Yonsei Medical Journal
Vol. 29, No. 3, 1988

Olivopontocerebellar Atrophy

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Between 1985 and 1987, 31 patients with sporadic olivopontocerebellar atrophy (SOPCA) and 3 patients with familial olivopontocerebellar atrophy (FOPCA) were examined in the Neurologic Clinic of Yongdong Severance Hospital. The incidence of the disease among our neurology clinic patients was 0.9%, and 3.4% of those patients were admitted. Seventeen of them were men and seventeen women, and their ages of onset ranged from 16 to 75 years (mean, 48.2 years). In comparison with SOPCA, the disease began earlier in FOPCA (mean age, 51.0 VS 19.3 years), but there were no other differences in clinical feature of the disease. Four patients had parkinsonism, one dementia, and one ophthalmoplegia. None presented spinal involvement or abnormal movements. Eight had a coexisting disease; 3, chronic alcoholism; 2, hypertension; 2, diabetes mellitus; and 1, malignant neoplasm.

Key Words: Olivopontocerebellar atrophy, FOPCA, SOPCA

Olivopontocerebellar atrophy (OPCA) is a term coined by Dejerine and Thomas which comprises as series of heterogenous diseases whose only common fator is the loss of neurons in the ventral portion of the pons, inferior olives and cerebellar cortex. Presently the OPCAs are included under the general heading of multiple system atrophy.

OPCA may be clinically diagnosed by means of history, including pertient family history, characteristic signs, and in the past, a pneumoencephalogram (PEG). With the advent of computed tomography (CT), these patients may be evaluated without the need for PEG (Aita 1978).

Since Menzel's description of this disorder in 1981, numerous clinical studies have been performed in America and Europe (Konigsmark and Weiner 1970; Landis *et al.* 1974; Berciano 1982; Harding 1982). However, few reports about this order as it is found in Korea have appeared in print (Lim *et al.* 1984; Jeon *et al.* 1984; Lee *et al.* 1985).

Received March 30, 1988
Accepted May 24, 1988
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MATERIALS AND METHODS

Between 1985 and 1987, a total of 3,596 patients (994 admissions) were seen at the Neurologic Clinic, Yongdong Severance Hospital, Yonsei University Medical Center.

Of them, the diagnosis of OPCA was made in 34 cases, Parkinson's disease in 150 cases, and Alzheimer's disease in 5 cases.

Thirty-four patients with OPCA were classified according to incidence, sex, age, family history, duration of illness, clinical signs and symptoms, and coexisting diseases. The disease was divided into an hereditary type and a sporadic group, based on the Greenfield's mothed (Greenfield, 1954).

C-T brain scans were performed in all patients, EEG (electroencephalogram) in 15 patients, and BAEP (brainstem auditory evoked potentials) in.6 patients. No pathologic study was done.

The diagnostic criteria of OPCA were the following: 1) neurologic disturbances including cerebellar, pyramidal, extrapyramidal and/or spinal involvement; 2) family history; and 3) abnormal C-T brain scan findings such as atrophy of the pons and cerebellum, with enlargement of the 4th ventricle and ambient, prepontine, and quadrigerminal cisterns.

Table 1. Clinical summary of 34 patients with olivopontocerebellar atrophy

No	Sex	Age of onset	Duration of illness	Symptoms and signs			coexisting disorder
				cerebellar and pyramidal	extrapyramidal	other	
1	M	16	12	ataxia, dysarthria, spasticity, hyperreflexia	------	ophthalmoplegia	autosomal dominant
2	M	20	6	ataxia, dysarthria, hyperreflexia, pathologic reflex	------	------	"
3	F	22	4	ataxia, dysarthria	------	------	"
4	F	42	3	ataxia, hyperreflexia	bradykinesia, masked face, rigidity, short-step gait, tremor	inappropriate laughing	------
5	M	54	1	ataxia, hyperreflexia	bradykinesia, masked face, rigidity.	inappropriate laughing	DM
6	M	48	4	ataxia, hyperreflexia, intention tremor	bradykinesia, masked face, rigidity, short-step gait	------	------
7	M	40	10	dysarthria, dysphagia, hyperreflexia	masked face, rigidity, short-step gait, tremor	inappropriate laughing	alcoholism
8	F	59	3	ataxia, dysarthria, hyperreflexia	------	dementia, urinary incontience	uterine Ca
9	M	26	6	ataxia, dysarthria, hyperreflexia, nystagmus	------	hearing loss (o.u)	------
10	M	54	5	ataxia, dysarthria, dysphagia, spasticity, hyperreflexia, intention tremor	------	------	hypertension
11	F	46	1	ataxia, dysarthria	------	------	------
12	M	58	3	hyperreflexia, spasticity	------	------	hypertension
13	M	54	1	ataxia, dysarthria, hyperreflexia, nystagmus, pathologic reflex	------	------	alcoholism
14	F	53	2	ataxia, dysarthria, hyperreflexia, pathologic reflex	------	------	------
15	F	49	3	ataxia, dysarthria, dysphagia	------	------	----
16	F	60	7	ataxia, dysarthria, dysphagia, spasticity, hyperreflexia	------	------	-----
17	F	53	8	ataxia, dysarthria, spasticity, hyperreflexia	------	------	-----
18	M	68	1	ataxia, hyperreflexia	------	------	----
19	F	58	3	ataxia, dysarthria, spasticity, hyperreflexia	------	------	DM
20	F	54	10	ataxia, dysarthria	------	------	----
21	M	49	1	ataxia, dysarthria, spasticity, hyperreflexia, pathologic reflex	------	------	alcoholism
22	M	75	2	ataxia, dysarthria, spasticity, hyperreflexia, pathologic reflex	------	------	-----
23	F	51	2	ataxia, dysarthria, hyperreflexia, pathologic reflex	------	------	-----
24	M	55	10	ataxia, dysarthria, dysphagia, spasticity, hyperreflexia	------	------	-----
25	F	52	1	ataxia, spasticity, hyperreflexia	------	------	-----
26	F	43	1	ataxia, dysarthria, spasticity, hyperreflexia	------	------	-----

No	Sex	Age of onset	Duration of illness	Symptoms and signs: cerebellar and pyramidal	extrapyramidal	other	coexisting disorder
27	F	55	2	ataxia, hyperreflexia	-----	-----	-----
28	M	64	2	ataxia, dysarthria, dysphagia	-----	-----	-----
29	M	50	4	ataxia, dysarthria, spasticity, hyperreflexia	-----	-----	-----
30	F	56	2	ataxia, hyperreflexia, pathologic reflex	-----	-----	-----
31	F	37	6	ataxia, dysarthria	-----	-----	-----
32	M	27	2	ataxia, spasticity, pathologic reflex	-----	-----	-----
33	M	45	3	ataxia, spasticity, pathologic reflex	-----	optic atrophy with depigmentation	-----
34	F	45	7	ataxia, spasticity, nystagmus, pathologic reflex	-----	-----	-----

RESULTS

The incidence of OPCA was 0.9% of the total group in our neurologic clinic, and 3.4% of those admitted (cf Parkinson's disease, 4.1 and 15.1%; Alzheimer's disease, 0.14 and 0.5%).

A clinical summary of the 34 patients with OPCA is given in Table 1.

Of the 34 patients, 3 were classified as hereaitary, with an autosomal dominant transmission (Fig. 1), and 31 were sporadic.

There were 17 men and 17 women. The ages of onset in OPCA ranged from 16 to 75 years (mean, 48.2 years), with the peak incidence in the 5th and 6th decades. The age of onset in famial OPCA (FOPCA) ranged from 16 to 22 years (mean, 19.3 years), and that of sporadic OPCA (SOPCA), 26 to 75 years (mean, 51.0 years) (Table 2).

The duration of the disease varied between 1 year and 12 years (average duration, 3.9 years).

The initial symptom of OPCA usually was cerebellar ataxia, especially involving the gait, but 4 patients exhibited parkinsonian symptoms initially. All patients except two (94.5%) had ataxia, 25(73.5%) hyperreflexia, and 23 (67.6%) dysarthria. Other clinical features included spasticity, dysphagia, tremor, rigidity and pathologic reflexes. In rare cases, urinary incontinence, optic atrophy, dementia, and ophthalmoplegia were noted. None had spinal involvement or abnormal movements (Table 3). There was no difference in clinical manifestations except for age of onset between FOPCA and SOPCA.

Eight (23.5%) had a coexisting disease: 3, chronic alcoholism; 2, hypertension; 2, diabetes mellitus; and one, carcinoma of uterine cervix. EEGs in 15 patients

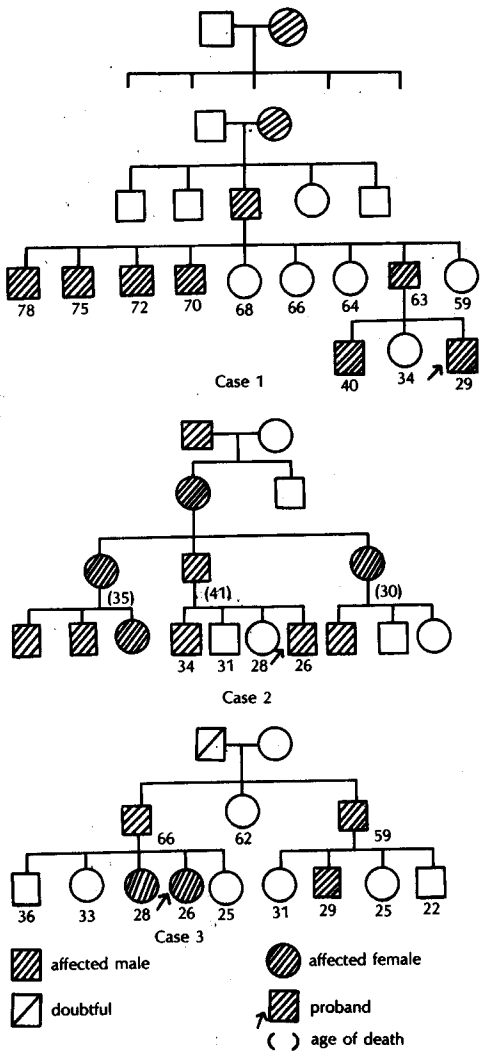

Fig. 1. Pedigrees of three patients with familial OPCA.

Table 2. Age of onset and sex distribution in 34 patients with OPCA

Age (years) \ Sex	Male	Female	Total
below 20	1	0	1
20-29	3	1	4
30-39	0	1	1
40-49	4	5	9
50-59	6	9	15
60-69	2	1	3
over 70	1	0	1
Total	17	17	34

Table 3. The fequencies of clinical features in 34 patients with OPCA

Clinical finding	No	%	Clinical finding	No	%
Ataxia	32	94.1	Bradykinesia	3	8.8
Hyperreflexia	25	73.5	Short-step gait	3	8.8
Dysarthria	23	67.6	Inappropriate laugh	3	8.8
Spasticity	15	44.1	Nystagmus	3	8.8
Pathologic reflex	11	32.4	Dementia	1	2.9
Dysphagia	6	17.6	Urinary incontinence	1	2.9
Tremor	4	11.8	Ophthalmoplegia	1	2.9
Rigidity	4	11.8	Optic atrophy	1	2.9
Masked face	4	11.8	Hearing loss	1	2.9

and BAEPs in 6 patients were obtained, and all were normal.

DISCUSSION

The olivopontopocerebellar atrophies (OPCA) are a group of diseases characterized by the loss of neurons in the cerebellar cortex, basis pontis and inferior olivary nuclei. There may be neuronal loss to a variable degree in the spinal cord, cerebral cortex and basal ganglia (Landis *et al.* 1974). Although OPCA was first reported by Menzel in 1981, OPCA is a term coined by Dejerine and Thomas who separated their isolated case from the familial type described by Menzel (Konigsmark & Weiner 1970). Thereafter several mothods of classification of OPCA have been suggested.

Greenfield (1954) divided the OPCA's into an hereditary type and a sporadic type. Pratt (1967) in a review of hereditary diseases of the nervous system, divided the OPCA's into 2 groups; those with spinal cord involvement and those with the absence of spinal cord involvement. Becker divided the OPCA's into 3 types: 1) a dominant type as described by Menzel; 2) a recessive type including sporadic; and 3) a typical types with varing clinical presentations (Harding, 1984). Konigsmark and Weiner (1970) divided the OPCA's into 5 categories; type 1, dominant; type 11, recessive; type 111, with retinal degeneration; type 1V, Schut and Haymaker; type V, with dementia, ophthalmoplegia and extrapyramidal signs.

The literature contains descriptions of various clinical studies of OPCA, but many of them were review article concerned with cases and families (Schut 1950; Landis *et al.* 1974; Berciano 1982; Harding 1982). OPCA is a rare disorder of multisystem degeneration. The incidence of OPCA herein is lower than that of Parkinson's disease, but higher than that of Alzheimer's disease. This finding differs between Korea and other countries. The age of onset in SOPCA is unually middle age or older, while FOPCA begins earlier than SOPCA. The reported sex ratios vary (Schut 1950; Landis *et al.* 1974; Berciano 1982), but gender does not appear to effect the incidence of OPCA. The duration of the disease varies between months and several years, and FOPCA usually lasts longer than SOPCA (Berciano 1982). As other authors have already indicated (Konigsmark and Weiner 1970; Landis *et al.* 1974; Berciano 1982), the clinical picture usually begins with cerebellar ataxia as we found herein. When parkinsonian symptoms are found among the first manifestations, they will always be important symptoms throughout the course of the disease.

In contrast with the greater frequency of ataxic gait in the early stages, as the disease progresses, the cerebellar syndrome always becomes static and kinetic. Dysarthria is also a constant symptom as we found herein. The type of dysarthria varies among bulbar or pseudobulbar, slow and monotonous, or as a mixture of these. Parkinsonian symptoms were reported in 25 of the 45 cases reviewed by Rosenhagen (1943), and in 40% of the patients of Jellinger and Tarnowska-Dziduszko (1971). Of the series herein, only 4 patients (12.9%) had parkinsonism. Abnormal movement considered as a whole are significantly more frequent in FOPCA (Bercino 1982).

None had abnormal movements in this series. Dementia was reported in 16 of the 25 cases reviewed by Jellinger and Tarnowska-Dziduszko (1971), and in 11.1 to 22.2% of the patients of Berciano (1982), but we had only one case of dementia. Spinal symptoms usually were associated with FOPCA, but those were significantly less frequent is SOPCA (Berciono 1982; Harding 1982). In the series herein, none had

spinal involvement. In addition, OPCA had various clinical features such as urinary incontinence, ophthalmoplegia, optic atrophy, and so on.

In the past, the pneumoencephlogram (PEG) had been the only diagnostic test available to confirm the diagnosis of OPCA during life (Aita 1978; Gilroy and Lynn 1978). With the advent of computed tomography (CT), OPCA may be evaluated without the need for PEG. The CT brain scan findings of OPCA were atrophy of the pons and cerebellum, with enlargement of the 4th ventricle and ambient, prepontine and quadrigerminal cisterns (Aita 1978). Gilroy and Lynn (1978) reported that their 3 patients with OPCA showed abnormal BAEP findings, and the innocuous AEP procedure might be used in conjunction with the CT scan in the diagnosis of OPCA, eliminating the need for PEG.

OPCA is differentiated from various neurologic diseases. OPCA is distinguished from Friedreich ataxia by the relatively late onset and the absence of sings and symptoms of the spinal cord disease (Thilenius and Grossman 1961). In familial cases, hereditary cerebellar ataxia is more difficult in view of persisting uncertainties regarding the classification of hereditary ataxia (Hoffman *et al.* 1971; Hanes *et al.* 1984). The family history is of primary importance. Posterior fossa tumor and cerebellar degeneration occurring as a remote effect of carcinoma should be considered in the differential diagnosis (Rowland 1984). Some cases with rigidity and tremor may initially be mistaken for Parkinson's disease. CT usually shows enlargement of the prepontine cistern and 4th ventricle (Rowland 1984). Recently, Plaitakis and co-workers (1980) described a significant reduction in the activity of the enzyme glutamate dehydrogenase in several patients with receissively inherited OPCA. If this finding is confirmed, it would provide a means to indentify a subgroup of patients and offer a marker for genetic counseling (Sorbi *et al.* 1986).

The literature defines OPCAs as a group of genetic disorders, but most of the cases herein are sporadic. The causes of SOPCA are unknown. Etiological possibilities include toxic factors, a specific deficiency or possibly a receissive hereditary disease of late onset.

In the series herein, 3 patients had a history of alcoholism. But alchol induced CNS lesions usually differ from those of OPCA (Victor *et al.* 1959). So we believe alcohol consumption does not contribute to the development of OPCA. It also appears that previous illnesses play no part either. Konigsmark and Weiner (1970) suggest that many sporadic cases probably reflect an unrecognized recessive heredity.

In conclusion, OPCAs are not rare in Korea, and it is a characteristic clinical feature of OPCA in Korea that SOPCAs are exclusively more common than FOPCAs.

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