

## Correlation of clinical, MRI and Tc-99m HMPAO SPECT findings in neuro-Behçet's disease

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### Abstract

*Behçet's disease (BD) is a systemic disorder of unknown cause. In our study, we investigated the utility of Tc-99m HMPAO SPECT and MRI in patients with neuro-Behçet's disease (n-BD).*

*Patients and Methods : Twelve patients (two females, ten males ; mean age  $33 \pm 9.6$  yr ; age range 18-45 yr) with n-BD, fulfilling the criteria of the International Study Group for BD, were included in the study. MRI was performed according to a standard protocol with 1 or 1.5 T imagers. Brain SPECT data were obtained using a single head gamma camera after 555 MBq Tc-99m HMPAO injections. Following image reconstruction, regional cerebral perfusion was evaluated both visually and semi quantitatively.*

*Results : Neurological examination showed parenchymal brain involvement in 6 of 12 patients (50%). All 6 patients had white matter lesions on MRI, while only 5 of them showed perfusion defects on brain SPECT. Out of 6 patients (50%) without clinical signs of parenchymal brain involvement, 1 patient showed a pathological brain SPECT and 3 patients showed pathological MRI findings. Semiquantitative analysis of brain regions on SPECT study showed statistically significant hypoperfusion of biparietal regions.*

*Conclusion : This study investigates the correlation between clinical, MRI and SPECT findings and it shows discrepancy between these findings in some cases. Brain SPECT may act as a complementary modality to increase the detection rate of affected regions in patients with n-BD.*

**Key words :** Behçet's disease ; neurological involvement ; MRI ; SPECT.

### Introduction

Behçet's disease (BD) is an inflammatory disorder of unknown origin. It has been described in 1937 as a clinical triad of uveitis and oral and genital ulcers by a Turkish dermatologist Hulusi Behçet (1). Other manifestations include synovitis, thrombophlebitis, and pulmonary, gastrointestinal and central nervous system (CNS) involvement. CNS involvement in BD is named as neuro-Behçet disease (n-BD). N-BD was reported in 4-48% of

patients with BD (2-5). Findings of brainstem involvement (cranial neuropathies, ocular motor dysfunction, nystagmus, dysarthria and ataxia), meningomyelitis (spinal cord and meningeal irritation signs), meningoencephalitis (resulting in the development of dementia, parkinsonism, pseudobulbar palsy and quadriparesis) and vascular complications (such as intracranial hypertension) can be observed when the disease progresses. Magnetic resonance imaging (MRI) has been used to demonstrate the lesions in patients with clinically diagnosis of n-BD (6-12). Cerebral perfusion studies with Single Photon Emission Computed Tomography (SPECT) were reported in a few studies with limited number of n-BD cases (13-23). Brain SPECT images with Technetium-99m hexamethylpropylene amine oxime (Tc-99m HMPAO) demonstrated perfusion defects in patients with or without pathologic MRI findings in BD. Perfusion defects were detected even in patients without any clinical evidence of neurologic involvement (19-20).

We performed this study to analyze the relationship between clinical abnormalities, MRI and Tc-99m-HMPAO images in n-BD, and the reasons of discrepancies between clinical and imaging findings.

### Patients and methods

Twelve patients (2 females, 10 males ; mean age  $33 \pm 9.6$  yr ; age range 18-45 yr) with n-BD, fulfilling the criteria of the International Study Group for Behçet's disease, were included in the study (24). Ten healthy controls (4 females, 6 males ; mean age  $40.3 \pm 8.1$ yr ; age range 25-51yr) were evaluated by SPECT study for comparison of brain perfusion data.

Brain MRI was performed in all patients at the beginning of the neurologic signs and symptoms, using 1 T and 1.5 T scanners in ten and two cases respectively. T1- and T2-weighted images were obtained in transaxial, sagittal and coronal orientations with a slice thickness of 5 mm. A brain SPECT study was performed in all patients within

Table 1  
Results of SPECT, MRI and neurological examination

Patient No	Age/gender (yr)	SPECT	MRI	Neurological Signs
1	22/M	R parietal	R mesencephalon	L body, R face hemihypoesthesia vertigo, nystagmus
2	41/M	L fronto-temporal	Bil mesencephalon, pons left cerebellar peduncle and thalamus	R hemiparesis, bulbar paralysis, bil cerebellar signs
3	41/M	R parieto-temporal, and thalamus	L mesencephalon, pons, cerebellar peduncle, R thalamic, internal capsule posterior limb	L hemiparesis, cerebellar signs, tactile agnosia, R spasticity and vertical gaze paralysis
4	29/M	Negative	R cerebellar peduncle	Bil cerebellar signs
5	45/M	Central parieto-occipital	R subcortical parietal and multiple periventricular	Dysphasia
6	41/M	L parieto-temporal and parieto-occipital	Negative	Recurrent headache, vomiting, normal CSF
7	40/M	L parietal, parieto- temporal and occipital	Centrum semiovale microangiopathic lesions	Meningoencephalitis, papilloedema, abnormal CSF (elevated protein/cell count)
8	27/M	Negative	L globus pallidus and capsula interna	ICH
9	21/M	Negative	Negative	ICH
10	43/M	Negative	Choroid plexus cyst	Normal
11	21/F	Negative	Sagittal and transverse sinus thrombosis	ICH
12	25/F	Negative	Negative	Anterior optic neuropathy

ICH : Intracranial hypertension, R : right, L : left, Bil : bilateral.

2 weeks. None of the patients had new neurologic findings or a treatment in this period. A single head gamma camera (GE, Starcam 4000i XC-T, Milwaukee, WI) fitted with a low energy high-resolution collimator was used for SPECT study. Sixty-four 30 s frames were collected during a 360° rotation in a 64 × 64 matrix. Acquisition was begun 15-20 min after the intravenous injection of 555 MBq Tc-99m HMPAO (Ceretek, Amersham, U.K.) while the patient was sitting, eyes open, in a quiet room. Image reconstruction was performed using ramp filtered back projection with a Butterworth filter without attenuation correction. Transaxial slices were re-oriented parallel to orbitomeatal line to obtain sagittal and coronal reconstructions. Cerebellar activity was chosen to normalize the brain slices. Regional cerebral perfusion was evaluated both visually and semiquantitatively. Transaxial slices parallel to orbitomeatal line (by adding 3 slices passing from the cerebellum, basal ganglia, supraventricular region and vertex) were used to determine perfusion index (PI) of total 16 brain regions. Nineteen rectangular regions of interest (ROIs) (5 × 5 pixel) were set on the brain regions of each hemisphere while irregular ROIs were drawn over the cerebellar hemisphere. To calculate PI, the average counts obtained from the cerebral regions were divided by the average counts, obtained from the ipsilateral cerebellum. Statistical analysis : The Mann-Whitney U test was used to compare the mean PI values for images in patients and controls. The results are presented as

the mean ± standard deviation (SD). P values of less than 0.05 were interpreted as significant.

## Results

On neurological examination 6 of 12 patients (50%) showed signs of parenchymal brain involvement (Table 1). All 6 patients had white matter lesions on MRI and 5 of them showed perfusion defects on SPECT (Fig. 1, 2). Amongst the other 6 patients (50%) without clinical signs of parenchymal brain involvement, 1 patient showed also pathological brain SPECT images and 3 patients showed abnormal MRI findings. MRI findings in these patients weren't correlated with clinical findings except one patient (patient 11).

MRI findings were abnormal in 9 of all 12 patients (75%) and showed thalamus, brainstem, basal ganglia and white matter lesions and sinus thrombosis. None of these patients had cortical gray matter lesions.

Brain SPECT showed hypoperfused areas in 6 of 12 patients (50%). One of the patients showed thalamic involvement in addition to cortical gray matter involvement. Four of 6 patients with normal brain SPECT findings had basal ganglia, choroidal plexus or cerebellar peduncle lesions or sinus thrombosis on MRI. In 1 of 3 patients with normal MRI findings, hypoperfusion was present on brain SPECT. Semiquantitative evaluation of all SPECT data showed that left and right supraventricular parietal PI values were lower in patients with n-BD

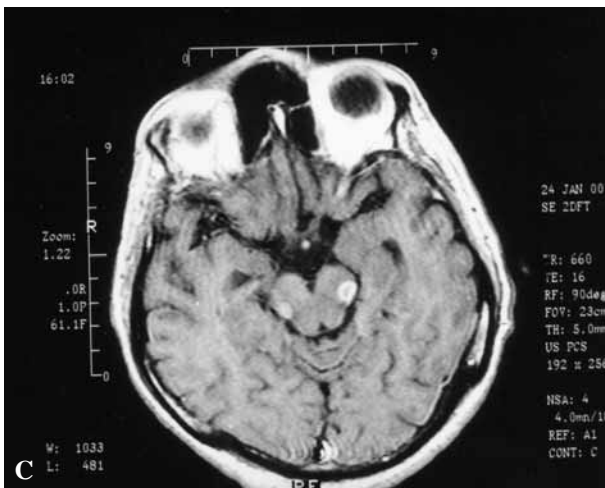
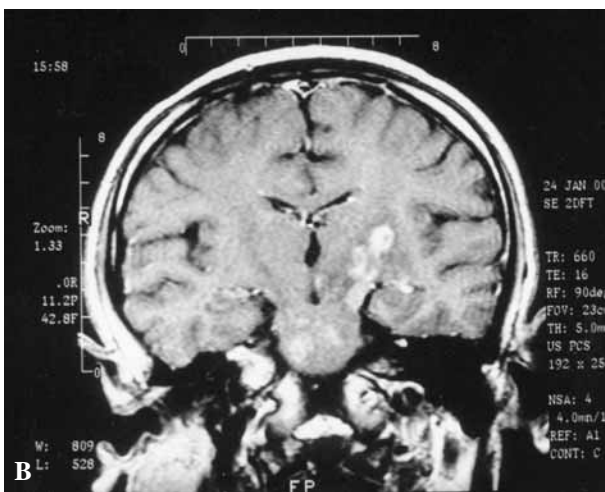
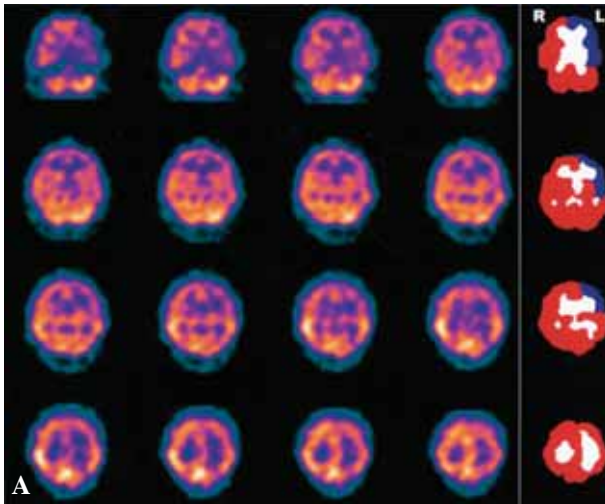


FIG. 1. — Tc-99m HMPAO brain SPECT and MR imaging slices of patient no. 2.

- A Axial slices of SPECT images from base to vertex showing left frontal hypoperfusion (Hypoperfused areas were shown as blue in the schematic arrangement).
- B Coronal T1 weighted MR images shows contrast enhancement of the meningeal cistern, bilateral mesencephalon, pons, left cerebellar peduncle and thalamus lesions.
- C Contrast enhanced axial T1 weighted MR image reveals enhancement of the mesencephalon bilaterally.

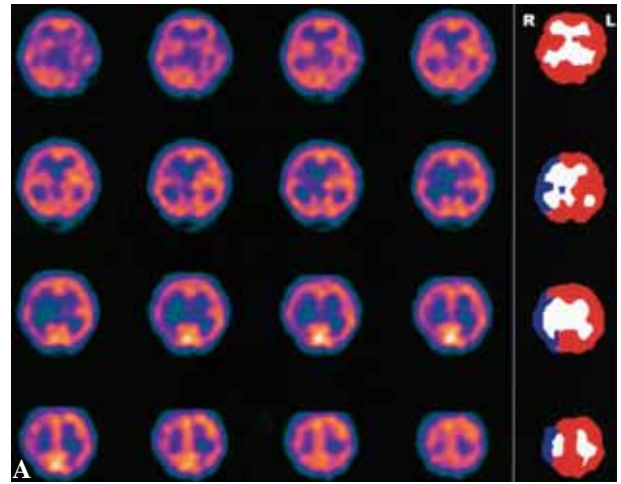


FIG. 2. — Tc-99m HMPAO brain SPECT and MR imaging slices of patient no. 3.

- A Axial slices of SPECT images from base to vertex showing right parietotemporal and thalamic hypoperfusion (Hypoperfused areas were shown as blue in the schematic arrangement).
- B Axial T2 weighted MR image reveals a left mesencephalon lesion.
- C Axial T2 weighted MR image reveals right thalamic and capsula interna lesion.

Table 2

Perfusion Index values obtained from brain SPECT study of 12 patients with n-BD and 10 controls

Brain regions	n-BD		Control	
	L	R	L	R
Frontal(Vertex)	1,06 ± 0,09 <sup>a</sup>	1,06 ± 0,10 <sup>a</sup>	1,04 ± 0,04	1,05 ± 0,05
Parietal(Vertex)	0,99 ± 0,10 <sup>a</sup>	1,04 ± 0,07 <sup>a</sup>	1,03 ± 0,02	1,05 ± 0,06
Frontal(SV)	0,99 ± 0,10 <sup>a</sup>	1,01 ± 0,11 <sup>a</sup>	1,06 ± 0,04	1,06 ± 0,04
Parietal(SV)	0,94 ± 0,12 <sup>b</sup>	0,95 ± 0,13 <sup>c</sup>	1,04 ± 0,05	1,05 ± 0,06
Occipital(SV)	1,11 ± 0,09 <sup>a</sup>	1,10 ± 0,11 <sup>a</sup>	1,08 ± 0,05	1,11 ± 0,02
Frontal(BG)	0,96 ± 0,13 <sup>a</sup>	1,00 ± 0,09 <sup>a</sup>	1,02 ± 0,04	1,03 ± 0,05
Temporal(BG)	1,01 ± 0,09 <sup>a</sup>	1,06 ± 0,09 <sup>a</sup>	1,03 ± 0,03	1,01 ± 0,02
Occipital(BG)	0,85 ± 0,05 <sup>a</sup>	0,90 ± 0,02 <sup>a</sup>	0,91 ± 0,02	0,87 ± 0,02

SV : supraventricular; BG : Basal ganglia ; <sup>a</sup>p > 0.05, <sup>b</sup>p = 0.041, <sup>c</sup>p = 0.043.

than in controls ( $p < 0.05$ ) whereas other PI values between two groups were not significantly different (Table 2).

### Discussion

MRI is the most useful tool in identifying the presence of brain lesions (25). In n-BD, the lesions frequently occur in the brainstem and cerebral white matter followed by the basal ganglia, thalamus, cerebellum and cerebral hemispheres. MRI showed pathological findings up to 70% patients in large n-BD study groups (6-12). However, there was no clear correlation between MRI and neurologic findings in some patients with n-BD (20-23). PET and SPECT studies already revealed abnormal cortical findings with normal MRI (19-20).

In our study we found a variable correlation between MRI and SPECT findings in n-BD patients. The areas of abnormalities detected on SPECT were more extensive than those detected on MRI in our 6 patients (50%) (patients 1,2,3,5,6,7). Scott reviewed the parenchymal brain involvement in n-BD and suggested that it would be the result of a combination of focal lesions in classical sides (i.e. upper brainstem, basal ganglia and white matter) and relatively low grade, diffuse inflammation of CNS. During n-BD, focal brain lesions were found more commonly in the brainstem, basal ganglia and hemispheric white matter but pathologic changes were widespread and might involve any part of CNS (28). SPECT might show cortical diffuse inflammation better than cranial MRI (16).

Patient 7's cerebrospinal fluid (CSF) findings were correlated with meningoencephalitis while MRI findings were not correlated with the clinical findings. Although he did not have focal neurologic findings, SPECT showed lateralized cortical hypoperfusion. Patient 6 had a history of episodic headache and vomiting. He had normal MRI but pathological brain SPECT imaging. Vignola *et al.* presented 7 juvenile n-BD patients. Three of their patients had normal MRI, but pathologic findings

on SPECT examinations (16). All their patients had clinical findings of meningoencephalitis. It was stated that in the absence of MRI alterations, brain perfusion defect in BD might be evidence of CNS involvement.

Patient 3 had cortical sensory deficit (tactile agnosia) and this finding was correlated with right parietal hypoperfusion on SPECT. MRI showed no cortical lesion. Cortical sensory deficit was correlated with right parietal hypoperfusion on SPECT imaging. An explanation for this discrepancy between SPECT and MRI findings may be deafferentation of the cortical area from deep gray structures such as thalamus. Cortical hypoperfusion has been interpreted as a result of cortical deafferentation from deep gray matter structures that are frequently impaired. Diaschisis ipsilateral to cortical gray matter can be characterized by changes in regional cerebral blood flow (26). Cortical hypoperfusion could be reversed after therapy (20). Pupi *et al.* has shown that cortical microcirculation has been preserved in n-BD by using acetazolamide (15). They explained this finding with vasculitic involvement in n-BD. This finding also supports possible presence of disconnection in n-BD.

Lakhanpal *et al.* reviewed that focal cerebral cortical involvement is infrequent in their pathologic series (27). Arai *et al.* reported a neuro-Behçet's patient with dementia. This patient had marked hypoperfusion in the frontal cortex (17). Post-mortem study showed pathological abnormalities in the midbrain and pons but not in the cerebral cortex. But there was clear evidence for lesion formation within gray matter of the cortex in n-BD patients. Patients showing involvement of the cortex with marked loss of neurons were also reported (29-30).

There were 2 patients (patients 8, 9) in our study with papilledema and intracranial hypertension. Their CSF findings weren't compatible with meningoencephalitis. SPECT findings were normal and correlated with the clinical findings in these

patients. Patient 8's MRI showed lesions at left globus pallidus and internal capsule which were not compatible with the clinical findings. The other patient had normal MRI compatible with the clinical findings.

One of our patients (patient 4) had a lesion at cerebellar peduncle on MRI with normal SPECT and showed clinical signs since 2 years with slow progression. Because of this long period, cortical inflammatory reactions may be little. Normal brain SPECT might show that there was no cortical inflammation since brain SPECT is very sensitive in detecting cortical abnormality in patients with n-BD (14, 16). Another patient (patient 8) had a lesion on the left globus pallidus and SPECT findings were normal. He had no focal neurological finding. Garcia-Burillio *et al.* showed three patients with abnormal MRI and normal SPECT (13). Lesions were in the putamen, subcortical white matter and bilateral subinsular white matter. These findings support the idea that MRI is more sensitive than SPECT in white matter lesions (14).

Patient 2 and 3 had thalamic lesions on MRI, but only one of them (patient 3) showed decreased perfusion on SPECT imaging. Brain SPECT perfusion with single head rotating gamma cameras shows decreased sensitivity in the detection of subcortical gray matter lesions due to relatively poor resolution. Therefore, all lesions on MRI could not be shown with SPECT. The non-visualization of thalamic involvement in patient 2 was possibly related to the small size and perfusion alteration of the lesions.

In our study, semiquantitative evaluation of brain perfusion showed non-significant values except biparietal regions in comparison with controls because of possibly small numbers in patients. Major involvement areas were found in parietal lobes while other cerebral regions showed limited number of involvements. This might be another explanation of non-significant values.

There are a few n-BD patients with optic neuropathy, which has been reported. Kocer *et al.* had reported one n-BD patient with optic neuropathy in their 65 n-BD patients (8). Akman-Demir *et al.* reviewed 200 patients with n-BD; there was only one patient with optic neuropathy (4). Patient 12's findings were similar to multiple sclerosis too. But she had bilateral anterior optic neuropathy and her visual accuracy was short. Anterior optic neuropathy is not very common in multiple sclerosis and oligoclonal banding in CSF was not detected in this patient. She didn't have pyramidal or cerebellar findings. MRI and SPECT findings were normal.

In conclusion, Tc-99m HMPAO brain SPECT demonstrated cerebral cortex lesions while MRI showed brain stem, thalamus, basal ganglia and white matter lesions. Therefore, brain SPECT may act as a complementary modality to increase the detection rate of affected regions in patients with

Behçet's disease. This study investigates the correlation between clinical, MRI and SPECT findings and it shows discrepancy between these findings in some cases. MRI and SPECT are useful and complementary investigations in the diagnosis of n-BD.

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