

Arnold-Chiari Malformation (Postmortem study of 6 cases)

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= Abstract = A total of 6 autopsy cases of Arnold-Chiari malformation was examined at the Department of Pathology of Seoul National University. These cases showed characteristic features of Chiari type II malformation, i.e., displacement of a portion of the inferior vermis, whole medulla oblongata and the fourth ventricle into the cervical canal and associated cerebellar dysplasia. All of the cases had hydrocephalus and accompanying meningo-myelocele at various levels. All cases showed polygyria but not micropolygyria, and in three cases there were craniolacunias. Three out of 6 cases showed severe malformations of the extraneural system. These malformations included bilateral renal agenesis, exstrophiasplanchnica, cardiovascular and skeletal abnormalities, etc. On the basis of our observations we think that multifactorial causes are involved in the pathogenesis of the Arnold-Chiari malformation.

Key words: *Arnold-Chiari malformation, Meningomyelocele, Chiari malformation, Neural tube defect, Hydrocephalus, Spina bifida*

INTRODUCTION

The Arnold-Chiari malformation is a congenital defect of the hindbrain characterized by displacement of a tongue of cerebellar tissue, an elongated medulla oblongata and the fourth ventricle into the cervical region of the spinal cord. This anomaly was first described by Cleland in 1883 in one infant in a series of 9 presenting with various combinations of spina bifida cystica, encephalocele and anencephaly. In that report the herniation of the vermis and the deformities of the medulla oblongata and tectal plate were illustrated (Carmel and MaKesbery, 1972). Since Chiari report (1891), Arnold (1984) and Schwalbe and Gredig (1907) described the malformations in detail. Now most books adopt the eponym "Arnold-Chiari malformation" for this condition,

However, there are still unsolved problems regarding the pathogenesis particularly in Chiari type II malformation. In this report, we reviewed 6 autopsy cases of Arnold-Chiari malformation, trying to elucidate the principal elements of the central nervous system lesions and also examine the extraneural malformations in these cases.

MATERIALS AND METHOD

A total of 6 cases was found in the autopsy file of the Department of Pathology, Seoul National University during last 20 years from 1969 to 1988. All these cases were from the file of Registry of Congenital Malformation Seoul National University Hospital, and SNU Children's Hospital. Age, sex, gestational age and the central nervous system malformations in these cases are summarized in Table 1.

Pre- and postnatal clinical information was not available in most cases. However lantern slides for gross and microscopic slides were available in

Table 1. Summary of 6 cases with the Arnold-Chiari malformation

Case	Age	Sex	GA	hydrocephalus (HC/CC)	craniolacunias	meningomyelocele	polygyria
1	22 days	M	?	+ (??)	?	T4-L4	+
2	3 days	F	38 wks	+ (31.5/27)	+	thoracolumbar (T7-L?)	+
3*	stillbirth	M	39 wks	+ (34/36)	+	sacral	+
4	1 hour	M	32 wks	+ (28.2/?)	-	lumbar	+
5	stillbirth	F	32 wk	+ (43/34.5)	-	lower lumbar	+
6	10 min	M	39 wks	+ (41/27)	-	lumbosacral	+

GA: gestational age

HC/CC: head circumference/chest circumference

*second of twin.

all cases together with the autopsy protocol. The slides were reviewed and analysed.

RESULTS

General features

Among 6 cases, 2 were female and 4 were male. Case 1 survived for 22 days but the remainder died either within 3 days or were stillborn. The gestational age ranged from 32 weeks to 39 weeks. Two cases were breech presentations and in case 6 Cesarean section was performed. Externally all these cases showed hydrocephalus of varying degrees and meningomyelocele at various levels. In case 3 and 6 deformity the ear lobe was observed.

Neuropathological Findings

In all cases, there was displacement of a "tail" of cerebellar tissue into the cervical region of the vertebral canal with the length of the "tail" ranging from 0.4 to 2.8 cms. The 'tail' was a midline structure continuous with the vermis. The herniated cerebellar tissue was firm, whitish and sclerotic and adhered to the surrounding leptomeninges. There was a well defined groove which marked the site of the invariably large foramen magnum at the upper end of the tail (Fig. 1). The cerebellum above the foramen magnum appeared somewhat small and the lateral lobes showed considerable asymmetry (Fig. 4).

The other characteristic feature of this malformation was a marked elongation and downward displacement of the brainstem (Fig. 2). This elongation involved the medulla oblongata and the fourth ventricle to a various extent, and fre-

quently included the pons. The medulla and fourth ventricle always extended into the spinal canal irrespective of the length of the cerebellar "tail". A deformity of the brainstem was particularly apparent on lateral view or when one elevated the herniated cerebellar tissue; it consisted of a caudal shifting of the entire dorsal aspects of the medulla oblongata, fourth ventricle and choroid plexus: the nuclear groups in the floor of the fourth ventricle were situated much farther caudal than would correspond to the landmarks at the ventral surface of the medulla.

Microscopically, the herniated cerebellar tissue showed loss of Purkinje and granular cells, with irregular sclerosis of the folia. The white matter was deficient of myelinated fibers. In addition to atrophy and sclerosis there was focal dysplasia in the cerebellar cortex (Fig. 9). In the white matter of the cerebellum, there were focal nests which consisted of Purkinje and granular cells. There was also a diffuse hypertrophy of astrocytes as well as increase of astrocytes in the cerebellar white matter.

In case 2, inflammatory cells infiltrated to the meninges and choroid plexus of the cerebellum. The source of suppurative meningitis was thought to be an abscess under the skin near the meningomyelocele. The choroid plexus and tela choroidea were congested and thickened.

The cervical roots were angulated at their origin and ascended cranially through their own intervertebral foramina, rather than taking their normal lateral or descending course. Diffuse dilatation of the central canal (hydromyelia) was found in cervical cord (Fig. 8).

Spina bifida was seen in all 6 cases. The level

was lumbar in two, thoraco-lumbar in two, lumbosacral in one and sacral in one. Case 3 showed shortest herniation length in which the meningomyelocele was restricted to the lumbar area. Case 1 showed longest herniation that extended from fourth thoracic to fourth lumbar vertebral level.

The most common change of the cerebral hemispheres consisted of hydrocephalus of varying degree. This change could be accounted either by cervical herniation or by stenosis of the aqueduct. The lateral and third ventricles were dilated in all cases, and in some cases the hydrocephalic change was so severe that the brain collapsed as soon as the brain was removed from the head. In case 6, the ventricular surface was covered by the ependymal lining focally and the remaining area showed disappearance of ependyma and replacement gliosis. The surface of the hydrocephalic cerebral hemispheres exhibited increased number of gyri (polygyria). This change varied markedly in the different case. Gray matter heterotopia was observed on the ependymal surface of the lateral ventricle. Small bean-sized nodules were scattered in case 2

(Fig. 13 and 14). Craniolacunias were present in case 2 and 3 (Fig. 6 and 7). After reflection of the scalp, marked variation of the thickness of the skull was noted. It involved the whole skull diffusely with round defects of varying size separated by bony ridges.

Extraneural findings

Malformations of extraneural systems in this series are summarized in table 2. They were especially prominent in case 3, 4 and 6. Case 3 was a second cotwin and was a typical sirenomelia that was previously reported by Kim and Chi (1982). In this case there were anal atresia as well as agenesis of kidneys, urinary bladder, rectum, urethra and prostate. Hypoplastic lungs and hiatal hernia were observed as well as malformed external ear. Case 4 was a case of exstrophism splanchnica. There were gastroschisis, exstrophy of the bladder associated with imperforate anus and ambiguous genitalia. The terminal ileum opened to the exstrophied bladder and the large bowel was represented by a 10 cm long blind sac with two appendices opened into the terminal ileum. There were bilateral dys-

Table 2. Associated extraneural malformations in Arnold-Chiari malformation

Case	Genito-urinary system	Alimentary system	Respiratory system	Skeletal system	Cardiovascular system	Others
1				clubfoot		
2						
3	bilateral renal agenesis, agenesis of bladder and prostate rudimentary phallus intra-abdominal testis	imperforate anus	hypoplastic lungs hiatal hernia	sirenomelia		malformed external ear
4	exstrophy of bladder cystic kidney, type IV left hydroureter agenesis of phallus undescended testis	gastroschisis anal atresia double appendices		agenesis of sacrum clubfoot		
5			incomplete three lobes			
6	fused kidney with single anterior ureter. undescended testis		hypoplastic lungs diaphragmatic mass	kyphoscoliosis hemivertebrae absence of right ribs clubfoot	tetralogy of Fallot patent ductus arteriosus	low-set ears hypertrichosis

plastic kidneys with a marked hydroureter on the left side and a small atropic ureter on the right. This case was previously reported. (Suh and Chi, 1984).

In case 6 there were multiple anomalies in the thorax such as kyphoscoliosis and hemivertebrae of the right thoracic and lumbar spine, absence of right ribs and rib cage, diaphragmatic mass, bilateral pulmonary hypoplasia, tetralogy of Fallot and patent ductus arteriosus. Additionally, there were fused kidneys with a single anterior ureter and undescended testes.

Club foot, pes equinovarus, was observed in three cases (Fig. 5). Other minor abnormalities are summarized in table 2. There were 3 cases of urogenital abnormalities in this series. Kyphoscoliosis was observed in case 6. There were two cases of anal atresia which were associated with sirenomelia and exstrophia splanchnica, respectively.

DISCUSSION

In this series, all cases showed typical Chiari type II malformation (A-C malformation) and other associated abnormalities such as the meningomyelocele, craniolacunia, hydrocephalus, cerebellar dysplasia, cerebral and cerebellar cortical heterotopia, etc.

Spina bifida has been almost always present in the Arnold-Chiari malformation of infants (Peath, 1964). But not every spina bifida case is associated with Arnold-Chiari malformation. During the period of this study, 4 additional meningomyelocele cases were found. These cases were not associated with Arnold-Chiari malformation. In other words, 6 out of 10 meningomyelocele cases in our series had A-C malformation. Generally the severity of the deformity of the posterior fossa structures corresponds to the severity of the lumbosacral spina bifida. A similar relationship is shown in experimental data of Gunberg (1956) who observed lesions comparable to the Arnold-Chiari malformation in the progeny of trypan blue injected rats. In this study, this phenomenon could be generally approved.

Craniolacunia were found in 43 percent of 120 patients with spina bifida (Vogt and Wyatt, 1944). They discovered that it was more frequently found with meningomyelocele than with simple meningocele, and that it was an unfavor-

able prognostic sign. According to Cameron (1957), congenital abnormalities of the urogenital tract were found in 8 cases of 26, such as horseshoe kidneys, cystic kidney, intradddominal hypoplastic testicles, bilateral hydroceles and bilateral double renal arteries.

PATHOGENESIS

The Arnold-Chiari or Cleland-Chiari malformation was first described by Cleland in 1883 as herniation of the cerebellar vermis and deformities of the medulla oblongata and tectal plate. Later, Chiari attributed the malformation to embryonic hydrocephalus causing caudal herniation of the posterior fossa contents.

Those anomalies seen in the posterior fossa in this series are compatible with Chiari type II anomaly which defines as "displacement of part of the inferior vermis, pons, medulla oblongata and fourth ventricle into the cervical canal". He emphasized that cerebellar dysplasia, brainstem displacement, and elongation of the fourth ventricle should be present. This type is now widely recognized as the Arnold-Chiari malformation.

Arnold's (1984) contribution is a report of an infant with meningomyelocele and absence of the sacrum, sacral teratoma, and deformities of the lower extremities. Many reports have documented the variation of the type II malformation and have presented various theories on its morphogenesis. Although many different theories have been presented, no single theory can explain the pathogenesis of the Arnold-Chiari malformation fully.

Chiari attributed herniation of the posterior fossa contents to hydrocephalus of the cerebrum (Chiari, 1891) and this has been supported by others (Cameron, 1957). This theory does not explain those cases of this malformation without hydrocephalus, nor those occasional cases without spina bifida that have been reported (Peath, 1964).

A small posterior fossa is frequently demonstrated by necropsy and radiographic studies (Kruffy, 1966). Barry, Patten, and Stewart (1957) felt that excessive volume of the cerebrum, which they attributed to overgrowth, caused caudal displacement of the tentorium. As a result, the cerebellum and medulla herniated to the cervical region of spinal canal. But there has been little acceptance or further confirmation by

other workers of the theory that the disorder is due to a primary defect in posterior fossa development. The micropolygyria and polygyria associated with the disorder tends to suggest the primary lesion is neural rather than cranial.

Because almost all the patients with the Arnold-Chiari malformation show spina bifida, most authors focus on the relationship of meningomyelocele with this malformation. One mechanism proposed is that the spinal cord fixed at the meningomyelocele creates downward traction on the hindbrain as the fetus grows. This hypothesis has been disproven experimentally (Goldstein and Kepes, 1966), and pathologically (Barry, Patten, and Stewart, 1957). It has been shown that traction is dissipated within four segments of the nonmobile defect. In addition, this theory cannot explain the Arnold-Chiari malformation without spina bifida.

Cameron (1957) proposed a myelomeningocele hydrodynamic theory. He proposed that all the abnormalities found in the Arnold-Chiari malformation are the consequence of an escape of cerebrospinal fluid from the spina bifida into the amniotic cavity during the first half of intrauterine life. So an increase in intraamniotic pressure would be transmitted to the fetal skull, and this downward pressure from the skull was thought to force the hindbrain into the upper cervical cord. However, the hydrodynamic theory fails to explain the Arnold-Chiari malformation cases without hydrocephalus and those without spina bifida.

Daniel and Strich (1958) proposed that the abnormalities of the skull and dura are the consequence of the hindbrain abnormality, since the development of the cerebral malformation precedes the development of the skull in fetal life. He proposed that the primary disturbance is a failure of formation of the pontine flexure. Lack of flexion would cause the hindbrain elongation typical of this anomaly.

Barry, Patten and Stewart (1957) introduced the concept of overgrowth of the cerebellum, akin to the overgrowth of spinal cord tissue near a myelomeningocele. There was no doubt about that the overgrowth can and does occur, but there was no evidence of the that the overgrowth cause the Arnold-Chiari malformation experimentally and pathologically.

ACKNOWLEDGEMENT

We wish to thank the staff of Seoul Adventist Hospital and Cheil General Hospital for referring case 4 and 5. We would also like to acknowledge Dr. Jung Ran Kim for providing important informations on case 2.

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= 국문초록 =

Arnold-Chiari기형 (6 부검예의 분석)

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시제근 · 박원서

Arnold-Chiari기형 또는 Cleland-Chiari기형을 뇌간과 소뇌를 침범하는 비교적 흔한 병변이다. 특징으로는 수두증, 소뇌의 탈출증, 소뇌의 이형성, 뇌간의 전위, 제 4 뇌실의 신장, 작은 수두와, 척수야분증, 두개와 (craniolacuni)등을 보인다. 저자들은 1969년 이래 서울대학교 의과대학 병리학교실에서 검색된 총 6례의 Arnold-Chiari기형을 분석하고 그 병리학적 특징과 그에 동반된 기형에 대해 기술하고 문헌고찰과 함께 병인론에 대한 고찰을 하였다.

LEGENDS FOR FIGURES

- Fig. 1. Arnold-Chiari malformations and exposed during exploration of the posterior fossa, showing downward displacement of dysplastic cerebellum. arrow: the level of foramen magnum, arrow head: medulla oblongata.
- Fig. 2. Midline section of Fig. 1. Herniated cerebellar vermis and hump of medulla oblongata are seen. (arrow).
- Fig. 3. Another case of Arnold-Chiari malformation, posterior view. arrow: the level of foramen magnum.
- Fig. 4. Arnold-Chiari malformation, ventral view. In addition to the herniated cerebellar vermis, asymmetry of the cerebellum is noted. arrow: the level of foramen magnum.
- Fig. 5. Clubfoot.
- Fig. 6. Roentgenogram of skull, lateral view. Note multiple radiolucent areas representing craniolacunia.
- Fig. 7. Skull vault of Fig. 6.
- Fig. 8. Spinal cord. Horizontal section showing the cavity of a hydromyelia in free communication with the central canal. The cavity is lined by delicate glial tissue and ependymal tissue. H & E, × 40
- Fig. 9. Cerebellar dysplastic focus in which the granular and Purkinje cells are intermingled irregularly. H & E, × 100
- Fig. 10. Midline sectioned brain. Increased number of gyri is observed and the lateral ventricle is dilated severely.
- Fig. 11. Roentgenogram of case 6, severe hydrocephalus is noted and absence of right ribs, hemivertebrae and kyphoscoliosis are observed.
- Fig. 12. Part of a structure resembling choroid plexus from the posterior lumbar arachnoid tissue. H & E, × 40
- Fig. 13. Nodules of heterotopic cortex in the wall of the lateral ventricle.
- Fig. 14. a: Microscopic view of Fig. 13. Heterotopic cortical tissue in the lateral ventricle. The nodule is composed of cells resembling matrix cells. b: The overlying cortex shows no significant changes. H & E. × 40





