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# Olivopontocerebellar Atrophy in an Infant (an Autopsy Case)

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= **Abstract** =Olivopontocerebellar atrophy (OPCA) is a group of neurologic multisystem disorders with some trait of heredity which is characterized clinically by cerebellar ataxia and histologically by widespread neuronal loss in the inferior olives, pons and cerebellar cortex. It is generally acknowledged that the OPCA usually begins at middle or older age of life, although the pediatric age group can also be involved. Recently, we have experienced an autopsy case of 10-month-old boy demonstrating the characteristic features of OPCA. Family history was unavailable as nothing was known except the fact that both parents were in their early thirties. We report this case in view of its occurrence in such a young age and the first pathologic documentation of this entity in the Korean literature.

Key words: ***Olivopontocerebellar atrophy, Spinocerebellar degeneration, Floppy infant syndrome***

## INTRODUCTION

Olivopontocerebellar atrophy (OPCA) is a rare form of spinocerebellar degeneration, which shows a slowly progressive cerebellar ataxia and other symptoms such as autonomic deficit and abnormal sleep (Chokroverty *et al.* 1984b; Salva and Guilleminault 1986). It is characterized by selective atrophy involving cerebellum, olive and pons, for which the condition is named. Microscopically, the degeneration and atrophy of neuronal cells, particularly of Purkinje cells, and the cellular and fibrillar gliosis of white matter are the prominent features. Since Dejerine and André-Thomas reported the disorder in 1900, many cases of various neurological manifestations have been reported in the literature, occurring sporadically and familially. The greater majority of cases of OPCA showed the onset of disease at their middle or late age of life (Berciano 1982; Eadie 1975b). However, OPCA may occur rarely in very young age and even show congenital onset (Norman and Urich 1958; Gross and Kaltenbäck 1959). Though there were several clinical cases of OPCA in adult, the occurrence in an infant and first autopsy experience on this disease in Korea prompted this report.

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## CASE HISTORY

This legal autopsy was performed for the evaluation of sudden and unexpected death of a 10-month old boy. Several months prior to death, he was once referred to a university hospital because of generalized muscular weakness. He apparently had no demonstrable abnormalities except for floppy muscles and slightly microcephalic head. The olivopontocerebellar atrophy was not considered at that time. He was recommended to visit for further neurologic examinations and close follow-up. But he never came back. He was found dead in his room on June 19th, 1986. No other details about the child's circumstances were known except that his parents are in their thirties.

## AUTOPSY FINDINGS

The general features of the dead were compatible with those of a 10- month old boy. The internal findings were of acute death with abnomalities only of the central nervous system and lungs. The cranial sutures were closed. The dura was normal.

The brain demonstrated well developed symmetrical cerebral hemispheres and a strikingly small cerebellum, weighing 700 gm together (Fig. 1). While the cerebrum showed unremarkable outer surface and coronal sections, the cerebellum was

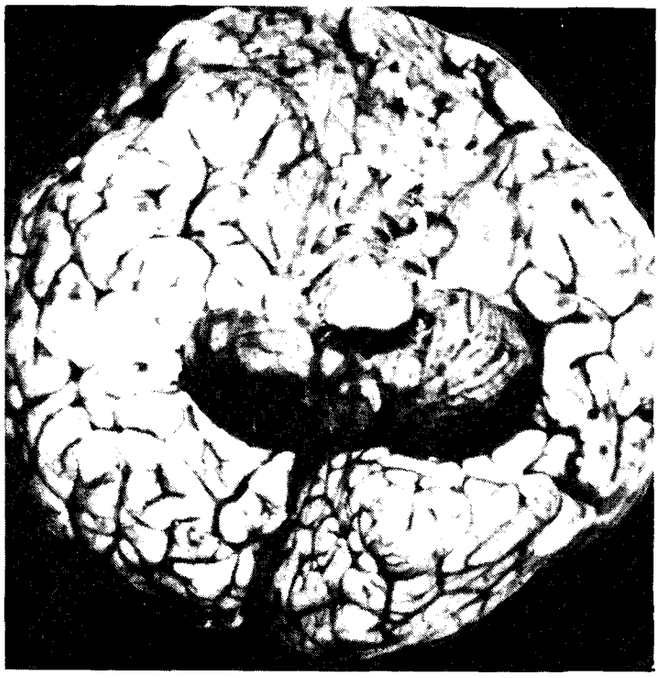

Fig. 1. Posterior basal view of the brain shows strikingly small cerebellum in proportion to cerebral hemispheres.

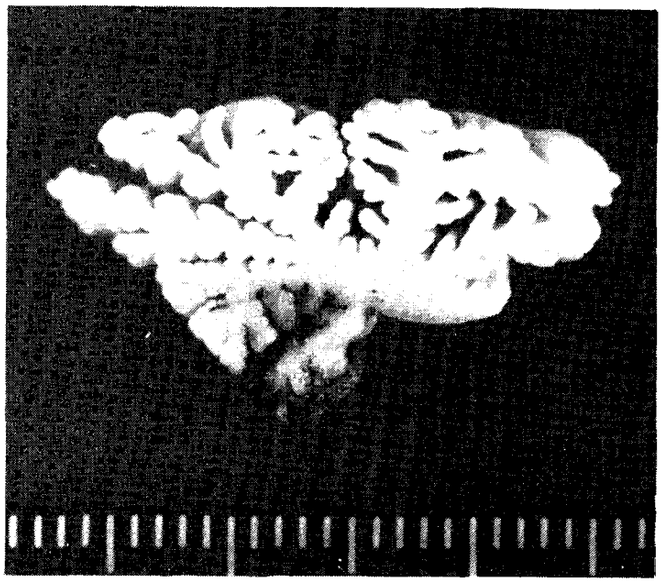

Fig. 2. A sagittal section of cerebellar vermis, showing markedly atrophic folia with prominent subarachnoidal spaces.

evidently small and measured 8.5 cm in width, 3 cm in antero-posterior diameter and 2.5 cm in height. The cerebellar hemispheres were covered by fairly thick opaque leptomeninges. The leptomeninges stripped off with ease from the underlying cerebellar folia. Peeling off the meninges revealed diffuse atrophy of cerebellar folia involving both vermis and cerebellar hemispheres. The number of folia appeared unremarkable. However, the cerebellum in general felt firm. Sagittal sections of the cerebellum showed a considerable atrophy of the individual folium, and this atrophy was equally outstanding in both vermis and hemispheres. The cut sections were generally pale and firm with very prominent subarachnoid space and finger-like projections of folia (Fig. 2). Deep nuclei of cerebellum could not be easily seen. The pons was firm and measured 1.8 cm in width. The middle cerebellar peduncle seemed to be small and firm. The 5th nerves were bilaterally smaller. The cerebellopontine angle was prominent on both sides. However, the 6th, 7th and 8th nerves were normal in size. The horizontal section of the midbrain showed a small rhomboid cerebral aqueduct and slightly grayish inferior colliculus. The teg mental area of the brainstem appeared dusky with a butterfly appearance. Basis pontis was smaller almost proportional to the size of the tegmentum pontis. The medulla oblongata showed normal pyramides and less prominent olives. Serial horizontal sections of the pons and medulla showed a generally firm appearance without any focal lesion. Because of limitation on the autopsy, we could not examine the spinal cord.

Lungs weighed about 60 gm, respectively. The right lung consisted of two lobes and the left, three lobes. But no other features of abnormal situs was present. Within larynx, trachea and bronchi were the partly digested milkish and food materials, suggestive of aspiration.

## MICROSCOPIC FINDINGS

Granular cell layer of cerebellum showed a marked reduction of cell population. Reduction of the thickness of the molecular layer was not so pronounced. Although the vermis was severely involved, cerebellar hemispheres were more prominently atrophied. The whole granular layer of cerebellar cortex demonstrated widespread loss of its granule cells. Also the Purkinje cells were seldom seen. In contrast, the layer of Bergmann astrocytes and basket cells was prominent (Fig. 3). Luxol fast blue staining of cerebellar white matter revealed marked loss of myelin fibers, and the neuropil was replaced by cellular and fibrillary gliosis. However, the dentate nucleus was intact with its normal neuronal population and myelin fibers (Fig. 4). In pons, there was a great reduction in the number of

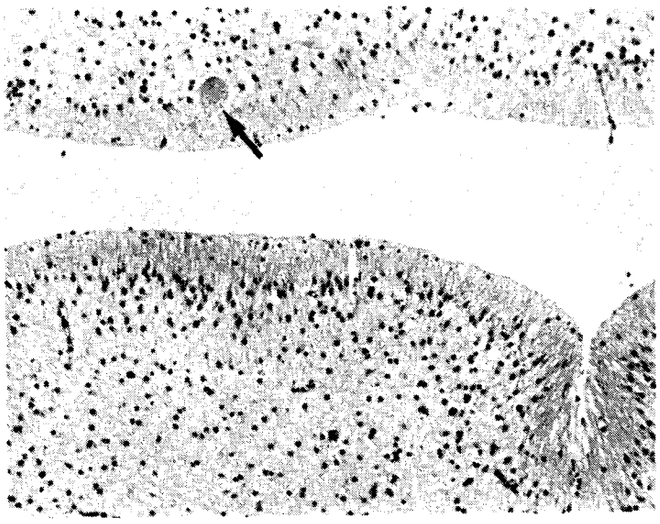

Fig. 3. Photomicrograph of cerebellar cortex demonstrates diffuse loss of granular cells and shrunken molecular layer. Instead of granular cells, proliferated Bergmann astrocytes and a ghost cell (arrow) are seen. (H&E, X100)

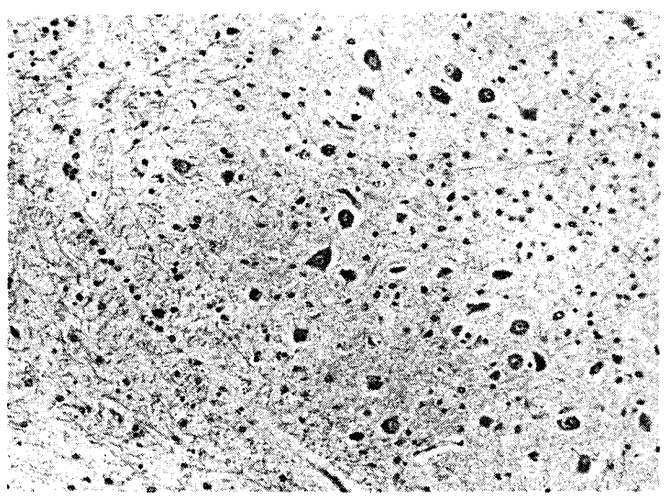

Fig. 4. Dentate nucleus of the cerebellum shows preserved neuronal cells and adjacent myelinated fibers. (H&E-LFB, X200)

transverse pontocerebellar fibers, while the longitudinal fibers with their myelin were preserved (Fig. 5). Tegmentum was intact. The small and shrunken inferior olivary nucleus demonstrated a considerable loss of neurons. A few scattered neurons showed chromatolysis or pyknosis. There was pallor of myelin staining of the intra-, inter-, and peri-olivary fibers. The arcuate nuclei appeared to be intact despite the changes of olivary nuclei. The pyramides were of normal size and showed normal myelination and cell population (Fig. 6 and 7). All

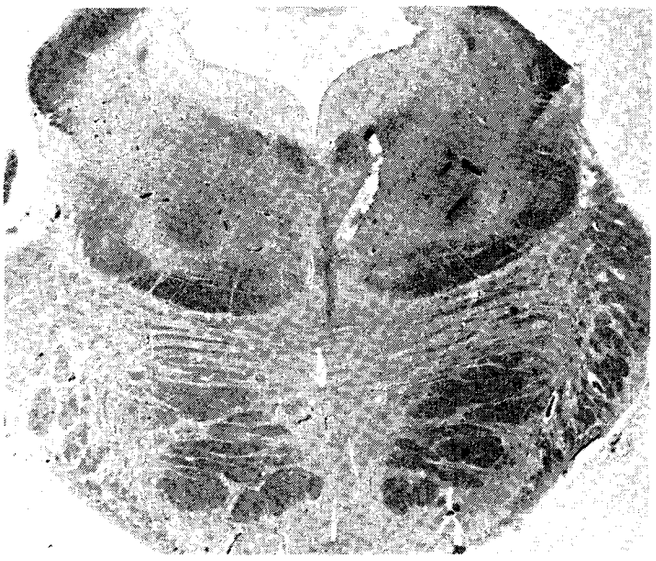

Fig. 5. Low power photomicrography of a transverse section of pons, showing proportionally small griseum pontis and crossing fibers. Note prominent descending longitudinal fibers. (H&E-LFB, X4)

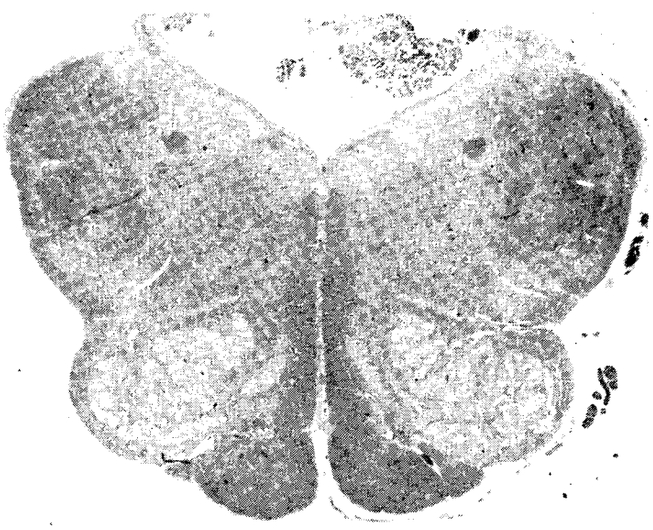

Fig. 6. Transverse section of medulla oblongata shows atrophic inferior olivary nuclei with pale staining hilus. The pyramis and medial lemniscus are well preserved. (H&E-LFB, X4.5)

the examined tissues of central nervous system were devoid of inflammatory process, such as necrosis or perivascular cuffing. Sections of brain above the midbrain were not available for examination. However, it was presumed that they would show no significant histologic finding based on gross appearance.

Multiple areas of lung demonstrated cellulose

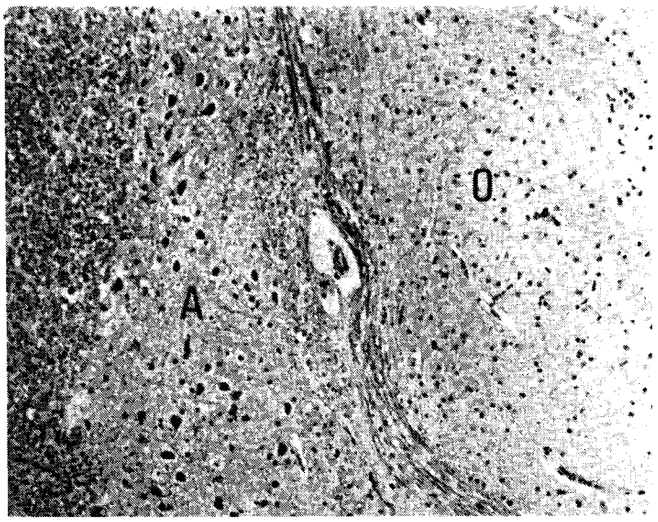


Fig. 7. Photomicrograph of the olivary nucleus(O) showing no visible neuronal cells, while those of arcuate nucleus(A) are well preserved. (H&E-LFB, X100)

and granular materials in bronchial lumen without associated inflammation, indicating aspirated materials.

## DISCUSSION

The presented case showed the typical pathological features of olivopontocerebellar atrophy. Microscopically, the extensive loss or degenerative changes of neuronal cells, demyelination of selective fibers and bundles, and cellular or fibrillary gliosis were characteristic. The ample number of folia easily excluded the possibility of cerebellar hypoplasia. However, this case demonstrated some unusual features. Firstly, the patient is unusually young. In regard to the age of onset and duration of OPCA, Eadie (1975b) reviewed the literatures and reported that the mean age of onset for OPCA was 50.1 year, with three-quarters beginning between 40 and 60 years. The usual course of the disorder, from onset to death, averages 6.3 years. In Berciano's review of 117 cases (1982), the average age of onset is 28.35 years in familial OPCA and 49.22 for the sporadic type. The course was 14.88 years for familial type and 6.31 years for sporadic type, respectively. A few cases found in pediatric age were reported in sporadic form. There was a case of congenital onset of disease (Berciano 1982). It is generally agreed that OPCA is not an inborn disease, mainly because of its late onset in the great majority of cases, despite the fact that trait of heredity is known. Secondly, in spite of the young age of our case, the cerebellum demonstrated the extensive pancerebellar cortical atrophy with near-total loss of cells in the granular layer, which was unique in our case. These findings strongly indicate that the disease started much earlier than the age at death (10 months), suggesting a possibility of congenital nature. As other degenerative spinocerebellar diseases, the etiology of OPCA is obscure. Landis *et al.* (1974) suggested a viral infection as a cause in their ultrastructural study. However, it is generally accepted that the pathology of OPCA begins in the terminal axons of the olivo-cerebellar and ponto-cerebellar fibers, and later involves the cerebellar cortex by a process of trans-synaptic atrophy. Therefore, an autopsy at an appropriate evolutional stage of the disorder might demonstrate the intact cerebellar cortex and demyelinated white matter as Eadie (1975a) suggested. Recent reports described neurochemical abnormalities of cerebellum in OPCA (Kish *et al.* 1984; Whitehouse *et al.* 1986; Chokroverty *et al.* 1984a).

The familial history of this case could not be known, but both of the parents were apparently healthy, suggesting that this case would be a sporadic form instead of the familial type (Koligsmark and Weiner 1970).

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= 국문초록 =

# 유아에서 관찰된 감람-교-소뇌 위축증 (1 부검례 보고)

국립과학수사연구소 법의과* · 서울대학교 의과대학 법의학교실 및 병리학교실**

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감람-교-소뇌 위축증(olivopontocerebellar atrophy)은 대부분 중년에 그 증상이 나타나 진행성 운동실조의 증세를 보이며, 병리학적으로는 선택적으로 감람핵, 뇌교 및 소뇌에서 심한 신경세포의 소실과 신경섬유의 탈수초 현상을 보이는 비교적 드문 질환이다.

저자들은 기도내의 이물질 흡입으로 사망한 것으로 여겨지는 10 개월된 남아의 부검에서 본 증을 경험하였다. 환아는 사망 수 개월전의 진찰에서 다소 머리가 작았던 것외에 외형상 특기할 소견이 없었으며, 지능의 저하도 없었다. 다만 전반적인 운동실조의 증상을 보여 근긴장이 완아 증후근(floppy infant syndrome)을 의심케 하였다. 부검상 소뇌회가 얇고 그 사이가 넓어진 작은 소뇌를 관찰하였으며, 감람핵의 돌출은 미약하였으며 뇌교도 작았다. 현미경적으로 소뇌, 감람핵 및 뇌교의 전반적인 신경세포의 소실과 신경초의 탈실을 보였다. 특히 소뇌 피질의 과립층과 Purkinje 세포의 소실은 현저하였으나 분자층의 위축은 상대적으로 미약하였다. 소뇌 백질, 특히 피질에 가까운, 신경초에서 유수섬유는 거의 관찰되지 않았다. 뇌교에서는 특징적으로 횡 교-소뇌 섬유 (transverse pontocerebellar fiber)는 감소하였으나 종 신경초는 잘 유지되어 있었다.

비록 본 예에서 중추신경계 전반에 대한 검색이 이루어지지 않았으며 자세한 가족력을 알 수 없어 완전한 증례가 될 수는 없으나, 문헌상 이 연령층에서 본 증의 보고가 거의 없으며 특징적인 병리학적 소견을 보여 이를 보고하는 바이다.