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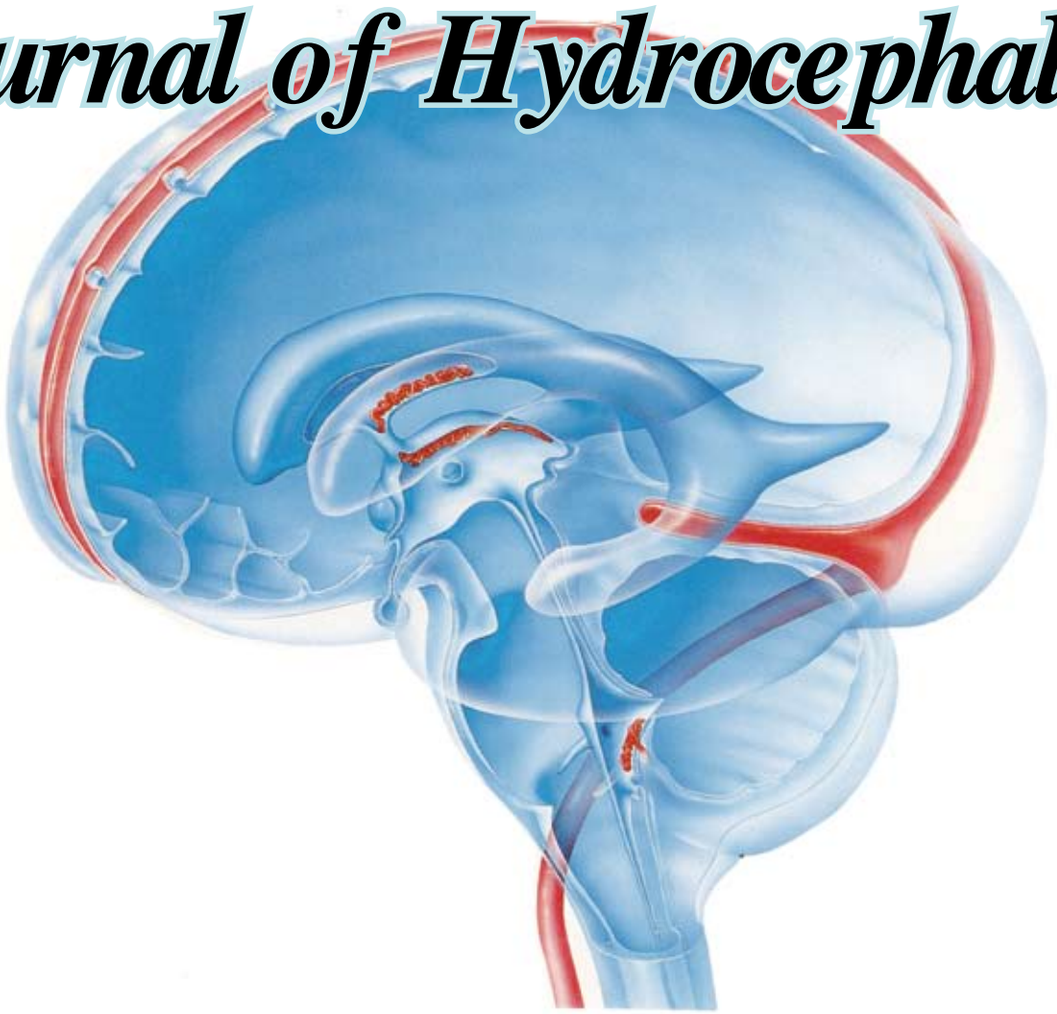

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Evolution Theory in Cerebrospinal Fluid Dynamics: A Hypothesis for Failure of Neuroendoscopic Ventriculostomy in Treatment of Hydrocephalus in Fetal, Neonatal and Early Infantile Periods

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Abstract

[Object] The aim of this study was to discuss the underlying pathophysiology in failure of neuroendoscopic ventriculostomy during treatment of "non-communicating hydrocephalus" with reference to findings from analyses of specific cerebrospinal fluid (CSF) dynamics in the immature brain.

[Materials and Method] Prospective analysis was performed for 12 hydrocephalic neonates and infants suspected as non-communicating hydrocephalus as the initial impressions on magnetic resonance imaging (MRI) to undergo the preoperative CSF dynamic studies using cine-mode MRI and computed tomography (CT) ventriculo-cisternography.

[Results] Of the 12 cases, 9 (75%) in the prospective study of CSF dynamics revealed misdiagnosis compatible with "communicating hydrocephalus". The pattern in the ventriculo-cisternography in all these cases revealed intra-parenchymal predominant CSF flow (minor pathway) in the CSF dynamics, rather than passage in the major pathway. Four patients were selected as displaying definitive indications for neuroendoscopic ventriculostomy. Postoperatively, all 4 patients were improved with stabilized intracranial pressure (ICP), as in the condition of "post-endoscopic ventriculostomy arrested hydrocephalus". However, symptoms of increased ICP recurred in all 4 patients at a mean of 5.5 weeks (range, 4-9 weeks). Ventriculo-peritoneal (V-P) shunt was subsequently performed in all 12 patients except one who underwent craniotomy for cyst removal, with improvements noted in each case.

[Discussion and Conclusion] The high incidence of "failure of neuroendoscopic ventriculostomy" in treatment for hydrocephalus in the neonatal and infantile periods may depend on the specific CSF dynamics, in which the major CSF pathway has not developed and the minor pathway plays a significant role in the individual maturation process. This clinical evidence may be supported by the hypothesis that CSF dynamics develops according to evolutionary theory, from an immature brain as seen in animals with minor CSF pathway predominance,i.e., "Minor Pathway Hydrocephalus" towards a mature adult human brain together with completion of the major CSF pathway, i.e., "Evolution Theory in CSF Dynamics".

Key Words: evolution theory • CSF dynamics • neuroendoscopic ventriculostomy • hydrocephalus • major and minor pathway • age-difference • V-P shunt

I. Introduction

The treatment goal for hydrocephalus is normalization of the disturbed cerebrospinal fluid (CSF) dynamics, resulting in a state of "arrested hydrocephalus" [4), 24), 25)]. The most widely accepted treatment modalities at present involve either CSF diversion (shunt placement) or ventriculostomy (neuroendoscopic procedure). The final individual goal after treatment is defined as "shunt-dependent arrested hydrocephalus" in cases with shunt placement, or "post-ventriculostomy arrested hydrocephalus" after neuroendoscopic procedures.

Neuroendoscopic ventriculostomy is typically indicated for treatment of hydrocephalus in cases of "non-communicating hydrocephalus" (according to Dandy' s definition, 1919) [8)], involving hydrocephalus due to a blockage located in the CSF

pathway between the (lateral) ventricles and the lumbar subarachnoid space [8)], with marked tri-ventriculomegaly except of the fourth ventricle in cases of aqueductal stenosis. The success rate for "post-ventriculostomy arrested hydrocephalus" under neuroendoscopic procedures is extremely high, approaching 100% in adulthood (long-standing overt ventriculomegaly in adult : LOVA, Oi S et al, 2000)[26)] or late childhood [3) 17)]. However, success rates reported in treatment of hydrocephalus by neuroendoscopic procedure are much lower in the immature brain, at 0-64% in patients <1-year-old [6) 13) 17) 18) 20)], and 53% under 2 years [3)].

In our recent clinical experience, no successful cases of "post-ventriculostomy arrested hydrocephalus" have been encountered in patients <1-month-old, including hydrocephalus during fetal life, as in prematurely born neonates. Based on the literature and our own experience, we initiated prospective analyses of CSF dynamics in hydrocephalus of the immature brain using cine-mode magnetic resonance imaging (MRI) to observe CSF movements and computed tomography (CT) ventriculo-cisternography with water-soluble contrast to reveal CSF flow. In a preliminary study before designing the prospective study, early experience with CSF dynamics indicated specific patterns in this age group of immature patients, and we have already tentatively proposed a hypothesis concerning "Evolution Theory in CSF Dynamics" [28)].

The purpose of this study was to analyze specific CSF dynamics in cases of hydrocephalus within 1 year after birth, including the fetal period for premature births, with special reference to possible mechanisms underlying the failure of neuroendoscopic ventriculostomy in immature brain.

II. Material and Method

Analysis of CSF dynamics was scheduled prospectively for hydrocephalic neonates and infants under 1-year-old with hydrocephalus that was suspected as non-communicating hydrocephalus following plain CT and MRI. In order to select the most-indicated surgical modality, i.e., shunt placement vs. neuroendoscopic procedure, informed consent was obtained to analyze the pattern of disturbed CSF dynamics using CT ventriculo-cisternography. The patients selected to undergo this study were all macrocephalic with a head circumference enlarged by more than +2 standard deviations (SDs) and ventricles dilated more than 50% according to Evan's Index (EI). All patients underwent preoperative studies of psychomotor development, with analysis of developmental quotient (DQ) using the new K-edition DQ test [29)], CSF dynamics using cardiac-gated cine-mode MRI and CT ventriculo-cisternography using injection of 2 ml water-soluble contrast media (Omnipaque 240; iodine) via an Ommaya reservoir placed in the frontal horn of the lateral ventricle. CT scanning was repeated 1, 6 and 24 h (and 48 h, if requested) after contrast injection.

III. Results

1) Primary impression of hydrocephalus type on MRI
Between September 2001 and April 2004, a total of 12 hydrocephalic neonate/infants (9 girls, 3 boys) participated in this prospective study for selection of the most-indicated therapeutic modalities at Jikei University Hospital Women's and Children's Medical Center (JWCMC). Mean age at diagnosis was 17.2 weeks (range, 0-50 weeks). Underlying pathology was congenital/simple hydrocephalus (n = 6), intraventricular hemorrhage during fetal life (n = 3), arachnoid cyst (n = 1), encephalocele (n = 1), and myeloschisis (n = 1) (TABLE 1). Type of disturbed CSF circulation was considered "non-communicating hydrocephalus" as the initial impression, with MRI indicating occlusive changes in the major CSF path at the foramen of Monro (n = 1), aqueduct (n = 5), outlet of the fourth ventricle (n = 4) and basal cistern (n = 2) (TABLE 1).

2) Analyses of CSF Dynamics
CSF dynamic studies with CT ventriculo-cisternography demonstrated definitive findings of communicating hydrocephalus in 9 of the 12 cases (75.0%), with free communication between the ventricular system and basal cistern at 6 h after injection of contrast into the lateral ventricle (TABLE 2 Note:75% of cases estimated as

TABLE 1

CSF dynamic study in neonatal/infantile hydrocephalus - 1: Indicated initial operative procedures based on CSF dynamics

Case No.	Age (weeks)/ Sex	Underlying disease	Primary Impression for Occlusive Site	CSF Dynamics	Initial Operative Modality
1	0/F	Myeloschisis	IV Ventricle Outlets	Non-communicating	Shunt
2	0/F	Fetal IVH	Aqueduct	Communicating	Shunt
3	0/M	Fetal IVH	IV Ventricle Outlets	Non-communicating	ETV/EAP
4	0/F	Fetal IVH	Foramen of Monro	Non-communicating	ESS
5	1/F	Congenital	Aqueduct	Communicating	Shunt
6	8/M	Congenital	Aqueduct	Communicating	Shunt
7	20/F	Congenital	IV Ventricle Outlets	Communicating	Shunt
8	24/M	Congenital	Aqueduct	Communicating	Shunt
9	28/F	Congenital	Basal Cistern	Communicating- obstructive	ETV
10	32/F	Congenital	Basal Cistern	Communicating	ETV
11	44/F	Arachnoid Cyst	IV Ventricle Outlets	Communicating	Craniotomy
12	50/F	Encephalocele	Aqueduct	Communicating	Shunt

IVH: intraventricular hemorrhage, ETV: endoscopic third ventriculostomy, EAP: endoscopic aqueductal plasty, ESS: endoscopic septostomy

TABLE 2

Accuracy of indications for endoscopic ventriculostomy from initial impression following MRI.

Primary Impression for Occlusive Site	CSF Dynamics with CT Ventriculo-	
	Communicating	Non-
Aqueduct (5)	5 (100%)	0
IV Ventricle Outlets (4)	2 (50.0%)	2 (correct: 1, incorrect site: 1)
Basal Cistern (2)	2 (100%)	
Foramen of Monro (1)	0	1 (correct:1)
Total (12)	9 (75.0%)	Occulusion Site Correct : 2 (16.7%) Incorrect : 1 (8.3%)

"non-communicating hydrocephalus" were incorrect and CT ventriculo- cisternography confirmed "communicating hydrocephalus"; FIG. 1). Although cine-mode MRI was suggestive for detecting occlusive site, no definitive judgment could be obtained (FIG. 1-B) and final diagnosis was made using CT ventriculo-cisternography in all cases.

In CT ventriculo-cisternography at 24 h, contrast material filled the entire subarachnoid space over the cerebral convexity and Sylvian fissures in all except 2 of the 9 cases, in whom contrast material stayed in the basal cistern, suggesting a blockage or occlusion site around the tentorial notch. The finding allows communication between the ventricles and prepontine/posterior fossa cisterns but obstructing in the subarachnoid space: non-communicating by Dandy [8] but obstructive hydrocephalus by Russell [32]. Regardless of the pattern of disturbed CSF circulation in the major pathway, contrast distributed diffusely throughout the entire ventricular space and cerebral parenchyma (FIG. 1-C). Contrast tended to clear from the ventricle but remained much longer in the cerebral parenchyma (FIG. 2).

3) Operative Indications Based on CSF Dynamics

Based on findings form the analysis of CSF dynamics, indications for neuroendoscopic ventriculostomy were discussed regarding 5 patients (non-communicating, n = 3; communicating-obstructive n = 2). The remaining 7 patients with communicating type hydrocephalus immediately underwent ventriculo-peritoneal (V-P) shunt, except in 1 case with posterior fossa cyst in which craniotomy was performed. Among the 5 patients discussed for treatment modalities, V-P shunt was performed in 1 patient with myeloschisis due to possible technical difficulties in such a small third ventricle with large massa intermedia. The other 4 patients underwent neuroendoscopic procedures, with third ventriculostomy alone (n = 2), and third ventriculostomy with either aqueductal plasty (n = 1) or septostomy (n = 1) (TABLE 1).

4) Post-ventriculostomy CSF Dynamics

At the end of each neuroendoscopic procedure, contrast media was injected into the ventricle and postoperative CT ventriculo-cisternography as well as by cine-mode MRI Post operative. cine-mode MRI suggested all ventriculostomied sites were patent. Postoperative

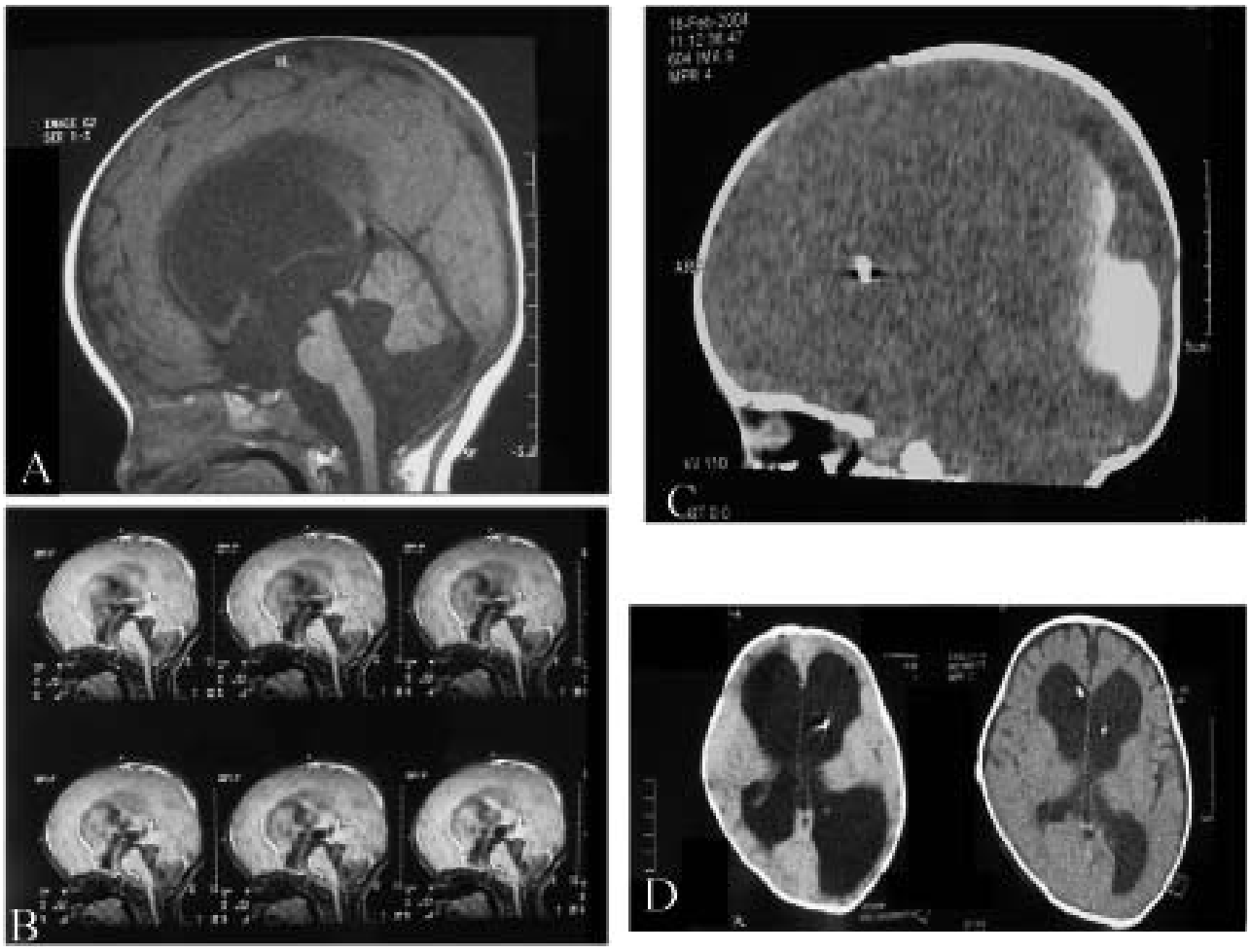

FIG. 1: Case #7. A 5-month-old girl with congenital hydrocephalus. **A:** T1-weighted midline-sagittal MRI revealing disproportionately large fourth ventricle with marked dilatation of all ventricles and aqueduct of Sylvius. The primary impression for the occlusive site was outlets of the fourth ventricle with a suggestive cystic lesion in the posterior fossa. **B:** Cardiac-gated cine-mode MRI midline-sagittal image. Findings were not definitive for communication or obstruction at the outlets of the fourth ventricle. **C:** CT Ventriculo-cisternography at 6 h after injection of water-soluble contrast via Ommaya reservoir. Note complete communication between ventricles and cisterns/subarachnoid space. This case was evaluated as "communicating hydrocephalus". **D:** Pre- (left) and postoperative CT 1 month after ventriculo-peritoneal shunt (right). The brain mantle is in the process of reconstitution by shunt.

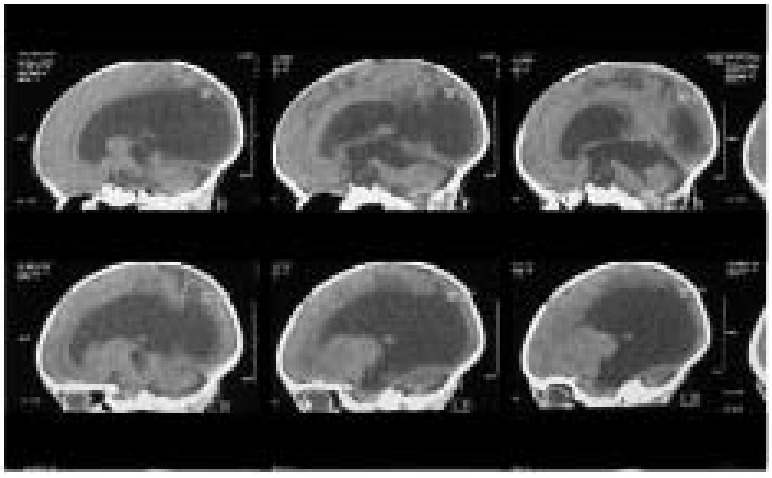

FIG. 2: Case #3. A 4-day-old girl with fetal IVH and Hydrocephalus. **A:** Primary impression for occlusive site was the outlets of the fourth ventricle. CSF dynamics confirmed non-communicating hydrocephalus with aqueductal occlusion.

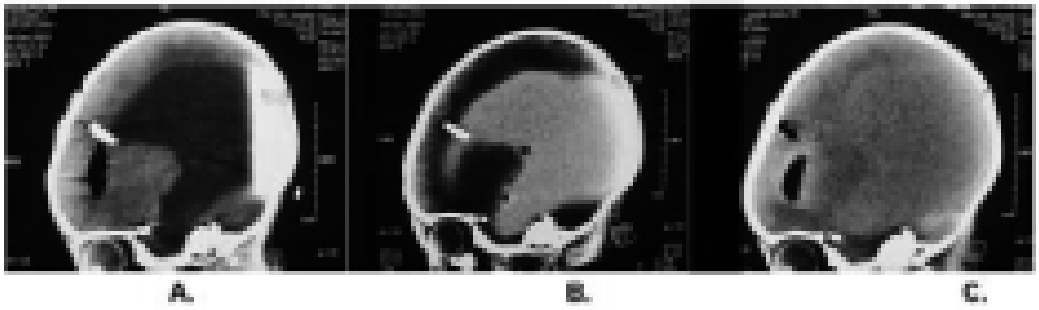

FIG. 2-B: Case #3. Post-endoscopic ventriculostomy CSF dynamic analysis. Contrast
A. Post-ETV contrast injection: CT at 1 h later.
B. Post-ETV contrast injection: CT at 24 h (1 day) later.
C. Post-ETV contrast injection: CT at 72 h (3 days) later.

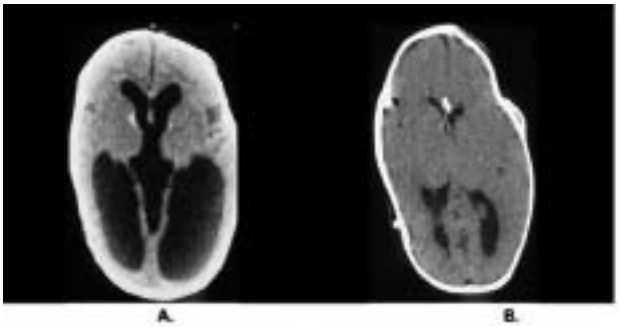

FIG. 2-C: Case #3. Post- shunt reconstitution of the cerebral mantle.
A. CT: Pre-shunt. B. CT: Post-shunt, after 3 months.

TABLE 3
CSF dynamic study in neonatal/infantile hydrocephalus – 2: Post-endoscopic ventriculostomy

Case No.	Age (weeks)/ Sex	Underlying disease	Occlusive Site	Post-Initial Op CSF Dynamics	Final Operative Modality*
3	0/M	Fetal IVH	Aqueduct	Pot-ETV/EAP communicating	Shunt
4	0/F	Fetal IV	Foramen of Monro	Post-Ess communicating	Shunt
9	28/F	Congenital	Basal Cistern	Post-ETD Non-obstructive	Shunt
10	32/F	Congenital	Basal Cistern	Post-ETD Non-obstructive	Shunt

ventriculo-cisternography revealed communicating CSF dynamics throughout the entire major CSF pathway between the ventricular system and convex subarachnoid space and Sylvian fissures. Contrast distribution, however, again revealed significant intraparenchymal stasis, even over 3 days after contrast injection, suggesting a condition of "post-ventriculostomy communicating hydrocephalus" (FIG. 2-B).

Postoperative courses were uneventful in all patients, with no developing morbidity or mortality. Patients who had undergone V-P shunt all displayed clinical improvements, with normalized head circumference within normal limits and significant brain mantle reconstruction on radiology (FIG. 1-D, 2-C). All 4 patients who had undergone neuroendoscopic procedures did well clinically without developing symptoms and signs of increased intracranial pressure, displaying soft and sunken or flat anterior fontanels and unchanged head circumferences. However, at a mean of 5.5 weeks (range, 4-9 weeks) after the operation, clinical symptoms and signs of increased intracranial pressure reappeared, with tense anterior fontanel and increased head circumference (TABLE 3). Postoperative CT and MRI revealed re-expanded ventriculomegaly, progressed beyond preoperative findings from before neuroendoscopic ventriculostomy. All 4 patients consequently underwent V-P shunt. Before placing the ventricular tube, a 1.9-mm diameter fine rigid-rod neuroendoscopy lens (Oi-Samii Handy Pro; Karl Storz, Tuttlingen, Germany) [25] was inserted in the direction of the foramen of Monro and the patency of the third ventriculostomy fenestrated opening was confirmed. Post-shunt course was uneventful with satisfactory outcomes on clinical and radiological follow-up (FIG. 2) to a mean of 18 months (range, 8-36 months).

IV. Discussion

Patterns of Disturbed CSF Dynamics and Indications for Neuroendoscopic Ventriculostomy

The major CSF pathway starts from bilateral lateral ventricles with fluid from the choroid plexus, the major source of CSF, merging with fluid produced in the third and fourth ventricles. CSF then 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 [4, 33]. Absorption occurs primarily at the arachnoid granulation (Pacchionian

body) or villi that soak CSF into the sinus, mainly the superior sagittal sinus [35]. With the bi-directional volume movement of CSF in the major pathway, CSF dynamics created bulk flow [9]. Rate of CSF production is approximately 500 ml over 24 h in humans and the CSF major pathway contains some 130-140 ml, indicating a physiological turnover of CSF 3-4 times daily.

Based on these traditional concept of CSF dynamics, hydrocephalus has been defined as a state of "disturbed CSF circulation and classified classically into two types, communicating and non-communicating" [8]. In the definition used by Dandy of communicating and non-communicating hydrocephalus, communications in the CSF pathway occur between the lateral ventricle and the lumbar subarachnoid space (confirmed by injection of dye into the lateral ventricle and subsequent detection by lumbar puncture). However, obstructive hydrocephalus [32] 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 the causes of non-obstructive hydrocephalus are limited to either CSF overproduction by choroid plexus papilloma or CSF malabsorption due to events such as sinus thrombosis. These two classifications are based on the classification of hydrocephalus from the perspective of disturbed CSF dynamics in the major CSF pathway alone, as "Major Pathway Hydrocephalus" [28].

The most crucial indication for neuroendoscopic ventriculostomy is the specific pattern of the disturbed CSF dynamics causing hydrocephalus in the individual case, if the shortest route is functioning as the alternative "major pathway". On considering definitive indications for neuroendoscopic ventriculostomy, the classification "communicating vs. non-communicating" described by Dandy [8] may still be the most valid of the presently available classifications [24]. Since the basic concept in this classification involves the site of occlusion in the major CSF pathway, particularly the outlet of the fourth ventricle or intraventricular passage, the interact draining route after each individual ventriculostomy procedure is key to normalization of the disturbed CSF dynamics. In a strict sense, there may be one exceptional condition, which cannot be included in this criterion. Even in "communicating-type hydrocephalus", third ventriculostomy may still be indicated, if the blockage is localized and limited to the prepontine/quadrigeminal/ ambient cisterns before the floor of the third ventricle. The classification of "non-obstructive vs. obstructive" hydrocephalus by Russell [32] is not suiTABLE when considering indications for any type of ventriculostomy. Actually, "obstructive hydrocephalus" can occur by occlusion not only within the ventricular system, but also in any spot blocking CSF flow in the subarachnoid space before absorption via arachnoid granulations/villi (Pacchionian body). Third ventriculostomy, for example, may not be effective if covert blockage remains in the subarachnoid space before CSF absorption by the Pacchionian body.

Development of CSF Dynamics and Role of the "Minor Pathway"

CSF circulation starts to develop when the choroid plexus is created in the primitive lumen as the ventricle at embryonic day 41-44 embryonic days in the fourth ventricle, day 44 in the lateral ventricle and day 57 in the third ventricle [7]. The roof of the fourth ventricle (area membranecca inferior; AMI) opens by gestational week 8, immediately after choroidal differentiation in the fourth ventricle is observed [36]. The primitive meninx begins to develop at 8 weeks, with the arachnoid mater being first observed at 12 weeks and separating from the dura mater at gestational week [21] [29].

Regarding the development of CSF absorption sites, the absence of arachnoid granulations (Pacchionian body) in mice, rats, rabbits, cats and Japanese monkeys, even in adult animals, is well known [15]. In large mammals and humans, arachnoid granulations (Pacchionian body) appear microscopically in postnatal life or just before birth as villi [12] [15], and begin to function as the route of CSF reabsorption in later life [23]. Since the arachnoid villi are microscopic structures whereas granulations are prominent gross anatomical findings, the development of arachnoid granulations (Pacchionian body) [34] has been used as a marker of age in radiological identification with findings of parasagittal depression of the caldarium [1]. Radiological evidence of the presence of arachnoid granulations is usually obtained first at around 7-years-old, developing progressively up to about 20-years-old [14]. CSF reabsorption by the arachnoid graduations may begin from the late infantile period [23]. Without the expected functional development of the arachnoid granulations, CSF dynamics may be maintained by the minor pathway with drainage via the perineural space to the lymphatic system [5] [10] [11] [23] [32], via transependymal-interstitial route to the perivascular /subpial space both in the brain and spinal cord [2] [16] [19], and via the epithelium of the choroid plexus to the fenestrated capillaries and finally to the Galenic venous system [15]. These "minor CSF pathways" represent the main route for CSF dynamics in both rodents and other small mammals [30] [31] [33] [35] and the developing immature brain in humans 12,36) (See illustrative diagrams in reference 28) [28]. We summarized the ontogenetic aspects of the development of CSF circulation and proposed the "Evolution Theory

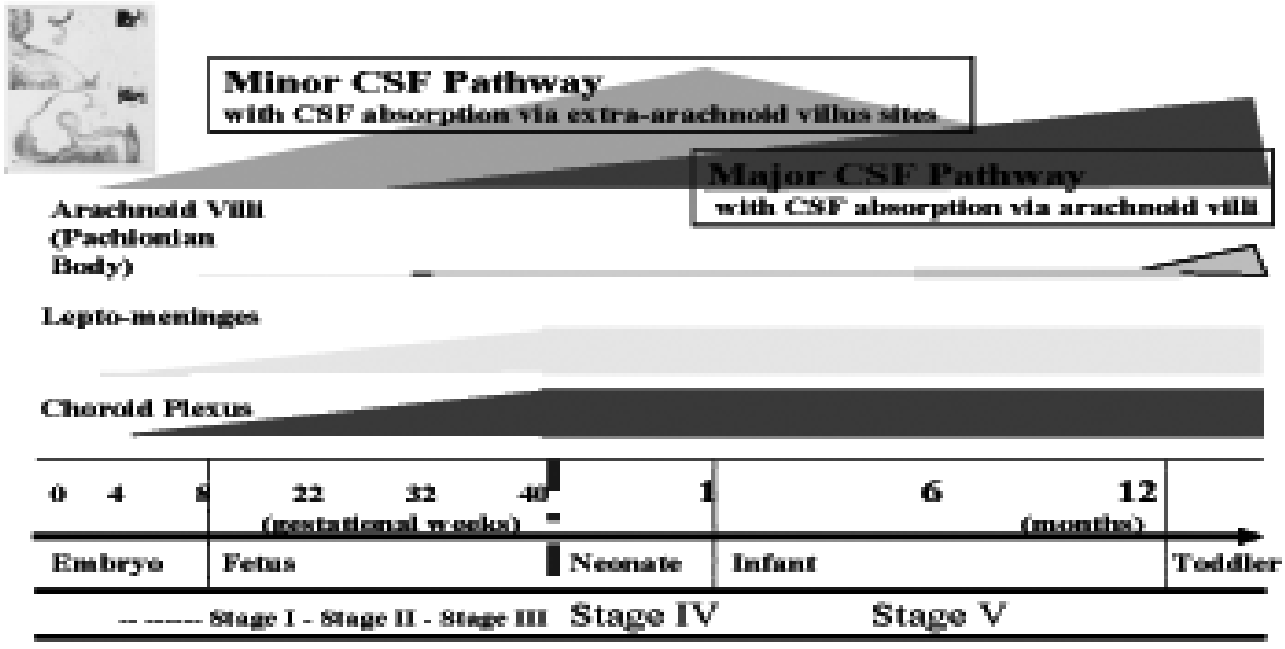

FIG. 3: CSF Dynamics Maturation [CSFDM] Stages I-V (Oi, S et al 2006, with permission) [28]

in CSF Dynamics" [28]. The developmental stage of CSF dynamics is also described in various processes, divided into Stages I-V (CSF Dynamics Maturation [CSFDM]: Stage I (gestational age, ≤22 weeks), primitive formation of the choroid plexus and sub-arachnoid space; Stage II (gestational age, 23-32 weeks), organization of 3 layers of the meninges; Stage III (gestational age, 33-40 weeks), functional maturation of choroid plexus; Stage IV (neonatal period up to 4 weeks after birth), CSF formation approaching adult level.The meridian of "Minor CSF Pathway"; Stage V (infantile period, 5-50 weeks after birth) maturation of Pacchionian body and superior sagittal sinus [Maturation of Major CSF Pathway]CSFDM stages are also compatible with our perspective classification of congenital hydrocephalus [PCCH] stages [27] (FIG. 3). Catala [7] reported that the epithelium of the choroid plexus in the human fetus contains large amounts of glycogen, as seen in the plexus in lower vertebrates (adult fish and amphibians). This high content of glycogen is likewise observed in hibernating mammals, in which choroid plexus cells are again filled with glycogen during hibernation. These data suggest that the glycogen content parallels the metabolic status of the subject and that human fetal life is very similar to a hibernating period.

"*Minor CSF Pathway Hydrocephalus" and Failure of Neuroendoscopic Ventriculostomy*

Since CSF dynamics during fetal and neonatal/early infantile periods are mainly maintained by the "minor CSF pathways", hydrocephalus occurring during these periods should be defined as disturbed CSF circulation in the "minor CSF pathway" ("Minor CSF Pathway Hydrocephalus") [28]. The mechanisms or pathogenesis of hydrocephalus may thus differ from "Major CSF Pathway Hydrocephalus". The classical classification of "communicating vs. non-communicating" [8] or "obstructive vs. non-obstructive" [32] do not properly reflect the disturbance of CSF circulation at this stage in life. Causative underlying conditions may include various pathologies, as in our PCCH [27]; i.e., primary dysgenesis or secondary causes 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 the 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 from CT ventriculo-cisternography demonstrated marked 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). In several cases, the major CSF pathway was blocked by a certain lesion, such as clot from IVH blocking the foramen of Monro or aqueduct of

Sylvius, this did not represent the single cause underlying hydrocephalus. Neuroendoscopic ventriculostomy would represent the definitive therapeutic method if the above CSF absorption routes remained intact. However, after successful ventriculostomy CSF dynamics changed to "communicating hydrocephalus" with contrast stasis in all communicating ventricles, cisterns and the subarachnoid space. Furthermore, the prominent stasis of contrast material in the cerebral parenchyma was observed in some cases [Minor CSF Pathway Hydrocephalus] as a form of "post-ventriculostomy communicating hydrocephalus".

The condition of "minor CSF pathway hydrocephalus", however, can improve later with the development of the Pacchionian body in late infancy increasing CSF absorption. The high success rate of neuroendoscopic surgery, and even spontaneous arrested hydrocephalus and disappearance of external hydrocephalus are all expected after this period (CSFDM Stage V), when the "major CSF pathway" is completed.

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Impact of a portable neuroendoscopic equipment system to provide an outreach service in Sub-Saharan Africa

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Abstract

Hydrocephalus in the pediatric population is an enormous burden in developing countries worldwide. In Kenya, and its surrounding East, Central and Southern Africa region, with a population of 250,000 million, a conservative estimate suggests an annual incidence of nearly 14,000 infants developing hydrocephalus within the first year of life. Hydrocephalus, largely a disease of poverty in this region, becomes even more challenging to treat due to lack of neurosurgical manpower, inadequately equipped public health care facilities, meager resource allocation, high rates of neonatal infection including meningitis, difficulty of access to hospitals able to treat hydrocephalus, and high complication rates in patients who are able to access and receive shunting procedures.

Definitive treatment of Hydrocephalus, yet avoiding shunting procedures and long-term shunt dependence is a safer option. In environments such as Sub-Saharan Africa and, indeed, in other similar resource challenged regions, neuroendoscopic ventriculostomy (NEV), in appropriately selected patients, can overcome the problems associated with shunting, as well as long term shunt dependence.

Lack of neurosurgeons and those trained to perform neuroendoscopy, and non availability of neuroendoscopy equipment is a further challenge in such environments. Where such manpower and equipment is available, the challenge is for the multitude of patients in the rural population to access sites within their easy reach, which can offer NEV

The novel approach promoted by volunteer neurosurgical teams in Kenya is described, and the its potential role in successfully providing NEV at hospitals in regional sites away from main referral tertiary hospitals is outlined. Using a single portable neuroendscopy equipment system, and a versatile free-hand, single operator neuroendoscope, the outreach, and mobile portable model has been successfully utilized to perform 177 procedures including NEV, cyst fenestration, and cerebral abcess cavity washout, in 17 different hospital sites in 5 different countries within the East African region

The merits of performing this current best-practice procedure in a convenient, cost effective and safe way as an outreach, mobile service, for a condition that mainly affects children in rural populations, is highlighted.

Key Words: Hydrocephalus • Neuroendoscopic ventriculostomy (NEV) • Portable outreach neuroendoscopy • East African neurosurgery

I. Introduction

The primary aim of treatment for hydrocephalus is normalization of impaired cerebrospinal fluid (CSF) flow, aimed at achieving a state of "arrested hydrocephalus" [(1, 5)]. The final goal after treatment being defined as "shunt dependent arrested hydrocephalus" in cases of shunt placement, or "post-ventriculostomy arrested hydrocephalus" after neuroendoscopic ventriculostomy procedures. Of the large number of patients developing hydrocephalus within the first year

of life, only about a fifth of the overall number are able to access shunting procedures in established centers in Kenya, and an even lower number can do so in other countries within this Sub-Saharan region, with the majority being treated by a handful of neurosurgeons, a few general surgeons and occasionally by pediatric surgeons. Shunts are expensive to purchase by the family, and often unavailable altogether. However even when affordable shunts are utilized, shunt failure through infection, shunt blockage, distal migration, scalp erosion, shunt extrusion through anal passage are a significant cause of morbidity and mortality in up to 25% of the treated patients [4]. Thus, in developing regions, shunt placement procedures and shunt dependency pose an additional burden on the health care systems as well as on the care receivers and indeed upon the handful of specialist care providers, whose time is further expended in managing the disproportionately high rates of complications of shunting in these environments.

It is therefore better to pursue a definitive approach to treating Hydrocephalus, while, at the same time, avoiding shunt dependency. Neuroendoscopic ventriculostomy (NEV) has the advantage of achieving normalization of CSF flow dynamics and avoiding shunt related morbidities and dependency in the majority of children [2, 3]

The equipment used for Neuroendoscopic Ventriculostomy (NEV) in centres able to provide this service include a Camera control Unit, a Cold Light Source unit, a High Frequency Electrosurgical cautery unit, a Flat screen Monitor Display unit, all placed on a mobile cart riding on casters, which incorporates shelves and drawers (FIG. 1)

The use of this set of equipment, albeit very robust and mobile within an operating suite of individual hospitals, is restricted to provision of NEV procedures to only those patients who are able to reach the hospital facility. It cannot be utilized as a convenie and readily accessible service to patients in low economic profile regions where the purchase cost of providing such equipment in distant and rural settings is neither feasible nor affordable, and nor is it safely and easily transportable. In essence this implies that the large majority of patients who reside in rural communities cannot be offered the preferred mode of treatment utilizing NEV procedures.

II. Material and Method

In October 2006, a neurosurgical team that had established an outreach mission program to provide specialized neurosurgical services in regional hospitals outside the capital Nairobi (FIG. 2), purchased a compact neuroendoscopic Karl Storz Telepack system (FIG. 3) This incorporates a processing unit, combined with a

FIG. 1

FIG. 2

FIG. 3

FIG. 4

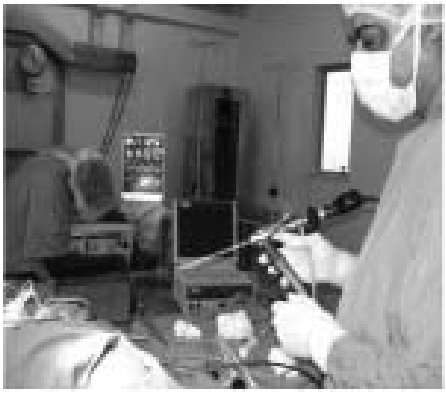

FIG. 5

FIG. 6

FIG. 7

TABLE 1

KENYATTA NATIONAL HOSPITAL NAIROBI	KENYA ……..80
AGA KHAN UNIV HOSPITAL NAIROBI	KENYA…….6
ERTRUDE CHILDREN's HOSPITA NAIROBI	KENYA ……6
L MOI TEACHING HOSPITAL ELDORE	KENYA ……5
COAST PROV GEN HOSP MOMBASA	KENYA ……6
MEWA MISSION HOSP MOMBASA	KENYA ……5
AGA KHAN HOSPITAL MOMBASA	KENYA ……4
AGA KHAN HOSPITAL KISUMU	KENYA ……2
KIJABE MISSION HOSPITAL RIFT VALLE	KENYA…….6
MULAGO MEDICAL COMPLEX KAMPALA	UGANDA ……....5
MUHIMBILI INSTITUTE DAR-ES-SALAAM	TANZANIA …...30
MNAZI MOJA HOSPITAL ZANZIBAR	TANZANIA……..4
BLACK LION HOSPITAL ADDIS-ABABA	ETHIOPIA ……..3
BETHEL TEACHING HOSPITAL ADDIS-ABABA	ETHIOPIA ……..3
MYUNSUNG CHRISTIAN MISSIO ADDIS- ABABA	ETHIOPIA ……..4
KIGALI UNIVERSITY TEACHINGSP KIGALI	RWANDA……..8
TOTAL between October 2006 and Februa 2009	177 cases

Camera Unit and Light source, all conveniently and safely transportable in a portable suitcase. An equally versatile and easy to use rigid rod neuroendoscope, the Oi Handy-Pro[Karl-storz, Tuttlingen, Germany] [(6)], with a 0 degree autoclavable Hopkins II Telescope (FIG. 4) was also purchased. The system offers a single surgeon the free hand ability to perform neuroendoscopy safely (FIG. 5). The image quality has been excellent. The system has revolutionized the management of children with hydrocephalus in this region.

III. Results

In tandem with providing an opportunity of treatment through NEV for patients (FIG. 6), the program has been a source of training of local teams, both neurosurgical and nursing, in performing the NEV procedure, sterilization and care of the equipment. The same single equipment system has been utilize to train 24 MDs (FIG.7), including 16 neurosurgeons and 8 neurosurgery residents to perform the procedure, and 14 operating room nurses in the care, assembly and sterilization of the equipment. The number of cases at sites served by one single unit include the following (Table. 1):

Discussion

Post -ventriculitis aqueductal obstruction is amongst the commonest cause of hydrocephalus in East African studies, and the same is likely to be the case in other developing countries [8]. Definitive treatment of hydrocephalus, while avoiding shunting , is a desirable mode of treatment, provided it can be achieved without increasing the management morbidity and mortality. NEV has been shown to have the potential for avoiding shunt dependency in the majority of children, with lower morbidity and mortality [3, 7]. With the high burden of disease in developing regions, such as Sub-Saharan Africa, as well as the recognized dangers posed by shunt dependency, the cost of purchasing the shunt (as well as subsequent shunts, external drains, reservoirs, sterile collection bags, repeated CSF microbiology studies, etc, in the event of shunt infection and failure), the life long potential for shunt dysfunction, the wider use of NEV, as the primary option for treatment, has significant merit. On the other hand, the inadequate numbers of neurosurgical practitioners and their total absence in rural areas of developing countries, poses a challenge that require a novel approach. It is not feasible to offer expensive Neuroendoscopy equipment at rural sites, as this does not justify such large investment vis-à-vis the overall clinical workload at such rural hospitals. However, the population of hydrocephalus patients presenting at these rural sites cannot, equally, be denied appropriate care that is currently possible through NEV procedures.

IV. Conclusion

The outreach, portable, neuroendoscopy model developed in Kenya and now being promoted across the broader East African region, is one that can achieve the objectives of NEV treatment with ease, safety, convenience and in a cost effective manner. Its main requisites are a recognition that NEV is a preferred option of management, equipment that is readily portable in a safe and reliable way, and a dedicated team willing to volunteer its time and skills to, not only provide care, but also to organize a consistent and structured approach to training as many of the neurosurgical specialists available across the region.

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Complications of Neuroendoscopy

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Abstract

The technical advances in endoscopic tools have extended the indications of neuroendoscopy in the neurosurgical practice. Endoscopy is currently used in most pediatric neurosurgical centers on a daily base. Hydrocephalus, intracranial cysts and intraventricular tumors are commonly treated nowadays with this minimally invasive technique.

While the advantages of this method have been the subject of many reports, its complications have not been described sufficiently and are difficult to evaluate on the grounds of the published reports. The knowledge of these complications is of paramount importance to try to reduce the steep learning curve of neurondoscopic procedures.

In the attempt to provide a pratical assessment of neuroendoscopic complications we have reviewed the recent literature classifying the complications according to their time of occurrence and/or clinical recognition: peroperative, immediate post-operative, and late.

Key Words: endoscopic surgery • ventricles • hydrocephalus, • intraventricular tumors • intracranial cysts • morbidity • mortality

Since the first endoscopic procedures reported more than a century ago [6, 56] the improvement of neuroendoscopic tools in the recent years has enlarged the spectrum of its indications [42]. The anatomy of ventricular cavity lends in fact itself to a direct approach for hydrocephalus, intraventricular lesions (cysts or tumors) but the endoscope has been successfully used also to gain access to lesions adjacent to subarachnoid spaces such as sylvian cysts. Endoscopy is currently used to treat children with hydrocephalus, intracranial cysts and intraventricular tumors in most pediatric neurosurgical centers on daily base. While the advantages of the technique have been the subject of many reports, its complications have not been described sufficiently and are difficult to evaluate on the grounds of the published reports. In fact, the rate of complications of neurodoscopic procedures is extremely variable in the literature, going from 0 to 20% [59], and most of the papers dealing with these subject are anecdotic case reports or coming from the same institutions and authors [10, 54, 55, 58, 59].

Though life threatening complications may occur during endoscopy [33], the endoscopic mortality and permanent morbidity are usually low in large series (0.6% and 4.4%, respectively in Schroeder et al series on 344 endoscopic procedures [59]. The transient morbidity rate is higher. For instance in Schroeder et al series transient complications were found in 9.3% of the patients [59]. The time distribution of the complications in most centers underlines the steep learning curve associated with these procedures, most of fatal and permanent complications occurring within the initial period of the series [11, 12, 23, 58]. The knowledge of such events is of paramount importance to try to avoid the repetition of potential errors and mistakes and thus reduce the risk of complications. It might therefore be possible to reduce the steepness of the learning curve.

The evaluation of complications related to neuroendoscopy is also complicated by the fact that

they depend on the type of neuroendoscopic procedure: endoscopic third ventriculostomy (ETV) or septa fenestrations intracranial cyst fenestration, endoscopic biopsy for intraventricular lesions or endoscopic tumor removal [8, 22]. All these procedures in fact carry a specific risk of morbidity [3, 8, 10, 15, 22, 50, 52 - 54,61- 64].

Complications can be further subdivided according to the impact they have on the outcome (transient vs permanent or symptomatic vs asymptomatic) or on the grounds of their occurrence (during the operation, in the immediate postoperative period or in the late postoperative phases).

In the attempt to provide a pratical evaluation of neuroendoscopic complications we have reviewed the recent literature classifying the complications according to their time of occurrence and/or clinical recognition: peroperative, immediate post-operative, and late.

Peroperative complications

1. Haemorrhagic complications and vascular injuries. Injuries to cerebral blood vessels or surgically induced haemorrhages from cerebral or tumoral tissue are a relatively common complication, mostly in the course of the operation. The haemorrhage is usually caused by mechanical and/or thermal (coagulation) direct injury. The bleeding might occur as early as at the introduction of the endoscope itself in the ventricle due to its impaction on subependymal vessels (FIG. 1). Usually it is only mild and can be controlled by irrigation. Sometimes the bleeding might be more important, coming from thalamic or septal veins. The visibility might be affected and the procedure abandoned [11, 36].

Endoscopic view at the insertion of the scope. The vision is blurred by an ependymal haemorrhage. The foramen of Monro in the center, the septal vein and choroid plexus on the left can be hardly recognized.

Arterial injuries are rare, occurring in about 1-2% of ETV [1, 13; 58]. The basilar artery or its branches within the interpeduncular cistern are involved [14].

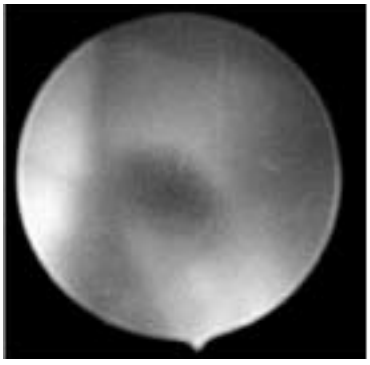

FIG. 1

Injury of such vessels is a dramatic event even if cases of successful management are reported [1, 60]. The risk factors for vascular complications are represented by a poor intraoperative visibility and/or unfavourable anatomical conditions [14]. Formation of traumatic basilar tip aneurysm after ETV has also been described [45]. Involvement of anterior cerebral arteries and/or its branches has been exceptionally reported [7].

The control of intraoperative bleeding during endoscopic procedures is challenging. In fact, not only it is difficult to control it with the minimally invasive tools currently available, but blood can also rapidly and dramatically reduce the vision, consequently complicating or making impossible to continue the procedure. When irrigating during surgery, attention should be paid to several factors: infusion rate, temperature of the irrigation, inward and outward flow [48]. Aggressive irrigation can in fact increase the ICP or in other cases distort the ventricular anatomy [37, 66]. Cold saline has been reported to produce an altered mental status after surgery [48].

In some cases, the haemorrhage might be found on post-operative imaging within the parenchyma due to a damage of pial vessel during the introduction of the endoscope. However the occurrence of intracerebral haematoma is rather uncommon [58].

Epidural hematomas can also bee found (3/134 procedures in Oertel et al series [54]). The rate of haemorrhage seems similar in ETV and in intracranial cyst endoscopy. However, haemorrhage seems to be more frequent during endoscopic tumor biopsy or removal procedures. Intraoperative bleeding of any degree is, in fact, frequent. It was noted in 17 out of 31 cases in Depreitere et al series 14 of which from the tumor itself [18]. But only rarely it results in an interrupted procedure or clinically significant sequelae (1/31 in Depreitere et al series, 3.5%.in Luther et al series [18, 43]).

2. Aborted procedures and technical failures

Although peroperative failures are mainly due to the interruption of the procedure for a bleeding that affect the visibility, the abort of the operation may be also due to an abnormal anatomy [12, 23, 48]. In most cases the potential anatomical limitations can be predicted by a careful examination of preoperative MR especially taking into consideration axial and sagittal T2 weighted MR images which better delineate the shape of the ventricles, the position and thickness of the floor of the third ventricle and the size of the Monro foramen [47]. However in some instances, an unexpected small foramen of Monro or an excessively malformed anatomy of the third ventricle as in myelomeningocele, may still be found during the procedure with the consequent impairment to introduce

the endoscope within the ventricle. In other cases the presence of thick membranes may hinder the recognition of the landmarks usually utilised to perforate the floor of the ventricle or cyst wall.

The reported rates of aborted procedures are higher in case of intraventricular tumors and intracranial cysts (1-9.5%) than in ETV (0.4-5.8%). In cases of intraventricular tumors, the procedure may also fail because of an excessive tumor consistency [59]. Conversion to an open transcortical craniotomy with standard microsurgical technique might then be necessary [26, 64].

Technical failure can also be secondary to defective material during the procedure as in the case reported by Grotenhuis et al with a dislocation of the distal lens of the endoscope [30]. A careful check of the tools, before any endoscopic procedure of all the elements from the scope and instruments, through the optic fibers and camera to the monitor should always be performed. In other cases, complications due to defective tools can be seen only in the postoperative period. Schroeder et al described multiple metal artefacts on the ventricular wall in one patient from an abraded trocar [58].

More in general, even though the success rate of intraventricular tumor biopsy remains high [52] some drawback may result from the histological analysis because of the limited sample size [16]. Also this last limit might be considered as a complication of the neuroendoscopic procedure.

3. Hemodynamic modifications during neuroendoscopy

During endoscopic procedures, especially ETV, cardiac rhythm changes may be seen (bradycardia more commonly, tachycardia or arrest very rarely [14, 15, 21]. Several hypothesis have been suggested: direct compression on the brain stem or on the basilar artery or its braches; increased ICP by irrigation, direct disturbance of hypothalamic nuclei in the floor of the third ventricle [2, 23].

Immediate post-operative

1. Infections

Infection may occur in all types of procedures. CSF infections might occur in 1 to 7% of the cases [3, 15, 23, 58, 59, 61]. Fatal septic multiorgan failure due to a meningitis following ETV has also be described [58, 60].

In ETV procedures, however, postoperative meningitis might result in a closure of the stoma [25]. Skin infection is a non specific complication of endoscopic procedures.

2. Neurological complications

The incidence of neurological complications is low [3]. In most of the cases they are transient. The rate of long term neurological complications reported in the literature is lower than 1% [3, 58]. More commonly clinically silent contusions of neurological structures such as fornix, thalamus or mamillary bodies can be found on postoperative imaging studies without any apparent clinical manifestations [58]. The planning of the burr hole placement and endoscope trajectory are important to try to reduce any damage during the procedure.

Neurological complications might be secondary to vascular injuries or result by direct lesion.

The anatomical structures more often damaged during ETV are those delimiting the Monro foramen and the walls of the third ventricle. In some cases however postoperative focal deficits may be due to a lesion of the internal capsule (Hemiparesis, hemiplegy) or of the cranial nerves (palsies). Cases of Parinaud or Horner's syndrome, peduncular hallucinosis due to mesencephalic/diencephalon injuries have also been described after ETV [14, 15].

The most frequent non-focal neurological deficits after ETV are the impairment of consciousness and confusion, late arousal or memory loss. They are due mainly to diencephalic or forniceal lesions. Personality disorders have been described after ETV [4].

Transient but also permanent hypothalamic and neurovegetative disorders have also been reported (increase in thirst and appetite, diabetes insipidus, hormonal changes, pubertas praecox, thermic dysregulation …), the most common being transient diabetes insipidus and transient hyperthermia They result from injury or distortion of hypothalamic nuclei and infundibulum. [58, 63].

Similar complications are also found after the endoscopic management of intracranial cysts or intraventricular tumors depending on their location.

Seizures related to bleeding, hyponatremia, subdural effusions have also been reported after endoscopic procedures [3, 65]. Seizure incidence following ETV is estimated around 1% [15, 19].

3. CSF related complications

Subgaleal CSF collections and CSF leak have been described after ETV with an overall incidence of 2% to 18% [14, 15, 58]. CSF may tend to flow along the lower resistance pathway offered by the ETV tract. This phenomenon might occur during the first postoperative days secondarily to the transitory increase in ICP found after ETV [49]. Lumbar punctures after the ETV might control the ICP protect the wound, and promote flow through the stoma while a normal CSF absorption is recovered.

Subdural collections are also found after endoscopic procedures with a ventricular access. Acute and

chronic collections have been reported [5, 23, 38, 46]. Both symptomatic and asymptomatic collections have been described [58]. In some cases surgery for the subdural collection is needed [35]. Conversely, asymptomatic collections are seldom reported and probably underestimated in the literature [5, 39, 45]. Postoperative collections have been found in 20% of the cases in Hopf et al series [35]. A packing of the endoscopic tract by fibrin glue and hemostatic mesh has been proposed to reduce the risk of such complication [41]. Subdural spinal hematoma has also been reported [9] .

Pneumocephalus can occur due to the perioperative CSF leak [15]. Only rarely it can become hypertensive [32].

These complications are also shared with the other types of endoscopic intraventricular procedures.

4. Failures

Symptom resolution is the best indicator of a functioning procedure and effective treatment [28]. The success rate of ETV in the literature is estimated to 60-90% [11, 15, 19, 28]. That means that in around 10-40% of the cases the ETV fails to treat the hydrocephalus. Some preoperative and intraoperative criteria have been proposed to predict the efficacy of the ETV. The stronger predictors of failure seem to be the intraventricular scarring or a distorted intraventricular anatomy [29].

A diminished ventricular volume, a flow void signal trough the stoma, as well as a modification of the ventricular shape are radiological criteria to assess on postoperative MR [25, 28, 40, 57]. However the ventricular volume might remain enlarged in the early postoperative imaging so that persisting ventriculomegaly should not be considered necessarily a failure of the procedure [28, 40].

The failure of a technically successful ETV might occur early that is within the first days/weeks, marked by an initial resolution of the symptoms due to the ventricular tapping. In such a cases, symptoms recur in the early post-operative period despite the patency of the stoma confirmed at MR imaging. The cause of such failure is to be searched in an impaired CSF dynamics beyond the obstructed aqueduct [51]. Post-infectious and post-haemorrhagic hydrocephalus for instance are less prone to respond to ETV [13, 24, 34]. Age appears in some studies to play a role, with a progressive increase in success rate with increasing age [19].

In other cases, the patency of the stoma cannot be assessed, due to a cicatrisation of the stoma (FIG. 2) or an incomplete opening of the stoma. These cases will respond to a repeated procedure.

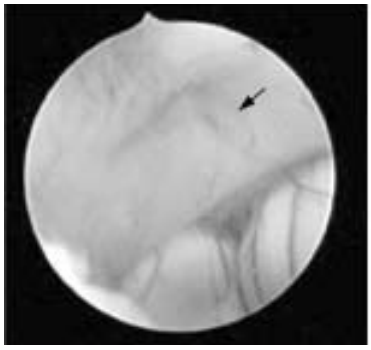

FIG. 2

Endoscopic view of the floor of the third ventricle during a repeated ETV. The stoma is obliterated by a scarring tissue (arrow).

Late and delayed complications

Late complications of endoscopic procedures are mainly represented by the delayed reocclusion of the stoma with the risk of symptom recurrency.

Delayed failure after an initially successful ETV is uncommon (3.4% in Ershain et al series with a mean delay of 105 weeks (23)). However, late failure occurring after 6 years has been reported [11, 12]. In some cases, the late closure may be recognized by a progressive clinical deterioration and symptom recurrence. In others, a rapid clinical deterioration can occur that needs to be promptly diagnosed. A repeated ETV is generally effective. However, cases of delayed sudden death after a functional ETV have also been reported [20, 31]. All patients in whom an autopsy or repeated ETV were performed were found to have an occluded ETV [12, 20, 67] usually by a new membrane or scar and rarely by a clot or tumoral extension [25, 44]. Education of patients and their families about the risk of a late deterioration is of paramount importance to allow for a rapid management and timely intervention. Similarly, cystostomies may close, with consequent cyst enlargement and symptoms recurrence (2/23 in Tamburrini et al series [62]). Large fenestrations in the cyst wall are often necessary to avoid cyst's recurrence [27]. The opening of the cyst in the ventricles and in the cisterns (ventriculo-cysto-cisternostomy) may reduce such risk of secondary closure [17].

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