Brain SPECT Imaging for Lamina Heterotopia

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Brain perfusion SPECT was performed in an epileptic patient with a rare form of diffuse subcortical laminar heterotopia using $^{99m}$Tc-HMPAO. MRI demonstrated generalized laminar heterotopia underlying the cortical mantle. Intercital SPECT imaging revealed identical or increased perfusion of the laminar heterotopia as compared with that of the overlying cortical mantle. Moreover, SPECT revealed low perfusion in the left temporal lobe that agreed with the seizure type of complex partial seizures and the EEG finding of frequent generalized spike-wave complexes with a slight left-sided dominance. Brain SPECT imaging may be useful for appropriate diagnosis of gray matter heterotopia and for detection of functionally focal abnormality associated with epilepsy.

Key Words: SPECT; $^{99m}$Tc-HMPAO; epilepsy; heterotopia


Cerebral malformations due to neuronal migration anomalies are frequently associated with mental retardation and epileptic seizures (1). These malformations include agria, pachygyria, polymicrogyria, schizencephaly and heterotopia (2). Heterotopia is a collection of gray matter located abnormally in the brain and classified into two distinct types, the subependymal nodular and the laminar. A rare form of diffuse subcortical laminar heterotopia, called “double cortex”, (3–10) has been observed recently by MRI. On the other hand, nuclear medicine studies on heterotopia are limited. In this study, we present SPECT images from an epileptic patient with subcortical laminar heterotopia.

CASE REPORT

A 35-yr-old right-handed female with moderate mental retardation was evaluated for epileptic seizures. She had two normal siblings, and there was no family history of epilepsy or other neurological disorders. Perinatal history was unremarkable. Birth was uncomplicated. Developmental milestones were delayed: she started to walk at 18 mo, and by 2 yr could say only a few words. She was clumsy, easily upset and had poor impulse control. Her epileptic attacks, starting at age ten, comprised sudden disturbance of consciousness, leading to complex partial seizures accompanied by automatism. Despite sufficient anticonvulsants, she continued to suffer from complex partial seizures that sometimes evolved into secondarily generalized seizures at a frequency of several times per month in the second decade. However, the frequency of seizures decreased to several times per year in the third decade. Physical examination showed the patient to be of adult height and obese. Neurologic examination was normal. Intercital electroencephalograms (EEGs) demonstrated slow background activity and frequent generalized spike-wave complexes with a slight left-sided dominance.

A 1.0 T unit was used for MRI. Imaging parameters included: spin-echo sequences with repetition time msec/echo time msec = 500/20 for T1-weighted images and 2500/90 for T2-weighted images and 2500/20 for proton-density images; 8-mm section thickness with a 2-mm interslice gap; 256 × 256 acquisition matrix. MRI revealed a bilateral layer of tissue that had the same signal intensity as gray matter (Fig. 1A, B) located in both hemispheres between the wall of the lateral ventricle and the cerebral cortex from which it was divided by a thin layer of normally interdigitating white matter. The tissue, interpreted as heterotopic gray matter, symmetrically extended from the frontal to the occipital region. Moreover, MRI revealed diffuse atrophy of cerebral hemispheres as manifested by enlarged ventricles and enlarged cortical sulci, but the overlying cortex was normal with respect to convolutional pattern and gyral thickness. The structures of the limbic system were normal.

Brain perfusion SPECT images were acquired following a 740-MBq dose of $^{99m}$Tc-HMPAO. Imaging was performed using a high-resolution SPECT system with three-head rotating cameras equipped with high-resolution, low-energy, parallel-hole collimators. Acquisition of projection data started from 10 min after injection and lasted for 20 min. Data were accumulated for 24 angles (5° step, 120°) with 50 sec per angle for each detector. A Shepp and Logan filter with 0.85 cycles per cm cutoff frequency was used for image reconstruction of axial, coronal and sagittal sections in a 128 × 128 image matrix. Attenuation correction was performed using Chang’s method. The resolution was 8.5 mm FWHM in the center of the reconstructed slice (11) and the computer slice was 3.5 mm wide. Brain SPECT images of a 30-yr-old normal male volunteer (Fig. 2) obtained in the same manner as this patient showed high-resolution images comparable to those obtained using the other brain-dedicated SPECT system (12). Intercital SPECT imaging of this patient revealed much thicker cortical activity than that in the normal control (Fig. 3). This thick cortical activity may comprise the activity of the subcortical laminar heterotopia and that of the superficial cortical mantle. Spatial resolution of the SPECT system was not sufficient for separating these two structures. However, in some areas, the low activity of the white matter intervened between the heterotopia and the cortical mantle. The subcortical heterotopia showed identical or even increased perfusion as compared with that of the
superficial cortical mantle. Moreover, the left temporal lobe showed slightly low activity. Regions of interest (ROIs) were drawn over three homotypic regions of the bilateral temporal lobes in the same manner as in the previous report (13); superior temporal gyrus and insula cortex (T1), inferior and middle temporal gyrus (T2) and temporal poles (T3). Quantitative analysis was used for each pair of bilateral ROIs using an asymmetry index, determined by the equation: \(200 \times \frac{(R - L)}{(R + L)}\). In eight age-matched normal controls (six males and two females, aged 30–39 yr), the asymmetry indices ranged from −5.4 to 6.2 (0.4 ± 2.9, mean ± s.d.) in T1, from −8.3 to 9.7 (0.7 ± 4.5) in T2, and from −5.4 to 9.0 (1.8 ± 3.6) in T3. This patient showed significantly higher values of asymmetric indices, 19.0 in T1, 15.1 in T2, and 13.4 in T3, indicating relatively low perfusion in the left temporal lobe.

**DISCUSSION**

Since Barkovich et al. (3) described the MRI picture of a rare form of laminar heterotopia referred to as “band heterotopia,” several investigators (4–10) have reported similar MRI findings in patients with developmental delay and seizures. This is also called “double cortex,” which is characterized by an extensive linear subcortical neuronal heterotopia parallel to the cortical surface. An apparent predilection for females is observed in this anomaly. Although Barkovich et al. (3) described the poor prognosis and intractable nature of the associated seizures, other reports (4–10) clarified a broad spectrum of severity in this anomaly, including patients with very severe neurological abnormalities, different types of epilepsy, and occasionally, nearly normal subjects. Response to antiepileptic medication also varied greatly. Some patients became seizure-free when receiving medication (4,5), but others required corpus callosotomy because of intractable seizures (10).
Although several reports (14–18) have addressed brain PET or SPECT findings in gray matter heterotopia, to our knowledge this is the first report on subcortical laminar heterotopia using a nuclear medicine technique. All but one reported identical or increased perfusion of gray matter heterotopia as compared with that of the overlying cortical mantle. Preserved perfusion of heterotopia may be related to the microscopic finding of a normal six-layered cortex in laminar heterotopia (2). On the other hand, Palmi

in et al. (5), in a microscopic study of laminar heterotopia obtained by brain biopsy, described poor demarcation of cortical layers 5 and 6 in spite of well-preserved isocortical lamination in cortical layers 1 to 4. This minor alteration in lamination could be associated with epileptogenicity. In this case SPECT provided additional information of slightly low perfusion in the left temporal cortex. This finding is in good agreement with the seizure type of complex partial seizures and the EEG finding of generalized spike-wave complexes with a slight left-sided dominance. The usefulness of $^{99m}$Tc-HMPAO SPECT imaging has been reported in patients with focal epilepsy (19,20). Brain SPECT imaging may be a valuable adjunct in diagnosing heterotopia and in evaluating co-existing functionally focal abnormality associated with epilepsy.

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REFERENCES