Frequency and long-term follow-up of trapped fourth ventricle following neonatal posthemorrhagic hydrocephalus

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OBJECTIVE Intraventricular hemorrhage (IVH) is a common complication of premature neonates with small birth weight, which often leads to hydrocephalus and treatment with ventriculoperitoneal (VP) shunting procedures. Trapped fourth ventricle (TFV) can be a devastating consequence of the subsequent occlusion of the cerebral aqueduct and foramina of Luschka and Magendie.

METHODS The authors retrospectively reviewed 8 consecutive cases involving pediatric patients with TFV following VP shunting for IVH due to prematurity between 2003 and 2012. The patients ranged in gestational age from 23.0 to 32.0 weeks, with an average age at first shunting procedure of 6.1 weeks (range 3.1–12.7 weeks). Three patients were managed with surgery. Patients received long-term radiographic (mean 7.1 years; range 3.4–12.2 years) and clinical (mean 7.8 years; range 4.6–12.2 years) follow-up.

RESULTS The frequency of TFV following VP shunting for neonatal posthemorrhagic hydrocephalus was found to be 15.4%. Three (37.5%) patients presented with symptoms of posterior fossa compression and were treated surgically. All of these patients showed signs of radiographic improvement with stable or improved clinical examinations during postoperative follow-up. Of the 5 patients treated conservatively, 80% experienced stable ventricular size and 1 patient experienced a slight increase (3 mm) on imaging. All of the nonsurgical patients showed stable to improved clinical examinations over the follow-up period.

CONCLUSIONS The frequency of TFV among premature IVH patients is relatively high. Most patients with TFV are asymptomatic at presentation and can be managed without surgery. Symptomatic patients may be treated surgically for decompression of the fourth ventricle.

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KEY WORDS fourth ventricle; shunt; pediatric neurosurgery; hydrocephalus

INTRAVENTRICULAR hemorrhage represents a common complication in premature neonates with small birth weight and has been reported in up to 70% of infants weighing less than 1500 g, born before 35 weeks gestation, and/or requiring ventilator support.^{2,23} Similar hemorrhage can occur at term birth, with an estimated 35% of these infants requiring intervention.²⁹ While a specific pathophysiological link remains unclear, posthemorrhagic hydrocephalus may result from an inflammatory response (e.g., ependymitis, arachnoiditis) with attendant occlusion of the cerebral aqueduct and foramina of Luschka and Magendie or scarring and obstruction of the surface

absorptive mechanisms.^{9,21} CSF shunting has become the foremost therapeutic intervention to relieve ventricular dilation and prevent progressive symptoms secondary to hydrocephalus.^{7,17,23}

An isolated trapped fourth ventricle (TFV) describes a phenomenon when CSF shunting of the lateral ventricles fails to adequately drain the fourth ventricle. The clinical antecedents leading to TFV most commonly involve intraventricular inflammatory reactions, including bacterial infection or hemorrhage. Delayed diagnosis of TFV can lead to severe neurological dysfunction and/or death.^{14,32} To date, the treatment modalities have ranged from open

ABBREVIATIONS IVH = intraventricular hemorrhage; TFV = trapped fourth ventricle; VP = ventriculoperitoneal.

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surgery (fourth ventriculocisternostomy) to CSF diversion (transcerebellar, transaqueductal, transforaminal, or transcortical) and endoscopic procedures (aqueductoplasty and/or stenting, cystoventricular stenting). Conservative management without surgery has been shown to be effective for patients with unequivocal clinical and radiographic stability.¹⁴

With previous reports of fourth ventricular enlargement limited to isolated cases, the literature remains sparse regarding the frequency, natural and surgical histories, and long-term clinical and radiographic outcomes of TFV.^{14,23,31,32} Udayakumaran et al. reported 13 posterior fossa craniotomies and opening TFV in the spinal subarachnoid space across 12 patients and found that 100% showed clinical improvement and 75% showed radiographic improvement over an average follow-up period of 6.1 years.³⁵ More recently, Raouf and Zidan reported universal radiographic and clinical improvement over 23 months in 13 patients with symptomatic TFV managed with suboccipital endoscopic trans-fourth ventricular aqueductoplasty.²⁶ The purpose of the present study is to review the long-term clinical and radiographic outcomes for conservatively and surgically managed pediatric patients with TFV following neonatal posthemorrhagic hydrocephalus. In so doing, we better understand the frequency and natural and surgical histories of TFV in the pediatric population.

Methods

Following institutional review board approval, we retrospectively reviewed premature infants with intraventricular hemorrhage (IVH) who were treated with ventriculoperitoneal (VP) shunting procedures at the University of Virginia over a 10-year period from 2003 to 2012. Fifty-two patients with IVH due to prematurity and subsequent hydrocephalus treatment with VP shunting were reviewed. Eight patients developed TFV following shunted hydrocephalus secondary to IVH. Three of these patients were managed with surgery. Five patients were managed conservatively with serial radiographic imaging and clinical examinations.

Clinical Evaluation

All 52 patients underwent comprehensive multidisciplinary evaluation, including neonatal intensive care and child neurology consultations with information available about history, neurological examination findings, and postpartum and/or postoperative (from the initial CSF shunting procedures) complications. The patients were treated/operated on by the same pediatric neurosurgeon.

Imaging

All patients underwent preoperative CT and/or high-resolution MR imaging using standard T1- and T2-weighted spin echo sequences. Imaging studies were independently reviewed at diagnosis by a neuroradiologist and pediatric neurosurgeon to determine the degree of aqueductal and fourth ventricular outlet patency as well as the amount of fourth ventricular enlargement (Fig. 1). Surgery was indicated for patients with clinical symptoms, in addition to progressive enlargement of the fourth ventricle. We compared the baseline imaging parameters to the findings on postoperative imaging.

tion to progressive enlargement of the fourth ventricle. We compared the baseline imaging parameters to the findings on postoperative imaging.

Results

Patient Characteristics

In total, 8 pediatric patients were evaluated for and diagnosed with TFV following shunted IVH due to prematurity; all patients underwent neurological examinations and radiographic follow-up. Three of these patients presented with the symptoms of posterior fossa compression and were managed with surgery. Five patients were managed conservatively with serial radiographic imaging and clinical examinations. There were notably more female ($n = 7$) than male ($n = 1$) patients. For all patients, the mean gestational age was 26.3 weeks (range 23.0–32.0 weeks), which was slightly higher in the surgical cohort (27.0 weeks) than the nonsurgical cohort (25.8 weeks) ($p = 0.65$). The total clinical follow-up was 7.8 years (range 4.6–12.2 years) and radiographic follow-up was 7.1 years (range 3.4–12.2 years). The demographic characteristics and follow-up length by group are summarized in Table 1.

TFV Characteristics

Over the examined 10-year time period, 52 patients with IVH due to prematurity received treatment with VP shunting. Of these 52 patients, 8 patients subsequently developed TFV, suggesting a total frequency of 15.4%. Three of the 52 (5.8%) IVH patients were treated surgically (37.5% of TFV patients), and 5 of 52 (9.6%) patients were managed conservatively (62.5% of TFV patients). The temporal relationship between initial shunting for IVH and diagnosis and treatment for TFV was further classified. In total, the mean age at the first shunting procedure was 6.1 weeks (range 3.1–12.7 weeks). Patients in the surgical group underwent their initial shunting procedures at 5.6 weeks (range 3.6–6.8 weeks), which was slightly earlier than the nonsurgical group at 6.3 weeks (range 3.1–12.7 weeks) ($p = 0.78$). This difference likely did not reach significance due to the relatively small number of patients. Following the first shunting procedure, the average time to TFV diagnosis across all patients was 19.3 months (range 1.5–69.7 months), which was higher for the surgical group (mean 21.1 months; range 2.5–55.3 months) than the nonsurgical group (mean 18.3 months; range 1.6–69.8 months) ($p = 0.89$). On average, the nonsurgical group received a higher number of initial VP shunt revisions prior to TFV diagnosis (mean 5.4; range 1.0–11.0) than the surgical group (mean 2.3; range 1.0–5.0) ($p = 0.28$) (Table 2).

Clinical Characteristics

At the time of IVH diagnosis and treatment, half of the patients had Grade 3 IVH and the other half had Grade 4 IVH. All 52 patients who were treated with VP shunting for lateral ventricle hydrocephalus were followed with yearly serial neurological examinations and imaging. At the time of TFV diagnosis, all 8 patients showed isolated fourth ventricular enlargement on neuroimaging. Three (37.5%) of these patients presented with the symptoms of posterior fossa compression. The indications for surgery

FIG. 1. T2-weighted MRI brain scans showing TFV shunting in a 32-week premature neonate at 2 months following Grade 4 IVH diagnosis. **A–D:** The patient presented with emesis, lethargy, and dysconjugate gaze (**A** and **B**) and exhibited an enlarged fourth ventricle on radiographic imaging 2 months later (**C** and **D**). **E and F:** The patient showed initial improvement with fourth ventricular shunting but required 2 revisions with improvement each time. **G and H:** At the last follow-up at 5 years hence, the patient exhibited stable neurological examination findings as well as fourth ventricular size on radiographic imaging.

were symptoms of posterior fossa compression, and thus all of these patients were treated with surgery. One patient had unrelated sleep apnea related to seizure episodes. Of the 3 surgical patients, all (100%) had lethargy and 2 (67%) patients had abnormal gaze. One (33%) patient presented with spontaneous bradycardic episodes. All of the patients in the nonsurgical group showed only radiographic signs of TFV without any clinical symptoms (Table 3).

All of the nonsurgical patients experienced a stable TFV course. Over the course of 7.1 years (range 3.4–10.8 years) of radiographic follow-up in the nonsurgical group, 4 (80%) patients exhibited stable size of the fourth ventricle and 1 patient (20%) exhibited a slight increase in size (3 mm). This patient was carefully followed and, due to the lack of symptoms, was not treated. Over the course of 7.1 years (range 4.6–10.8 years) of clinical follow-up in the nonsurgical group, all 5 (100%) patients showed either

stable or improved clinical examinations. All of the surgical patients (100%) showed signs of radiographic improvement over 7.4 years (range 4.9–12.2 years) of follow-up. All patients (100%) also had a stable or improved clinical examinations over 7.7 years (range 5.2–12.2 years) of follow-up (Table 3). The patients who were treated surgically had several procedures performed on the fourth ventricle, and all ended up with a fourth ventricular shunt. One surgical patient initially underwent endoscopic fenestration of the right lateral ventricle and the fourth ventricle, another initially underwent an endoscopic cerebral aqueduct fenestration, and the third patient initially underwent fourth ventricular shunting. Also, these patients all had 3 subsequent revision surgeries after the fourth ventricular shunting procedures (i.e., 4 total procedures on the fourth ventricle for the 2 patients who initially underwent endoscopic fenestrations). Prior to revision surgery, they all presented with symptoms and radiographic evidence of failed fourth ventricular drainage.

Discussion

An isolated or trapped fourth ventricle can be a consequence of hemorrhagic, infectious, or inflammatory insults to the brain, particularly after lateral ventricular shunting for neonatal posthemorrhagic hydrocephalus. The occlusion of the aqueduct is largely irreversible and is thought to be associated with overdrainage of the supratentorial shunt.^{19,25,33} While the neurosurgical treatment armamentarium has broadened to include open surgery, CSF diversion, and endoscopic techniques, serious complications ranging from cranial nerve to brainstem dys-

TABLE 1. Patient demographics*

Characteristic	Surgical	Nonsurgical	p Value
Sex			
M	0	1	
F	3	4	
Gestational age, wks	27.0 (24.0–32.0)	25.8 (23.0–29.0)	0.65
Clinical follow-up length, yrs	7.7 (5.2–12.2)	7.8 (4.6–11.0)	0.92
Radiographic follow-up length, yrs	7.4 (4.9–12.2)	7.1 (3.4–10.8)	0.89

* All values are shown as the number of patients or mean (range).

TABLE 2. TFV and VP shunt characteristics

Characteristic	Surgical	Nonsurgical	Total	p Value
TFV frequency of all IVH patients	3/52 (5.8%)	5/52 (9.6%)	8/52 (15.4%)	
Mean age at 1st shunt, wks				0.78
Mean	5.6	6.3	6.1	
Range	3.6–6.8	3.1–12.7	3.1–12.7	
Mean time to TFV diagnosis after 1st shunt, mos				0.89
Mean	21.1	18.3	19.3	
Range	2.5–55.3	1.6–69.8	1.6–69.8	
Mean no. of shunt revisions prior to TFV diagnosis				0.28
Mean	2.3	5.4	4.3	
Range	1.0–5.0	1.0–11.0	1.0–11.0	

function as well as a high rate of failure often hinder a complete cure.^{1,3,5,14,20,36} In the present series, the 3 surgical patients all required multiple revision surgeries after fourth ventricular shunt placement. Specifically, the 2 patients who initially underwent endoscopic fenestration procedures ultimately underwent 4 total procedures related to the fourth ventricle.

The pathological underpinnings of fourth ventricular hydrocephalus span a diverse spectrum from congenital (Dandy-Walker malformation) to posthemorrhagic (subarachnoid or intraventricular hemorrhage), infectious (bacterial, fungal, parasitic), and neoplastic (carcinomatous meningitis) processes.¹⁴ Most cases of TFV in the literature have been linked to inflammatory processes, chief among them infection and intraventricular hemorrhage.^{6,8,13,16,18,22} Isolated enlargement of the fourth ventricle is presumably a byproduct of inflamed ependymal surfaces that result in obstructive adhesions and hence aqueductal stenosis and obstruction of the foramina of Luschka and Magendie.^{10,14} The consequent disruption of fourth ventricular outflow and retrograde flow through the aqueduct can result in trapping of the fourth ventricle,

which progressively enlarges insofar as CSF production by ependymal and choroid plexus continues.^{10,27,28}

In 1978, Hawkins et al. published their seminal report of post-shunting TFV in 3 patients with cerebellar signs.^{14,15} Fourteen years later, a review unearthed IVH in 50% of 1535 neonatal ultrasonography studies and 10 cases of significant fourth ventricular enlargement before shunt placement. Following lateral ventricular shunting procedures, 6 of these 10 patients experienced TFV.¹² Since then, most reported cases of TFV in children have focused more on operative technique, short-term postoperative outcomes, and complications without attention to the incidence or respective outcomes in the nonsurgical counterparts.

Endoscopic transaqueductal or interventricular stenting has been considered safe and effective. Recent series of endoscopic treatment for TFV suggest a success rate of 25% to 33% over 9.8 to 29.7 months with aqueductoplasty alone, but as high as 71% to 100% when aqueductoplasty or interventriculostomy was followed by fourth ventricular stenting.^{4,11,30} Ogiwara and Morota studied 8 pediatric patients who underwent endoscopic stent placement for TFV (n = 5) or pre-TFV (aqueduct still patent) (n = 3).

TABLE 3. Clinical characteristics of the TFV patients

Sex	Gestational Age (wks)	Grade IVH	Signs at Diagnosis	Treatment	TFV Course	Radiographic Outcome*	Clinical Outcome
F	25	4	Lethargy, downward gaze, abnormal head position	Endoscopic 4th ventricle fenestration, 4th ventricle shunt	3 shunt revisions w/ improvement	Improved	Improved
F	32	4	Lethargy, emesis, dysconjugate gaze	4th ventricle shunt	2 shunt revisions w/ improvement	Improved	Stable
F	24	3	Lethargy, apnea, bradycardia	Endoscopic cerebral aqueduct fenestration, 4th ventricle shunt†	No revision, stable	Improved	Stable
F	29	3	Radiographic only	Conservative	Stable	Stable	Stable
M	29	3	Radiographic only	Conservative	Stable	Slight increase‡	Stable
F	24	4	Radiographic only	Conservative	Stable	Stable	Slight improvement
F	23	3	Radiographic only	Conservative	Stable	Stable	Stable
F	24	4	Radiographic§	Conservative	Stable	Stable	Stable¶

* In comparison to TFV diagnosis.

† Performed 6 years later.

‡ 3-mm increase.

§ Sleep apnea attributed to seizure episodes.

¶ No sleep apnea.

They found that all patients experienced improvement in symptoms and reduction in fourth ventricular size with reoperation in 33% of patients over a mean follow-up of 49.6 months.²⁴ Teo et al. reported successful procedures and universally good outcomes in 16 patients with TFV (8 patients treated with endoscopic approach, 4 patients by fenestration, and 4 patients by aqueductoplasty), though 50% of shunted patients required revision with a complication rate of 25%.³⁴ More recently, Raouf and Zidan demonstrated both clinical and radiographic improvement over a follow-up period of 23 months in all 13 patients with symptomatic entrapped fourth ventricle who underwent suboccipital paramedian aqueductoplasty.²⁶

In this study of a cohort of 8 pediatric patients diagnosed with TFV following shunted posthemorrhagic hydrocephalus due to prematurity, 3 patients underwent surgery for symptoms related to an enlarging fourth ventricle and 5 patients were managed without surgery. The initial surgical technique included endoscopic fourth ventricle fenestration, endoscopic cerebral aqueduct fenestration, or fourth ventricular shunting, and all surgical patients ultimately received a fourth ventricular shunt. Surgical intervention was associated with improvement in radiographic evidence of fourth ventricular dilation over a mean follow-up of 7.4 years (range 4.9–12.2 years) and stable or improved symptoms and signs on clinical examination over a mean follow-up of 7.7 years (range 5.2–12.2 years). Of the 5 patients treated conservatively, 80% experienced stable ventricular size and only 1 patient experienced minimal increase (3 mm) on imaging. All of the nonsurgical patients showed stable to improved clinical examination findings over the follow-up period of 7.8 years (range 4.6–11.0 years). This finding elucidates a possible benign natural history of asymptomatic TFV, which should be further explored. Asymptomatic patients can likely be watched with close clinical and radiographic follow-up with operative intervention withheld for symptomatic progression.

One of the more salient findings of this review was the relatively high frequency (15.4%) of TFV following VP shunting for neonatal posthemorrhagic hydrocephalus. Hall et al. previously reported the neurosonographic enlargement of the fourth ventricle in 10 (4%) of 229 premature infants with severe intracranial hemorrhage. Six (60%) of these 10 patients (2.6% total) experienced TFV following lateral ventricular shunting procedures.¹² The previously underreported incidence of TFV highlights its possible benign nature. Given this relatively high frequency, premature infants with IVH and shunting should be closely monitored for posterior fossa symptoms and TFV.

The primary limitation of this study is the small number of patients and the attendant constraints of drawing statistical inference from surgical versus conservative treatment groups. Going forward, longitudinal follow-up studies should focus on comparing the management strategies of symptomatic patients to those without symptoms. These studies will help to further elucidate the natural and surgical histories of TFV and, more appropriately, gauge the risk-benefit trade-off of a growing spectrum of surgical interventions. Surgical technique, including endoscopic (aqueductoplasty and/or stenting) and open (fourth ventriculocisternostomy) approaches, and the resolution

of clinical symptoms and radiographic signs should also be explored with more patients as there is no consensus regarding the most appropriate surgical technique. With further study over longer time horizons meant to capture all cases of clinical and/or radiographic deterioration, we may further be able to refine diagnostic criteria, predict symptomatic progression, and, accordingly, match appropriate surgical and nonsurgical therapeutic modalities to patient functioning.

Conclusions

The frequency of TFV among premature IVH patients is relatively high (15.4%). Most patients with TFV are asymptomatic at presentation and can be managed without surgery. Symptomatic patients should be treated surgically for decompression of the fourth ventricle.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: all authors. Acquisition of data: all authors. Analysis and interpretation of data: all authors. Drafting the article: all authors. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Statistical analysis: Jane, Pomeraniec, Ksendzovsky. Administrative/technical/material support: Jane, Pomeraniec, Ksendzovsky. Study supervision: Jane, Pomeraniec, Ksendzovsky.

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