active inflammation. Cerebrospinal fluid examination showed increases in the number of cells (542/mm³, mononuclear cells 28%), glucose (54 mg/dl), and protein (60 mg/dl). Radiograph computed tomography (Radiograph CT), MRI, and SPECT with Tc-99m-HMPAO were performed on the first hospital day. Radiograph CT did not reveal any abnormality. The T2 weighted image (TR = 2000 msec/TE = 100 msec) of MRI performed on a unit with a 0.5 T superconducting magnet, however, depicted multiple abnormal high signal intensity, especially in the left basal ganglia, internal capsule, and corona radiata (Fig. 1-A).

A Tc-99m-HMPAO SPECT study was performed as follows. Twenty min after injection with Tc-99m-HMPAO (740 MBq), sixty-four projection data were acquired in a 128 × 128 matrix (pixel size: 2 × 2 mm), in a 360-degree step rotation mode with an acquisition time of 25 sec each, by means of a triple head digital gamma camera equipped

with low energy high resolution collimators. The in-plane spatial resolution of this gamma camera was 6.1 mm FWHM. The image reconstruction was performed by a filtered back-projection method with a Ramp filter after pre-processing with a Butterworth filter (cutoff frequency, 0.5 cycle/cm; order 10) to obtain 6 mm thick transaxial images. Tc-99m-HMPAO SPECT did not show any apparent decrease in regional cerebral blood flow, but high tracer fixation was obviously delineated in the left basal ganglia extending to the left frontal cortex, where abnormal signal intensity was depicted on MRI (Fig. 2). Cerebral angiography performed on the third hospital day did not show any abnormality, indicating that the main trunks and branches were not involved. Tc-99m-ECD SPECT was performed on the fifth hospital day with the same data acquisition method as in the Tc-99m-HMPAO SPECT except for the injected dose (600 MBq for Tc-99m-ECD). In Tc-99m-ECD SPECT, left basal ganglia, where Tc-

99m-HMPAO SPECT showed high uptake, did not show corresponding high uptake but demonstrated rather decreased uptake (Fig. 3). The patient's condition and clinical manifestations had not changed significantly between the two SPECT examinations.

On the basis of multiple disseminated lesions depicted on MRI, cerebrospinal fluid abnormality, and a history of Behçet's disease, a diagnosis of neuro-Behçet's disease was made. From the sixth hospital day, the patient began to receive prednisolone therapy. The T2 weighted image (TR = 2000 msec/TE = 100 msec) of follow-up MRI performed on the eighth hospital day still showed similar abnormal finding to the previous one (Fig. 1-B), but the clinical manifestations had gradually improved after the prednisolone therapy was begun, and cerebrospinal fluid examination results returned to normal on the eighteenth hospital day. The T2 weighted image (TR = 3500 msec/TE = 100 msec) of follow-up MRI performed after five months showed marked improvement (Fig. 1-C), indicating amelioration of the lesions and the effectiveness of prednisolone therapy.

DISCUSSION

Neuro-Behçet's disease produces a subacute hemorrhagic and necrotizing meningo-encephalitis.³ Pathologically, exudative inflammatory change in vessel walls, gliosis, demyelination, and microthrombi are observed.^{5,9,10} These pathological changes most typically affect the hypothalamus and brain stem. In addition to these structures, basal ganglia and internal capsule are also commonly affected, as seen in this case.^{3,11}

In this case, Tc-99m-HMPAO showed high uptake in the basal ganglia where MRI depicted abnormal signal intensity. This high uptake could represent reactive hyperemia caused by the inflammatory changes,⁹ although the possibility of spurious "hyperfixation" of Tc-99m HMPAO¹² could not be denied. In contrast to Tc-99m-HMPAO, Tc-99m-ECD did not show corresponding high uptake. Although there was an interval of four days between the two SPECT examinations, a change in hemodynamics was unlikely to be the cause of this discordance. Since SPECT examinations were performed after about one month from the onset of clinical manifestations, the disease was thought to be already in a subacute phase at this time. Considering the histopathological features of neuro-Behçet's disease analogous to subacute encephalitis,³ an acute change in hemodynamics in this phase was unlikely. In fact, the clinical manifestations were stable and no obvious change was observed in this short interval. And MRI performed before and after this interval did not show any apparent differences.

Tc-99m-ECD has been developed as a new cerebral blood flow tracer which has superior labeling stability to Tc-99m-HMPAO. Both tracers are reported to show similar brain distribution reflecting regional cerebral blood

flow with the exception of luxury perfusion syndrome in subacute cerebral infarction.^{13,14,15} Since the retention mechanism of Tc-99m-ECD is thought to be related to its metabolism in brain tissue,¹⁶ it is likely that Tc-99m-ECD could not be retained in the damaged neuronal tissue associated with impaired metabolism even if high perfusion existed there. Being independent of the etiology, a perfusion/metabolism mismatch could cause failure of Tc-99m-ECD retention. The discordance between Tc-99m-HMPAO and Tc-99m-ECD seen in this case could be explained by the same mechanism expected for luxury perfusion syndrome, although the initially affected regions returned almost to normal on MRI. In subacute stroke, the region showing luxury perfusion syndrome may well lead to infarction, but luxury perfusion syndromes associated with reversible neurological deficits were also reported.^{17,18} In these cases, hyperperfusion was thought to come from vasodilation of noninfarcted vessels caused by local cerebral hypoxia. In the present case, local hypoxia or acidosis induced by the inflammatory changes originating in neuro-Behçet's disease may have caused similar hyperperfusion and impairment of metabolism. These possible pathophysiological changes could be responsible for the discordance between Tc-99m-ECD and Tc-99m-HMPAO. To prove this hypothesis, the dynamic SPECT technique would be valuable. It could depict initial Tc-99m-ECD uptake and subsequent washout due to the failure of the retention mechanism. Further clinical experience would clarify the implications of Tc-99m-ECD washout as a marker of neuronal tissue damage.

REFERENCES

1. Behçet H. Ueber rezidivierende, aphthöse, durch ein virus verursachte geschwüre am mund, am auge und de genitalien. *Dermato Wehnschr* 105: 1152, 1937.
2. Chajek T, Fainaru M. Behçet's disease. Report of 41 cases and a review of the literature. *Medicine* 54: 179, 1975.
3. Bousser MG, Rougemont D, Youl BD, Wechsler B. Neurological manifestations of Behçet's disease. *J Mal Vasc* 13: 231-234, 1988.
4. Campanile S, Amore M, Cerisoli M, Agati R, Campanile A. Neurological complications in Behçet's disease. *Riv Patol Nerv Ment* 105: 229-237, 1984.
5. Sugihara H, Mutoh Y, Tsuchiyama H. Neuro-Behçet's syndrome: report of two autopsy cases. *Acta Pathol Jpn* 19: 95-101, 1969.
6. Ferrer C, Cervello A, Barranco MJ, Carrasco R, Cervera E, Navarro V, et al. Behçet's syndrome with neurological involvement: value of magnetic resonance. *Neurologia* 7: 194-197, 1992.
7. Fukuyama H, Kameyama M, Nabatame H, Takemura M, Nishimura K, Fujisawa I, et al. Magnetic resonance images of neuro-Behçet syndrome show precise brain stem lesions. Report of a case. *Acta Neurol Scand* 75: 70-73, 1987.
8. Watanabe N, Seto H, Sato S, Simizu M, Wu Y, Kageyama

- M, et al. Brain SPECT with neuro-Behcet disease. *Clin Nucl Med* 20: 61–64, 1995.
9. Sugihara H, Ichinose T, Tsuchiyama H. Neuro-Behçet's syndrome: report of an autopsy case. *Acta Pathol Jpn* 21: 563–569, 1971.
 10. Koga M, Suetsugu M, Umeda Y. An autopsy case of chronic nodular encephalomyelitis simulating neuro-Behcet syndrome. *Jpn J Psychiatry Neurol*. 40: 669–676, 1986.
 11. Mrabet A, Saidi H, Touibi S, Kchouk M, Laouiti H. Value of cerebral tomodensitometry in Behçet's disease with neurological manifestations (50 cases). *Tunis Med* 71: 523–528, 1993.
 12. Sperling B, Lassen NA. Hyperfixation of HMPAO in subacute ischemic stroke leading to spuriously high estimates of cerebral blood flow by SPECT. *Stroke* 24: 193–194, 1993.
 13. Leveille J, Demonceau G, Walovitch RC. Intrasubject comparison between technetium-99m-ECD and technetium-99m-HMPAO in healthy human subjects. *J Nucl Med* 33: 480–484, 1992.
 14. Moretti J, Defer G, Cinotti L, Cesaro P, Vigneron N, Pethe C. Comparative tomoscintigraphic study of strokes using Tc-99m-ECD, Tc-99m-HM-PAO and I-123-IMP. *Eur J Nucl Med* 12: 311, 1988.
 15. Shishido F, Uemura K, Murakami M, Inugami A, Ogawa T, Higano S, et al. Arterial clearance and cerebral uptake of Tc-99m ECD in patients with cerebrovascular disease compared with PET. *KAKU IGAKU (Jpn J Nucl Med)* 29: 27–35, 1992.
 16. Walovitch RC, Cheesman EH, Maheu LJ, Hall KM. Studies of the retention mechanism of the brain perfusion imaging agent ^{99m}Tc-bicisate (^{99m}Tc-ECD). *J Cereb Blood Flow Metab* 14: S4–11, 1994.
 17. Higashi S, Matsuda H, Fujii H, Ito H, Yamashita J. Luxury perfusion syndrome confirmed by sequential studies of regional cerebral blood flow and volume after extracranial to intracranial bypass surgery: case report. *Neurosurgery* 25: 85–89, 1989.
 18. Strashun A, Dunn EK, Sarker SS, Abel W, Hotson G, Scalfani S. Reversible increased technetium-99m-HMPAO cerebral cortical activity: a scintigraphic reflection of luxuriant hyperperfusion. *J Nucl Med* 33: 117–119, 1992.