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Unique discrepancy between cerebral blood flow and glucose metabolism in hemimegalencephaly

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Summary Hemimegalencephaly (HME) presents as severe refractory seizures and requires early surgical treatment to prevent progression to catastrophic epilepsy. Single-photon emission computed tomography (SPECT) and positron emission tomography (PET) are useful imaging techniques for the presurgical evaluation of patients with intractable epilepsy. However, the results in HME are variable and no study has compared SPECT and PET performed at around the same time. We performed SPECT and PET for nine patients with HME, which was defined as a whole or part of affected hemisphere enlargement (three males, six females; age range 0.5—20 years). The ictal and interictal states were determined based on the presence or absence of clinical seizures during all PET examinations and majority of SPECT examinations. The perfusion pattern in the malformed hemisphere was increased or equal, despite the reduced glucose metabolism in six out of nine patients. Five of the six patients who underwent early surgical treatment showed this kind of perfusion/metabolism discrepancy. Importantly, even the

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non-affected hemisphere in early infantile cases already lacked the normal hypoperfusion and hypometabolism patterns of immature frontal lobes, which was most prominent in case with poor surgical prognosis. In all six surgical patients, epileptic seizures appeared before 4 months of age. By contrast, none of the non-surgical patients had seizures before 4 months of age. In conclusion, although the number of patients examined is small and the result is still preliminary, the perfusion/metabolism discrepancy found in this study may show potential characteristic aspect of HME and further study with simultaneous EEG recording will make clear if this finding can be useful indicator for early surgical treatment in HME.

Introduction

Hemimegalencephaly (HME) is a malformation of cortical development characterized by unilateral enlargement of the cerebral hemisphere (Tinkle et al., 2005). It is generally defined as the enlargement of at least one lobe of the cerebral hemisphere confirmed by head magnetic resonance imaging (MRI) (Barkovich, 2005; Barkovich and Chuang, 1990; Flores-Sarnat, 2002). The pathogenesis is unknown, although several hypotheses have been reported (Baybis et al., 2004a; Flores-Sarnat, 2002; Geschwind and Miller, 2001; Gupta et al., 2004; Sarnat and Flores-Sarnat, 2004; Sun and Walsh, 2006). Clinically, most patients exhibit severe refractory seizures and psychomotor retardation within the first 6 months of life. Early diagnosis and an early surgical treatment are required to prevent progression to catastrophic epilepsy (Devlin et al., 2003; Di Rocco et al., 2006; Jonas et al., 2004), but the incidence of surgical complications is higher in very young patients (Di Rocco and Iannelli, 2000).

Single-photon emission computed tomography (SPECT) and positron emission tomography (PET) of the brain are useful functional imaging techniques for studying cerebral blood flow (CBF) and glucose metabolism, respectively. Typically, both CBF and glucose metabolism are increased in the epileptogenic zone during ictus, while both are decreased during the interictal period (Buch et al., 2008; Henry and Van Heertum, 2003; Maehara, 2007). Consequently, ictal perfusion SPECT and interictal PET are useful for the presurgical evaluation of partial epilepsy (Henry and Van Heertum, 2003; Nelissen et al., 2006; Spencer, 1994; Van Paesschen et al., 2007). In HME, however, the results are variable, with increased or decreased CBF and glucose metabolism interictally (Rintahaka et al., 1993; Soufflet et al., 2004), and no comparative study has performed SPECT and PET at around the same time.

In this study, we investigate clinical findings in patients with HME and compared CBF and glucose metabolism in the affected lesion using SPECT and PET to identify useful indicators of surgical intervention.

Methods

Patients

We conducted a retrospective study of nine patients (three males and six females) with HME who had visited Tohoku University Hospital between 1990 and 2008 (Table 1). Informed consent regarding the examination was obtained from the parents before each patient's studies. HME was diagnosed based on the typical MRI signs, including whole or part of brain hemisphere hypertrophy with lateral ventricle dilatation, abnormal gyral patterns, and abnormal white matter intensity (Barkovich, 2005) (Fig. 1). The malformation was on the left in four patients and on the right in five. It involved the entire hemisphere in two, frontal and parietal lobes in four, and parietal and occipital lobes in three. The non-affected hemisphere appeared normal in all patients. All but one patient (Patient 8) had refractory complex partial seizures, which appeared within the first 6 months of life, originating from the HME hemisphere, as confirmed by ictal electroencephalography (EEG). All patients had various levels of hemiplegia and mild to severe developmental retardation. As part of the preoperative evaluation, they underwent additional examinations, including long-term video-EEG monitoring, magnetoencephalography (MEG), and nuclear functional imaging at ages ranging from 0.5 to 23 years (mean 5.8 years). The EEG taken nearest the time (within two weeks in Patient 1—7, within six months in Patients 8 and 9) of SPECT and PET was considered in this study.

Six of the nine patients (Patients 1—6) underwent functional hemispherectomy at ages ranging from 5 to 41 months (mean 12.5 months); as a result, four patients became seizure free, one showed a dramatic reduction, and one did not change (Patient 2; Table 1). Patient 2 had very frequent apneic and tonic seizures on her left side from the early neonatal period. Considering her young age (2 months) and low bodyweight (4500 g), she underwent a callosotomy initially. However, a hemispherectomy was performed at 6 months of age, since the seizure frequency was not reduced. This patient's EEG showed independent multifocal spike foci in the non-affected hemisphere at 5 months of age (Fig. 2).

Three patients (Patients 7—9) did not undergo surgical treatment. Patient 7 developed daily epileptic seizures at 4 months of age, but antiepileptic medication reduced the seizure frequency to monthly. Patient 8 was diagnosed with Klippel—Weber syndrome and afebrile seizures occurred only a few times throughout her life. The EEG showed continuous alpha wave-like spikes in the affected right posterior hemisphere. Patient 9 had an afebrile right hemiconvulsion at 6 months of age and subsequently improved on antiepileptic medication with occasional partial seizures. Unfortunately, she drowned at 28 years of age and it is not known whether an epileptic seizure was the cause.

MEG recording

Magnetoencephalography was performed in six patients (Patients 3—7, 9). EEG and MEG were recorded simultaneously in a magnetically shielded room. The MEG data were recorded with a whole-head MEG system with 204 spatial-type gradiometers (VertorView; Neuromag, Helsinki, Finland). The scalp EEG used the standard international 10—20 EEG electrode placement with additional anterior temporal electrodes. EEG and MEG data were acquired with sampling at 500 Hz and bandpass filtering between 0.10 and 160 Hz. MEG and EEG were recorded for 30-min periods while awake and asleep. This study analyzed the current orientation at the main peak latency of the MEG spike, while the simultaneously recorded scalp EEG, if available, indicated negative spikes. Only equivalent current dipoles with adequate goodness of fit (>85%)