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## Technetium-99m-HMPAO SPECT and MRI of Brain in Patients with Neuro-Behçet's Syndrome

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Involvement of the brain is one of the most important complications of Behçet's disease (BS). It is difficult to diagnose, however, because of the lack of effective imaging methods. **Methods:** Thirteen BS patients with neuropsychiatric symptoms or signs [Neuro-Behçet's syndrome (NBS)] were included in this study. We combined two routine brain imaging modalities—brain SPECT with <sup>99m</sup>Tc-hexamethyl propyleneamine oxime (HMPAO) and brain MRI—with clinical manifestations to diagnose brain involvement. **Results:** Technetium-99m-HMPAO brain SPECT findings were abnormal in 100% (13/13) of patients. Brain MRI findings were abnormal in 31% (4/13) of patients. Gray matter was involved more commonly than white matter. In the gray matter, the cerebral cortex was the most commonly involved area and the cerebellum was the least commonly involved area in NBS. **Conclusion:** SPECT is a more sensitive and useful tool in detecting brain involvement in NBS patients compared with brain MRI. The combination of HMPAO and MRI is necessary to detect brain lesions in both gray and white matter in NBS.

**Key Words:** MRI; SPECT; Behçet's syndrome

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**B**ehçet's syndrome (BS) is a rare disorder of unknown etiology and is characterized by recurrent oral and genital aphthous ulcers, ocular inflammation and neurological involvement (1). Neurological complications occur in approximately 10%-25% of all patients (2). Common neurological manifestations include cerebral venous thrombosis and cerebrovascular

accident (3). The diagnosis and management of BS with neuropsychiatric symptoms or signs [neuro-Behçet's syndrome (NBS)] are critical (4,5). Due to the lack of effective imaging techniques, however, diagnosis of brain involvement in NBS patients is difficult.

MRI has been used to detect structural lesions in NBS patients (6-8). The most typical MRI findings in NBS are brain lesions of high signal intensity on T2-weighted images (6-8). In a significant proportion of patients with clinically evident brain involvement, however, brain MR images are normal (9). SPECT brain imaging with <sup>99m</sup>Tc-hexamethyl propyleneamine oxime (HMPAO) is an alternative modality that is used to assess regional cerebral blood flow (rCBF). Compared with MRI, <sup>99m</sup>Tc-HMPAO brain images have proven to be more accurate in detecting brain involvement in autoimmune connective tissue disease and to have better correlation with clinical diagnosis (10-13).

In this study, we investigated the potential of <sup>99m</sup>Tc-HMPAO brain images compared with brain MRI to detect cerebral anomalies, including lesions of the gray and white matter, in BS patients with neuropsychiatric symptoms or signs.

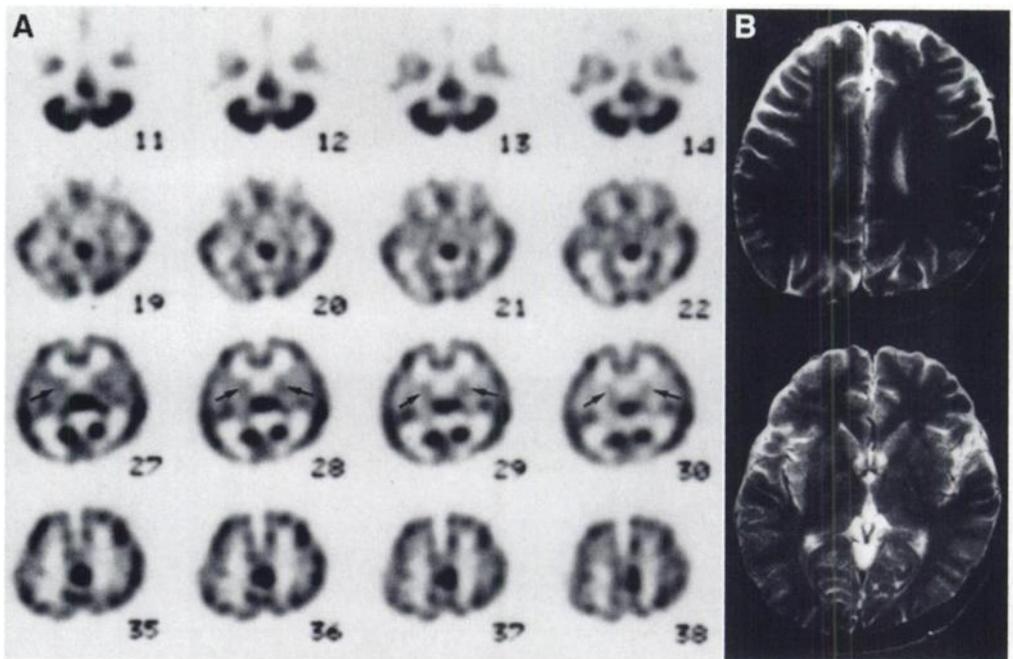
### MATERIALS AND METHODS

#### Patients

Thirteen patients (7 women, 6 men; aged 28-62 yr) with BS were enrolled in this study. The diagnosis of BS was established on the basis of the criteria of the Behçet's Disease Research Committee of Japan (14): the presence of a triple-symptom complex, including recurrent aphthous stomatitis, genital ulcers and relapsing uveitis. Besides this triad, additional features, including synovitis, cutaneous vasculitis and meningoencephalitis, are recognized

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**FIGURE 1.** (A) Technetium-99m-HMPAO brain SPECT in 51-yr-old woman reveals bilateral and multiple hypoperfusion areas in cerebral cortex and basal ganglia (arrows). (B) Brain MR image looks normal.

as part of the syndrome. A neurological consultant evaluated the patients for neuropsychiatric symptoms or signs. Neuropsychiatric symptoms or signs associated with NBS were defined as those that could not be attributed to any other cause (such as uremia, hypertension or infection). Brain  $^{99m}\text{Tc}$ -HMPAO and MRI were arranged on the same day as the neurologic assessment to detect cerebral anomalies.

#### Technetium-99m-HMPAO Brain Images

Technetium-99m-HMPAO was prepared from a freeze-dried kit (Ceretek; Amersham International, Little Chalfont, Bucks, United Kingdom) by the addition of approximately 1250 MBq freshly eluted  $^{99m}\text{Tc}$ -pertechnetate to 5 ml saline solution. The solution was injected no more than 30 min after preparation. Patients were placed in a supine position in a quiet room with dimmed lights and were allowed to relax with their eyes closed for 15 min before intravenous administration of 1110 MBq (30 mCi)  $^{99m}\text{Tc}$ -HMPAO. After  $^{99m}\text{Tc}$ -HMPAO injection, patients were asked not to move or talk for at least 10 min. The scan was obtained 90–120 min after injection. During imaging, patients were in the supine position on the imaging table with forehead and chin restrained. The scanning equipment consisted of a rotating, large-field-of-view, dual-head gamma camera (Helix HR; Elscint Ltd., Haifa, Israel) fitted with a fanbeam collimator. Data were collected in a  $64 \times 64$  matrix with 1.3 zooming, through a  $360^\circ$  ( $180^\circ$  for each camera head) rotation at three intervals, for 25 sec per arc interval. Approximately 7.5 million counts were acquired. The SPECT images (coronal, sagittal and transaxial sections) were reconstructed using a Metz filter (power 5.00), backprojection and attenuation correction. Transaxial sections were reoriented parallel to the base of the brain to obtain sagittal and coronal reconstructions. The spatial resolution of the camera with fanbeam collimator was 6.3 mm FWHM. To identify local areas of abnormal hypoperfusion, the brain SPECT images were interpreted visually by two experienced observers blinded to the clinical information. Abnormal findings on  $^{99m}\text{Tc}$ -HMPAO brain imaging consisted of heterogeneous rCBF in the gray matter of the cerebral cortex and basal ganglia/thalamus, with focal hypoperfusion or visible asymmetry (Figs. 1 and 2). Otherwise, the findings were considered to be normal (Fig. 3) (12,13,15).

#### Brain MRI

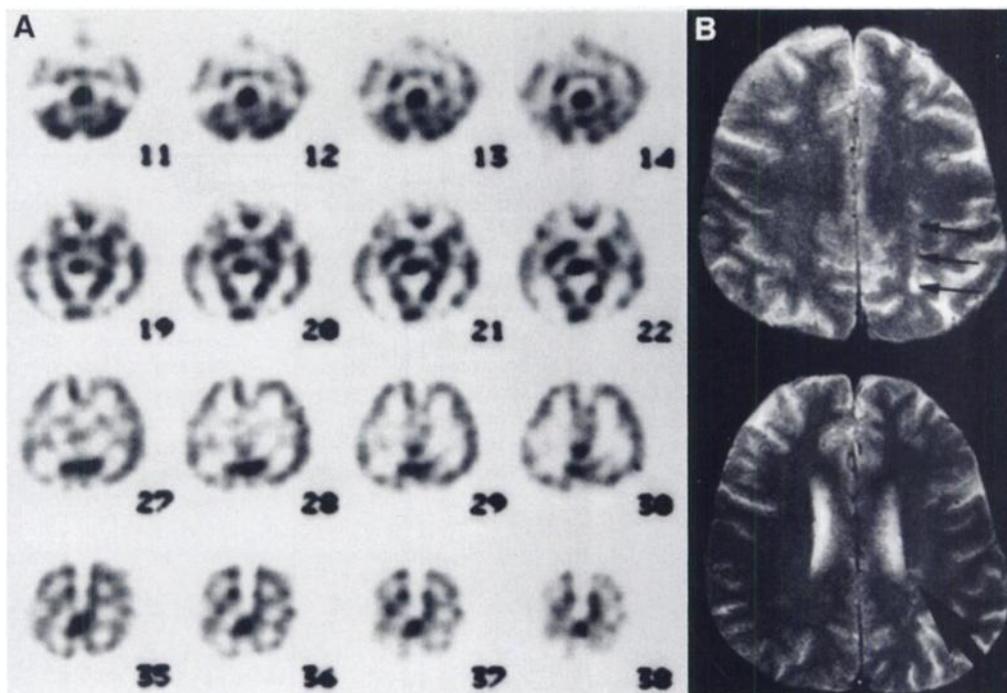
Contrast enhanced brain MR images were obtained using a Vista MR2055 HP 1.0-T scanner (Picker International, Cleveland, OH), with a spin-echo T1-weighted sequence of 500–750/20/1–2 (repetition time/echo time/number of excitations), a proton density-weighted sequence of 2000–3000/20/1–2 and a T2-weighted sequence of 2000–3000/80–100/1–2. The section thickness was 5–7 mm with an intersection gap of 1 mm. To detect local areas of abnormal signal intensity, the brain MR images were interpreted visually by two experienced observers blinded to the clinical information. Abnormal findings of brain MRI consisted of foci of high signal intensity on T2-weighted images in the white matter of the brain stem, basal ganglia, cerebral hemispheres and cerebellum (Fig. 2). Otherwise the findings were considered normal (Fig. 1) (16–19).

#### RESULTS

The detailed data are presented in Table 1. The results showed that  $^{99m}\text{Tc}$ -HMPAO brain SPECT was abnormal and hypoperfusion lesions in gray matter were observed in 100% (13/13) of the patients. No white matter abnormalities were found on  $^{99m}\text{Tc}$ -HMPAO brain SPECT. Brain MRI findings were abnormal, and high-signal-intensity lesions were observed in the white matter in 31% (4/13) of the patients. No gray matter abnormalities were found on brain MRI. Gray matter was involved more commonly than white matter: 12 patients with lesions in the cerebral cortex, 6 patients with lesions in the basal ganglia and 2 patients with lesions in the cerebellum.

#### DISCUSSION

BS, originally described as a triple-symptom complex consisting of oral aphthous ulceration, genital ulceration and hypopyon iritis (20), is recognized now as having a wide systemic spectrum. It is generally rare but is more prevalent in Japan and many Mediterranean and Middle Eastern countries. Complications usually appear several months or even years after presentation of the dermatologic features (1–3,9). Neurologic findings of the brain vary and include loss of vision, cranial nerve palsies, speech disorder, cerebellar ataxia, sensory and motor disturbances and dementia. Histopathological findings of NBS consist of brain involvement in gray and white



**FIGURE 2.** (A) Technetium-99m-HMPAO brain SPECT in 29-yr-old man reveals bilateral and multiple hypoperfusion areas in gray matter, including cerebral cortex, basal ganglia and cerebellum. (B) Brain MR image shows normal gray matter but high signal area in white matter of the left parietal-occipital lobe close to trigone of left lateral ventricle (arrows).

matter (1-3,9). Early institution of corticosteroids or other immunosuppressive agents is necessary to obtain the best response and to decrease the risk of fatality (2,21). Therefore, exact sensitivity data of diagnostic modalities, for detecting brain anomalies in NBS patients, are important.

From a review of the literature, only a small number of case reports concerning the use of brain SPECT to evaluate rCBF in NBS have been published (22-28). Our results show that  $^{99m}\text{Tc}$ -HMPAO brain SPECT, in conjunction with a high-resolution, fanbeam collimator, is a sensitive method for detecting brain involvement in NBS patients. Compared with brain MRI, 100% (13/13) of patients had hypoperfusion areas in the gray matter on  $^{99m}\text{Tc}$ -HMPAO SPECT. In addition, with improved fanbeam SPECT resolution (FWHM 6.3 mm), visualization of deep-seated structures of the brain, such as the basal

ganglia, has become possible. In this study, we were able to detect anomalies in the basal ganglia in 46% (6/13) of NBS patients. However, these SPECT findings of multiple hypoperfusion lesions in the cerebral cortex are not specific, because similar findings can be found in a variety of neuropsychiatric disorders, including cocaine abuse, acquired immunodeficiency syndrome dementia complex, multi-infarct dementia, chronic fatigue syndrome, major unipolar depression and neuropsychiatric systemic lupus erythematosus (29-33). Therefore, the definite diagnosis of BS must depend on clinical observations. In addition, only 31% (4/13) of patients had abnormal signal intensity in the white matter on MRI.

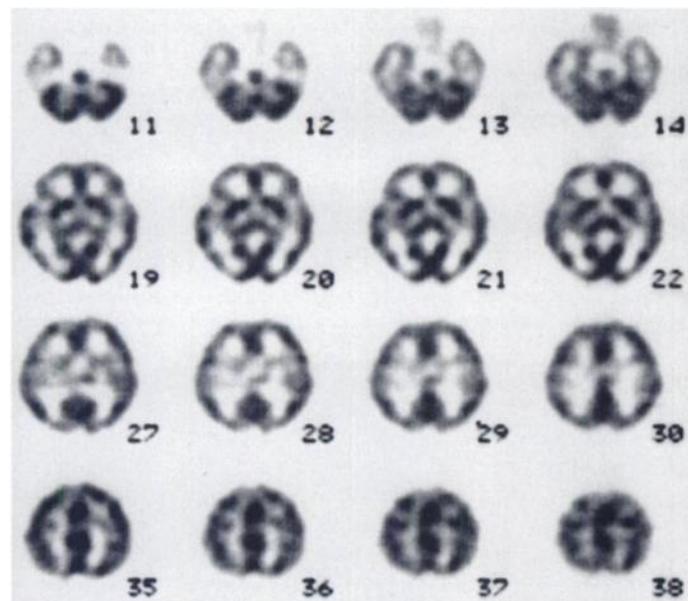
Our results show that  $^{99m}\text{Tc}$ -HMPAO brain SPECT is more sensitive than MRI. These findings are consistent with previous reports (24,27,28). Discrepancies between the less obvious morphological changes on MRI and the more conspicuous functional changes on  $^{99m}\text{Tc}$ -HMPAO brain images are most apparent in brain cortex and the basal ganglia (Fig. 1). From these results, we believe that metabolic or functional changes in the brain, such as fluctuations in rCBF, may be more easily detected than changes in anatomic structure of the brain in NBS patients. However, MRI seems to be more sensitive than  $^{99m}\text{Tc}$ -HMPAO brain SPECT in detecting white matter lesions (Fig. 2).

### CONCLUSION

In this study,  $^{99m}\text{Tc}$ -HMPAO brain SPECT detected changes in rCBF in gray matter in 69% (9/13) of NBS patients with normal brain MRI findings. In addition, the brain abnormalities detected by  $^{99m}\text{Tc}$ -HMPAO SPECT were more compatible with clinical symptoms or signs than brain abnormalities detected by MRI in NBS patients. Therefore, we conclude that  $^{99m}\text{Tc}$ -HMPAO brain imaging, in conjunction with fanbeam SPECT, should be a standard procedure in evaluating brain involvement in NBS patients. However, MRI is also necessary for detecting white matter lesions.

### ACKNOWLEDGMENTS

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**FIGURE 3.** Normal  $^{99m}\text{Tc}$ -HMPAO brain imaging findings in 40-yr-old healthy man consisted of homogeneous regional cerebral blood flow in gray matter of cerebral cortex and basal ganglia/thalamus without focal hypoperfusion or visible asymmetry.

**TABLE 1**  
Results of Brain Technetium-99m-HMPAO SPECT and MRI in Neuro-Behçet's Patients

Patient no.	Age (yr)	Sex	<sup>99m</sup> Tc-HMPAO brain imaging		Brain MRI		Neuropsychiatric symptoms and signs
			Gray matter	White matter	Gray matter	White matter	
1	62	F	Rt Co	Negative	Negative	Rt Fr	Convulsion, Lt hemiparesis
2	40	F	Lt BG	Negative	Negative	Negative	Gait disturbance
3	29	M	Bil Co, Bil Ce, Lt BG	Negative	Negative	Lt P-O	Dementia, bil cerebellar ataxia
4	51	F	Bil Co, Bil BG	Negative	Negative	Negative	Headache, speech disturbance, personality change
5	34	F	Bil Co, Bil Ce	Negative	Negative	Bil P	Dementia, aphasia, bil cerebellar ataxia
6	44	M	Bil Fr	Negative	Negative	Negative	Personality change, mutism
7	55	M	Lt Fr-T	Negative	Negative	Negative	Somnolence, aphasia, Rt hemiparesis
8	32	F	Bil Co	Negative	Negative	Negative	Somnolence, mutism
9	63	M	Rt Co	Negative	Negative	Negative	Dementia, Lt hemiparesis
10	49	M	Bil Co, Rt BG	Negative	Negative	Lt Fr	Headache, dementia
11	28	M	Bil Co, Lt BG	Negative	Negative	Negative	Headache
12	37	F	Bil P, Lt BG	Negative	Negative	Negative	Dementia
13	38	F	Bil P-T-O	Negative	Negative	Negative	Headache, impaired vision

Rt = right; Lt = left; Bil = bilateral; Co = cerebral cortex; Fr = frontal lobe; P = parietal lobe; T = temporal lobe; O = occipital lobe; Ce = cerebellum; BG = basal ganglia.

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