Journal of Korean Medical Science
Vol. 8, No. 6, 476-481 December 1993

Delayed-onset Focal Dystonia After Diffuse Cerebral Hypoxia

— Two Case Reports —

Young Chul Choi, M.D., Myung Sik Lee, M.D., Il Saing Choi, M.D.

Department of Neurology, Youngdong Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

The delayed-onset focal dystonia is a rare sequela of cerebrovascular disease or diffuse cerebral hypoxic damage. The responsible lesion sites for the dystonia are variable and the pathogenesis is uncertain.
We describe two children with delayed-onset focal dystonia as a complication of perinatal anoxia. The intervals between hypoxic insult and onset of dystonia were 6 years in one and 3 in the other case. Our patients did not have a focal lesion; one had scattered white matter lesion and the other had a diffuse frontoparietal atrophy. Delayed-onset dystonia after perinatal anoxia can be also caused by non-focal lesion such as diffuse frontoparietal atrophy or cerebral white matter lesion with long interval delay.

Key Words: *Delayed-onset dystonia, perinatal anoxia*

INTRODUCTION

Dystonia is characterized by sustained muscle contraction, which leads to abnormal posture and/or twisting and repetitive movements(Fahn, 1988). Since the first description by Hammond in 1871, delayed-onset dystonia is a rare but well known sequela of diffuse cerebral hypoxic damage(Burke et al, 1980;Marsden et al, 1985; Pettigrew and Jancovic, 1985; Saint-Hilaire et al, 1991) or cerebrovascular disease(Traub and Ridley, 1982; Demierre and Rondot, 1983; Russo, 1983; Obeso et al, 1984; Chiang and Lu, 1990).

It can occur immediately after a brain damage, but more frequently it develops after a variable period(Russo, 1983; Marsden et al, 1985; Pettigrew and Jancovic, 1985). Caudate nucleus, lentiform nucleus, thalamus, internal capsule, or variable combinations of them have been reported as the responsible sites for delayed-onset dystonia, especially in stroke patients(Marsden et al, 1985; Pettigrew and Jancovic, 1985). However, Glatt and Nausieda(1984) had reported 2 patients with lesion outside the extrapyramidal system and there were several reports of delayed-onset dystonia caused by perinatal anoxia without focal basal ganglia lesion(Table 1).

The pathologic process responsible for the dystonia during the initial recovery period is unknown. Burke et al.(1980) have hypothesized that the neuronal regeneration with brain maturation is responsible for the delayed-onset. Some authers have compared the interval and frequency of delayed-onset dystonia in patients of perinatal anoxia and stroke and they concentrated only on the age of hypoxic injury deciding the duration of delay in spite of the differences of etiology(Pettigrew and Jancovic, 1985).

We present two patients with delayed-onset focal dystonia after perinatal anoxia and review the related literature.

CASE REPORTS

Patient 1

An 8-year-old boy was referred due to dystonic posture in the left arm for 2 years. He was a prod-

Address for correspondence: *Young Chul Choi, Department of Neurology, Yongdong Severance Hospital, Yonsei University, College of Medicine, Seoul, Korea(Tel.: 569-0110 Ext. 2230).*

Table 1. Clinical characteristics and anatomical lesion in dystonic patients reported in the literature after perinatal anoxia and childhood asphyxia.

Reference	Age at insult	Age of onset	Duration of delay	Site of dystonia	Etiology & pathology		Anatomical site
Burke	birth	7	7yr	Lt U/E	Perinatal	anoxia	Rt cerebral hemiatrophy
(1980)	birth	14	14yr	Rt U/E	Perinatal	anoxia	Normal
	birth	13	13yr	Lt arm	Perinatal	anoxia	Normal
	birth	9	9yr	Rt U/E	Perinatal	anoxia	Not obtained
	birth	6	6.5yr	Lt hemi.	Perinatal	anoxia	Normal
Pettigrew	birth	29	29yr	Lt hemi.	Perinatal	anoxia	Rt cerebral hemiatrophy,arachnoid cyst
(1985)	birth	2	2yr	Rt hemi.	Perinatal	anoxia	Lt cerebral hemiatrophy,porencephalic
	birth	32	32yr	Lt hemi.	Perinatal	anoxia	Rt putamen
Marsden	birth	4	4yr	Rt hemi.	Perinatal	anoxia	Lt cerebral hemiatrophy
(1985)	birth	1	1yr	Lt hemi.	Perinatal	anoxia	Rt cerebral hemiatrophy
Saint Hilaire	birth	5	5yr	Lt hand	Perinatal	anoxia	Normal
(1991)	birth	8	8yr	Lt hemi.	Perinatal	anoxia	Rt hemiatrophy
	birth	15	15yr	Lt hemi.	Perinatal	anoxia	Normal
	birth	9	9yr	Rt arm	Perinatal	anoxia	Normal
	birth	14	14yr	Rt arm	Perinatal	anoxia	Normal
	birth	14	14yr	Rt arm	Perinatal	anoxia	Normal
	birth	13	13yr	Neck	Perinatal	anoxia	Normal
	birth	13	13yr	Rt arm	Perinatal	anoxia	Bilateral basal ganglia
	birth	21	21yr	Face	Perinatal	anoxia	Normal
	birth	17	17yr	Neck	Perinatal	anoxia	Cerebellar atrophy
	3yr	9	6yr	Both arm	Asphyxia		Normal
	18mon	17	16yr	Face	Asphyxia		Normal
Present case	birth	6	6yr	Lt U/E	Perinatal	anoxia	Rt frontoparietal atrophy
	birth	3	3yr	Lt L/E	Perinatal	anoxia	White matter lesion

uct of a full-term pregnancy and normal delivery. Severe jaundice and cyanotic apnea developed in the early neonatal period and he received intensive treatment for 3 weeks in the hospital. Developmental milestones were normal until the age of four years. Thereafter, he had a frequent partial seizure. He slowly developed walking difficulty and clumsiness in the left arm. At the age of six, he developed definite dystonic posture of the left upper extremity which was intensified by standing or walking. This consisted of abduction of the shoulder, flexion and external rotation of the elbow and wrist with flexion of the metacarpophalangeal joints and extension of the interphalangeal joints (Fig.1). There was no family history of metabolic or degenerative neurologic disease and no medication history such as neuroleptics. On examination, he had a mild left hemiparesis and muscle wasting. Deep tendon reflexes were hyperactive on the left side. Cranial nerve tests were normal. Cerebellar function revealed no abnormality. Deep and superficial senses were normal. There was no Kayser-Fleischer ring. Normal and negative tests included complete blood count, urinalysis, electrolyte, renal function tests and serum ceruloplasmin. But liver enzymes(SGOT/SGOP) were elevated due to hepatitis B virus infection. An electroencephalogram showed intermittent bilateral sharp waves at the parieto-occipital region. The computed tomography scan of the brain showed right frontoparietal atrophy(Fig. 2). The frequency of the seizure attacks was reduced markedly after carbamazepine administration. There were no changes in the dystonic movement of the left hand with adminstration of trihexyphenidyl.

Patient 2

A 9-years-old girl was referred due to walking difficulty for 6 years. The pregnancy was normal and full-term, but delivery was complicated by amniotic fluid aspiration.

Developmental milestones were normal until the age of three years. At the age of 3, she developed a spontaneous and action-induced dystonic posture in the left foot. It started gradually and progressed to produce plantar flexion of the left foot during sitting position in a chair(Fig. 3) which was aggravated by walking. There was no family history of metabolic or degenerative neurologic disease and no medication history such as neurolep-

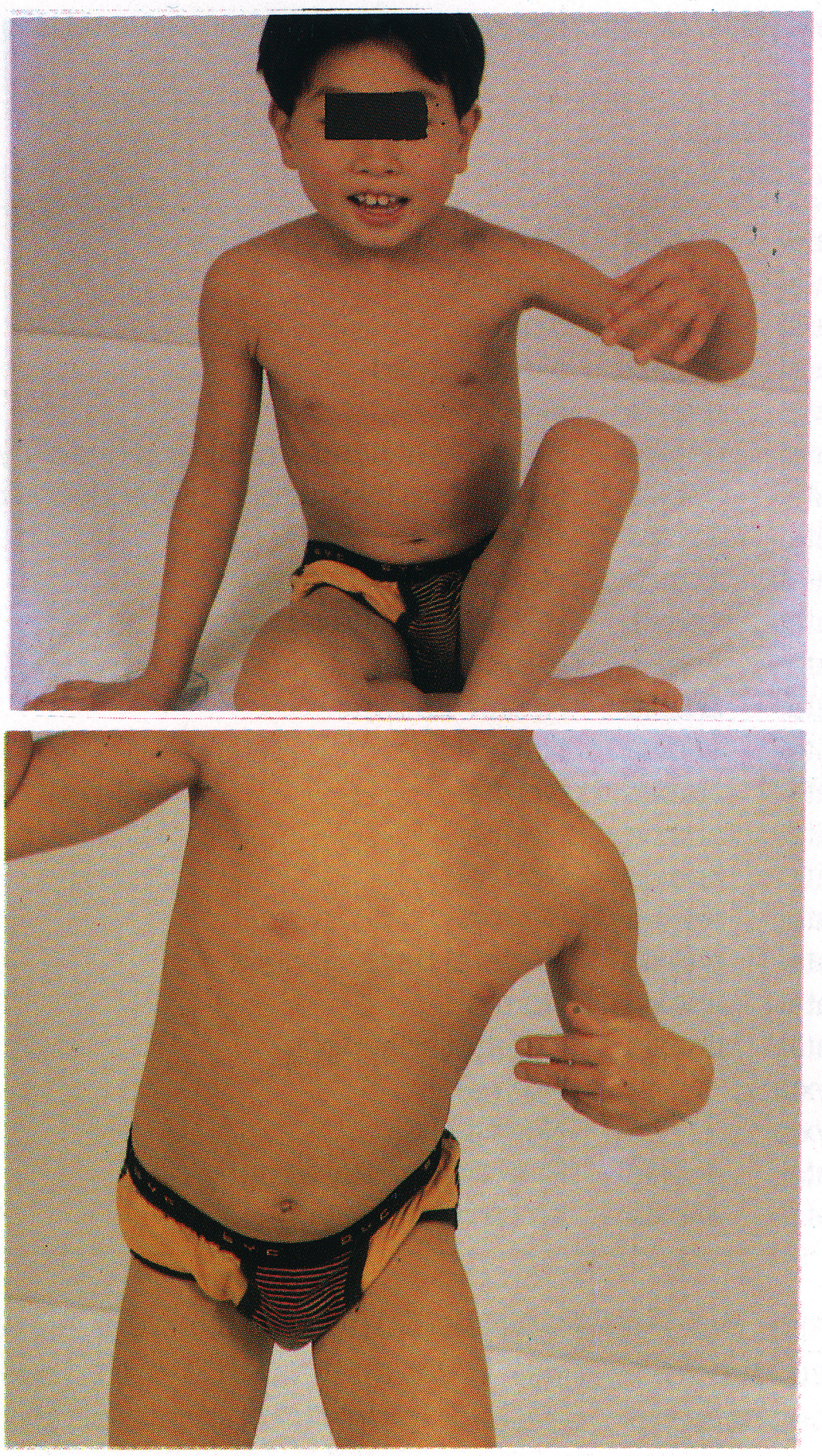

Fig. 1. The dystonic movement of left arm in patient 1(A) intensified by standing up(B).

tics. On examination, her mental function was normal. There was no motor weakness. Cranial nerves were normal. Cerebellar function test was normal. A slit-lamp examination revealed no Kayser-Fleisher ring. Complete blood count, urinalysis, serum electrolytes, renal function test were normal. Liver function tests and seurm ceruloplasmin were normal. The MRI of the brain showed scattered high signal intensity in the white matter, especially at the bilateral occipital and parietal area (Fig. 4). Mild improvement of dystonic posture was noted after an administration of clonazepam.

DISCUSSION

Delayed-onset dystonia is a rare sequela of cerebral hypoxic insult(Dooling and Adams, 1975) such as perinatal anoxia(Burke et al, 1980; Marsden et al, 1985; Pettigrew and Jancovic, 1985; Saint-Hilaire et al, 1991) or cerebrovascular disease(Traub and Ridley, 1982; Demierre and Rondot, 1983;Russo, 1983; Obeso et al, 1984). It may also develop as a sequela of many other disorders such as; trauma(Andrew et al, 1982; Brett and Hoart, 1981; Krauss et al, 1992), tumor(Marsden et al, 1985; Glatt and Nausieda, 1984; Narbona et al, 1984), infection(Dooling and Adams, 1975), vasculitis and SLE(Anegawa et al,1986; Daras et al, 1988). It can occur immediately after hemiplegia, but more frequently much later with the recovery from hemiplegia. In our series, two patients developed dystonia after perinatal hypoxia. The latency between brain hypoxic insults and the onset of dystonia were 6 years and 3 years.

The anatomical basis and pathogenesis of de-

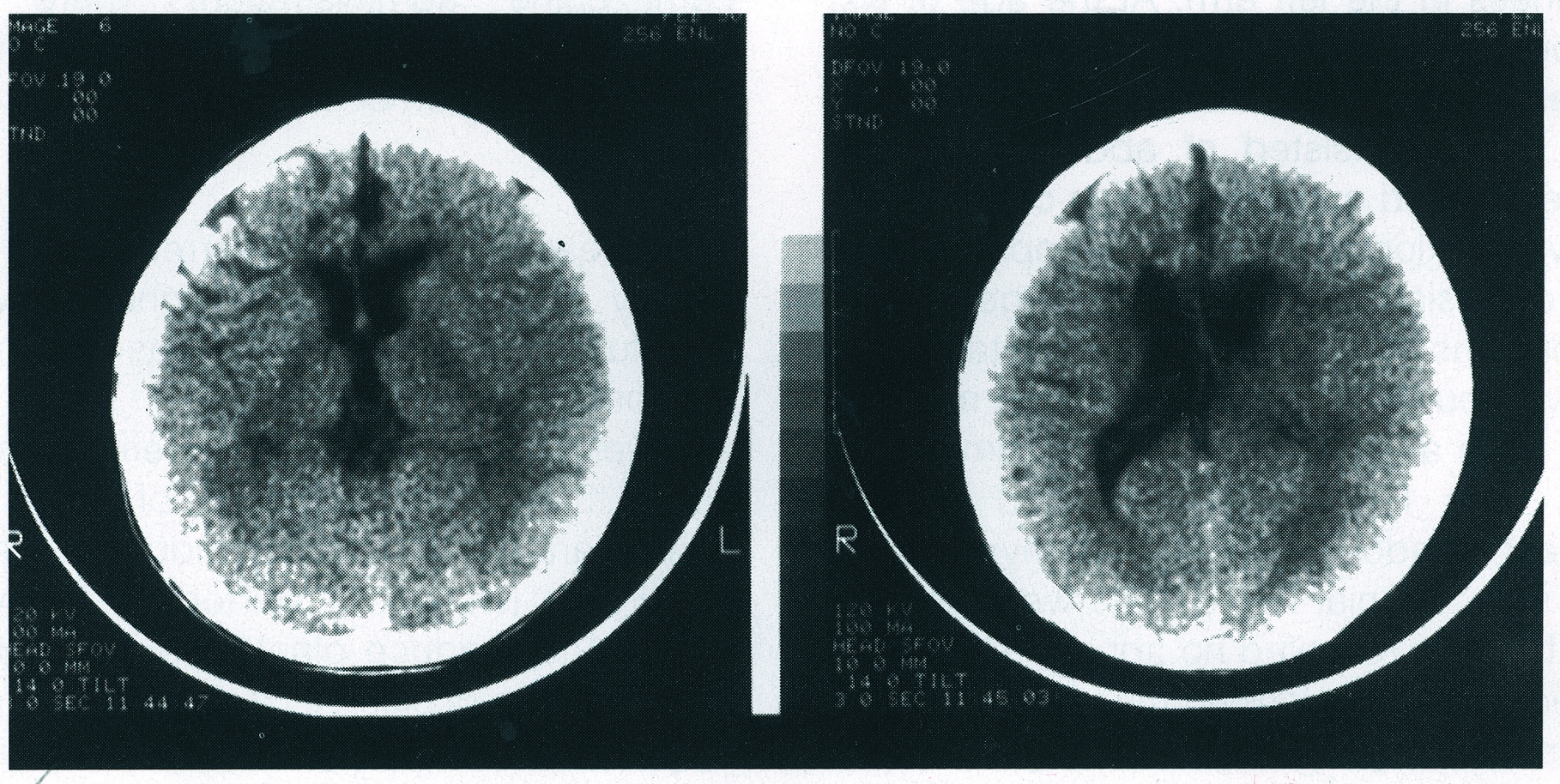

Fig. 2. A brain CT of Patient 1 revealed diffuse frontoparietal atrophy.

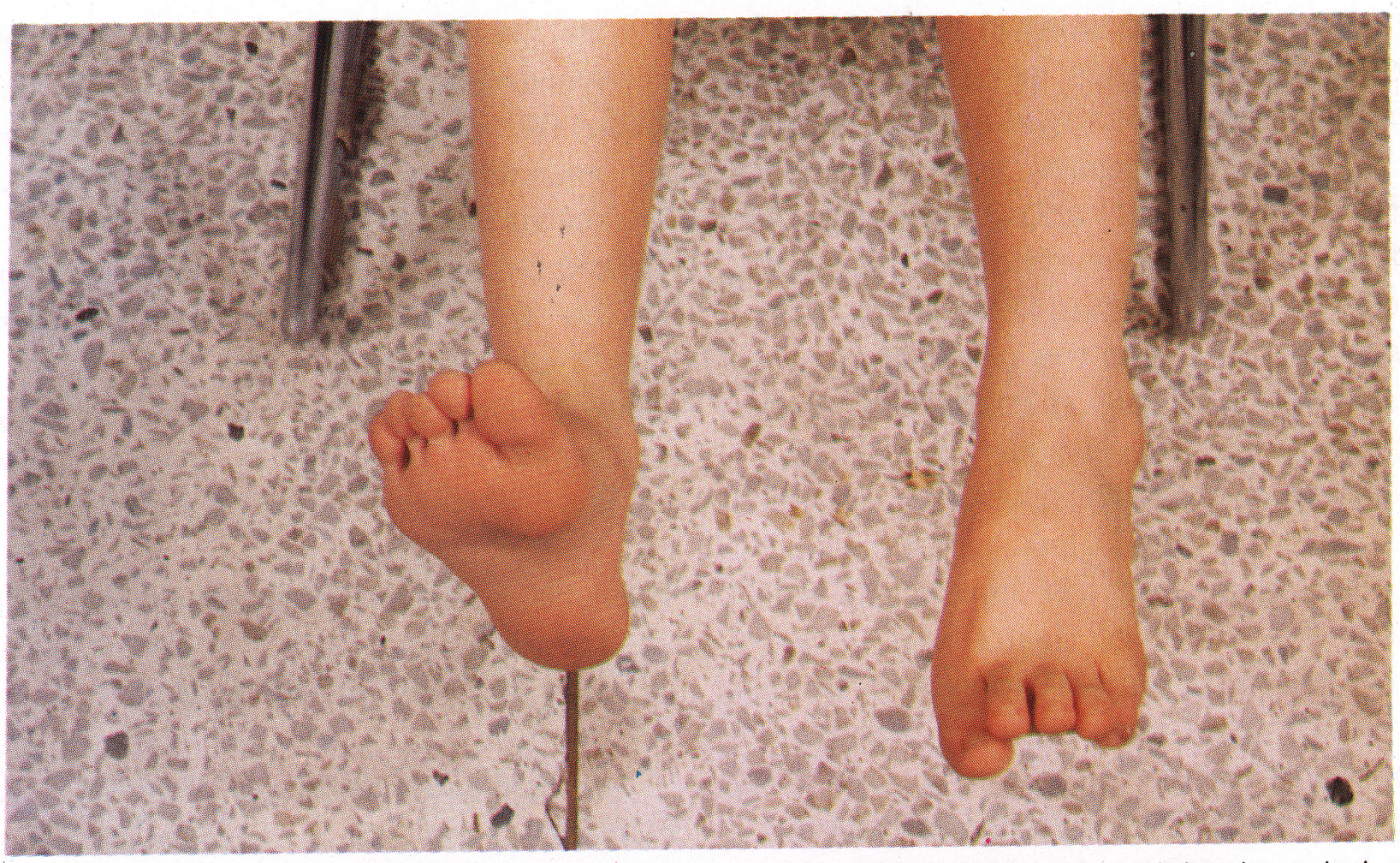

Fig. 3. The dystonia of patient 2 showed plantar flexion of the left foot while sitting in a chair.

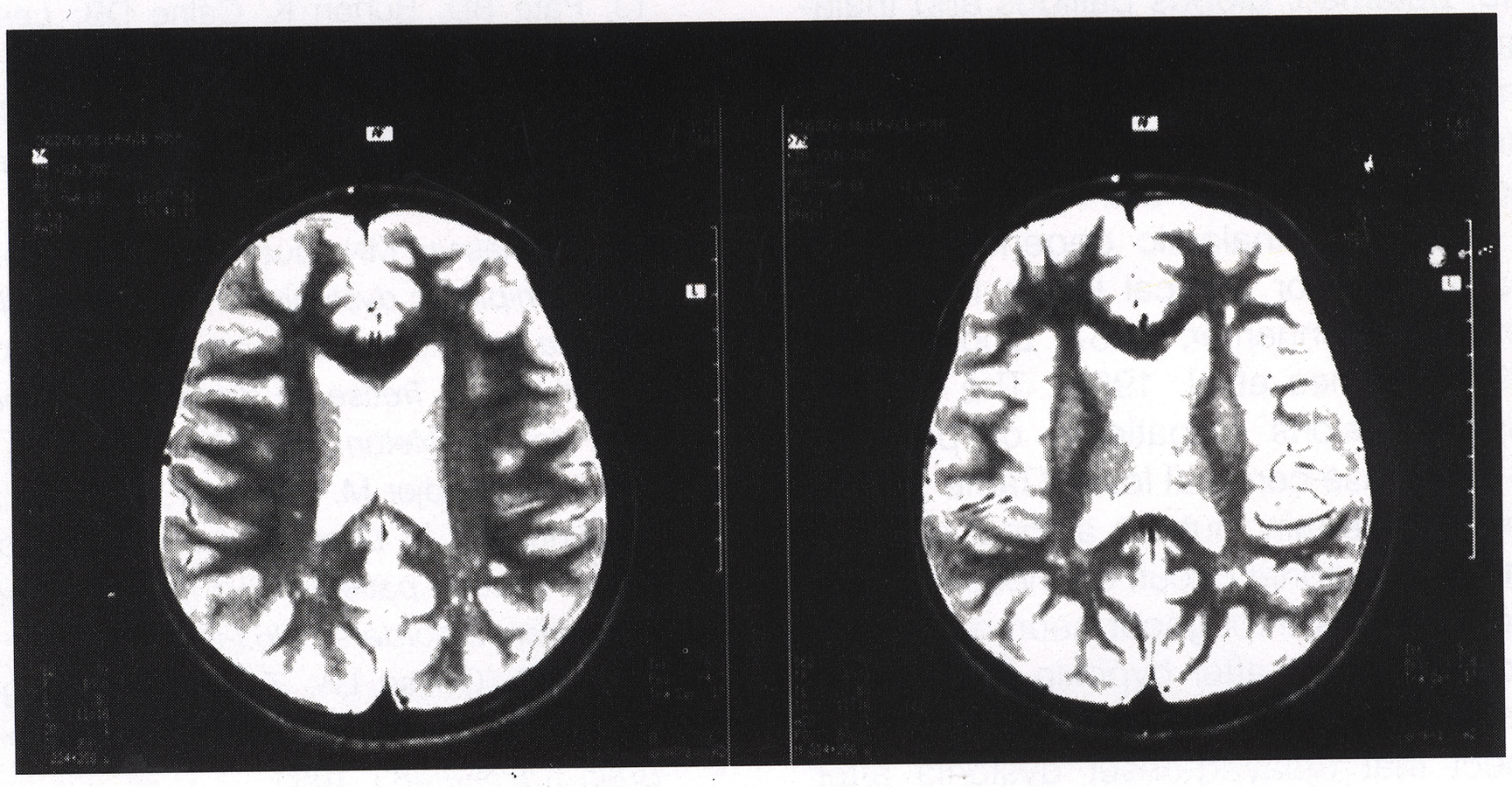

Fig. 4. A MRI of the brain of patient 2 showed abnormal high signal intensity in bilateral occipital and parietal deep white matter(repetition time, 3000 msec; echo time, 80 msec).

layed-onset dystonia is uncertain. Mitchell(1974) has suggested that the delay in the onset of hemichorea or athetosis following hemiplegia was caused byy progressive changes in the original brain lesion. Burke(1980) has hypothesized that the mechanism of delayed-onset dystonia occurring a year or more after the insult may be due to aberrant neuronal sprouting with brain maturation. Pettrigrew and Jankovic(1985) studied 22 patients of delayed-onset dystonia following variable causes. They found that the mean interval in the seven patients who had brain lesions below the age of 7 was much longer than the remaining patients above the age of 7, and postulated that the age of the patient at the time of cerebral injury decides the duration of delay after the acute brain damage. However, these hypothesis have limitation. Some patients with immediate onset can not be explained by neuronal regeneration. Because if the delayed-onset dystonia is caused by neuronal regeneration with brain maturation, the patients of hypoxic injury at the perinatal and early childhood period would have shorter duration of delay than that of hypoxic injury after early childhood.

Therefore we reviewed the literature to further characterize the relationship between anatomical

lesion site and the latency of delay in perinatal hypoxia brain damage. 20 cases of delayed-onset dystonia after perinatal anoxia(Burke et al, 1980; Marsden et al, 1985; Pettigrew and Jancovic, 1985: Saint-Hilaire et al, 1991) and 2 cases of delayed-onset dystonia after early childhood asphyxia(Saint-Hilaire et al, 1991)(Table 1) have been reported. The intervals between the onset of dystonia and perinatal hypoxic brain damage were varied from 1 year to 32 years(mean delay: 12.3 years). Dystonia following childhood asphyxia appeared 6 years and 16 years after hypoxic insult. After studying our cases and the literature, it became clear that the delay of dystonia following perinatal anoxic brain damage is long and there are variety of anatomical lesion sites such as non-focal diffuse cerebral lesion.

The pathological lesions in patients of delayed onset dystonia have a variety of anatomical lesion sites. Damage to the neuronal circuit connecting the caudate, putamen, globus pallidus and thalamus(Pettigrew and Jancovic, 1985; Fross et al, 1987) seems to be responsible for the dystonia following cerebrovascular disease. However, it can occur without evidence of striatal lesion(Glatt and Nausieda, 1984) and thalamic degeneration following striatal lesion or cortical lesion have also been reported(Oppenhemer, 1967; Dooling and Adams, 1975; Grimes et al, 1982). The responsibe pathologic lesions in patients of perinatal anoxia can be diffuse cerebral lesion(Table 1). The pathogensis is uncertain, but the authosr suggest that effect to the neuronal circuit connecting basal ganglia and thalamus throughout neuronal regeneration or degeneration after hypoxic injury seem to be the contributing mechanism.

We suspect that delayed-onset dystonia after perinatal anoxia have a long duration of delay and can be also caused by non-foacal lesion such as diffuse frontoparietal atrophy or cerebral white matter with a long delay interval.

REFERENCES

Andrew J, Fowler C, Harrison MJG. *Hemi-dystonia due to focal basal ganglia lesion after head injury and improved by sterotaxic thalamotomy. J Neurol Neurosurg Psychiatry 45;276, 1982.*

Anegawa T, Harada K, Akiguchi I: *Two cases of posthemiplegic dystonia and controlateral low density area on CT caused by inflammatory vasculitis. Clin Neurol 26:180-183, 1986.*

Brett EM, Hoart RD: *Progressive hemi-dystonia due to focal basal ganglia lesion after mild head trauma. J Neurol Neurosurg Psychiatry 44;460, 1981.*

Burke RE, Fahn S, Gold AP: *Delayed-onset dystonia in patients with "static" encephalopathy. J Neurol Neurosurg Psychiatry 43;789-797, 1980.*

Chiang CY, Lu CS: *Delayed-onset posthemiplegic dystonia and imitation synkinesia. J Neurol Neurosurg Psychiatry 53;623, 1990.*

Daras M, Georgakopoulos T, Adelidis D: *Late onset posthemiplegic dystonia in systemic lupus erythematosus. J Neurol Neurosurg Psychiatry 51;151-152, 1988.*

Demierre B, Rondot P: *Dystonia caused by putamino-capsulo-caudate vascular lesions. J Neurol Neurosurg Psychiatry 46;404-409, 1983.*

Dooling EC, Adams RD: *The pathological anatomy of posthemiplegic athetosis. Brain 98;29-48, 1975.*

Fahn S: *Concept and classification of dystonia. Adv Neurol 50;1-8, 1988.*

Fross RD, Martin WRW, Li D, Stoessl AJ, Adam MJ, Ruth TJ, Pate BD, Burton K, Calne DB: *Lesions of the putamen. Neurology 37;1125-1129, 1987.*

Glatt SL, Nausieda PA: *Posthemiplegic dystonia: radiographic and pharmacologic analysis. Neurology 34 (Suppl 1):290-291, 1984.*

Grimes JD, Hassan MN, Quarrington AM: *Delayed-onset posthemiplegic dystonia: CT demonstration of basal ganglia pathology. Neurology 32;1033-1035, 1982.*

Hammond WA: *A Tretise on disease of the nervous system. New: Appleton, 655-662. 1871.*

Krauss JK, Mohadjer M, Braus DF, Wakhloo AK, Nobbe F, Mundinger F: *Dystonia following head trauma: a report of nine patients and review of the literature. Movement Disorders 7;263-272, 1992.*

Marsden CD, Obeso LA, Zarranz JJ, Lange AE: *The anatomical basis of symptomatic hemidystonia. Brain 108;468-483, 1985.*

Mitchell SW. Post-paralytic chorea. Am J Med Sci 68; 342-352, 1974.

Narbona J, Obeso JA, Tunon T, Martinez-Lage JM, Marsden CD: *Hemi-dystonia secondary to localized basal ganglia tumor. J Neurol Neurosurg Psychiatry 47; 704-709, 1984.*

Obeso JA, Martinz-Vila E, Delgado G, et al: *Delayed onset dystonia following hemiplegic migraine. Headache 24;266-268, 1984.*

Oppenhemer DR: *A case of striatal hemiplegia. J Neurol Neurosurg Psychiatry 30;134-139, 1967.*

Pettigrew LC, Jancovic J. Hemidystonia: *a report of 22 patients and a review of literature. J Neurol Neurosurg Psychiatry 1985;48;650-657.*

Russo LS: *Focal dystonia and lacunar infarction of basal ganglia. Arch Neurol 40;61-62, 1983.*

Saint-Hilaire M-H, Burke RE, Bressman SB, Brin MF, Fahn S: *Delayed-onset dystonia due to perinatal or early childhood asphyxia. Neurology 41:216-222, 1991.*

Traub M, Ridley A: *Focal dystonia in associated with infarction. J Neurol Neurosurg Psychiatry 45;1073-1074, 1982.*