Journal of Hydrocephalus

The 10 Major Subjects in Hydrocephalus Research Fields

HRF subject I-X

Subject I.	**Definition and Terminology of Hydrocephalus**		
Subject II.	**Classification of Hydrocephalus**		
Subject III.	**Pathophysiology 1. Cerebrospinal Fluid (CSF) Physiology**		
	Pathophysiology 2. Intracranial Pressure (ICP) Physiology		
	Pathophysiology 3. Miscellaneous		
Subject IV.	**Hydrocephalus Chronology**		
Subject V.	**Specific Forms of Hydrocephalus**		
	1. Pathogenic Concepts	**1) Congenital Hydrocephalus**	
		2) Acquired Hydrocephalus	
		3) Idiopathic	
	2. Pathophysiological Concepts	**1) Intracranial Pressure (ICP)**	
		2) Cerebrospinal Fluid (CSF)	
		3) Miscellaneous	
	3. Chronological Concepts	**1) Phase**	
		2) Progression	
	4. Miscellaneous		
Subject VI.	**Associated Congenital Anomalies/ Syndrome and Underlying Conditions**		
Subject VII.	**Diagnostic Procedures for Hydrocephalus**		
Subject VIII.	**Treatment Modalities in Hydrocephalus**		
Subject IX.	**Experimental Hydrocephalus and Invention**		
	1. Hydrocephalus Model		
	2. Diagnostic and Therapeutic Methodology and Invention		
	3. Miscellaneous		
Subject X.	**Ethics & Moral/ Society/ Education in Hydrocephalus Medicine and Science**		
	1. Medico-ethics/ Medico-social/ Medico-legal/ Medico-economical Issue		
	2. Federation/ Society/ Association/ Research Foundation/ Study Group and Education for Hydrocephalus		
	3. Miscellaneous		

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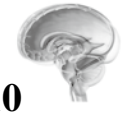
Volume 2, Number 1 2010

Hydrocephalus Research: Current Topics of the Year 2010
"Definition and Classification of Hydrocephalus"



Hydrocephalus Research: Current Topics of the Year 2010
"Definition and Classification of Hydrocephalus"

KEY NOTE PAPER

A Proposal of "Multi-categorical Hydrocephalus Classification": Mc HC — Critical Review in 72,576,000 Patterns of Hydrocephalus —

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Abstract

Objective: Hydrocephalus is defined as a pathophysiology with disturbed cerebrospinal fluid (CSF) circulation. There have been numerous numbers of classification proposed based on various aspects, such as associated anomalies/ underlying lesions, CSF circulation/intracranial pressure (ICP) patterns, clinical features, and other categories. However, no definitive classification exists comprehensively to cover the variety of these aspects.

The purpose of this paper is to design and develop a new classification of hydrocephalus, "Multi-categorical Hydrocephalus Classification": [Mc HC] to cover the entire aspects of hydrocephalus with all considerable classification items and factors.

Materials & Method: Considerable items in classification for hydrocephalus among 3 subjects: patient, CSF and treatment are divided into 10 categories, "Mc HC" Category I: Onset (age, phase), II: Cause, III: Underlying Lesion, IV: Symptomatology, V: Pathophysiology 1. CSF circulation, VI: Pathophysiology 2. ICP dynamics, VII: Chronology, VIII: Post-shunt, IX: Post-Endoscopic Ventriculostomy (EVS), and X: Others. There were 54 subtypes of hydrocephalus listed up, and these were divided into the 10 "Mc HC" Categories, 2-7 in each respectively.

Results & Discussion: In order to cover all these combinations, there could be theoretically 72,576,000 patterns of hydrocephalus classified. This new classification of hydrocephalus, "Mc HC", shall be applied to analyze the clinical data prospectively corrected from the most-experienced centers in Japan as a part of the nationwide cooperative study for fetal and congenital hydrocephalus as "Center of Excellence (COE) - Fetal Hydrocephalus Top 10 Japan nominated from the retrospective survey for the year of 2008.

Conclusion: In the preliminary clinical application, it was concluded that "Mc HC" is extremely effective to express the individual state in the past and present condition of hydrocephalus along with the possible chronological change in future.

Key Words: Hydrocephalus, Definition, Classification, Cerebro-spinal Fluid (CSF), Multi-categorical Hydrocephalus Classification, Shunt, Neuroendoscopic Surgery, Chronology

I. Introduction

The definition of hydrocephalus remains still debatable. Since hydrocephalus is not a single pathological disease but a pathophysiological condition of disturbed cerebrospinal fluid (CSF) dynamics with or without the underlying disease, the classification is often confused and complex. There are numerous numbers of the classification categories, items and criteria. Since hydrocephalus in each patient shall be classified along with the individual categories, and items, such combination of the classified subtypes of hydrocephalus can be uncountable, i.e. "*congenital-fetal/ progressive/ high-pressure/ non-communicating/ idiopathic/ macrocephalic/ internal-triventricular*" hydrocephalus with a cyst in the fourth ventricle etc..

In fetal hydrocephalus, for example, it is the major concern to predict the postnatal clinical feature in prenatal diagnosis of the individual type of hydrocephalus. We have promoted the hydrocephalus research for fetal hydrocephalus in the track of rapidly developing neuroimaging modalities with ultrasonography, magnetic resonance (MR) imaging[19), 23)], and have enabled prenatal diagnosis of fetal hydrocephalus in its morphology. A few of the presently available classification systems takes into account the chronological changes of the hydrocephalic state from the fetal to neonatal and infantile periods, and reflect the underlying developmental or embryological stages of the brain, especially the neuronal maturation process. The postnatal prognosis may also depend on the progression of the hydrocephalus and the affected brain and on the degree of damage to the neuronal maturation process.

In the field of hydrocephalus research in adults, there are growing new consensus other than classical "normal pressure hydrocephalus" (NPH), which has been always debatable in the concept of this entity[24, 27)]. Based on such variety of characteristics in hydrocephalus, recently with more and more new aspects disclosed not only in fetal and pediatric but also in adult hydrocephalus, the current status of classification of hydrocephalus in the individual subgroup was reviewed focusing on the critical points of the individual category of hydrocephalus.

The purpose of this paper is to design and develop a new classification of hydrocephalus, "Multi-categorical Hydrocephalus Classification": [Mc HC] to cover the entire aspects of hydrocephalus with current considerable classification categories and subtypes.

II. Material and method

1. The 10 major subjects in hydrocephalus research field: HRF Subject I-X (Table 1)

In order to design the new classification of hydrocephalus, "Mc HC", the 10 major subjects in hydrocephalus research field were listed up for understanding of the general consensus [HRF Subject I-X]. The research for the "Classification of Hydrocephalus" was considered as one of the major subject, HRF Subject II, after "Definition and Terminology" (HRF Subject I).

2. The 10 major classification categories of hydrocephalus in "Mc HC" (Table 2)

Considerable items in classification for hydrocephalus among 3 subjects: patient, CSF and treatment are divided into 10 categories, "Mc HC" category I: Onset (age, phase), II: Cause, III: Underlying Lesion, IV: Symptomatology, V: Pathophysiology 1. CSF circulation, VI: Pathophysiology 2. ICP dynamics, VII. Chronology, VIII: Post-shunt, IX: Post-Endoscopic Ventriculostomy (EVS), and X: Others. There were 54 subtypes of hydrocephalus listed up, and these were divided into the 10 "Mc HC" Categories: 2-7 in each respectively.

3. Possible hydrocephalus patterns combined with 54 subtypes in 10 categories in "Multi-categorical Hydrocephalus Classification" [Mc HC].

In the 10 categories of "Mc HC" (Table 2), there were 2 subtypes in Mc HC category I. Onset (Pre-/post-natal), 5 in (Age), 3 in II. Cause, 5 in III. Underlying Lesion, 3 in IV. Symptomatology(head), 3 in (Symptom), 4 in (Consciousness and Mentality), 4 in V. Pathophysiology: CSF Circulation (Occlusion), 5 in (Accumulation), 7 in (Isolated Compartment), 2 in VI. Pathophysiology(ICP Dynamics), 3 in VII. Chronology (Phase), 2 in (Progression), 2 in VIII. Post-shunt Dependency and 2 in (Overdrainage), and 2 in IX. Post-EVS Dependency.

4. Reference search for the past publications 1950-2010 regarding hydrocephalus classification

The related publication to classification of hydrocephalus was performed using "PubMed advanced search" during the period of 1950 to April 20, 2010 with the key words, "Hydrocephalus Classification" either in the "key words" or the title from all English publications.

III. Results

1. Possible hydrocephalus patterns in "Multi-categorical Hydrocephalus Classification" [Mc HC].

Possible hydrocephalus patterns combined with 54 subtypes in 10 categories in "Mc HC" was mathematically estimated.

The formula to count all possible subtype combinations,

Table 1

The 10 Major Subjects in Hydrocephalus Research Fields

HRF Subject I-X

Subject I.	Definition and Terminology of Hydrocephalus	
Subject II.	Classification of Hydrocephalus	
Subject III.	Pathophysiology 1. Cerebrospinal Fluid (CSF) Physiology	
	Pathophysiology 2. Intracranial Pressure (ICP) Physiology	
	Pathophysiology 3. Miscellaneous	
Subject IV.	Hydrocephalus Chronology	
Subject V.	Specific Forms of Hydrocephalus	
	1. Pathogenic Concepts	1). Congenital Hydrocephalus
		2). Acquired Hydrocephalus
		3). Idiopathic
	2. Pathophysiological Concepts	1). Intracranial Pressure (ICP)
		2). Cerebrospinal Fluid (CSF)
		3). Miscellaneous
	3. Chronological Concepts	1). Phase
		2). Progression
	4. Miscellaneous Concepts	
Subject VI.	Associated Congenital Anomalies/Syndrome and Underlying Conditions	
Subject VII.	Diagnostic Procedures for Hydrocephalus	
Subject VIII.	Treatment Modalities in Hydrocephalus	
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Subject X.	Ethics & Moral/ Society/ Education in Hydrocephalus Medicine and Science	
	1. Medico-ethics/ Medico-social/ Medico-legal/Medico-economical Issue	
	2. Federation/ Society/ Association/ Research Foundation/ Study Group	
	3. Education for Hydrocephalus	
	4. Miscellaneous	

Table 2

$\mathcal{M}c\ \mathcal{H}C$: Multi-categorical Hydrocephalus Classification [Oi, S: Journal of hydrocephalus Vol.2 No.1, 2010]

Subjects	Categories	Subtypes		**/***[reference]
Patient	I. Onset (Pre-/Post-natal)	1 Congenital	2 Acquired	
	Onset (Age)	1 Fetal [PCCH Stage ( )]	2 Neonatal	3 Infantile
		4 Child	5 Adult	**[Oi, S]
	Others	( )		
	II. Cause	1 Primary	2 Secondary	3 Idiopathic
	III. Underlying Lesion	1 Dysgenetic	Syndromic ( )	
		2 Post hemorrhagic	3 Post meningitic	4 Post traumatic
		5 With Tumor / Cyst / Mass Lesions		others ( )
	IV. Symptomatology (Head)	1 Macrocephalic	2 Normocephalic	3 Microcephalic
	(Symptom)	1 Occult (asymptomatic)	2 Symptomatic	3 Overt
	(Conciousness & Mentality)	1 Comatose	2 Stuporous	3 Dementia
		4 Retarded	others ( )	***[Hakim, S]
	(Syndrome:)	1 Hydrocephalus / Parkinsonism Complex		**[Oi, S]
CSF	V. Pathophysiology:	1 Communicating	2 Noncommunicating	***[Dandy, WE]
	CSF Circulation (Occlusion)	3 Non-obstructive	4 Obstructive	***[Russell, DS]
	(Accumulation)	1 External	2 Internal	3 Interstitial ***[Raimondi, AJ]
		4 Localized	5 Minor Pathway	***[Sato, O], **[Oi, S & Di Rocco, C]
	(Isolated Compartment)	Isolated Compartment: [1 UH 2 IFV 3 IRV 4 ICCD 5 DCH		
		6 DLFV 7 HMH others ( )]		***[Rekate, H]**[Oi, S]
	VI. Pathophysiology (ICP Dynamics)	1 High Pressure	2 Normal Pressure	***[Hakim, S] ***[Di Rocco, C]
	VII. Chronology (Phase)	1 Acute	2 Chronic	3 Long standing
	(Progression)	1 Progressive	2 Spontaneously Arrested	**[Oi, S]
Treatment	VIII. Post-shunt	1 Shunt dependent	2 Shunt independent	
	IX. Post-neurondoscopic	1 Slit ventricle syndrome	2 Postoperative Subdural Hematoma	
	Ventriculostomy [NEV]	1 NEV dependent	2 NEV independent	
	X. Others	Others ( )		

* ICP = Intracranial Pressure, CSF = Cerebrospinal Fluid, NEV = Neuroendscopic Ventriculostomy, UH = Unilateral Hydrocephalus, IFV = Isolated Fourth Ventricle, IRV = Isolated Rhombencephalic Ventricle, ICCD = Isolated Central Canal Dilatation, DCH = Double Compartment Hydrocephalus, DLFV = Disproportionately Large Fourth Ventricle, HMH = Hydromyelic Hydrocephalus

**Reference: 1. Hydromyelic Hydrocephalus: Oi, S et al: Journal of Neurosurgery 74: 371-379, 1991
2. Experimental Models of Congenital Hydrocephalus and Compatible Clinical Types: Oi, S et al: Child's Nerv Syst 12: 292-302, 1996.
3. Perspective Classification of Congenital Hydrocephalus[PCCH Stage I-V]: Oi, S et al: Journal of Neurosurgery 88: 685, 1998
4. Long-standing Overt Ventriculomegaly in Adults [LOVA]: Oi, S et al: Journal of Neurosurgery 92: 933-940, 2000
5. Hydrocephalus-Parkinsonism Complex: Oi, S et al: Child's Nerv Syst 20: 37-40, 2004
6. Evolution Theory of CSF Dynamics and Minor Pathway Hydrocephalus: Oi, S and Di Rocco, C: Child's Nerv Syst 22: 662-669, 2006
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***Reference: 8. Communicating/ Non-communicating Hydrocephalus: Dandy, WE: Ann Surg 70: 129-142, 1919 and Dandy, WE & Blackfan, KD: Am J Dis Child 8: 406-482,1914
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12. Ventriculomegaly induced by Pulse Pressure: Di Rocco C et al: J Neurosurg 42: 683-689, 1975
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14. Dynamics of CSF as a Hydraulic Circuit: Rekate, HL Semin Pediatr Neurol 16: 9-15, 2009

$2 \times 5 \times 3 \times 5 \times 3 \times 3 \times 4 \times 4 \times 5 \times 7 \times 2 \times 3 \times 2 \times 2 \times 2 \times 2 = 72,576,000$, suggested that one single hydrocephalus entity can exist in 72,576,000 patterns at least without counting the "other "possible subtypes in "Mc HC".

2. Reference search for the past publications 1950-2010 related to hydrocephalus classification (Table 3)

The "PubMed advanced search during the period of 1950 to April 20, 2010 for the related publications to classification of hydrocephalus listed 83 papers previously published (Table 3). It was convinced in these publications that the "Mc HC" category I-X could cover the multiple aspects of hydrocephalus in order to classify one single case in variety of concepts.

IV. Illustrative Cases

Case 1. A 27-week-old fetus to a 30-yeay-old gravid-0/para-0 mother underwent fetal MR imaging study because of progressively increasing bi-parietal distance (BPD) of the fetus suggesting progressive "macrocephalus" in the ultrasonography. The heavily-T2-weighted fast-spine-echo MR image (Fig. 1 A, C, E) demonstrated moderate ventriculomegaly of the bilateral lateral ventricle. The follow up fetal MR imaging at 33 weeks gestational age (B, D, F) disclosed more expanded ventriculomegaly and macrocephalus with more severely compressed/thinning brain mantle suggesting a fact of "rapid progression of fetal hydrocephalus before birth". The data presented here imply that the neuronal maturation process could be affected by progression of ventriculomegaly in fetal life during the period before pulmonary maturation, up to 32 weeks gestational age (PCCH Stage II).

Mc HC in case 1 (Prenatal): Congenital-Fetal-PCCH Stage II (Mc HC Category I) -primary (II) -Macrocephalic-Overt (IV) -Noncommunicating-Obstructive-Internal (V) -High Pressure (VI) -Acute -Progressive (VII) Hydrocephalus

Case 2. A 30-week-old fetus to a 22-yeay-old gravid-0/para-0 mother underwent fetal MR imaging study because of progressively increasing bi-parietal distance (BPD) of the fetus suggesting progressive "macrocephalus" in the ultrasonography. The heavily-T2-weighted fast-spine-echo MR image of the fetus (Fig. 2 A) demonstrated a neoplastic mass, likely originated in the pineal region, compressing the aqueduct with non-communicating hydrocephalus.

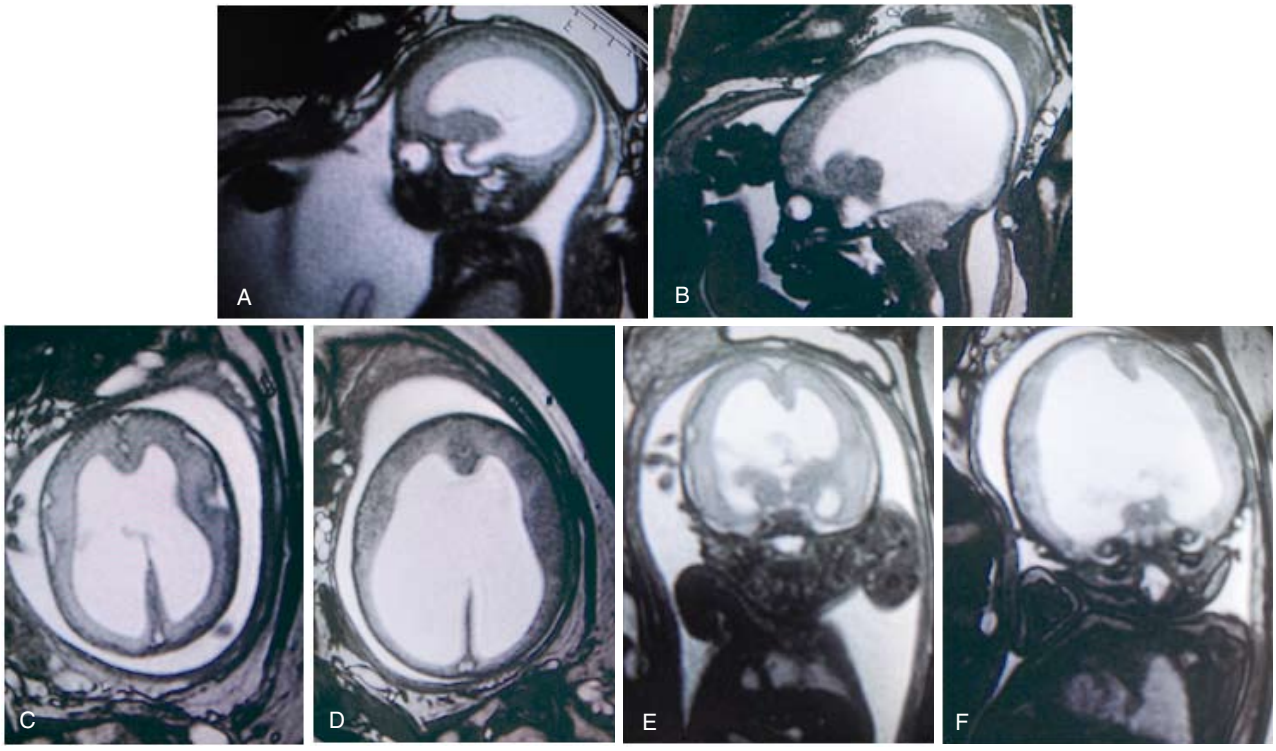

FIG. 1 A, B, C, D, E, F: The heavily-T2-weighted fast-spine-echo MR image demonstrated severe triventricular hydrocephalus, likely due to aqueductal stenosis, at 27 weeks in gestational age (**A, C, E**). The fetal MR imaging follow up at 33 weeks gestational age (**B, D, F**) disclosed more expanded ventriculomegaly and macrocephalus with more severely compressed/thinning brain mantle suggesting a fact of "rapid progression of fetal hydrocephalus before birth".

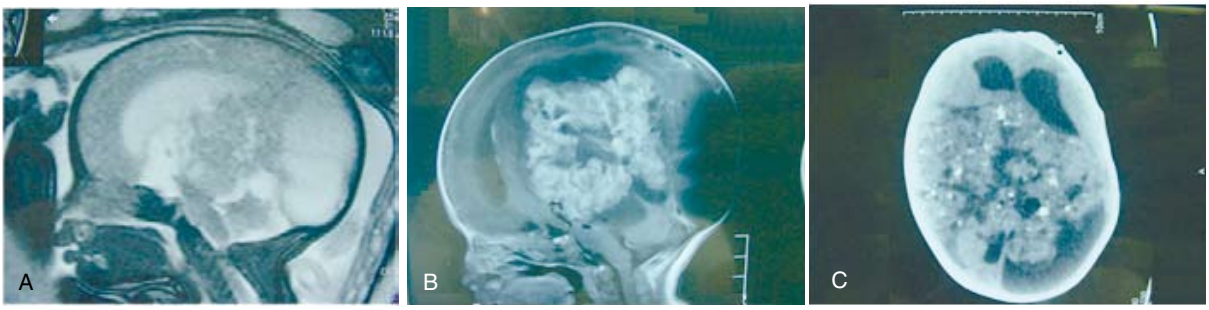

FIG. 2 A: MR image in case 1 (Prenatal): The heavily-T2-weighted fast-spine-echo demonstrated a neoplastic mass, likely originated in the pineal region, compressing the aqueduct with non-communicating hydrocephalus. **B, C:** MR image in case 1 (Postnatal): T1-weighted fast-spine-echo.

Mc HC in case 2 (Prenatal): Congenital-Fetal-PCCH Stage II (Mc HC Category I) -Secondary (II) -with tumor (III) -Macrocephalic-Overt (IV) -Noncommunicating-Obstructive-Internal (V) -High Pressure (VI) -Acute -Progressive (VII) Hydrocephalus

The patient was delivered at 34 weeks of gestational age with Cesarian section. The T1-weighted MR image on day 3 after birth (Fig. 2 A, B) revealeda rapid growth of the neoplastic mass, occupying the entire third and bilateral lateral ventricles, compressing the aqueduct and bilateral foramen of Monro, resulted in triventricular hydrocephalus.

Mc HC in case 2 (Postnatal): Congenital-Neonatal (Mc HC Category I) -Secondary (II) -with tumor (III) -Macrocephalic-Overt (IV) -Noncommunicating-Obstructive-Internal-Triventicular (V) -High Pressure (VI) -Acute-Progressive (VII) Hydrocephalus

Case 3. A 1-week-old male baby with prenatal fetal MR imaging of holoprosencephaly, most likely alobar type, underwent postnatal studies.

At birth, the patient had findings of cleft lip/palate on the examination (Fig. 3 A), and monoventricle with a dorsal sac on MR imaging (Fig. 3 B, C). The cine-mode MR imagings suggested some independent cerebrospinal flow movements between the monoventricle and dorsal sac likely with patient aqueduct (Fig. 3 D). Ommaya reservoir was placed and ventriculo-cisternography was performed. The repeated computerized tomography (CT) immediately after (Fig. 3 E, G), and 6 hours after water-soluble contrast injection (Fig. 3 F) demonstrated #1. Patient aqueduct, #2. Completely isolated dorsal sac from the CSF major pathway (Fig. 3 E, F, G).

Mc HC in case 3 (Postnatal): Congenital-Neonatal (Mc HC Category I) -Dysgenetic -Holoprosencephaly (II) -with Cyst (III) -Normocephalic-Overt (IV) – Noncommunicating-Obstructive-Internal (V) -High Pressure(VI) -Subacute-Progressive (VII) Hydrocephalus

Case 4. A 2-week-old macrocephalic neonate with a finding of ventriculomegaly involving all ventricular system in prenatal fetal MR imaging. The postnatal MR imaging suggested that all ventricles and aqueduct were fully open and expanded (Fig. 4 A, B). The cine-mode MR imaging suggested all independent CSF movements in each compartment and also in the basal cistern without significant to-and-fro movements in the widely open aqueduct (Fig. 4 C). Ommaya reservoir was placed and ventriculo-cisternography was performed. The repeated computerized tomography (CT) immediately after and 6 hours after water-soluble contrast injection suggested all communicating CSF "Major" pathway, and after 24 hours later, it demonstrated significant CSF flow in the trans-ependymal-interstitial brain parenchymal route, so called CSF "Minor" pathway, with stagnation of the contrast [A typical CT cisterno-ventriculography finding of "*Minor Pathway Hydrocephalus*" : Oi S & Di Roco C, 2006] (Fig. 4 D, E, F).

Mc HC in case 4 (Postnatal): Congenital-Neonatal (Mc HC Category I) -Primary (II) -Macrocephalic-Overt (IV) -Communicating-Nonobstructive-Internal-Interstitial (V) -High Pressure (VI) -Subacute -Progressive (VII) Hydrocephalus

Case 5. A premature baby was born at 37-week-gestational age after the prenatal diagnosis of unilateral ventriculomegaly with fetal ultrasonography finding at 36 weeks gestation. The MR imaging suggested occlusion of right foramen of Monro resulted in unilateral hydrocephalus.

Mc HC in case 5 (Postnatal): Congenital-Neonatal (Mc

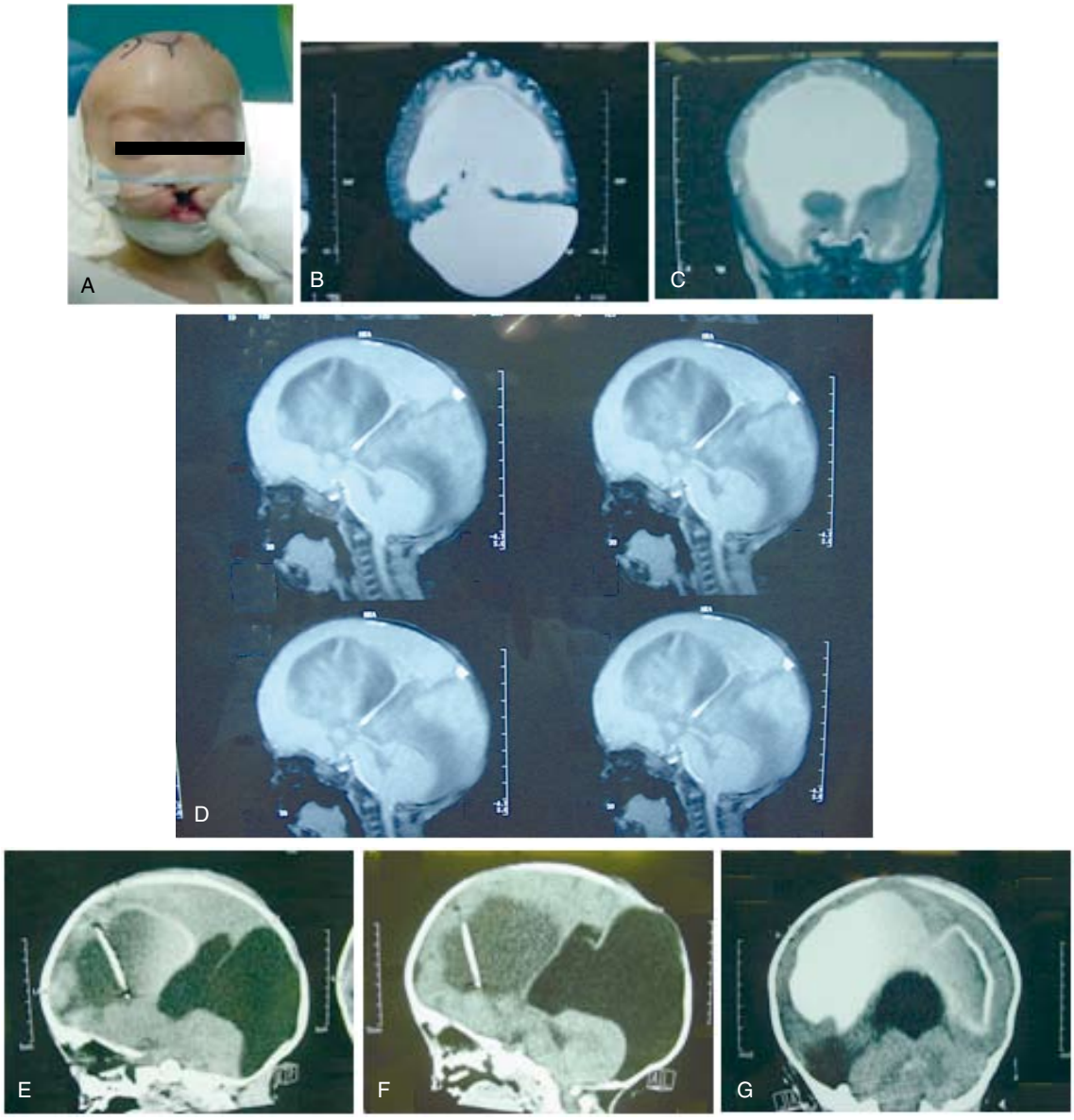

FIG. 3 **A, B, C:** The physical examination revealed cleft lip/plate and monoventricle with a dorsal sac on MR imaging, T2-weighted image. **D:** The Cine-mode MR image. **E, F, G:** The Ventriculo-cisternography performe via Ommaya reservoir (immediately after contrast injection [**E**], and 6 hours injection [**F**]) revealed patient aqueduct and isolated dorsail sac from the major CSF pathway. Furthermore, significant CSF flow in the trans-ependymal-interstitial brain parenchymal route, so called the "Minor" CSF "Minor" pathway (**E, F, G**).

HC Category I) -Primary (II) -Macrocephalic-Overt (IV) -Noncommunicating-Obstrucive-Internal-UH (V) -High Pressure (VI) -Subacute -Progressive (VII) Hydrocephalus.

The patient underwent neuroendoscopic septostomy and foraminoplasty of the occluded foramen of Monro in right side. During the procedure, multiple clots were recognized on the ventricular wall, which suggested "Post-intraventricular hemorrhagic [IVH] hydrocephalus" resulted in secondary occlusion of the foramen of Monro. The immediate postoperative CT revealed the findings of all communicated ventricular system with filling of the contrast injected during the surgery (Fig. 5 C, D). Postoperatively, the patient has been normal neurologically without any neurological deficit and psychomotor developmental delay. The follow up MR imaging at 4 years of age demonstrated nearly normalized ventriculomegaly with just a small subependymal scar of hemorrhagic cavity (Fig. 5 E, F, G).

Mc HC in case 5 (Postoperative & Long-term Follow up):

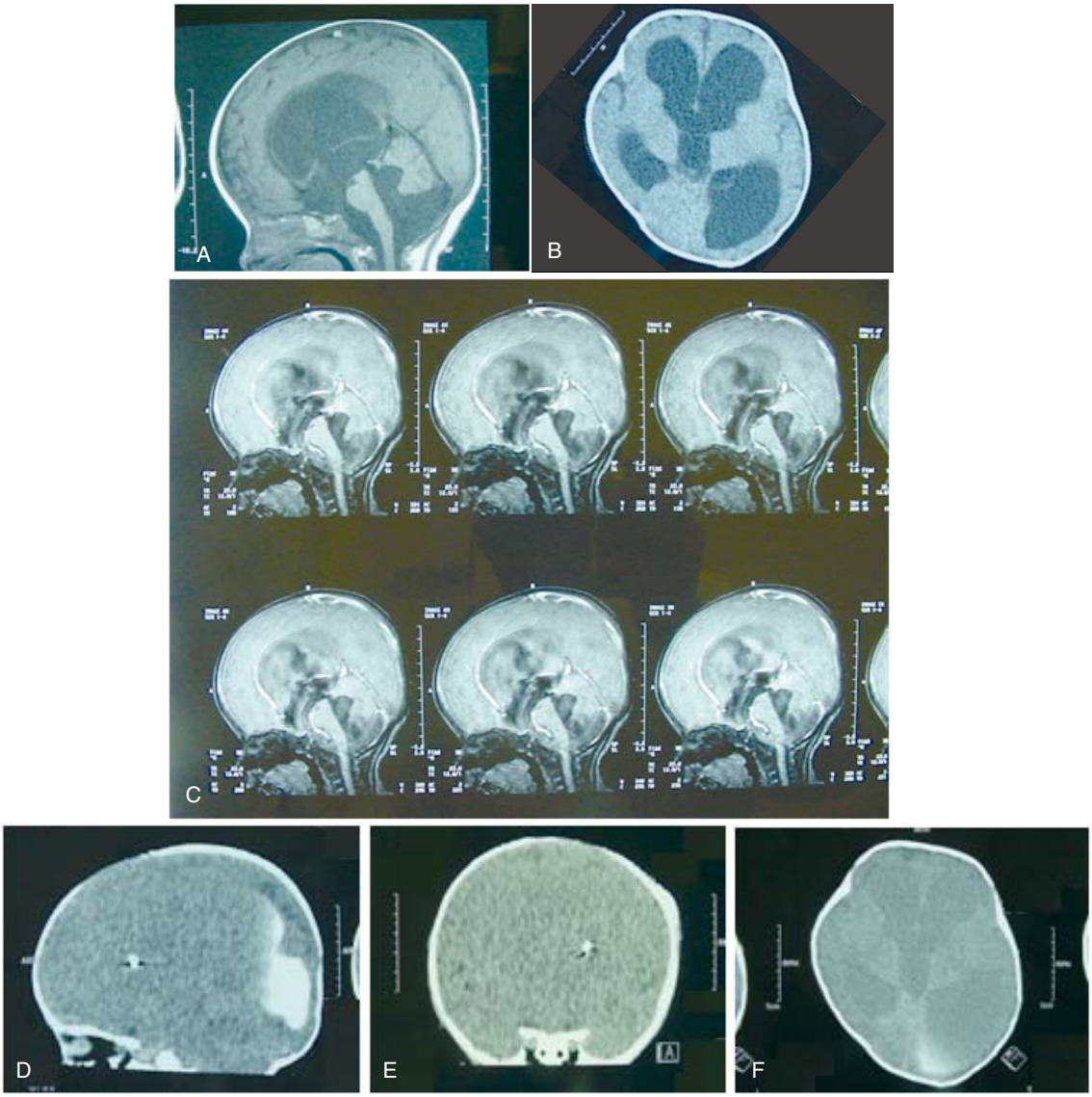

FIG. 4 **A, B:** The postnatal MR imaging (**A**), and CT (**B**) demonstrated fully open and expanded all ventricles and aqueduct. **C:** The Cine mode-MR imaging suggested all independent cerebrospinal flow movements in each compartment and also in the basal cistern without significant to-and-fro movements in the widely open aqueduct. **D, E, F:** The Ventriculo-cisternography at 24 hours after contrast injection demonstrated significant CSF flow in the trans-ependymal-interstitial brain parenchymal route, so called the CSF "Minor" pathway [A typical CT Cisterno-ventriculography findings of "*Minor Pathway Hydrocephalus*" : Oi S & Di Roco C, 2006]

Congenital-Infantile (Mc HC Category I) -Secondary (II) –Posthemorrhagic (III) -Normocephalic-Asymptomatic (IV) -Communicating-Nonobstructive-Internal-UH (V) -Normal Pressure (VI) -Arrested (VII) -EVS dependent (IX) Hydrocephalus.

Case 6. A 11-year-old macrocephalic boy was admitted to our hospital with intractable generalized convulsion. He has a history of neuroendoscopic third ventriculostomy (EVS) at 1 year of age for dysgenetic hydrocephalus with aqueductal stenosis. He had been well until 1 month prior to admission, when he started intermittent severe headaches. The neurological examination disclosed severe papilledema in bilateral optic fundi suggesting increased intracranial pressure (Fig. 6 A). The MR imaging suggested expanded third/lateral ventricles as a single cavity without clearly identified midline structure and downward compressed floor of the third ventricle without recognizable flow void at the EVS site (Fig. 6 B, C)

Mc HC in case 6 (Emergency Admission after Postoperative & Long-term Follow up): Congenital-

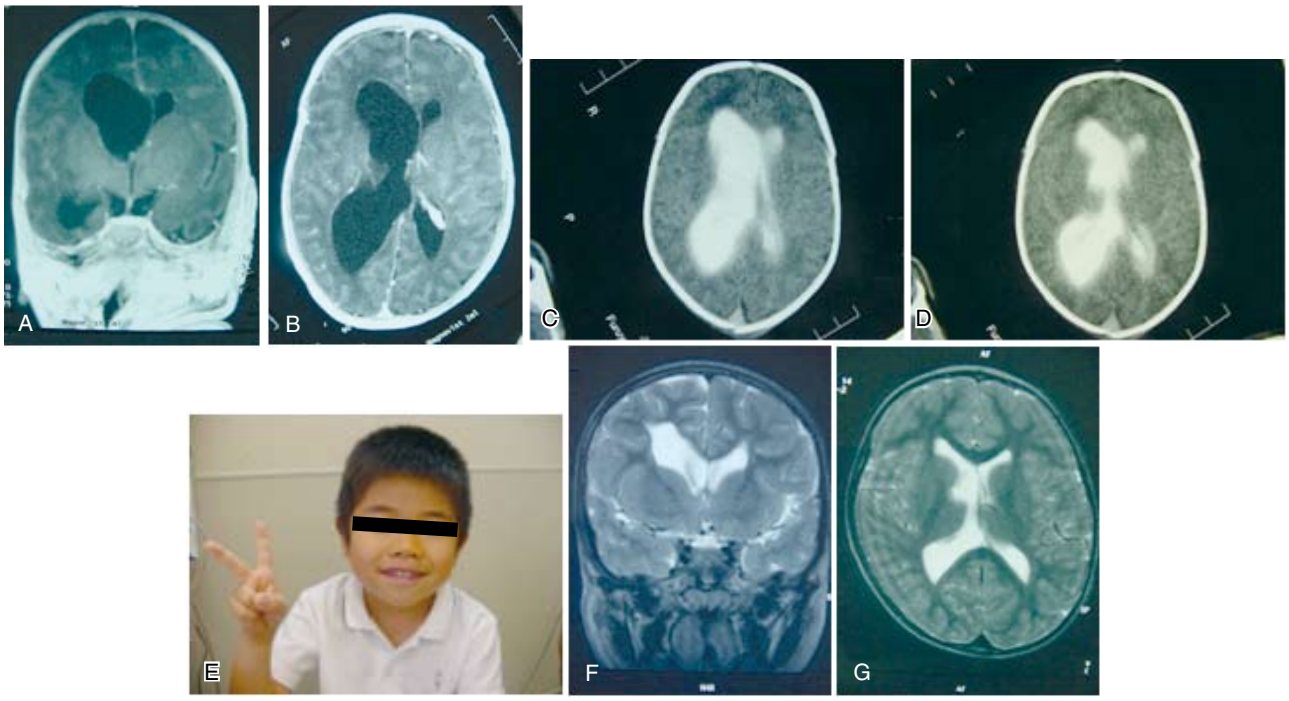

FIG. 5 **A, B:** The MR imaging suggested occlusion of right foramen of Monro resulted in unilateral hydrocephalus. **C, D:** The immediate postoperative CT revealed the findings of all communicated ventricular system with filling of the contrast injected during the surgery. **E, F, G:** Follow up MR imaging at 4 years of age (**E**) demonstrated nearly normalized ventriculomegaly with just a small subependymal scar of hemorrhagic cavity (**F, G**)

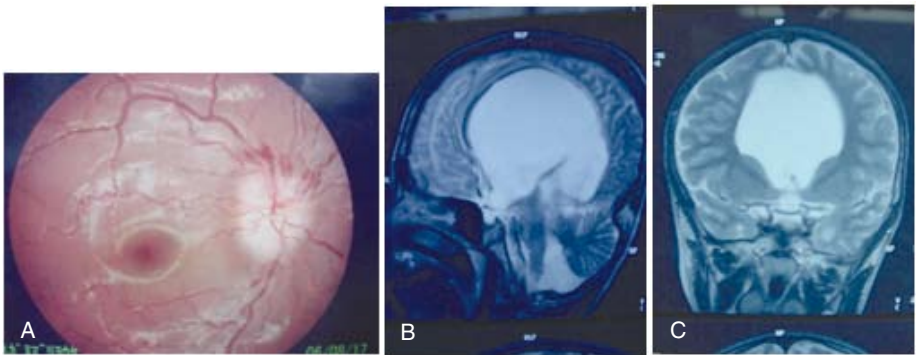

FIG. 6 **A, B, C:** Severe papilledema in bilateral optic fundi suggesting increased intracranial pressure (**A**). The MR imaging revealed expanded third/lateral ventricles as a single cavity without clearly identified midline structure and downward compressed floor of the third ventricle without recognizable flow void at the EVS site (Fig. 6 **B, C**)

Child(Mc HC Category I) -Primary (II) -Dysgenetic (III) -Macrocephalic-Coma (IV) -Noncommunicating-Obstructive-Internal (V) -High Pressure (VI) -Acute-Progressive (VII) -EVS independent (IX) Hydrocephalus.

Case 7. A 61-year-old mildly macrocephalic woman was admitted to our hospital with progressive gait disturbance. On neurological examination, she had also mild parkinsonism, such as bilateral fine tremor of the fingers and rigidity of upper extremity tonus. Her mentality was within normal limit, but mild masked-face appearance was noted. She was admitted to neurology service in our hospital first with a diagnosis of Parkinsonism. However, MR imaging demonstrated severe ventriculomegaly and suggestive finding of aqueductal stenosis with "Phantom sella" on the MR imaging (Fig. 7, A, B). She was transferred to our neurosurgery service with a diagnosis of "Long-standing Overt Ventriculomegaly in

Adults" [LOVA] with some tendency of "Hydrocephalus-Parkinsonism Complex", and underwent neuroendoscopic third ventriculostomy. In the end of the procedure, water-soluble contrast was injected in the third ventricle for the postoperative "Cisterno-ventriculography". Together with postoperative MR imaging (Fig. 7 C) and repeated CT confirmed aqueductal stenosis at immediately postoperative study (Fig. 7 D), good CSF circulation through the NEV site to the prepontine/ basal cistern (Fig. 7 E), and clear up within 24 hours (Fig. 7 F) suggesting "normalized" CSF "Major" pathway circulation. Her clinical symptoms and signs were dramatically improved in all.

Mc HC in case 7 (Pre-operative)): Adult (Mc HC Category I) -Primary (II) -Macrocephalic-Hydrocephalus/ Parkinsonism Complex (IV) -Noncommunicating-Obstructive-Internal (V) -High Pressure (VI) -Long standing-Progressive (VII) Hydrocephalus.

Case 8. A 64-year-old woman was referred to our outpatient clinic with progressive gait disturbance (Fig. 8 A). On neurological examination, she had also mild parkinsonism, such as rigidity of upper extremity tonus. Her mentality was within normal limit. She was evaluated first at neurology service outside hospital first with a diagnosis of LOVA with MR imaging which demonstrated severe ventriculomegaly of bilateral lateral ventricles (Fig. 8 B, C). She underwent first tap test which suggested low range of ICP at around 5-8 cm in H_2O. The withdrawal of 20 ml of CSF made her completely unambulatory for several days. It was reported also that Radio-isotope cisternography, performed at outside hospital, confirmed all communicating ventricular system and subarachnoid space. The diagnosis was made as "True NPH".

Mc HC in case 8 (Pre-operative)): Adult (Mc HC Category I) -Primary (II) -Hydrocephalus/Parkinsonism Complex (IV) -Communicating-Nonobstructive -Internal (V) -Normal Pressure (VI) -Chronic -Progressive (VII) Hydrocephalus.

V. Discussion

Concepts in Classification of Hydrocephalus

The classification of hydrocephalus is the most crucial but the most complicated academic challenge among the 10 major hydrocephalus research fields (Table 1). The major difficulty in this challenge arises from a fact that the classification shall be based on almost all these subjects in hydrocephalus research fields, i.e. Definition and Terminology of Hydrocephalus [HRF Subject I], Pathophysiology (1, 2, 3) [III], Hydrocephalus Chronology [IV], Specific Forms of Hydrocephalus (1, 2, 3, 4) [V], Associated Congenital Anomalies/Syndrome and Underlying Conditions [VI], Diagnostic Procedures for Hydrocephalus [VII], Treatment Modalities in Hydrocephalus [VIII], and Experimental Hydrocephalus and Invention (1, 2,3) [IX] in the list of Table 1.

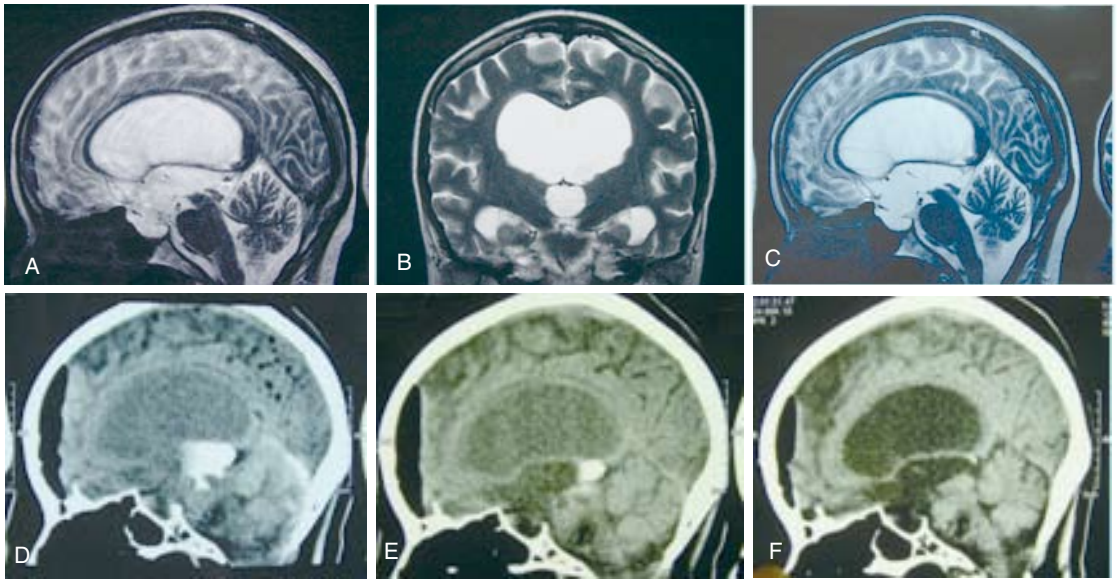

FIG. 7 A, B: MR imaging demonstrated severe ventriculomegaly and suggestive finding of aqueductal stenosis with "Phantom sella" compatible with "Long-standing Overt Ventriculomegaly in Adults" [LOVA]. **C, D, E, F:** Post-operative MR imaging (**C**), and CT Ventriculo-cisternography revealed aqueductal stenosis at immediately postoperative study (**D**), good CSF circulation through the NEV site to the prepontine/ basal cistern (**E**), and clear up within 24 hours (**F**).

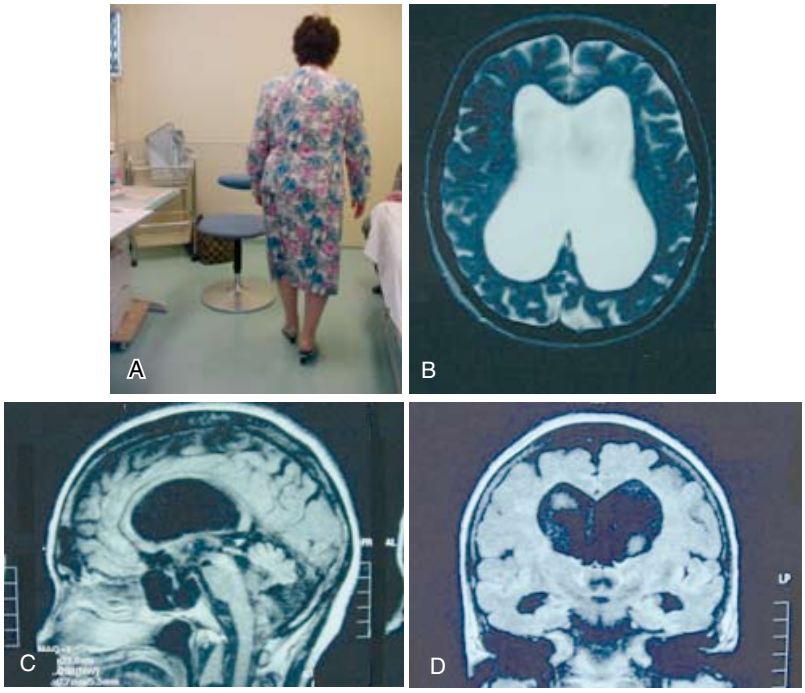

FIG. 8 A, B, C, D: A 64-year-old woman with progressive gait disturbance (**A**). MR imaging demonstrated severe ventriculomegaly of bilateral lateral ventricles (**B, C, D**)

To assure the establishment of the universal overview classification of hydrocephalus, this specificity of the multiplicity concept in hydrocephalus must be prioritized.

"Mc HC" Category I. Onset, II. Cause, and III. Underlying Lesions

The category in classification of hydrocephalus is first focused on the onset of hydrocephalus, either in the fetal / prenatal or postnatal period, and either in neonatal or infantile if diagnosed not before birth. At the same time, the causative factors may differ completely in the perinatal period from the childhood or adulthood. These two categories are most essential in classification of hydrocephalus, and the underlying lesion, if any, is the most considerable factor for the cause of hydrocephalus.

The neuroimaging modalities such as ultrasonography and MRimaging have enabled prenatal diagnosis of fetal hydrocephalus in its morphology, however, the understanding of the character of individual fetal hydrocephalus remains still a difficult challenge. The decision making in each case is often not conclusive. One major reason for the difficulty is the multifactorial nature of the conditions affecting postnatal outcome in congenital hydrocephalus. No single category or clinical feature adequately predicts the likely outcome. Up to late 1990s, there was no available classification systems takes into account the chronological changes of the hydrocephalic state from the fetal to neonatal and infantile periods, and reflect the underlying developmental or embryological stages of the brain, especially the neuronal maturation process. It was essential to have some definitive method with which to estimate postnatal prognosis in fetal hydrocephalus. The prognosis may also depend on the progression of the fetal hydrocephalus and the affected brain and on the degree of damage to the neuronal maturation process.

From this standpoint, Oi, S et al[19), 23)] have developed a new classification system for congenital hydrocephalus, "Perspective Classification of Congenital Hydrocephalus" (PCCH) 52,53. This classification is based on the stage, type, and clinical category of congenital hydrocephalus. Regarding the clinicoembryological stages, each stage reflects both clinical and embryological developmental aspects of the neuronal maturation process in the hydrocephalic fetus or infant, as summarized in Fig. 9.

The clinicoembryological stages [PCCH Stage I-V] are as follows.

Stage I occurs between 8 and 21 weeks of gestation, which is the period of legally permissible termination of pregnancy in Japan. Cell proliferation is the main process in neuronal maturation.

Stage II extends from 22 to 31 weeks of gestation, the period of intrauterine preservation of the fetus before pulmonary maturation is completed. Cell differentiation and migration are the main processes in neuronal

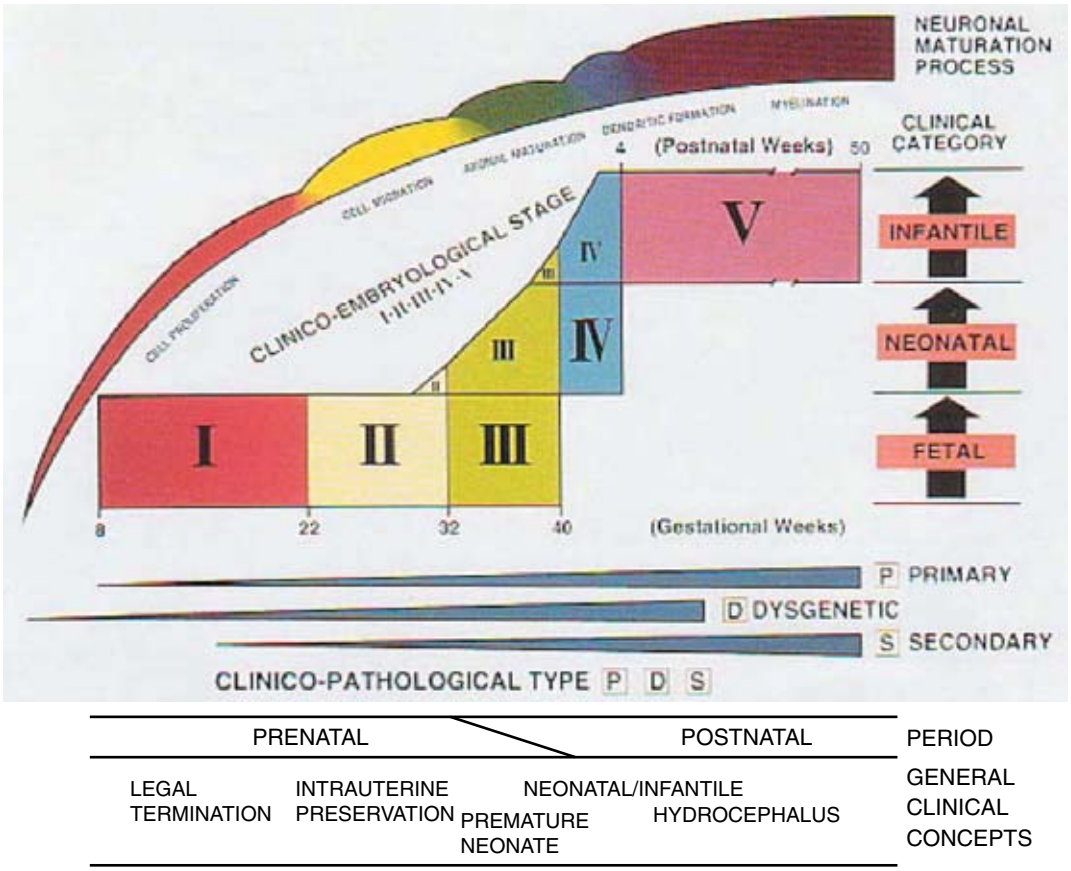

FIG. 9 "Perspective Classification of Congenital Hydrocephalus" [PCCH] (Reprinted with permission from Oi, S et al, Jpn J Neurosurg 3: 124, 1994) Reference: Oi et al : J. Neurosurg. 88: 685-694, 1998 [19), 23)]

maturation.

Stage III extends from 32 to 40 weeks of gestation, a period of possible premature/preterm neonatal hydrocephalus, if delivery occurs. Axonal maturation is the main process in neuronal maturation.

Stage IV occurs between 0 and 4 weeks of postnatal age, the period of neonatal hydrocephalus. Dendritic maturation is the main process in neuronal maturation.

Stage V extends from 5 to 50 weeks of postnatal age, the period of infantile hydrocephalus. Myelination is the main process in neuronal maturation.

In each stage, individual conditions with differing features of hydrocephalus can be classified along with the embryological or developmental background of the affected brain and the cerebrospinal fluid (CSF) circulation in each pathological type with subtypes. The clinicopathological subtypes are: 1) primary hydrocephalus, including communicating or noncomplicated hydrocephalus, aqueductal stenosis, foramen atresia, and others; 2) dysgenetic hydrocephalus, including hydrocephalus with spina bifida, bifid cranium, Dandy-Walker cyst, holoprosencephaly, hydranencephaly, lissencephaly, congenital cyst, and others; and 3) secondary hydrocephalus, hydrocephalus due to brain tumor, hemorrhagic or other vascular disease(s), infection, trauma, subdural fluid collection, and others. These conditions should be considered in the standard clinical categories of fetal, neonatal, and infantile hydrocephalus, based on essential differences in their pathophysiological appearance, including the dynamics of intracranial pressure and CSF circulation. This classification should be applied when the diagnosis of hydrocephalus is made before any procedures have been performed.

The further analysis performed using the new classification, PCCH, suggests that postnatal outcomes differ, depending on the time of onset of the hydrocephalus, even within the same category or sub types. The intelligence quotient (IQ) or developmental quotient (DQ) of patients whose hydrocephalus was diagnosed at PCCH Stage III was higher compared with those diagnosed at Stage II in cases of primary hydrocephalus and compared with those cases with some types of dysgenetic hydrocephalus such as myeloschisis [23)].

Intensive efforts have been made to identify the type(s) of fetal hydrocephalus in which there will be irreversible

damage if left untreated [18), 19), 23)]. The data presented here in Fig. 1 imply that the neuronal maturation process could be affected by progression of ventriculomegaly in fetal life during the period before pulmonary maturation, up to 32 weeks gestational age (PCCH Stage II).

The "Mc HC" Category III. Underlying Lesion is the most considerable factor related to Category II. Cause of Hydrocephalus, if known. It may explain the totally different outcomes in the long term followup in the individual case with similar findings of massive ventriculomegaly in Case 1 - 8 of illustrative cases.
This classification category is also acceptable in a proposal of the new concept of fetal hydrocephalus classified as "*Secondary Congenital Hydrocephalus*" such as with brain tumor as in Case 2, or intraventricular hemorrhage as in Case 5 involving the fetal brain before birth resulted in secondary fetal / congenital hydrocephalus..

" Mc HC" Category V. Pathophysiology (CSF dynamics)

The major CSF pathway starts from the bilateral lateral ventricles with choroid plexus as the significant CSF production source merging with CSF produced in the third and fourth ventricles and CSF passes outside the ventricular system into the cisterns or subarachnoid space. An appreciable volume of CSF comes from sources other than choroid plexus in animals (Bering & Sato, 1963) [1)], (Sato etal, 1975) [39)]. The major absorption site is the arachnoid granulation (Pacchionian body) or villi which soaks CSF up into the sinus, mainly superior sagittal sinus (Weed, 1914, 1916) [40), 41)]. With the bi-directional volume movement of CSF in the major pathway, the CSF dynamics created the bulk flow (Dandy & Blackfan, 1914) [3)]. The rate of CSF production is approximately 500 ml over 24 hours in humans and the CSF major pathway is some 130-140 ml, there may be physiologic turnover of the CSF three or four times every day.

Based on these traditional concept of CSF dynamics, the hydrocephalus has been defined as a state of "disturbed CSF circulation and classified classically into two types, communicating and non-communicating (Dandy, 1919) [2)]. In the definition of Dandy's Communicating/ non-communicating hydrocephalus the communication of the CSF pathway is between the lateral ventricle and the lumbar subarachnoid space (confirmed by injection of dye into the lateral ventricle and detection by lumbar puncture). However, the terminology of obstructive and non-obstructive hydrocephalus (Russel, 1949) [38)], is defined as a condition of disturbed CSF circulation due to a blockage at any region in the major CSF pathway including the ventricular system and cistern/ subarachnoid apace, so that the causes for non-obstructive hydrocephalus are limited to either CSF overproduction by choroid plexus papilloma or CSF malabsorption due to sinus thrombosis or fetal/ neonatal hydrocephalus during the period of immature development of Pacchionian bodies, etc. These two classifications are based on a concept to classify the type of hydrocephalus considering the disturbed CSF dynamics only in the major CSF pathway : "Major Pathway Hydrocephalus" [28)].

Since the CSF dynamics during the fetal and neonatal/early infantile periods is mainly maintained in the "minor CSF pathway", hydrocephalus occurring during these periods shall be defined as disturbed CSF circulation in the "minor CSF pathway" ("Minor CSF Pathway Hydrocephalus") [28)]. So that, the mechanism or pathogenesis of hydrocephalus maybe for different from the "Major CSF Pathway Hydrocephalus". The classical

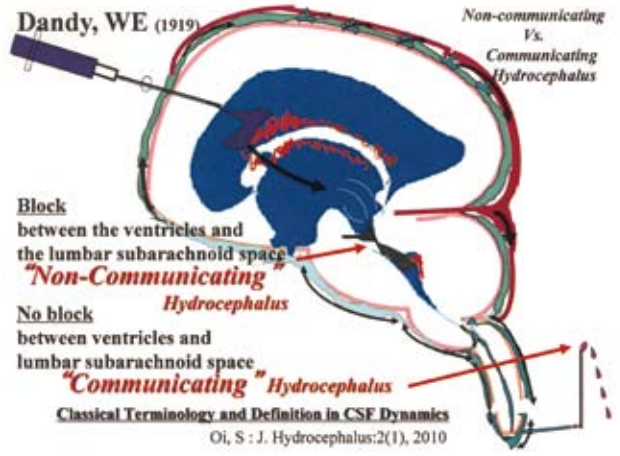

FIG. 10 Illustrative drawing ofc ommunicating and non-communicating hydrocephalus (Dandy, WE 1919) [8)]

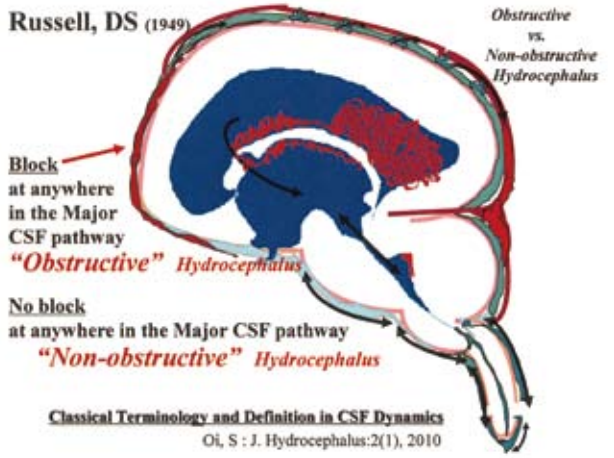

FIG. 11 Illustrative drawing of obstructive and non-obstructive hydrocephalus (Russell, D 1949) [2)]

classification of communicating vs. non-communicating" (Dandy) [2] and "Obstructive vs. non-obstructive" (Russell) [38] are not proper reflecting the disturbed CSF circulation. The causative underlying conditions may include various pathologies, as in our perspective classification of congenital hydrocephalus (PCCH) [23] i.e. primary dysgenetic or secondary such as Intraventricular hemorrhage (IVH) in the fetal brain.

In the CSF circulation, as in the immature form, CSF absorption may possibly be disturbed at the various absorption sites including subpial space -> perivascular space -> subarachnoid space -> neuroepithelium intracellular space, choroid plexus epithelium -> venous fenestrated capillary -> Galenic system, and/or perineural space -> lymphatic channel. Our data in CT ventriculo-cisternography demonstrated remarkable intraparenchymal CSF passage and delayed clearance of the contrast not only in the ventriculo-cisternal space ("major CSF pathway") but moreover from the cerebral parenchyma as in the "minor CSF pathway" [Minor CSF Pathway Hydrocephalus]. There were several cases in which the major CSF pathway was blocked with certain lesion, such as lot from IVH blocking formen of Monro or aqueduct of Sylvius, it was not simply the single causative change of hydrocephalus. The neuroendoscopic ventriculostomy was definitive therapeutic method if the above CSF absorption routs are infact. However, after the successful ventriculostomy the CSF dynamics changed to "communicating hydrocephalus" with stais of contrast in the all communicating ventricles, cisterns and subarachnoid space. Furthermore, major prominent stasis of the contrast in the cerebral parenchyma was observed in some cases [*Minor CSF Pathway Hydrocephalus*][28] as a form of "Post-ventriculostomy communicating hydrocephalus".

The condition of "*Minor CSF pathway hydrocephalus*" [28], however, has a chance to be improved later with development of Pacchionian body in late infancy to increase the CSF absorption function. The high success rate of neuroendoscopic surgery, even spontaneous arrested hydrocephalus and disappearance of external hydrocephalus are all expected after this period, when the "Major CSF pathway" is completed [28].

" Mc HC" Category IV. Symptomatology, VI. Pathopysiology (ICP dynamics), and VII. Chronology

A specific form of hydrocephalus may be considered in combination of multiple subjects in hydrocephalus research (HRF Subject I – X) as described in table 1, i.e. Subject V.Specific Forms of Hydrocephalus 1. Pathogenic Concepts 1). Congenital Hydrocephalus, 2). Acquired Hydrocephalus, 3). Idiopathic, 2. Pathophysiological Concepts 1). Intracranial Pressure (ICP), 2). Cerebrospinal Fluid (CSF), 3). Miscellaneous, 3. Chronological Concepts 1). Phase, 2). Progression, 4. Miscellaneous Concepts. and/or new aspects of the 10 major subjects of hydrocephalus research [HCR subjects I-X]].

However, complex combinations of these concepts or subjects sometimes make a critical confusion. "Normal Pressure Hydrocephalus" is a typical such confusional concept of hydrocephalus. Hakim and Adams [7] in 1965 proposed a clinical entity of normal pressure hydrocephalus (NPH) in which hydrocephalus with "normal cerebrospinal fluid (CSF) pressure" and "prominent mental symptomatology" can be treated with CSF shunt. However, the definition and classification of hydrocephalus in adulthood are now so confused that almost all adult hydrocephalic cases with or without dementia are called "NPH", with or without reliable analysis of the CSF pressure dynamics. These include not only idiopathic communicating hydrocephalus in adults but also secondary hydrocephalus [24] with subarachnoid hemorrhage (SAH), head trauma, meningitis and even brain tumor. Since the technique of continuous intracranial pressure (ICP) monitoring was introduced, it has become clear that the majority of hydrocephalus cases with dementia have intermittent high ICP, or even high baseline pressure in some cases [24]. Since the term "NPH," as first proposed by Hakim and Adams [7], is based on the characteristics of ICP dynamics, there remains the contradiction that only a few patients with such "prominent mental symptomatology" come under this definition [7, 24]. "Normal pressure" is one subtype of hydrocephalus in pathophysiology, and "dementia" is also one subtype in symptomatology in the classification of hydrocephalus. These 2 categories should be separated using proper terminology. In our recent report, we proposed defining cases of such "prominent mental symptomatology" in a single classification category, namely "hydrocephalic dementia: HD"[24]. This is certainly one subtype of hydrocephalus that is defined as a symptomatological entity of progressive hydrocephalus with various ICP dynamics (Table 2). This terminology will solve the confused entity of treatable dementia, which should also be clearly defined as the entity of "hydrocephalic dementia" as a symptomatological concept.

"Mc HC" Category VI. Pathopysiology (ICP dynamics) and VII. Chronology

The ICP dynamics of hydrocephalus change chronologically. The authors reported the chronological changes in hydrocephalic ICP dynamics

and symptomatology in adult patients, namely, "Hydrocephalus Chronology in Adults"(HCA), and the Staging of I-V from the acute to chronic and post-shunt periods [26]. It was demonstrated that the triad of symptoms, dementia, gait disturbance and urinary incontinence, is observed even in cases revealing high ICP dynamics and non-communicating hydrocephalus before the truely-chronic stage, such as HCA Stage III [24]. Hydrocephalus in this stage can be treated with a medium-pressure shunt system. There is some phase discrepancy between the symptomatology of "NPH" (Hakim and Adams) [7] and the chronological change in ICP dynamics in hydrocephalus. In the truely chronic phase of hydrocephalus, it may be normalized in the ICP dynamics. ICP dynamics is associated with biomechanical changes in the hydrocephalic brain in the chronic stage.

The author proposed an unique category of hydrocephalus in adults, namely, a long-term of hydrocephalus, "long-standing overt ventriculomegaly in adult" (LOVA) [27]. Although its mechanism still remains unclear, patients with LOVA often suffer from a progressive course of hydrocephalus that continues into adulthood. We also reported that the hydrocephalic state in LOVA is extremely difficult to treat with a shunt because of lost intracranial compliance. Patients with LOVA in whom significant progressive symptoms of hydrocephalus had developed were first diagnosed as being hydrocephalic during adulthood [27]. In all patients, ventriculomegaly was prominent, involving the lateral and third ventricles as demonstrated on CT and/or MR images. None of the patients had any known underlying disease or symptoms or signs, indicating that the hydrocephalus had first occurred at birth or during infancy in accordance with neuroimaging findings of long-standing hydrocephalus. The specific diagnostic criteria for LOVA includes macrocephaly greater than two standard deviations in head circumference, 57 cm in female and 58 cm in male patients, and/or neuroradiological evidence of a significantly expanded or destroyed sella turcica in addition to the non-communicating overt ventriculomegaly [27].

The LOVA is a chronological concept of hydrocephalus. As described here, LOVA may be summarized as a complex entity with the following compatible subtypes: 1) onset may be congenital in origin but becomes manifest during adulthood; 2) the underlying lesion is aqueductal stenosis; 3) symptoms include macrocephaly, increased ICP symptoms, dementia and subnormal IQ, but occasionally high or even super-high IQ; 4) pathophysiological characteristics include noncommunicating CSF circulation and an ICP dynamics that mainly consists of high ICP; 5) the chronology is long term and progressive; and 6) the hydrocephalus becomes arrested again after shunt placement or neuroendoscopic ventriculostomy [27].

" Mc HC" Category VIII. Post-shunt, and IX. Post-neuroendoscopic Ventriculostomy (NEV) .

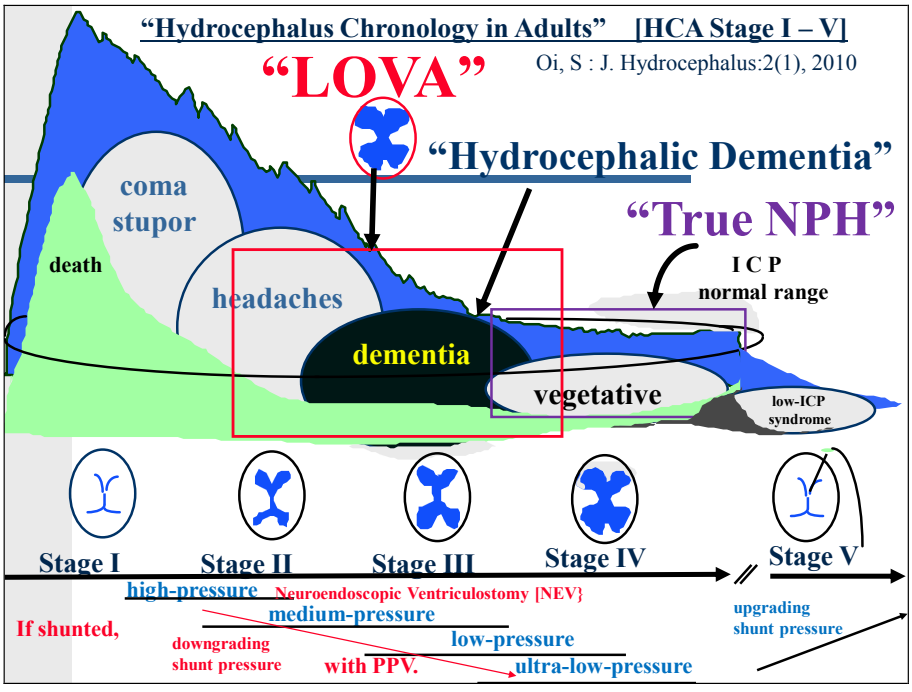

FIG. 12 "Hydrocephalus Chronology in Adults"(HCA), and the Stage I-V [HCA Stage I – V]

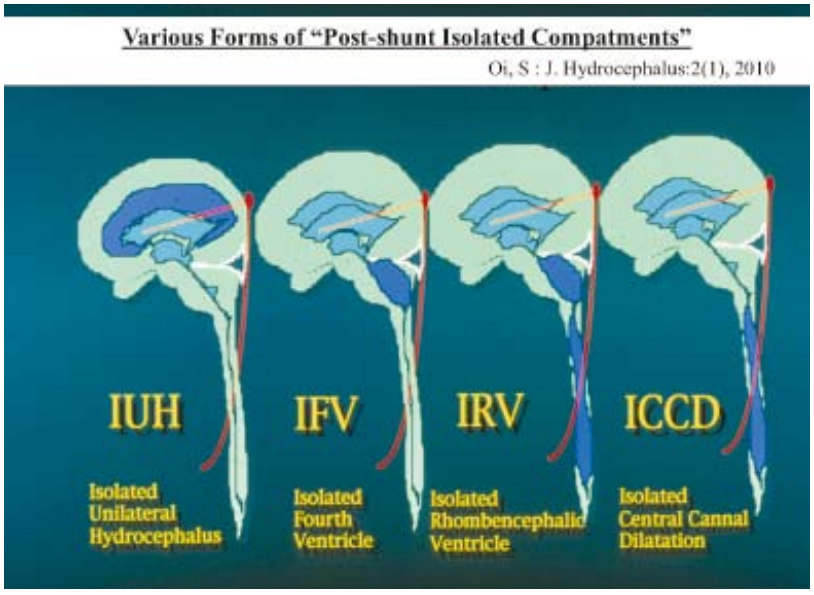

FIG. 13 Various forms of post-shunt isolated compartments (Types I – IV) depending upon the site of occlusion. (Oi, S et al) [17].

The shunt valve, designed basically with differential pressure as "low -medium - high" limits the range of the flow rate along with ICP. Approximately 50 ml/h of CSF shunt flow rate will be obtained when the ICP is around 90 mmH_2O with use of a low-pressure, 150 mmH_2O with a medium-pressure, and 220 mmH_2O with a high-pressure shunt system (personal data with OM-MAC Shunt System by Oi S et al, Kaneka Medics, Tokyo. Japan). The shunt system should be selected not routinely with one single pressure system, but depending upon the ICP dynamics in the individual case when we treat "progressive hydrocephalus". In the stage of relatively high ICP level, the shunt to be selected may be a medium-pressure system. In such ICP dynamics, usually in a relatively acute or subacute period in secondary hydrocephalus, the brain parenchymal compliance is well preserved. Small amounts of CSF withdrawal by the shunt may normalize the high amplitude of pressure waves (HCA stage III). In contrast, a low- or extremely low-pressure system may be necessary in the stage of relatively low ICP level. The compliance is lost and usually pulse pressure is small in range, with relatively low baseline pressure. However, it may still be reversible in the neuronal function, which is affected by such small but significant pressure waves (late HCA stage III and HCA stage IV). In these stages, a shunt system should delete the pressure waves ranging in a mildly abnormally high or even within a normal but relatively high ICP level in these cases. The medium-pressure shunt is not indicated in this stage of ICP dynamics.

The neuroendoscopic ventriculostomy is indicated for treatment of hydrocephalus, essentially in cases of "non-communicating hydrocephalus" (by Dandy's definition, 1919) [2], hydrocephalus due to blockage located in the CSF pathway between the (lateral) ventricles and lumbar subarachnoid space, as marked tri-ventriculomegaly except fourth ventricle in cases of aqueductal stenosis. The success rate for "post-ventriculostomy arrested hydrocephalus" by neuroendoscopic procedure is extremely high as upto nearly 100% in adulthood (LOVA) or elder childhood [27]. However, the success rates reported in treatment of hydrocephalus by neuroendoscopic procedure are much less in the immature brain ranging 0-64% under one year, and 53% under 2 years [25].

Base on these facts in the literature and our experience, the authors have started prospective analyses of CSF dynamics in hydrocephalus involving the immature brain in a use of cine-mode magnetic resonance (MR) imaging for CSF movements and computed tomography (CT) ventriculo-cisternography with water-soluble contrast for CSF flow. In the basic study before designing the prospective study, the early experience of the CSF dynamics has already demonstrated the specific pattern in these age groups of immature period, and the authors have tentatively proposed a hypothesis of "Evolution Theory in CSF Dynamics" [28] elsewhere.

We have previously reported that excess drainage of CSF via a ventricular shunt system will cause morphological changes in the CSF pathways and possibly lead to isolation of compartments [10), 11), 12), 13), 14), 16), 17)]. These phenomena produce a slit-like ventricle most commonly seen in young infants [11), 12), 14), 15), 17)] and occasionally

lead to the slitventricle syndrbme [15]. The mechanism of development of an isolated ventricle after shunting is closely related to the presence of a slit-like ventricle [14]. The mechanism of obstruction at the foramen of Monro in isolated unilateral hydrocephalus [64] and that of aqueductal obstruction in isolated fourth ventricles [11), 12)] occurring after shunt placement are essentially the same. Both occur in a previously communicating ventricular system, and in both cases reduction of the size of all ventricles is initially seen after shunting [8]. Isolation then gradually develops and relargement of the isolated compartment is observed. Dynamic studies of the CSF using metrizamide CT ventriculography have confirmed the presence of a one-way valve at either the foramen of Monro or the aqueduct [21), 29), 30)], and pressure gradients between the compartments have also been recorded. We suggest that similar isolation may occur after placement of a shunt in the lateral ventricle in cases of communicating holoneural canal dilatation. Various types of isolation (Types I to IV) may then develop, depending upon the site of occlusion (Fig. 2 and 8). Also, extracranial overdrainage of CSF via the shunt changes the intracranial pressure dynamics and produces a unique CSF circulatory disturbance.

We have reported that the excess drainage of CSF via a ventricular shunt system can cause morphological changes in the CSF pathways [11), 14), 15)] and possibly lead to the isolation of compartments. The obstruction at the foramen of Monro in isolated unilateral hydrocephalus [IUH] [17)] and aqueductal obstruction in isolated IV ventricle [IFV] after shunt placement occur in a previously communicating ventricular system, and in both cases a reduction in the size of all ventricles is initially seen after shunting [11)]. Isolation then gradually develops, and re-enlargement of the isolated compartment is observed. We suggested that similar isolation might occur after the placement of a shunt in the lateral ventricle in cases of communicating holoneural canal dilatation. [HNCD]. Various types of isolation may then develop, depending upon the site of occlusion [17)].

Neuroendscopic surgery was used to treat patients with various forms of isolated compartments with specific pathophysiology, including isolated unilateral hydrocephalus (IUH) (Fig. 3), isolated IV ventricle (IFV) (Fig. 4), disproportionately large IV ventricle (DLFV), isolated rhombencephalic ventricle (IRV) (Fig. 5), isolated quarto-ventriculomegaly (IQV), dorsal sac in holoprosencephaly (DS), and loculated ventricle (LV) [17)].

VI. Conclusions

A new classification of hydrocephalus, "Multi-categorical Hydrocephalus Classification": [Mc HC] was designed and developed to cover the entire aspects of hydrocephalus with current considerable classification categories and subtypes.

There were 54 subtypes of hydrocephalus listed up, and these were divided into the 10 "Mc HC" Categories, 2-7 in each respectively. In the result, in order to cover all these combinations, there could be theoretically 72,576,000 patterns of hydrocephalus classified. The current status of classification of hydrocephalus in the individual subgroup was reviewed and discussed focusing on variety of characteristics in hydrocephalus, recently with more and more new aspects disclosed not only in fetal and pediatric but also in adult hydrocephalus.

It was concluded that "Mc HC" is extremely effective to express the individual state in the past and present condition of hydrocephalus along with the possible chronological change in future.

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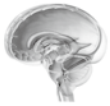

Hydrocephalus Research: Current Topics of the Year 2010
"Definition and Classification of Hydrocephalus"

Review Comment

Consideration of Modern Hydrocephalus Classification

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Summary

Hydrocephalus includes a variety of clinicopathological conditions of disturbed cerebrospinal circulation, and its classification is often complex and confused. Recent progress in neuro-imaging such as MRI and CT enables to understand clinicopathological conditions of hydrocephalus properly. Most widely accepted classification of hydrocephalus nowadays may be Dandy's classification of communicating/non-communicating hydrocephalus developed about 90 years before, and it seems to be important to develop new classifications of hydrocephalus from its underlining clinicopathological conditions that have been revealed along with the development of modern neurosurgery. Nowadays, there are a number of classification categories, parameters, and criteria proposed. Here, I have reviewed representative classifications of hydrocephalus proposed until now and discussed their validity.

Key Words: hydrocephalus, classification

Hydrocephalus is a clinicopathological condition of disturbed cerebrospinal fluid (CSF) circulation, but is not a single pathological disease, and its classification is often complex and confused. A variety of underlying etiologies result in hydrocephalus, and its classification and terminology are still controversial. There are numerous classification categories, parameters, and criteria. Most comprehensive and detailed classification of hydrocephalus may be the one by Oi in1998 that recognized the diversity in the category and the individual subtype. In the classification, Oi classified hydrocephalus from its many aspects such as their onsets, causes, underlying lesions, symptomatology, pathophysiology, and post-shunt reactivities. Since hydrocephalus comprised diverse clinicophysiological conditions that disturb CSF circulation, a detailed classification such as the one by Oi may be ideal.

Classifications of hydrocephalus themselves can be divided into three subgroups; (A) classifications in that any types of hydrocephalus can be included in anywhere in the classification, (B) classifications that focus on specific developmental stages (ex. neonates, infants, or adults), and (C) classifications that describes some specific forms of hydrocephalus.

A. Classifications in that any types of hydrocephalus can be included in anywhere in the classification.

1) Communicating/non-communicating hydrocephalus[1]

This is the most classical as well as widely accepted classification of hydrocephalus proposed by Dandy almost 90 years ago. Since neuro-imaging was not developed enough at that time, this classification was based on the behavior of dye injected in the lateral ventricle. In the definition of Dandy's communicating/non-communicating hydrocephalus, communicating hydrocephalus is the form of hydrocephalus in which the injected dye could be detected from the spinal subarachnoid space, and in non-communicating hydrocephalus dye did not reach the spinal subarachnoid space. Later in 1960 Ransohoff et al renamed non-communicating hydrocephalus as intraventricular hydrocephalus[2]. He focused on the point of obstruction.

2) Obstructive/non-obstructive hydrocephalus [3]

This classification was developed by Russell. The obstruction in the definition of obstructive hydrocephalus is at any region in the major CSF pathway including the ventricular system and entire cistern/subarachnoid space, so that the cause or condition for non-obstructive hydrocephalus is limited to either CSF overproduction by choroid plexus papilloma or CSF malabsorption due to sinus thrombosis.

3) Intraparenchymal/extraparenchymal type [4]

Raimondi suggested that hydrocephalus is a pathologic increase in intracranial CSF (he called it "brain fluid") volume, whether intra- or extraparenchymal, independent of hydrostatic or barometric pressure. He classified hydrocephalus into intraparenchymal (cerebral edema) and extraparenchymal, with the extraparenchymal types subclassified into subarachnoid, cisternal, and intraventricular forms. Mori supported this Raimondi' s suggestion, and reported that "one of the best classifications of hydrocephalus is the pathophysiological classification which devides hydrocephalus into intraparenchymal, extraparenchymal, or a combination of both"[5]. In the report, Mori also proposed a new classification of "intractable hydrocephalus" with diagnostic criteria.

4) Classification based on point of obstruction and developed on a mathematical model [6]

Rekate proposed to define hydrocephalus as "an active distension of the ventricular system of the brain related to inadequate passage of CSF from its point of production within the ventricular system to its point of absorption into the systemic circulation". With the definition, he classified hydrocephalus into 7 subgroups according to the site of obstruction.

B. classifications that focus on specific developmental stages (ex. neonates, infants, or adults)

5) Evolution theory in cerebrospinal fluid dynamics[7]

In 2006, Oi proposed "evolution theory in cerebrospinal fluid dynamics". In the theory, special attention was paid for the CSF circulation in the minor CSF pathway, i.e. "minor pathway hydrocephalus". Oi paid attention to the significantly high failure rate of neuroendoscopic ventriculostomy in treating hydrocephalus in neonates and infants with non-communicationg hydrocephalus as his initial impression. The pattern of ventriculo-cisternography in neonatal/infantile cases revealed intraparenchymal predominant pattern (minor pathway) of the CSF dynamics rather than passage in the major pathway, and the high incidence of "failure to arrest hydrocephalus" by neuroendoscopic ventriculostomy in fetal, neonatal and infantile periods was considered to depend on the specific CSF dynamics, in which the major CSF pathway has not developed and the minor pathway has a significant role. From these findings and speculations, Oi proposed a hypothesis that the CSF dynamics develop in the theory of evolution from the immature brain, as in the animals with the minor CSF pathway predominance, towards matured adult human brain together with completion of the major CSF pathway.

6) Hydrocephalus chronology in adult (HCA)[7]

Oi proposed hydrocephalus chronology in adult (HCA) in 1998 since it has become clear that pathophysiology of hydrocephalus do not remain constant but change at the time of passing[7]. In adult patients with secondary hydrocephalus in acute brain diseases, intracranial pressure (ICP) changes dramatically in combination with brain compliance. And Oi classified this chronology into five periods (Stage I to Stage V).

7) Perspective Classification of Congenital Hydrocephalus (PCCH) [8]

From the standpoint that postnatal prognosis of individual types of hydrocephalus may not be estimated solely on the basis of morphological analysis of prenatal diagnostic images; the prognosis may also depend on the progression of the hydrocephalus and the affected brain and on the degree of damage to the neuronal maturation process, Oi have developed a new classification system for congenital hydrocephalus, "Perspective Classification of Congenital Hydrocephalus" (PCCH), to determine the

factors that contribute to the postnatal prognosis of fetal hydrocephalus. This classification is based on the stage, type, and clinical category of congenital hydrocephalus. Regarding the clinicoembryological stages, each stage reflects both clinical and embryological developmental aspects of the neuronal maturation process in the hydrocephalic fetus or infant.

8) The occurrence of obstructive vs absorptive hydrocephalus: classification by Beni-Adani et al. [9]

Beni-Adani et al focused on "obstructive-communicating " hydrocephalus in pediatric subgroup. They suggested that obstructive hydrocephalus in the very young population may be rather a combination of obstuructive and absorptive problem. The authors categorized infants with active hydrocephalus into four groups along the spectrum of communicating vs obstructive hydrocephalus in an attempt to propose the relevance to treatment option.

C. Classifications that describes some specific forms of hydrocephalus.

9) Normal pressure hydrocephalus (NPH) [10]

The term "normal pressure hydrocephalus (NPH)" was firstly proposed by Hakim and Adams in 1964 and 1965[10, 11]. They defined this type of hydrocephalus as a syndrome with specific clinical features as treatable dementia. But he named the clinical entity as NPH from its pathophysiological aspects. This discrepancy of clinical and pathophysiological aspects cause the confusion in the classification of hydrocephalus in the adult at the present time, over 40 years after his initial proposal. Since a variety of ICP dynamics has become recognized in NPH patients in accordance with advances in continuous ICP monitoring and the technique of dynamic analyses, a new term, "hydrocephalic dementia" was proposed by Oi in 1998 in avoidance for misleading its pathophysiological aspect[12].

10) Longstanding overt ventriculomegaly in adult (LOVA) [13]

Longstanding overt ventriculomegaly in adult (LOVA) is specific form of non-communicating hydrocephalus that often causes hydrocephalic dementia. It is a unique category of hydrocephalus firstly presented by Oi in the middle of 1990's[13-16]. Before this new category developed, patients with LOVA might have considered as a part of normal pressure hydrocephalus (NPH), and were treated by shunts, but treatment of patients with LOVA is extremely difficult in terms of their sensitive compliance of brain parenchyma. LOVA patients definitely develop bilateral subdural hematoma when treated by differential pressure valve (DPV) shunts.

11) Hydrocephalus-parkinsonism complex[17]

Several reports [18-20] have noted that parkinsonism appeared as the initial sign of shunt malfunction. In combination with their own experience of cases in those parkinsonism appeared as the initial symptoms and signs of progressive hydrocephalus, Oi et al have speculated that mild to moderate ventriculomegaly involving the third ventricle in progressive hydrocephalus can affect factors involved in parkinsonism, and proposed the term "hydrocephalus-parkinsonism complex" to delineate this clinical entity.

12) Hydromyelic hydrocephalus[21]

In 1991, Oi investigated the role of hydrocephalus and postshunting alterations of CSF dynamics in the pathophysiology of hydromyelia. Staging of the hydrocephalic state and classification of the postshunting isolated compartment in communicating holoneural canal were developed.

In the present report, I have reviewed modern classifications of hydrocephalus. To classify hydrocephalus seems to be indispensable since it should be treated according to its underlining pathophysiology. Of mention, it seems to be important to recognize chronological change of hydrocephalus accurately especially in pediatric subgroups, since special attention should be paid for the CSF circulation in the minor CSF pathway. I think a classification of hydrocephalus should not be too simple because hydrocephalus implies a variety of clinicopathological conditions.

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HYDROCEPHALUS

On-line Journal Consensus Conference

[HCOL: JCC]

HCOL: JCC No.001

Prenatal Diagnosis of Fetal Hydrocephalus

Part 1: Holoprosencephaly

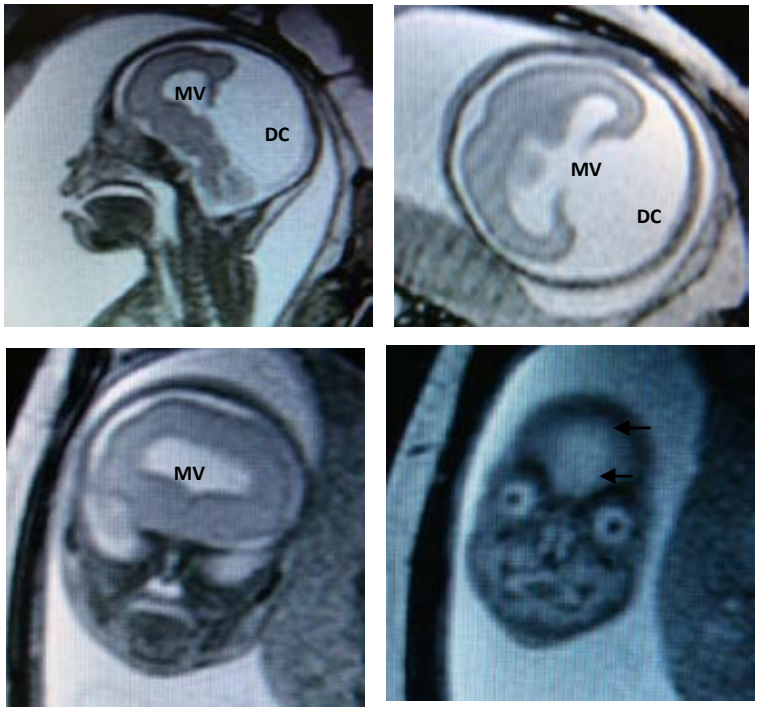
HCOL: JCC No.001
Prenatal Diagnosis of Fetal Hydrocephalus
Part 1: Holoprosencephaly

Case No.1 Case Illustration: Alobar versus Semilobar type of Holoprosencephaly in Prenatal Differential Diagnosis

History:

A 36-year-old healthy woman in 28 weeks gestation, gravida 3, para 2. She was attended to our outpatient clinic because ultrasonography at 23 weeks gestation revealed a monoventricle. The baby has had a normal growth. At 26 weeks of gestation fetal MRI revealed holoprosencephaly either alobar or semilobar type, and ultrasound monoventricle findings were confirmed also with this imaging study. The parents do not have history of familiar or personal genetic disorders neither underlying diseases. The other two children are normal and healthy. The mother has not been exposed to any known teratology agent during her pregnancy. Actually the pregnancy develops normal.

Neuroimaging: Fetal MRI



MV: monoventricle and DC: dorsal sac (cyst) in our opinion

QUESTION

What is your diagnosis, alobar vs. semilobar type of holoprosencephaly?

"My Opinion"

[ ]Fax: 0081-3-3235-9377 [ ]e-mail: shizambroi@aol.com

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on HCOLJCC No._____

[ ] I agree! [ ] I disagree!

What is your diagnosis on the fetal MR images?

[ ] Alobar Holoprosencephaly [ ] Semilobar Holoprosencephaly [ ] Other

Comment

Name: _____,M.D.

Institute: _____ City: _____, Country_____

[ ] I permit the above opinion and comment to be published with my name and institute/country in "Journal of Hydrocephalus"

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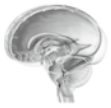
Journal of Hydrocephalus



HYDROCEPHALUS

On-line Journal Consensus Conference [HCOL:JCC No.001]

Case Report

Alobar versus Semi-lobar Types of Holoprosencephaly in Prenatal Differential Diagnosis

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Summary

Holoprosencephaly, which occurs through abnormal separation of prosencephalon, is the most common developmental defect of the forebrain. In this report we describe a case of holoprosencephaly in a fetus at 28 weeks gestation in a healthy mother and discuss the prenatal differential diagnosis of holoprosencephaly, considering its wide spectrum of presentation. The magnetic resonance (MR) imaging findings were not entirely compatible with either alobar or semilobar holoprosencephaly but were intermediate between the 2 types. The discordance between the severity of brain and facial abnormalities was evident on MR imaging. Because the prognosis is different for each type of holoprosencephaly, prenatal diagnosis is extremely important for a comprehensive approach to this disease from an early stage.

Key Words: Holoprosencephaly, Alobar, Semilobar, Prenatal diagnosis

I. INTRODUCTION

Holoprosencephaly (HPE) is a severe brain malformation, caused by abnormal cleavage of the prosencephalon in the fifth week of embryologic development. HPE represents a failure of the forebrain into to 2 hemispheres. The presentation rate is in 1 of 250 miscarriages and in 1 of 10,000-16,000 live births[10, 11]. These figures place it as the most common human malformation of the forebrain and associated to face defects. According to the severity, the brain defect is often associated with characteristic dysmorphic facies which are formed secondarily to the brain malformations[4, 5, 19, 24].

Moreover, the fusion of the cerebral hemisphere is

associated with a lot of midline anomalies, such as absence of a septum pellucidum and corpum callosum; even the less severe of forms of HPE show fusion of the thalamus, cingulum and caudate nuclei. The hypothalamus and pituitary may be also affected. Midline facial anomalies ranging from synophthalmia, cyclopia and proboscis to mild hypotelorism, can be present. Ethmocephaly, cebocephaly and cleft lip are also a possible finding[5, 23, 24].

The neurodevelopmental defects in HPE are variable; therefore HPE has been classified into 3 main types on the basis of severity: alobar, semilobar and lobar. Alobar is the most severe, the almost complete lack of separation or fusion of the cerebral hemispheres; it is accompanied by a monoventricle, the single ventricle is described in MR imaging like a horse-shape appearence[7], which often communicates with a dorsal cyst; and facial complex deformities, such as cyclopia, are common. Semi-lobar HPE type, often shows a lack of separation of the hemispheres anteriorly, but may show separation posteriorly; moreover, the ventricle formation is affected because there are no frontal horns formation, whereas the occipital horns are partially formed and the third ventricle is very small; midline structures such as the corpus callosum and septum pellucidum are partly formed or disappear when the interhemispheric fisure is absent, the thalami may be partially or completely fused; and facial deformities rang from none to minimal[7, 10, 21]. In the lobar form only minor changes may be seen, for example, the anterior falx cerebri and septum pellucidum are usually complete; the ventricle system do not suffer many anomalies just the frontal lobes and horns are hypoplastic; and facial malformations are rare or absent[6, 7, 10, 20, 24].

The etiology of HPE is heterogeneous and complex, including genetic and environmental causes and their interactions. Between environmental causes, the HPE has been associated with maternal exposure to retinoic acid and toxins, poorly controlled maternal diabetes and infectious diseases (rubella, cytomegalovirus infection) [17]. Among the genetic causes associated are chromosomal abnormalities (trisomies 13 and 18), triploidy, deletions, duplications, rearrangements of at least 12 gene loci and mendelian inheritance [4, 11, 17, 24].

The prognosis of alobar HPE is poor, only 50% of patients with alobar HPE will survive to 4 or 5 months of age, and only 20 to 30% will survive by 12 months of age[2]. On the other hand, 50% of the patients with semilobar or lobar types of HPE survive beyond 12 months[9]. The early diagnosis of fetal malformations, especially those of the central nervous system is very important, both because of the poor outcome and because of the emotional distress caused by the accompanying brain and facial malformation[11].

II. Case Illustration

A healthy 36-year-old woman (gravida 3, para 2) visited our outpatient clinic at 28 weeks gestation, because ultrasonography at 23 weeks gestation had revealed a monoventricle. The fetus had shown normal growth. At 26 weeks gestation MR imaging of the fetus revealed HPE of either the alobar or the semi-lobar type, and confirmed the as well ultrasound findings of a monoventricle. The parents had no history of familial or personal genetic disorders or underlying diseases. Their other 2 children were healthy. The mother had not been exposed to any known teratogen during her pregnancy.

MR imaging showed that the spine and cranium were well conformed. A single posterior ventricle was identified. The interhemispheric separation was not evident; moreover the thalami were fused, and the septum pellucidum and corpus callosum were absent (Fig. 1). On coronal MR imaging, craniofacial malformations were not apparent (Fig. 2-B). The MR imaging findings were not entirely consistent with either alobar or semilobar HPE, but were intermediate between the 2 types. In particular, discordance between the severity of brain and facial abnormalities was evident.

III. Discussion

The spectrum of facial and brain anomalies associated with HPE can be recognized in utero by means of neuroradiologic imaging, reason why they become in our primary tools for early diagnosis, besides they are non invasive techniques. A special attention should be paid to the facial morphology in aspects so simple like the interorbital distances; and also to the anatomical variations of brain, like the ventricular configuration, it is important to notice the presence or absence of the interhemispheric fissure[10]. Even though the ultrasonography gives the initial diagnostic impression, MR imaging is the most useful method for examining patients with HPE because of its superior definition of the corpus callosum, septum pellucidum, thalami and ventricle system[7, 9, 15]. Thus MR imaging allows the clear identification of the anatomical features of brain abnormalities and the differential diagnosis of HPE (Table 1).

The abnormalities of brain in the present case are more consistent with the alobar type. But the facial findings suggest a less severe abnormality of the brain, as in the

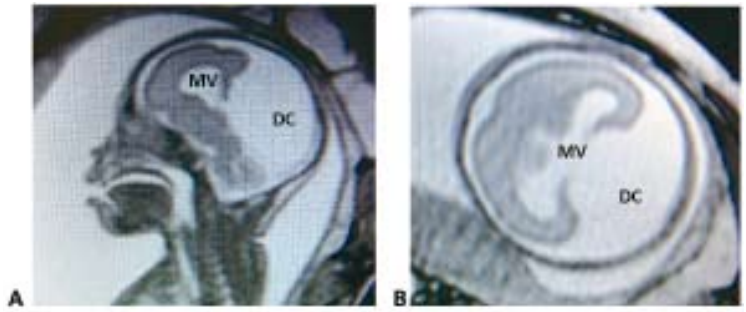

FIG. 1 Holoprosencephaly. A, Monoventricle (MV) and dorsal cyst (DC) are distingued in sagital MR imaging, with no corpus callosum. B, Single posterior monoventricle and talamus fused. A dorsal cyst can be recognized.

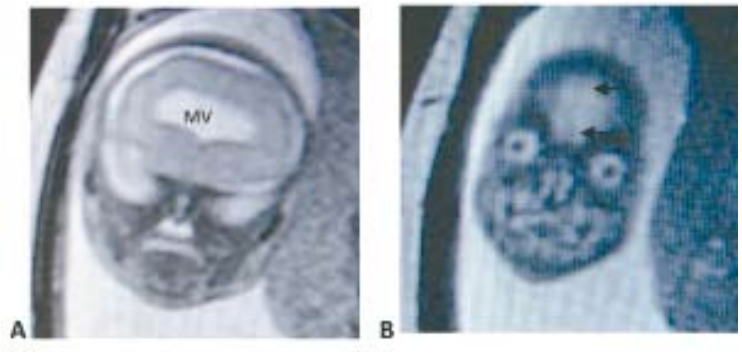

FIG. 2 A, Monoventricle (MV) in coronal MRI. B, On coronal MR imaging no craniofacial malformations are evident. Not even hypotelorism can be identified. An outline of the ventricular division can be observed in midline (arrow).

TABLE 1 Shows the MR imaging features of semi-lobar and alobar HPE and the findings of the present case. (Addapted from Grossman RI et al., 2005)

Feature	Semilobar	Alobar	Case
Facial deformities	None Minimal	Moderate Severe	None
Falx cerebri posteriorly	Absent	Present	Absent
Thalami	Partially fused	Fused	Fused
Interhemispheric fissure	Present posteriorly	Absent	Absent
Dorsal cyst	Absent	Present	Present
Frontal horns	Absent	Absent	Absent
Septum pellucidum	Absent	Absent	Absent
Splenium	Posterior may be present without genu or body	Absent	Absent
Third ventricle	Small	Absent	Absent
Occipital horns	Partially formed	Absent	Absent

semi-lobar type. The altered forebrain appears to be related directly to the mesoderm precordal mesenchymal tissue; this tissue is normally the responsible for the division of forebrain and the development of the mid-face.[12]. Patterson[17] (2002) in the paper "The face predicts the brain; the image predicts its function" also notes the close relationship to the development of both the brain and face, and suggest that the spectrum of facial dysmorphism broadly reflects the severity of the brain malformation. The phenotype is directly proportional to the separation and integrity of the brain, most of the time[17]. Multiple author Barkovich[1] (2000), Blaas[3] et al. (2002), Patterson[17] (2002), have proposed that only the less-severe forms of HPE do not have major facial anomalies, supporting the idea that "the face predicts the brain". Furthermore, Van Gool S et al. (1990)[22] have described a patient who have alobar HPE, diabetes insipidus and coloboma, but had no craniofacial abnormalities; results of an examination at birth were unremarkable, an alobar HPE was not diagnosed until the age of 2 months, when the infant was hospitalized with endocrine problems related to hypophyseal dysfunction, which is common in HPE[24].

Therefore, the case we described and Van Gool[21] case suggest that a broad range of phenotypes exist in HPE. This phenotypic variability could be associated to the etiological heterogeneity. The joint action of genetics and environmental factors could be responsible for the variables phenotypes found, and the apparent discrepancies between the developing brain and face. However, the mechanism by which environmental and genetic interaction lead to phenotypic variability remains unclear. Therefore, the notion that "the face predicts the brains", does not always hold true, like we were thinking. It is important to identify in prenatal life the variations of spectrum in the types of HPE, for make a more accurate diagnosis.

Clinical manifestations in HPE include mental retardation; developmental delay; hypogonadism; seizure; hypotonia or hypertonia; motor, endrocrine, and autonomic dysfunction, among others problems[9, 10]. Treatment is usually supportive; although the prognosis

of HPE depends on the type of HPE and the extent of facial abnormalities, it is generally extremely poor. We must concentrate our initial efforts on providing a comprehensive and multidisciplinary care of the delivery.

The combination of severe HPE of the alobar type, with an apparently normal facies, which is usually associated with less severe forms of HPE[18], suggest the deployed of a new view of the etiology and variability of the malformation. These findings stressed the importance of the prenatal diagnosis, not only in order to classify the HPE, moreover to give a broad understanding of the variability of the clinical phenotype, complications and survival. A complete analysis of the information is necessary.

IV. Conclusion

We have described a case of severe alobar HPE accompanied by less severe facial anomalies. The main objective of the prenatal diagnosis in case of HPE, is to identify the type and spectrum, so that its particular complications and prognosis can be understood at birth. The best neuroimaging tool for identifying the characteristics of each type is MR imaging, and the information provided facilitates a multidisciplinary approach to treatment. Moreover, prenatal diagnosis allows parent to better understand the nature of their child disease and its poor prognosis, and to prepare psychologically before delivery.

The diagnostic In utero should be extended to all medical practices to provide comprehensive and timely attention, even in cases that seem bleak as this, this provides the certainty of a diagnosis and the knowledge of identify what we are facing. We need to treat patient, not diseases, taking use of the classifications but observing the particularity of each case.

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