

# Patient With Unusual Alternating Hemiplegia

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**A patient with unusual alternating hemiplegia in childhood is reported. The frequency of hemiplegic episodes was lower than that in other reported patients. Interictal positron emission tomography revealed decreased cerebral blood flow in the left hemisphere. After cerebral angiography, postanesthetic irritability occurred which evolved into coma with hemiplegic episodes. We believe that cerebral angiography in a child with alternating hemiplegia may cause hemiplegic episodes and coma. The episodes disappeared almost completely for 6 years after treatment with flunarizine, thus indicating the benefit of the medication for the treatment of alternating hemiplegia.**

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## Introduction

Alternating hemiplegia in childhood was initially described by Verret and Steele in 1971 [1]. Aicardi and Krageloh delineated the clinical features, including onset before 18 months of age, repeated episodes of hemiplegia involving both sides of the body, other paroxysmal phenomena, and evidence of mental or neurologic deficit [2]. The pathogenesis of alternating hemiplegia in childhood remains unknown, but cerebral ischemia due to vasospasms of the cerebral vessels is one of the most probable causes [3-5]. Cerebral angiography is usually performed to diagnose or exclude cerebrovascular diseases, but there has been no report of a patient who developed coma with hemiplegia episodes after cerebral angiography. We report an unusual case of alternating hemiplegia in a child who suffered from coma after cerebral angiography and who responded well to flunarizine for 6 years.

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## Case Report

This patient was born at term after a normal pregnancy, labor, and delivery, weighing 3,950 gm. No perinatal problems were evident and no family history of migraine or epilepsy existed. At age 8 months, she had an initial episode of generalized clonic convulsions after crying. Developmental quotient was 96%. Thereafter, she had a generalized clonic convulsion twice a month which sometimes developed into status epilepticus. Paralysis of the extremities was uncertain. Electroencephalography (EEG) was normal at the time; therefore, no antiepileptic drug was administered. At age 12 months, cranial computed tomography (CT) revealed mild subdural fluid collection. Surgery was performed which involved burr hole placement and irrigation. After surgery, she was seizure-free, but exhibited minimally retarded verbal development and began physiotherapy.

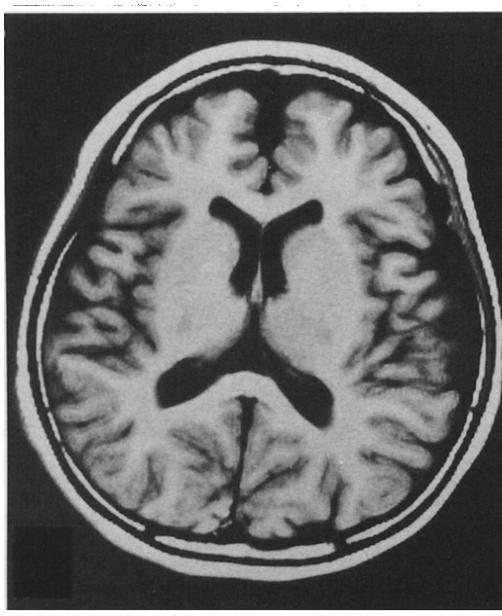
At age 3 years, she became semicomatose following crying and vomiting after stumbling. She was hospitalized for 1 month with the diagnosis of encephalopathy and she developed right-sided hemiparesis for several days. Ictal and interictal EEG demonstrated moderate slowing of background activity, especially on the left side, without paroxysmal epileptic discharges. Phenobarbital and phenytoin were administered.

At age 10 years, she hit her head and fell down. She vomited and developed impaired consciousness 20 min after the fall. She was admitted to the Department of Pediatrics, Kyoto Prefectural University of Medicine. She had a stiff right arm and deep tendon reflexes were increased bilaterally. Pupillary reaction was sluggish, but there was neither nystagmus nor eye deviation. She manifested no pellagraform rash or exacerbation of symptoms with exposure to sunlight. Laboratory examination results, including blood ammonia, liver function, blood amino acids, blood lactate and pyruvate, electrolytes, arterial gas analysis, and cerebrospinal fluid (CSF), all were within normal limits. The concentrations of 5-hydroxyindoleacetic acid (5-HIAA) and homovanillic acid (HVA) in CSF were 18.6 ng/ml (normal: 16.8-29.0 ng/ml) and 35.4 ng/ml (normal: 36.4-63.8 ng/ml), respectively. She recovered from right hemiplegia 2 days after admission. EEG demonstrated no paroxysmal epileptic discharges. There were no abnormal findings on cranial CT or magnetic resonance imaging (MRI; Fig 1). Interictal positron emission tomography (PET) revealed decreased cerebral blood flow (CBF) in the left hemisphere (Table 1; Fig 2).

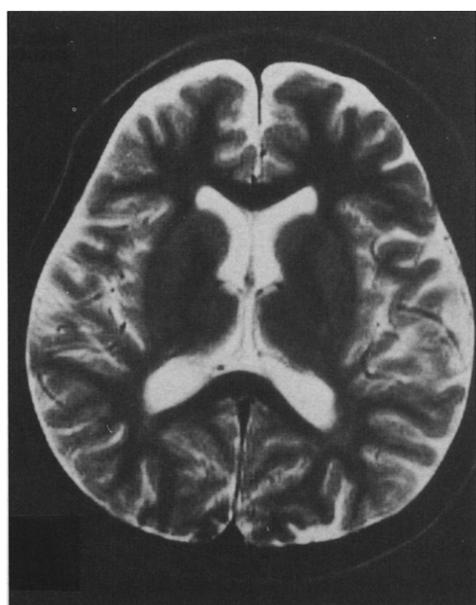
Cerebral angiography, performed under gas oxygen Fluothane anesthesia, revealed no abnormal findings; however, 2 hours after angiography, postanesthetic irritability and crying occurred, which developed into a semicomatose state. This episode was followed by left-sided hemiparesis and mild choreiform movements of the extremities. EEG disclosed marked slowing of background activity, but no paroxysmal epileptiform discharges. Cranial CT remained normal. Seven days after cerebral angiography, she had a clonic convulsion of the left upper extremity for 30 min, with tongue protrusion and sweating on the right side of the face. Papillary reaction was sluggish. Right-sided nystagmus and left-sided eye deviation was evident. Ictal EEG continued to manifest slowing of background activity without definite paroxysmal epileptic discharges. Ten days after angiography, she had a clonic convulsion of the left upper extremity for 5 min and left hemiparesis occurred again after crying. She recovered from the left hemiplegia 50 days after angiography. IQ score was 31 at discharge.

Five months after discharge the next episode of hemiplegia occurred on the right side, accompanied by vomiting. Since a calcium antagonist (flunarizine) was begun, there has been neither hemiplegia nor seizures for 6 years. There has been no neurologic regression. EEG continues to demonstrate no epileptiform discharges and mild slowing of the background activity which is maximal over the bilateral occipital regions. Cranial CT and MRI also continue to reveal no abnormal findings.

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Figure 1. No abnormality demonstrated by cranial MRI, horizontal sections. (A)  $T_1$ -weighted image (TR: 501 ms, TE: 15 ms). (B)  $T_2$ -weighted image (TR: 2,500 ms, TE: 90 ms).

## Discussion

Alternating hemiplegia in childhood was postulated to be related to hemiplegic migraine by Verret and Steele [1], Golden and French [3], and Hosking et al. [4]. Aicardi and Krageloh [2] and Aminian et al. [6] reported the clinical dissimilarities between these syndromes and delineated the clinical features, including the following:

- (1) Onset before 18 months of age;
- (2) Repeated episodes of hemiplegia involving both sides of the body;
- (3) Other paroxysmal phenomena, such as tonic episodes, dystonic posturing, choreoathetoid movements, nystagmus or other ocular motor abnormalities, and autonomic disturbance associated with episodes of hemiplegia or occurring independently; and,
- (4) Evidence of a mental or neurologic deficit, more or less early in the course.

This patient exhibited these clinical features except that the time of onset of hemiplegic episodes was uncertain. The frequency of hemiplegic episodes, involving both sides of the body, was lower than that in other reported patients [1,2,7,8]. The persistence of mental retardation and the persistent absence of features of classic migraine, even after 14 years of follow-up, exclude basilar artery migraine [2]. Normal serum and urinary amino acid analysis results exclude Hartnup disease and homocystinuria. Normal serum pyruvate and lactate levels exclude pyruvate decarboxylase deficiency and normal serum ammonia level excludes ornithine transcarbamylase deficiency. Normal cranial MRI and normal serum pyruvate and lactate levels eliminate MELAS syndrome (i.e., mitochondrial myopathy, encephalopathy, lactic acidosis, and recurrent episodes resembling strokes). Cerebral angiography was normal which eliminated moyamoya disease.

There are two hypotheses regarding the mechanism of alternating hemiplegia; one model comprises hypoperfusion due to intracranial vasospasms and the other a type of epileptic seizure [2,5,9]. The latter hypothesis is not supported by EEG findings obtained during ictus and interictus, no paroxysmal discharges being demonstrated

Table 1. Interictal  $C^{15}O_2$ ,  $^{15}O_2$  PET

		CBF*	OEF	CMRo <sub>2</sub> *	CBV (ml/100 gm)
Cortex frontal	R	50.3	0.32	2.76	4.26
	L	41.1	0.32	2.29	3.63
Cortex temporal	R	44.7	0.29	2.5	4.63
	L	38.7	0.34	2.3	4.33
Cortex occipital	R	39.0	0.39	2.57	5.28
	L	39.8	0.38	2.6	4.8
Cortex parietal	R	38.1	0.35	2.29	4.23
	L	34.7	0.35	2.12	4.17
Cortex mean	R	43.0	0.34	2.53	4.6
	L	38.6	0.35	2.33	4.23
White matter	R	25.8	0.39	1.73	2.81
	L	27.4	0.37	1.73	2.68
Basal ganglia	R	50.0	0.34	2.87	3.3
	L	51.1	0.34	3.01	3.47
Adult control		45-55	0.4-0.5	4.5	4.5

\* ml/100 gm/min.

### Abbreviations:

CBF = Cerebral blood flow  
 CBV = Cerebral blood volume  
 CMRo<sub>2</sub> = Cerebral metabolic rate of oxygen  
 OEF = Oxygen extraction fraction ratio

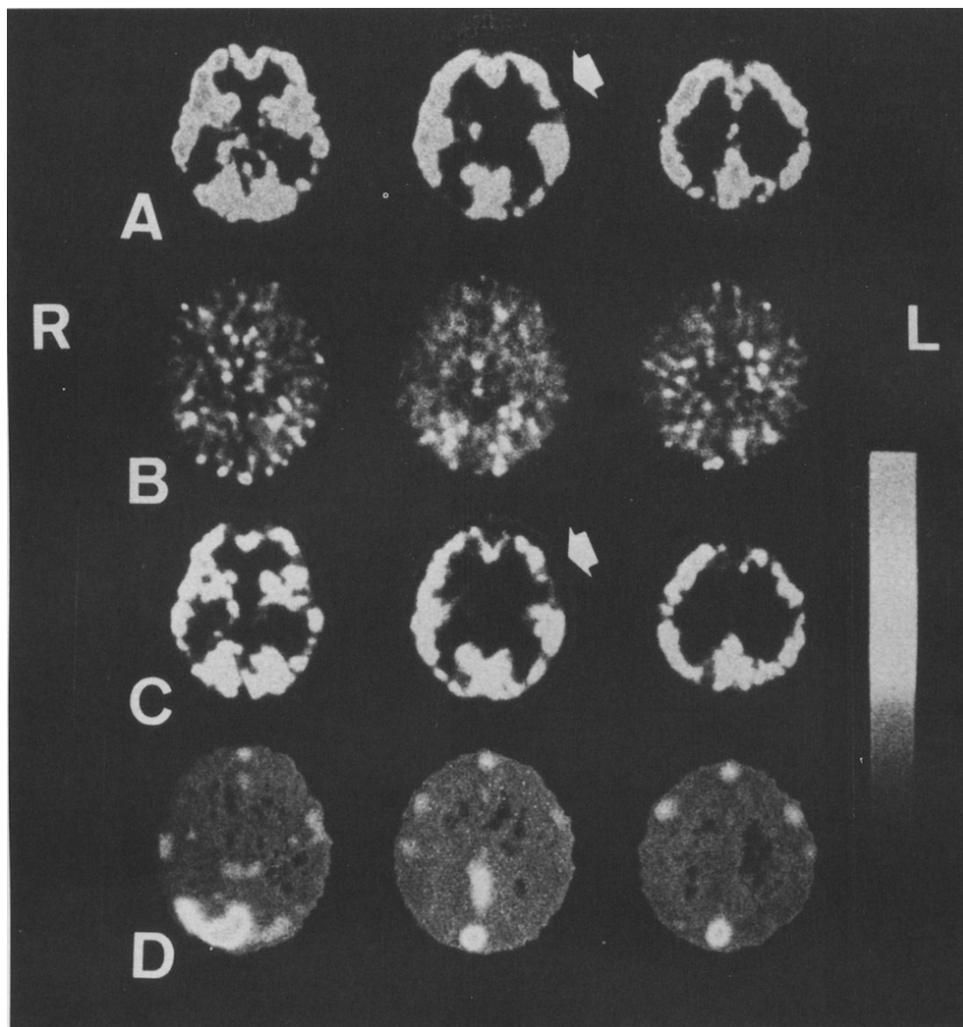


Figure 2. Interictal PET. (A) CBF revealed hypoperfusion of left frontal and temporal cortex (arrow). (B) Cerebral oxygen extraction fraction ratio (OEF) was normal. (C) Cerebral metabolic rate of oxygen ( $CMRO_2$ ) was also low in the left frontal and temporal cortex (arrow). (D) Cerebral blood volume (CBV) was normal.

[1,2,5]. In our patient, no paroxysmal epileptic discharges have been observed on EEG.

Interictal PET after the right hemiplegic episode revealed both decreased CBF and decreased metabolic rate of oxygen ( $CMRO_2$ ) in the left frontal and temporal cortex in our patient. A previous study involving measurement of CBF by PET revealed hypoperfusion of the left hemisphere [10] and another study reported normal results [8]. The decreased  $CMRO_2$  was probably due to decreased CBF.

Recently, single-photon emission computed tomographic (SPECT) brain images in alternating hemiplegia were reported [5,6,9]. Cranial  $^{123}\text{I}$ -iodoamphetamine SPECT images obtained during an acute episode of right hemiplegia demonstrated hypoperfusion of the left hemisphere [5]. Conversely, hyperperfusion of the contralateral hemisphere was suggested by asymmetric  $^{99\text{m}}\text{Tc}$ -hexamethylpropylene oxime ( $^{99\text{m}}\text{Tc}$ -HMPAO) uptake during episodes of ipsilateral hemiplegia [6,9]. There was no coincidence between the PET and SPECT findings

during the interictal period. There is no accepted conception of the circulatory dynamics in alternating hemiplegia in childhood.

The calcium-entry blocker, flunarizine, is the first drug that may be of benefit in the treatment of alternating hemiplegia [7,8,11]. Casaer reported that children treated with flunarizine responded favorably, with a reduction in the frequency and/or duration and severity of episodes [7]. Silver and Andermann treated 9 patients with flunarizine for up to 5 years, but the episodes only ceased completely in 1 patient [8]. In our patient, complete cessation of the episodes and seizures was obtained with flunarizine and has been maintained for longer than 6 years. There has been neither neurologic regression nor an adverse reaction. The mode of action of flunarizine is unknown. This drug has been reported to protect brain cells against hypoxia and to have an anticonvulsive effect [7].

Cerebral angiography is needed to demonstrate structural or dynamic changes in cerebral blood vessels. To our knowledge, there has been no patient with alternating

hemiplegia who developed a coma and hemiplegic episodes immediately after cerebral angiography. Postanesthetic irritability and crying appeared to trigger the episodes. Hemiplegic migraine, a typical complicated migraine, is sometimes accompanied by loss of consciousness [2]. It has been suggested that angiography of a hemiplegic migraine patient should be avoided because it worsens the episodes [12]. We believe that angiography should also be carefully considered in patients with alternating hemiplegia in childhood, especially in atypical ones, although cerebral angiography has to be performed in patients with alternating hemiplegia to eliminate cerebrovascular abnormalities, such as moyamoya disease.

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