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ORIGINAL ARTICLE

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Usefulness of Tc-99m ECD brain SPECT to evaluate the effects of methylprednisolone pulse therapy in lupus erythematosus with brain involvement: a preliminary report

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Abstract Methylprednisolone pulse therapy (MPT) was introduced to avoid life-threatening complications in systemic lupus erythematosus (SLE) with brain manifestations. However, its efficacy in SLE patients remains uncertain and needs to be objectively evaluated. In this study, technetium-99m ethyl cysteinate dimer (Tc-99m ECD) brain single photon emission computed tomography (SPECT) was used to detect regional cerebral blood flow (rCBF) in SLE patients with normal brain magnetic resonance imaging (MRI) findings. Twelve female SLE patients with neuropsychiatric symptoms were enrolled in this study. All patients had normal brain MRI and abnormal Tc-99m ECD brain SPECT findings. The Tc-99m ECD brain SPECT studies were performed 2 weeks after MPT. Pre- and post-MPT serum levels of anticardiolipin antibodies (ACA) and antiribosomal P antibodies (anti-P) were also measured. Before MPT, four patients had positive ACA and seven had positive anti-P. After MPT, all 12 patients demonstrated negative serologic findings and no neuropsychiatric symptoms. After MPT, ten patients showed complete recovery and two showed partial recovery of rCBF in the follow-up Tc-99m ECD brain SPECT images. This imaging is a logical and objective tool for measuring the effects of MPT in SLE patients with brain involvement by the determination of rCBF changes.

Keywords Methylpredisolone pulse therapy · Systemic lupus erythematosus · Tc-99m ECD brain SPECT

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Introduction

Involvement of the brain is one of the most serious complications of systemic lupus erythematosus (SLE). Of all SLE patients, 30–70% develop brain involvement manifested as cerebrovascular disease, seizures, cognitive disorders, headaches, and psychosis [1, 2, 3]. Large-dose methylprednisolone pulse therapy (MPT) was therefore introduced [4, 5]. However, due to the lack of effective imaging techniques, the efficacy of MPT in SLE patients with neuropsychiatric manifestations is still uncertain and needs to be objectively evaluated [5].

Single photon emission computed tomography (SPECT) with technetium-99m (Tc-99m) hexamethylpropylene amine oxime (HMPAO) has proven sensitive and useful for assessing regional cerebral blood flow (rCBF) in detecting brain involvement in SLE [6, 7]. Its potential in monitoring rCBF after MPT has been reported in only a few cases [8, 9]. However, Tc-99m HMPAO is limited in that its rapid decomposition in vitro necessitates usage within 30 min of preparation and that imaging needs to be performed within 40 min of injection for the results to be interpretable [10, 11]. Technetium-99m ethyl cysteinate dimer (ECD), a newer marker of rCBF, has better in vitro stability and brain-to-background signal ratio than Tc-99m HMPAO, resulting in better image quality [11, 12]. To date, very few reports

have been published concerning the clinical application of Tc-99m ECD brain SPECT in evaluating rCBF in SLE patients [13]. Therefore, in this preliminary study, we used it for determination of rCBF changes to monitor MPT results in SLE patients with brain involvement.

Materials and methods

After a neurology consultant evaluated patients for neuropsychiatric symptoms/signs due to SLE [14, 15], 12 female SLE patients (aged 28 to 41 years) who fulfilled the American College of Rheumatism criteria and with brain involvement and major neuropsychiatric manifestations (including psychosis, depression, confusion, seizures, and cerebellar ataxia) were selected for this study. The symptoms were defined as not attributable to any other cause (such as uremia, hypertension, or infection). The patients had normal brain MRI findings (excluding focal and diffuse hyperintensity lesions, infarcts, hemorrhage, and significant atrophy) and abnormal Tc-99m ECD brain SPECT findings. Follow-up Tc-99m ECD brain SPECT studies were performed on all patients 2 weeks after MTP (1 g/day), given intravenously for 3 consecutive days, and oral prednisolone (2 mg/kg per day) for 1 week. Also, pre- and post-MPT serum levels of anticardiolipin antibodies (ACA) were measured by enzyme-linked immunosorbent assay kits (Quanta Lite ACA IgG/IgM and IgA, INOVA Diagnostics, San Diego, Calif., USA) and antiribosomal P antibodies (anti-P) were measured by Western blot autoantibody profile kits (Immunovision, Springdale, Ariz., USA).

The Tc-99m ECD was prepared according to the formula of a commercial vial (Neurolite, Dupont, USA) [12]. In a dark and quiet room 15 to 45 min after intravenous Tc-99m ECD injection (740 MBq), SPECT data were obtained using a rotating, large field-of-view, dual-head, gamma camera fitted with fan-beam collimators. During the initial and follow-up Tc-99m ECD brain SPECT studies, the head was fixed in position by a hemicylindrical plastic head holder with a radiotranslucent plastic neck-contoured headrest and maintained in position during imaging using a laser beam. Data were collected from 64 projections in the 140-keV photopeak over 360° (180° for each head) in 128×128 matrices with an acquisition time of 30 s/projection. The images were reconstructed using attenuation correction with Hanning filters to produce transaxial sections. The same method of image reconstruction was used for initial and follow-up images: the transaxial sections were reoriented parallel to the base of the brain to obtain sagittal and coronal reconstructions. In addition, corresponding image pairs were referenced to prominent brain structures visible in the initial and follow-up images (landmarks included the caudate, putamen, thalamus, corpus callosum, ventricles, cingulate gyrus, and the cortical surface outline, particularly at the anterior point of the frontal lobe and the vertex of the occipital lobe).

Visual interpretation was performed according to the criteria established by Kao et al. [7, 16]. To identify areas of abnormal perfusion, simultaneous visual interpretation of the initial and follow-up SPECT images from each patient was carried out in random order. Normal or abnormal characterization was made by agreement of at least two of three independent, experienced observers unaware of the clinical information on the patients. Normal brain SPECT findings included homogeneous rCBF in the gray matter of the cerebral cortex and basal ganglia/thalamus without focal hypoperfusion or visible asymmetry. Abnormal brain SPECT findings were defined as heterogeneous rCBF with focal hypoperfusion or visible asymmetry in at least two consecutive slices in two sections.

Results

The detailed data, including serologic measurements and Tc-99m ECD brain SPECT findings before and after

Table 1 Detailed data of SLE patients

Case no. (age in years)	Disease duration (years)	Neuropsychiatric manifestations	ACA	Anti–P		Hypoperfusion lesions on Tc–99m ECD brain SPECT	
				Before MPT	After MPT	Before MPT	After MPT
		Memory impairment, cerebellar ataxia	No	–	–	–	Bil F–P–C	No
2 (29)	8	Seizure	No	–	–	–	Rt T	No
3 (30)	7	Memory impairment, seizure	No	–	–	–	Rt F–P–T	No
4 (31)	10	Confusion, psychosis, depression	No	–	+	–	Lt F–P–T–O, LT BS	No
5 (32)	14	Confusion, psychosis, depression, cerebellar ataxia	No	+	+	–	Bil F–P–T–O–C, Bil BS	Rt P–T–O, Lt C, Rt BS
6 (33)	11	Headache, depression	No	–	+	–	Rt F–P–T–O	No
7 (34)	13	Psychosis, seizure	No	+	+	–	Lt F–P–T,Lt BS	No
8 (37)	16	Headache, confusion, psychosis	No	+	+	–	Rt F–P–T, Rt BS	No
9 (37)	8	Memory impairment, depression	No	–	–	–	Lt F–P–T–C, Bil BS	Lt P–T, Lt BS
10 (39)	12	Psychosis, cerebellar ataxia	No	–	–	–	Bil F–P–T	No
11 (40)	16	Psychosis, depression	No	–	+	–	Bil P–T, Lt BS	No
12 (41)	10	Confusion, psychosis, seizure	No	+	+	–	Rt P–T–O, Bil BS	No

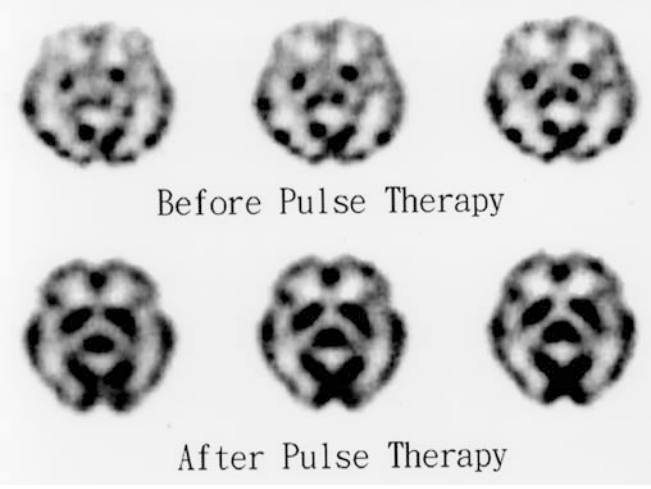

Fig. 1 Tc-99m ECD brain SPECT. Initial images before MPT (*upper row*) show diffusely decreased rCBF in the bilateral frontal-temporal-parietal-occipital-cerebellar regions and basal ganglia. Imaging 2 weeks after MTP (*lower row*) shows almost complete recovery of rCBF in the above areas

MPT, are listed in Table 1. Before MPT, four patients had positive ACA and seven had positive anti-P. After MPT, all 12 patients demonstrated negative serologic findings and no neuropsychiatric manifestations.

Before MPT, hypoperfusion lesions visualized in initial brain SPECT were most common in the temporal and parietal lobes (11/12, 91.7%) and least common in the cerebellum (3/12, 25.0%). After MPT, ten of the 12 (83.3%) patients showed complete recovery of rCBF in follow-up brain SPECT and the remaining two demonstrated partial recovery (Fig. 1).

Discussion

For detecting brain involvement in SLE, Tc-99m HMPAO brain SPECT has proven to be more sensitive than magnetic resonance imaging (MRI) and FDG positron emission tomography (-PET) [7, 16]. In previous reports comparing SPECT with Tc-99m ECD and Tc-99m HMPAO in healthy volunteers or patients, superior image quality was demonstrated with Tc-99m ECD [17, 18, 19, 20], making it easier to differentiate between affected and unaffected brain structures. Therefore, in this study, we used it to detect and visualize brain lesions in SLE patients.

Absolute quantification of rCBF is not feasible in routine clinical practice due to the required complex modeling of enzyme kinetics, careful correction for attenuation, and input functions from arterial blood samples for solving mathematical equations. All of the above procedures are very time-consuming for the nuclear medicine technician and invasive for patients undergoing clinical or practical brain imaging. Some semiquantitative methods for the interpretation of brain SPECT results have been reported [21, 22]. However, we did not think that such a method is valid for SLE patients with brain involvement, since brain lesions in SLE are always multifocal and can affect brain structures asymmetrically and/or bilaterally. Therefore, the visual interpretation of Tc-99m ECD brain SPECT images performed by independent and experienced observers and dependent on normal databases from our own laboratory was deemed sufficient for identifying lesions. Therefore, we selected a visual instead of quantitative method.

Methylprednisolone pulse therapy is used for managing acute lupus nephritis [23, 24, 25]. However, experience with MPT in SLE patients with brain manifestations is limited [5, 26]. As steroids reduce edema around infarcted areas, patients with acute stroke may improve with steroid treatment. Those with nervous vasculitis should also be treated with corticosteroids. High-dose steroids are indicated in cases of coma, seizures, psychosis, chorea, and transverse myelitis [27]. There have been several reports on pulse steroid therapy in the treatment of neuropsychiatric lupus [28, 29, 30]. Eyanson et al. reported two acutely ill patients who failed to respond to oral glucocorticoid therapy but responded dramatically to intravenous MPT [28]. The most common neuropathological changes observed in brain autopsies of SLE patients are multiple microinfarcts and vasculopathy with thickening of the intima and fibrinoid degeneration in the small vessels [31, 32]. Therefore, detection of changes in rCBF by Tc-99m ECD brain SPECT should be a sensitive tool for monitoring therapeutic effects.

Conclusion

Decreased rCBF can be reversed by MPT, and the recovery observed in brain SPECT images can also be used for monitoring MPT in SLE with brain involvement. Technetium-99m ECD brain SPECT, which is noninvasive, safe, practical, and reliably indicates changes in rCBF, seems to be the logical and objective choice for this purpose.

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