Congenital Hydrocephalus

— Analysis of 49 Cases —

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The causes of congenital hydrocephalus vary widely and have an important effect in determining the future counseling of affected cases. We analyzed the postmortem findings of 49 autopsies diagnosed as hydrocephalus to find the causes and related conditions. The cases were collected during the last 10 years (1981-1990). The cases consisted of 25 cases associated with various congenital malformations of the central nervous system (CNS), 14 cases of posthemorrhagic hydrocephalus, 4 cases of postinfection hydrocephalus, and 2 cases of hydranencephaly. Four cases were associated with supracerebellar arachnoid cyst (1) and unknown causes (3). Twenty-five cases associated with congenital malformation of the CNS consisted of 10 cases of holotelencephaly, 5 cases of stenosis of the Sylvian aqueduct, 4 cases of agenesis of the corpus callosum, and 3 cases each of Dandy-Walker malformation and Arnold-Chiari malformation. Various malformations of other organs were associated with these cases. Cardiovascular malformations were common, consisting of 11 cases of patent ductus arteriosus (PDA), 7 cases of atrial septal defect (ASD), and 6 cases of patent foramen ovale (PFO). Among the anomalies of the respiratory system, abnormal lobation was commonly associated, as well as hypoplasia of the lung. Gastrointestinal malformations included Meckel's diverticulum, diaphragmatic hernia, mobile intestine, and midline small liver. Cryptorchidism was the most common malformation in the genitourinary system. Holotelencephaly cases showed multiple craniofacial anomalies, as well as other malformations in the central nervous system. Skeletal malformations included polydactyly, simian crease, and flexion deformity. There were no specific constellations of malformations in these different groups of CNS malformations associated with hydrocephalus.

Key Words: Congenital hydrocephalus, Malformation, Posthemorrhagic, Postinfection, Central nervous system, Brain

INTRODUCTION

With the development of various antenatal examination methods, chances of examining cases of congenital hydrocephalus are increasing. Hydrocephalus has been known to be associated with multiple congenital malformations, especially in cases of chromosomal

abnormalities (Suh and Chi, 1989; Wiswell et al., 1990). Knowing the exact cause of hydrocephalus and associated malformations is very important and helpful in the counseling process related to further pregnancies.

To determine the causes, pathogenetic mechanisms, and associated structural anomalies in congenital hydrocephalus we analyzed the autopsy findings of 49 cases of congenital hydrocephalus and listed the various types of malformations according to the organ system.

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MATERIALS AND METHODS

A total of 45 cases of congenital hydrocephalus were collected from the autopsy files of the Department of Pathology, Seoul National University Children's Hospital, between 1981 and 1990. An additional 2 cases were from Kangnam Sacred Heart Hospital of Hallym University and 2 cases from Ewha Womans University Hospital. Most of these cases were clinically suspected as hydrocephalus by antenatal sonographic examination.

The cases were classified according to the causes of hydrocephalus: malformation of the central nervous system (CNS), hydroanencephaly, posthemorrhagic, postinfection, and miscellaneous. Associated anomalies were analyzed by reviewing autopsy records of the cases and photographs taken at the time of the autopsy. The findings are presented in tabular form.

RESULTS

Table 1 shows the classification of the cases according to pathogenesis.

Congenital malformations of central nervous system

Twenty-five cases were associated with various congenital malformations. Holotelsoncephaly was the most common, followed by stenosis of the Sylvian

aqueduct, agenesis of the corpus callosum, Dandy-Walker malformation, and Arnold-Chiari malformation. In addition, 2 cases of hydranencephaly were present. Associated malformations are summarized in Tables 2-9.

Ten cases of holotelsoncephaly consisted of 2 males and 7 females. Sex was unknown in 1 case. The gestational age(GA) of 6 cases was between 26 to 38 weeks, and 2 of these were born dead at 26 weeks and 30 weeks. Of 4 cases of unknown GA, 2 cases lived 1 day. One case was born dead. Age was unknown in 1 case. One case showed trisomy 18 (Edward's syndrome), which was presented in the previous study by one of us (Suh and Chi, 1988). Craniofacial and central nervous system anomalies were characteristic in these cases with ocular, aural, and nasal malformations (Tables 2 and 3). Agenesis of the olfactory bulbs was the most common anomaly (4 cases), followed by aqueductal atresia, pituitary malformation, and microcephaly in 2 cases each. Agenesis of the corpus callosum, macrocephaly, and cystic change were noted in one case each. Cardiovascular malformations were frequently associated; they were patent ductus arteriosus (PDA) in 5 cases, atrial septal defect (ASD) in 4 cases, and patent foramen ovale (PFO) in 3 cases. In addition, various other anomalies were noted (Table 4). Abnormal lobation of the lung was the most common anomaly of the respiratory system (4 cases), followed by tracheoesophageal fistula (TEF) with

Table 1. Classification and Incidence of Congenital hydrocephalus: 49 cases

	M/F	Total (%)
I. Congenital malformation	10/14 (1)	25 (50)
A. Holotelsoncephaly	2/7 (1)	10
B. Stenosis of Sylvian aqueduct	3/2	5
C. Agenesis of corpus callosum	3/1	4
D. Dandy-Walker malformation	1/2	3
E. Arnold-Chiari malformation	1/2	3
II. Posthemorrhagic hydrocephalus	9/5	14 (29)
III. Postinfection hydrocephalus	2/2	4 (8)
IV. Hydranencephaly	2/0	2 (4)
V. Miscellaneous	2/1 (1)	4 (8)
A. Supracerebellar arachnoid cyst	1/0	1
B. Unknown cause	1/1 (1)	3
	25/22 (2)	49 (100)

(): unknown

Table 2. Malformations of central nervous system in congenital hydrocephalus

DISEASE	Holotelencephaly (n = 10)	Dandy-Walker (n = 3)	Arnold-Chiari (n = 3)	Agenesis of c.c. (n = 4)	Stenosis Aqueduct (n = 5)	Hydranencephaly (n = 2)	Total (n = 27)
Agenesis of olfactory	4						4
Atresia of aqueduct	2	1			5		8
Pituitary malformation	2		1				3
Abnormal circle of Willis	1						1
Cystic change	1						1
Porencephaly		1					1
Macrocephaly	1						1
Microcephaly	2						2
Micropolygyria		1					1
Agenesis of corpus callosum	1	1					2
Hippocampal anomaly		1		1			2
Dysplastic neural tissue			1				1
Meningomyelocele			2				2
Encephalocele		1	1				2
Agenesis of septum pellucidum				1			1
Pachygyria				1			1

Note: n: number of cases, c.c.: corpus callosum

esophageal atresia, hypoplasia of the lung, choanal atresia, and agenesis of the lung (2 cases each) (Table 5). Gastrointestinal and genitourinary malformations are listed in Tables 6 and 7. One case showed Potter's face associated with hydronephrosis, segmental atresia of the left ureter, multiple cortical cysts of the left kidney, and multilobulated right kidney. Associated skeletal malformations were varied including flexion deformity, rocker bottom foot, syndactyly, polydactyly, simian creases (2 cases each), and absence of extremity, oligodactyly, short fingers, and hypoplastic toe (1 case each) (Table 8). In addition, adrenal agenesis was noted in 2 cases (Table 9).

Five cases of stenosis or atresia of Sylvian aqueduct unassociated with other malformations of CNS occurred in 4 males and one female. Gestational age was 29-42 weeks in 3 cases, and the other 2 cases, which lived 3 and 10 days, were of unknown GA. One case, terminated at 33 weeks GA, showed multiple congenital malformations including tetralogy of Fallot (TOF), agenesis of right lung and thymus, cloacal anomaly (persistent urachus, atresia ani with hydrocolpos and rectovaginal fistula), bilateral renal dysplasia, and facial anomalies (cleft lip and palate, low-set ear, right anomalous ear). The second case, 29 weeks GA, showed ASD, PDA, bilateral simian crease, micrognathia, bilateral club feet, bilateral adrenal hypoplasia,

and multiple hemangiomas. The third case, stillborn at 42 weeks GA, showed extensive intraventricular hemorrhage, as well as subarachnoid hemorrhage. The fourth case, lived 3 days, showed dysplastic kidney on the left side. The last one, 10 days of age, showed multiple congenital anomalies of the cardiovascular system (preductal coarctation of aorta, VSD, PDA, persistent left superior vena cava, PFO, and left ventricular hypertrophy) and musculoskeletal system (inward curving of both 5th fingers and bilateral flattened and broad thumb tips). Also noted were incomplete lobation of the right lung and urachal remnant on the apex of the fundic area of the urinary bladder. In summary, PDA and dysplastic kidney were noted in 2 cases out of 5. In addition, aqueduct atresia was associated with 2 cases of holotelencephaly and 1 case of Dandy-Walker malformation (Table 2).

Four cases of total or partial agenesis of the corpus callosum were associated with variable abnormalities. Two of those cases were male. Two lived for 3 days and 11 days, respectively and pregnancy was terminated in 1 case at 30 weeks of GA. The last one lived 28 days after 41 weeks GA. The one that lived 11 days showed multiple anomalies compatible with trisomy 18. There were ASD, muscular VSD, PDA, and persistent left superior vena cava (Table 4). Also associated were hypoplastic labia majora with prominent clitoris and ab-

Table 3. Craniofacial anomalies

DISEASE	Holotel- encephaly (n=10)	Dandy- Walker (n=3)	Arnold- Chiari (n=3)	Agenesis of c.c. (n=4)	Stenosis Aqueduct (n=5)	Hydranen- cephaly (n=2)	Total (n=27)
Ocular Malformation							
Proboscis	2						2
Hypertelorism	1	2					3
Hypotelorism	3						3
Epicanthal fold		1					1
Microphthalmia	4		1				5
Microcornea	1						1
Cyclopia	2						2
Corneal opacity	1						1
Optic nerve hypoplasia	1						1
Aplasia of eyeball	1						1
Aural Malformation							
Low-set ear	4	2	1		1		8
Malformed ear	2			1	1		4
Blind ear canal	1						1
Nose Abnormalities							
Absent nose	4						4
Flat nasal bridge	1	1			1		3
Absent nasal cavity	1						1
Beaked nose		1		1			2
Craniofacial							
Prominent occiput	1			1	1		3
Micrognathia	2	1		1			4
High arch palate	2			1			3
Receding chin					1		1
Cleft lip and palate	4	2	1	1	1	1	10

Note: n: number of cases, c.c.: corpus callosum

normal lobation of the lung. The other case, which lived 3 days, had multiple malformation syndrome (chromosome 4p- syndrome) consisting of oligomeganephronic hypoplasia, bilateral cleft palate, scoliosis with hemivertebrae, ASD, midline liver, intestinal malrotation, and agenesis of the right thyroid. The third case, terminated at 30 weeks GA (1800 gms), showed agenesis of the septum pellucidum and other abnormalities of telencephalic structures arising from the commissural plate (This case was reported previously). The last case showed a combination of malformations of the telencephalic structures such as agenesis of the septum pellucidum, anomaly of hippocampi, and diffuse pachygyria, as well as marked periventricular leukomalacia with cystic changes. Other organs were

unremarkable except for the bilateral undescended testis. In summary, 2 cases associated with chromosomal anomalies showed multiple malformations in other organs. Agenesis of the corpus callosum was also associated with 1 case each of holotelencephaly and Dandy-Walker malformation.

Two cases of Arnold-Chiari malformation were born dead and the other lived 10 min. The male to female ratio was 2:1. Two cases were type II with lumbosacral meningocele. One case was type I associated with frontal encephalocele. One case of type II malformation was associated with skeletal abnormalities, i.e., kyphoscoliosis, hemivertebrae, and the absence of right ribs and rib cage (Table 8). The heart showed TOF and PDA (Table 4). Various malformations of other

Table 4. Cardiovasuclar malformations

DISEASE	Holotel- encephaly (n = 10)	Dandy- Walker (n = 3)	Arnold- Chiari (n = 3)	Agenesis of c.c. (n = 4)	Stenosis Aqueduct (n = 5)	Hydranen- cephaly (n = 2)	Total (n = 27)
Patent ductus arteriosus	5	2	1	1	2	2	13
Atrial septal defect	4			2	1		7
Ventricular septal defect	1			1	1		3
Patent foramen ovale	3	2			1	1	7
Coarctation of aorta					1		1
Tetralogy of Fallot	1	1	1		1		4
Bilateral superior vena cava	1	1		1	1		4
Bicuspid pulmonary valve	1						1
Hypoplastic pul. artery	1						1
Aortic atresia	1						1
Dextrocardia		1					1
Rudimentary heart with one vein and one artery	1						1
Single umbilical artery	1						1
Right ventricular enlargement		1					1
Left ventricular hypertrophy					1		1

Note: n: number of cases, c.c.: corpus callosum, pul: pulmonary

Table 5. Anomalies of respiratory system in congenital hydrocephalus

DISEASE	Holotel- encephaly (n = 10)	Dandy- Walker (n = 3)	Arnold- Chiari (n = 3)	Agenesis of c.c. (n = 4)	Stenosis Aqueduct (n = 5)	Hydranen- cephaly (n = 2)	Total (n = 27)
Abnormal lobation of lung	4	1		2	1		8
Tracheo-esophageal fistula with esophageal atresia	2						2
Hypoplasia of lung	2	2	1	1			6
Choanal atresia	2						2
Agenesis of lung					1		1

Note: n: number of cases, c.c.: corpus callosum

organs were also noted: a fused kidney with a single anterior ureter, a bilateral hypoplastic lung, an undescended left testis and right anorchia, and a bilateral pes equinovarus deformity. The other type II case was 39 weeks GA and did not show malformation of other organs. The case of type I malformation was combined with encephalocele of the right forehead, a bony defect of the right half of the frontal bone, left microphthalmia, and multiple digital anomalies. All the malformations in the other organs associated with Arnold-Chiari malformation occurred in 1 case, each.

Three cases of Dandy-Walker malformation consisted of 2 females and 1 male. Two lived 1 day (35 weeks GA and premature of unknown GA, respectively) and 1, 28 days. One case, born after 35 weeks of gestation, showed Potter's syndrome associated with facies renalis, type IIb congenital cystic disease of the kidney, congenital hepatic fibrosis, as well as hypoplasia of the lungs and urinary bladder and simian crease. The central nervous system revealed Dandy-Walker malformation with occipital meningoencephalocele, aqueduct atresia, posterior porencephaly and

Table 6. Gastrointestinal malformations

DISEASE	Holotel- encephaly (n = 10)	Dandy- Walker (n = 3)	Arnold- Chiari (n = 3)	Agenesis of c.c. (n = 4)	Stenosis Aqueduct (n = 5)	Hydranen- cephaly (n = 2)	Total (n = 27)
Meckel's diverticulum	2						2
Diaphragmatic hernia		1		1			2
Mobile intestine	2						2
Malrotation				1			1
Agenesis anus					1		1
Midgut atresia	1						1
Midline small liver	1			1			2
Congenital hepatic fibrosis		1					1
Agenesis gallbladder		1					1
Heterotopic pancreas	1						1

Note: n: number of cases, c.c.: corpus callosum

Table 7. Malformations of genitourinary system

DISEASE	Holotel- encephaly (n = 10)	Dandy- Walker (n = 3)	Arnold- Chiari (n = 3)	Agenesis of c.c. (n = 4)	Stenosis Aqueduct (n = 5)	Hydranen- cephaly (n = 2)	Total (n = 27)
Horseshoe kidney			1				1
Cystic kidneys		1					1
Dysplasia					2		2
Cortical cyst	1	1					2
Multilobulation	1						1
Agenesis of kidney						1	1
Oligomeganephric hypoplasia				1			1
Hydronephrosis	1						1
Hydroureter	1						1
Single ureter			1				1
Hypoplasia of bladder		1					1
Cryptorchidism	1		1	2	1	1	6
Hypoplasia of uterus	1						1
Hypoplasia of ovary	1						1
Bicornuate uterus	1	1					2
Double vagina	1						1
Large clitoris	1						1
Small genitalia	1						1
Herniated testis through skin defect				1			1
Urachal remnant					1		1

Note: n: number of cases, c.c.: corpus callosum

micropolygyria, and a marked hydrocephalus (Table 2). Multiple skeletal abnormalities such as broad and short hand with contraction deformity of both thumbs, curved fifth fingers, and rocker bottom feet were noted,

as well as dextrocardia and PDA (Tables 4 and 8). The second case showed features compatible with trisomy 18 syndrome, although a chromosomal study failed to show any abnormalities because of blood clotting and

Table 8. Skeletal malformations in congenital hydrocephalus

DISEASE	Holotel- encephaly (n = 10)	Dandy- Walker (n = 3)	Arnold- Chiari (n = 3)	Agenesis of c.c. (n = 4)	Stenosis Aqueduct (n = 5)	Hydranen- cephaly (n = 2)	Total (n = 27)
Flexion deformity	2		1				3
Overlapping fingers				1			2
Absence of extremity	1						1
Rock bottom foot	2	1					3
Syndactyly	2						2
Polydactyly	2			1		1	4
Oligodactyly	1						1
Fusion of phalanges			1				1
Short fingers	1		1				2
Hypoplasia of toe	1						1
Simian crease	2	1			1		4
Creases anomaly					1		1
Abnormal ribs and vertebrae			1	1		1	2
Kyphoscoliosis			1				2
Pes equinovarus		2	1	1	1	1	6
Flattened broad thumb tips							1

Note: n: number of cases, c.c.: corpus callosum

Table 9. Other malformations

DISEASE	Holotel- encephaly (n = 10)	Dandy- Walker (n = 3)	Arnold- Chiari (n = 3)	Agenesis of c.c. (n = 4)	Stenosis Aqueduct (n = 5)	Hydranen- cephaly (n = 2)	Total (n = 27)
Abnormal lobation of spleen	1		1				2
Asplenia	1						1
Accessory spleen	1	1	1				3
Adrenal agenesis	2						2
Adrenal hypoplasia					1	1	2
Ectopic adrenals			1				1
Agenesis of thyroid				1			1

Note: n: number of cases, c.c.: corpus callosum

autolysis of the organs. The heart showed PDA, PFO, and right ventricular enlargement (Table 4). The brain showed Dandy-Walker malformation associated with partial agenesis of the corpus callosum and hypoplasia of the cerebral peduncle, pyramidal tract, and cerebellar vermis (Table 2). The third case lived 28 days with multiple congenital heart disease such as TOF bilateral superior vena cava, right subclavian artery arising from descending aorta with retroesophageal course, and PFO (Table 4). The right lung was bilobated. In summary, 2 out of 3 cases showed PDA, PFO, hypoplastic lung, pes equinovarus, hypertelorism,

low-set ear, and cleft lip and palate. Other malformations occurred in 1 case, each.

An additional 2 cases showed hydranencephaly. Both were male. One lived 2 months and the other was 33 weeks GA. One case, 33 week GA, showed multiple anomalies such as PDA, PFO, agenesis of the right kidney, preaxial polydactyly of the right hand, scoliosis, and complete left cleft palate and lip. The other case, which lived 2 months, showed PFO, an undescended right testis, and severe jaundice. In summary, holotelencephaly was most commonly associated with other central nervous system and

Table 10. Posthemorrhagic hydrocephalus: 14 cases

Case No.	Age/Sex	GA (wks)	Brain Wt (gm)	Other Pathologic Changes
1	3d/M	Uk	201	
2	2d/M	32	277.4	Brain edema
3	4d/F	30	204.3	Intracerebral hemorrhage
4	5hr/M	40	483	Achondroplasia
				Edema, marked
5	29hr/M	Uk	163	Hyaline membrane disease
6	5d/F	Uk	306	Lobar pneumonia, DIC
				Leukomalacia
7	16d/F	Uk	248	Systemic candidiasis
				DIC, PDA, leukomalacia
8	1d/M	Uk	428	Diffuse pneumonia
				PDA, leukomalacia
9	T/M	37	Uk	IVH, SAH
10	2d/M	Uk	274.5	Germinal matrix cyst
				Obstructive hydrocephalus
				Multiple congenital anomaly
11	15d/F	Uk	488	Subependymal cyst
				SAH, Edwards syndrome
12	3d/M	Uk	522	Subependymal cyst, bilateral
				Congenital heart disease
13	SB/F	25	253.8	Sponge-like cystic change of cerebral white matter
				SAH
14	SB/M	35	Uk	Extradural hematoma, posterior fossa,
				PDA, fetal hydrops

Note: GA: gestational age
 DIC: disseminated intravascular coagulation
 PDA: patent ductus arteriosus
 IVH: intraventricular hemorrhage
 SAH: subarachnoid hemorrhage
 Uk: unknown

craniofacial anomalies (Tables 2 and 3). PDA was the most commonly encountered cardiovascular malformation and found in 50% of the holotelencephaly cases (Table 4). Among the malformations of the respiratory tract, abnormal lobation of the lung was the most common, followed by hypoplasia of the lung (Table 5). Cryptorchidism was present in 6 cases out of a total of 27 cases (Table 7).

Posthemorrhagic hydrocephalus

A total number of 14 cases of posthemorrhagic hydrocephalus was noted (Table 10). There were 9 males and 5 females. The age distribution was from 1 day to 16 days, except for 2 cases which were

stillborn after 25 and 35+4 weeks GA, respectively. These included 3 cases of subependymal cysts due to old hemorrhage, 1 case of cystic leukomalacia associated with subarachnoid hemorrhage, and 1 case of posterior fossa hematoma. The other 9 cases showed varying amounts of intraventricular hemorrhage. These cases were commonly associated with respiratory problems. Three cases with subependymal cysts showed multiple congenital malformations in the cardiovascular, genitourinary, and skeletal systems and 1 case showed trisomy 18.

Postinfection hydrocephalus

Four cases of postinfection hydrocephalus were

Table 11. Postinfection hydrocephalus: 4 cases

Case No.	Age/Sex	GA (wks)	Pathology Findings
1	3d/M	Uk	Obstruction of interventricular foramen, micropolygyria, old ependymitis, situs inversus
2	19d/F	32	Disseminated neonatal herpes infection with meningoencephalitis involving skin, liver, and eyeball
3	SB/F	34	Herpes simplex necrotizing meningoencephalitis, chorioretinitis, intestinal obstruction (sigmoid colon)
4	21d/M	Uk	Congenital CMV infection, multifocal ependymitis, subependymal cyst

Note: CMV: cytomegalovirus

GA: gestational age

SB: stillborn

Uk: unknown

present (Table 11). One case was a stillborn female at 34 weeks of GA and showed herpes simplex meningoencephalitis with periventricular calcification and chorioretinitis. Other abnormalities were patchy necrosis of the liver, ischemic myocardial necrosis, ischemic necrosis of the right adrenal, and intestinal obstruction at the sigmoid colon. The other case of disseminated herpes infection was born at 32 weeks gestation and lived 19 days. The body weight was 1,800 gms. The brain revealed necrotizing inflammation with multicystic change, calcification, gliosis, and meningitis. The eyeball showed chorioretinitis with focal calcification and focal retinal detachment. The skin lesion on the back, trunk, and buttock showed intraepidermal vesicle with inclusion bodies. There was 1 case of congenital cytomegalovirus (CMV) infection showing multifocal ependymitis and subependymal cysts. It was a male and lived 21 days. The last one was a 3-day-old male showing obstruction at the interventricular foramen with micropolygyria, old ependymitis, and situs inversus.

Miscellaneous

There were 1 case of supracerebellar arachnoid cyst and 3 cases with unknown causes. The case of supracerebellar arachnoid cyst, terminated after 29 weeks GA, was combined with hydrops fetalis, infantile polycystic kidneys, pulmonary hypoplasia, ASD, PDA, and abnormal positioning of the right hand.

There was a preterm female baby (33 weeks GA) with mild hydrocephalus who lived 3-4 hours. The cause of hydrocephalus was not clear. The other case, 38 weeks GA and male, showed hydrocephalus of unknown cause, as well as periventricular calcification around the lateral ventricles and periaqueductal area along with hypoplastic lung. Information was not available for the third case.

DISCUSSION

We analyzed the postmortem pathologic findings of patients with congenital hydrocephalus to see the causes and related conditions. All the cases diagnosed antenatally or during the early neonatal period were included in this study. This study included 10 cases of holotelencephaly because antenatal examination frequently described such cases as hydrocephalus even though they did not exactly fulfill the criteria of hydrocephalus.

The incidence of congenital hydrocephalus is estimated to be 1-3 out of 1000 live births. Wiswell et al. (1990) reported 370 cases of congenital hydrocephalus, unassociated with spina bifida, meningitis, or intracranial hemorrhage, out of 763,364 live-born and stillborn babies from 1971 through 1987 (0.48/1000 total births). The incidence was similar to that in other

previous major American studies (Stein et al., 1981, 1982). In their study, hydrocephalus was significantly more common among males of all racial categories ($p < .01$). Our study showed 10 male cases and 14 female cases in the hydrocephalus group associated with congenital malformations. The difference was probably due to inclusion of holotelencephaly (M:F = 2:7) which was not included in their study. The rest of the cases showed a male to female ratio of 8:7, but comparison of this study with theirs may not be significant because this study included only autopsy cases. In the study of Fernell et al. done in Sweden (1986), a total of 202 live-born infants between 1967 and 1982 showed hydrocephalus before the age of 1 year. Of these, 141 (70%) were born at term and 61 (30%) were preterm. The mean prevalence was 0.53/1000 births. The preterm group showed increased prevalence during the later period (1979) compared to the years 1967-70. In 12 out of 23 children born very early GA, cerebral hemorrhage was the origin of hydrocephalus. Pietrzyk et al. (1983) and Lorber and Ward (1985) have described the decreased incidence of hydrocephalus, although others have reported either no change (Edmonds and James, 1985; Stein et al., 1981) or increased incidence (Schule, 1985; Fernell et al., 1986). In Korea, overall study for the prevalence or trend of infantile hydrocephalus has not been done and would be necessary in the near future.

The causes of hydrocephalus are usually known in a small number of cases such as maternal infection (cytomegalovirus, toxoplasmosis, and possibly mumps, rubella, varicella), nutritional disorder (experimentally associated with hypo- and hypervitaminosis A), teratogenesis (radiation etc.), and genetic factors (X-linked). This study demonstrated that causes of congenital hydrocephalus fall into 3 categories: congenital malformation, posthemorrhagic, and postinfection. In addition, two cases showed hydranencephaly and four cases were hydrocephalus with unknown etiology. Congenital malformation of CNS was the most common cause of hydrocephalus diagnosed during the intrauterine and perinatal period, which comprised 49% of all cases. Most of congenital hydrocephalus due to congenital malformation are the noncommunicating type as in this study. Russell (1949) concluded that at least 99% of her cases resulted from impaired circulation of cerebrospinal fluid (CSF) caused by mechanical obstructions of the CSF flow. According to Milhorat (1972), obstruction at the aqueduct of Sylvius accounts for more than two-thirds of the noncommunicating hydrocephalus group. Statistics done by Ford in 1926 showed that the 3 most common causes were menin-

gitis and arachnoid fibrosis (53/100), Arnold-Chiari malformation (16/100), and aqueduct stenosis alone (14/100). Gilles and Davidson (1971) and Shillito (1970) found 97 cases of hydrocephalus among 1,050 consecutive autopsies. Neoplasia (27 cases), meningitis and arachnoid fibrosis (25 cases), and Arnold-Chiari malformation (22 cases) were the most common causes. This study showed 8 cases of aqueduct stenosis or obstruction, including 2 cases associated with holotelencephaly and 1 case with Dandy-Walker malformation. Other malformations such as Arnold-Chiari and Dandy-Walker malformations are well-known causes of noncommunicating hydrocephalus.

Various chromosomal abnormalities have been reported to be associated with a variety of CNS malformations. According to Suh and Chi (1988), malformations of CNS were more common in trisomy 13 or chromosome 4p- syndrome than trisomy 18. Nine of their 18 cases of chromosomal abnormalities showed anomalies of CNS, and 6 of them had a combination of anomalies. Hydrocephalus was noted in 1 out of 10 cases of trisomy 18. Agenesis of the corpus callosum was noted in 1 case and holotelencephaly was associated with 2 cases of trisomy 13. Trisomy 13 has been frequently associated with CNS anomalies, such as holotelencephaly, corpus callosum defect, and hydrocephaly (Warkany et al., 1966; Kim, 1987). Trisomy 18 frequently constellated as multiple anomalies including craniofacial malformations, as well as box-shaped brain with gyral abnormalities and dysplasia of the hippocampus and inferior olive. In addition, absence of the corpus callosum and holotelencephaly may occur in this syndrome (Taylor, 1968). This study includes 5 cases of chromosomal anomalies: 4 cases of trisomy 18 and 1 case of chromosome 4p- syndrome. Three cases of trisomy 18 were associated with holotelencephaly (1), agenesis of the corpus callosum (1), and subependymal cyst and subarachnoid hemorrhage (1), each. One case with features compatible with trisomy 18 showed Dandy-Walker malformation associated with partial agenesis of the corpus callosum. A case of chromosome 4p- syndrome was associated with agenesis of the corpus callosum.

Congenital hydrocephalus due to malformation often shows a constellation of malformations in various organs. According to Wiswell et al. (1990), 137 out of 370 cases of congenital hydrocephalus (37%) had congenital anomalies unrelated to the primary defect. The most common defects were TEF and genitourinary, cardiac, and multiple anomalies. Since major CNS malformations are so frequently associated with unrelated anomalies (Elwood JM and Elwood JH, 1980;

Warkany et al., 1981(1), 1981(2); Lemire FJ, 1988) all infants with CNS defects should be examined closely during the neonatal period to detect any other anomalies. This study showed 13 cases associated with PDA, 8 cases of abnormal lobation of the lung, 7 cases of ASD and PFO each, and 6 cases of pulmonary hypoplasia. Various other malformations were noted in less than 4 cases. A small fraction of stenosis of aqueduct occurs as a familial, sex-linked trait (Bickers and Adams, 1949; Warren et al., 1963; Needleman and Root, 1963). Edwards et al. (1961) described a coexistent deformity of the thumb, spasticity, and contractions. Thumb deformity was also noted by Jezequel et al. (1973). These cases had a stenotic aqueduct with a very narrow lumen lined with ependyma compared to the aberrant channels of ependyma seen in nonhereditary congenital stenosis (Homles et al., 1973). One of our 5 cases of pure aqueductal stenosis showed multiple anomalies including flattened and broad thumb tips. Familial study in this case was not performed. In the evaluation of hydrocephalus cases, the findings of other unrelated anomalies or chromosomal abnormalities are very important to define the exact nature of the case and future prognosis.

Hydrocephalus is the most frequent sequel of intraventricular hemorrhage requiring shunts. Ventricular dilatation may accompany intraventricular hemorrhage or may follow as a late complication. The degree of ventricular dilatation reflects the amount of blood released into the ventricular system, the pressure under which the blood is released, and whether the hemorrhage blocks the subarachnoid space. There are many controversial risk factors for hemorrhage, and it has been accepted that the premature infant is more prone to traumatic hemorrhage than the infant born at full term. The National Collaborative Perinatal Project showed the similarities of distribution of hemorrhage between live-born and stillborn infants (Dooling and Gilles, 1983). Germinal matrix hemorrhage is the most frequently encountered source of intraventricular hemorrhage and most frequently occurs during 26-31 weeks GA. The other major source of hemorrhage is choroid plexus. In this study, 9 cases showed intraventricular hemorrhage and 7 of them were prematurity. Associated conditions were quite varied including respiratory problems, infection, and cardiac malformations. Four cases showed late stage of intraventricular hemorrhage manifested as germinal matrix or subependymal cyst (3) and sponge-like cystic change of cerebral white matter (1). Associated conditions were also varied including multiple congenital cardiovascular, genitourinary, and skeletal system malformations,

as well as chromosomal anomaly.

Meningitis and arachnoid fibrosis with obstruction of the subarachnoid space is the most common cause of hydrocephalus in infancy (Friede, 1975). Fibrotic obstruction may also result from the organization of subarachnoid hemorrhages. Postinfection hydrocephalus could be communicating or noncommunicating according to the level of obstruction. One of our cases showed obstruction of the interventricular foramen due to old ependymitis. Two other cases showed necrotizing meningoencephalitis.

REFERENCES

- Bickers DS, Adams RD: *Hereditary stenosis of the aqueduct of Sylvius as a cause of congenital hydrocephalus*. *Brain* 72:246-262, 1949.
- Dooling EC, Gilles FH: *Intracranial hemorrhage: topography*. In: Gilles FH, Leviton A, Dooling EC (eds) *The Developing Human Brain: Growth and Epidemiologic Neuropathology*. Boston, Wright PSG, pp193-203, 1983.
- Edwards JH, Norman RM, Roberts JM: *Sex-linked hydrocephalus: report of a family with 15 affected members*. *Arch Dis Child* 36:481-485, 1961.
- Edmonds LD, James LM: *Temporal trends in the incidence of malformations in the United States, selected years, 1970-1971, 1982-1983*. *MMWR* 34 (No. 2SS): 1SS-3SS, 1985.
- Elwood JM, Elwood JH: *Epidemiology of anencephalus and spina bifida*. Oxford, England: Oxford University Press; 1980.
- Fernell E, Hagberg B, Hagberg G, von Wendt L: *Epidemiology of infantile hydrocephalus in Sweden. I. Birth prevalence and general data*. *Acta Paediatr Scand* 75:975-981, 1986.
- Ford FR: *Cerebral birth injuries and their results*. *Medicine* 5:121-194, 1926. In: Friede RL *Developmental Neuropathology* Springer-Verlag New York, 1975.
- Friede RL: *Developmental Neuropathology*. Springer-Verlag New York, 1975.
- Gilles FH, Davidson RI: *Communicating hydrocephalus associated with deficient dysplastic parasagittal arachnoidal granulations*. *J Neurosurg* 35:421-426, 1971.
- Holmes LB, Nash A, Zu Rhein GM, Levin M, Opitz JM: *X-linked aqueductal stenosis: clinical and neuropathological findings in two families*. *Pediatrics* 51:697-704, 1973.
- Jezequel C, Belloir D, Jehan P et al: *Congenital hydrocephalus. Bilateral abnormality of the thumbs and eye changes*. *Semaines Hopitaux* 49:927-934, 1973. In: Friede RL *Developmental Neuropathology* Springer-Verlag New York 1975.

- Kim KB: Chromosomal aberrations reported in Korea. *J Korean Pediatr Assoc* 30:602-612, 1987.
- Lemire RJ: Neural tube defects. *JAMA* 259:558-562, 1988.
- Lorber J, Ward AM: *Spina bifida: a vanishing nightmare?* *Arch Dis Child* 60:1086-1091, 1985.
- Milhorat TH: *Hydrocephalus and the cerebrospinal fluid.* Baltimore, Williams & Wilkins, 1972.
- Needleman HL, Root AW: Sex-linked hydrocephalus. *Pediatrics* 31:396-399, 1963.
- Pietrzyk JJ, Grochowski J, Kanska B: CNS malformations in the Krakow region. I: birth prevalence and seasonal incidence during 1979-1981. *Am J Med Genet* 14:181-188, 1983.
- Russell DS: *Observations on the pathology of hydrocephalus.* Medical Res Council, Special Report Series No. 265. London: HMSO 1949. In: Friede RL *Developmental Neuropathology* Springer-Verlag New York, 1975.
- Schule K: Aspects of the incidence of central nervous malformations in Cologne 1971-1980. *Klin Padiatr* 197: 277-281, 1985.
- Shillito J: Infantile hydrocephalus: retrocerebellar subdural hematoma. *J Pediatr* 76:529-537, 1970.
- Stein SC, Feldman JG, Apfel J, Kohl SG, Casey G: *The epidemiology of congenital hydrocephalus: a study in Brooklyn, NY 1968-1976.* *Childs Brain* 8:253-262, 1981.
- Stein SC, Feldman JG, Friedlander M, Klein RJ: Is myelomeningocele a disappearing disease? *Pediatrics* 69:511-514, 1982.
- Suh YL, Chi JG: Congenital malformations in chromosomal abnormalities: analysis of 18 autopsy cases. *Seoul J Med* 29: 333-342, 1988.
- Taylor AI: Autosomal trisomy syndrome: a detailed study of 27 cases of Edwards syndrome and 27 cases of Patau syndrome. *J Med Genet* 5:227-252, 1968.
- Warkany J, Lemire RJ, Cohen MM: Hydrocephaly. In: Warkany J, Lemire RJ, Cohen MM (eds) *Mental Retardation and Congenital Malformations of the Central Nervous System.* Chicago, Ill: Year Book Medical Publishers Inc; pp48-82(1), 1981.
- Warkany J, Lemire RJ, Cohen MM: Encephaloceles. In: Warkany J, Lemire RJ, Cohen MM (eds) *Mental Retardation and Congenital Malformation of Central Nervous System.* Chicago, Ill: Year Book Medical Publishers Inc; pp158-175(2), 1981.
- Warkany J, Passarge E, Smith LB: Congenital malformations in autosomal trisomy syndrome. *Am J Dis Child* 112:502-515, 1966.
- Warren MC, Lu AT, Ziering WH: Sex-lined hydrocephalus with aqueductal stenosis. *J Pediatr* 63:1104-1110, 1963.
- Wiswell TE, Tuttle DJ, Northam RS, Simonds GR: Major congenital neurologic malformations. A 17-year survey. *Amer J Diseased Child* 144:61-67, 1990.