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Surgical treatment of post-infectious hydrocephalus in infants

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Abstract
The management of post-infective hydrocephalus in infants remains a challenging task for the pediatric neurosurgeon. The decision-making curve is often complex in that appropriate temporizing measures need to be implemented to properly clear any infection within the CSF before any decision can be made regarding a permanent solution. The etiology differs at varying stages of neonatal development, and the weight of the child, skin fragility, and relevant surgical treatment options are often important limiting factors. Deciding on the optimal treatment option involves assessing the etiology, age, and clinical and radiological features of the individual case and selecting the most appropriate surgical option.

Keywords Hydrocephalus · Infection · Pediatric neurosurgery · Neuroendoscopy · Surgical treatment

Introduction

In children, hydrocephalus is a relatively common condition affecting the central nervous system, occurring in 0.36–0.9 per 1000 live births [1, 2].

Post-infectious hydrocephalus (PIH) refers to the accumulation of cerebrospinal fluid (CSF) within the ventricular system of the brain due to an acute or chronic infection. The development of fibrous adhesions either in the ventricles, the arachnoid villi, or the basal cisterns are considered to be the main contributors to this process [3–5]. The management of neonates and children with post-infectious hydrocephalus remains an ongoing challenge to pediatric neurosurgeons. This is mostly because the options for surgical treatment are quite limited, and while there have been some advances, there are described shortcomings to these options [3, 4].

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Etiology and pathophysiology

The incidence of PIH varies geographically, with descriptions of an increased incidence in developing countries [6, 7].

PIH is often classified according to the period during which the infection occurs, i.e., pre-natal, neonatal, and post-natal infectious hydrocephalus [8].

It can also be classified according to etiology, as viral, bacterial, tuberculous, or parasitic. It is important to remember that in this context, the infection can be either acute or chronic. For the purpose of this work, the discussion will focus on acute infection.

PIH is almost always obstructive in nature, with the level of obstruction ranging from intraventricular to the level of the arachnoid villi at the superior sagittal sinus.

Toxoplasmosis and cytomegalovirus have been identified as common causative agents in prenatal infection [3, 4]. The primary causative agents in neonatal infection are mostly bacterial, with *E. coli* and streptococcal infection implicated in early-onset infection and staphylococcus, and group B streptococci identified in the later onset infections [3]. Exudate may be deposited on the choroid plexus, in the basal cisterns, and over the arachnoid villi. The CSF may become turbid, with the development of septations in the ventricles and fibrotic adhesions in the basal cisterns. These are all related to the inflammatory response within the brain and thus contribute to the disturbance of CSF flow and loculations within the ventricular system [9].

Diagnostic imaging

Imaging modalities in pediatric hydrocephalus form a vital part of the decision-making process. The described imaging options range from a skull X-ray, ultrasound, and CT scan to various sequences of MRI scans.

Skull X-ray

The skull X-ray in this context is quite an antiquated modality, yet its role particularly in assessing the integrity of a V/P shunt is essential. The lateral skull X-ray, chest X-ray, and abdominal X-ray, usually referred to as the shunt series, is vital in detecting breaks or fractures in the V/P shunt, especially in the neck and over the clavicle, and assessing integrity of the valve as well as ventricular and abdominal catheter position.

Pneumoencephalography (PEG) may also be performed using the basic principles of a lumbar puncture (L/P). It is very important to have adequate imaging, either CT or MRI, to rule out any contraindication, prior to performing a lumbar puncture (L/P). Opening pressures are recorded via the L/P and CSF released prior to injection of about 5 m of air. A lateral skull X-ray is performed before and after the procedure to assess the presence and level of the air locule, i.e., within the lateral ventricle, below the level of the basal cisterns or no air at all. While the significance of this technique in modern neurosurgery is mostly historic, descriptions of its usefulness as an adjunct in the context of tuberculous meningitis (TBM) help differentiate communicating from non-communicating hydrocephalus and thus guide decision-making in this condition as it relates to the management of the hydrocephalus [10–12]; however, some authors do not recommend performing a PEG in this condition due to the risk associated with raised ICP [13, 14].

Ultrasound

Bedside ultrasound imaging is very helpful in assessing the brain and ventricles in neonates, especially when the anterior fontanelle is still open. In its current form, its role still remains that of a screening tool, but with advances in ultrasound probe design and size, the image quality has improved quite dramatically (Fig. 1) [15]. Limitations however, include user dependency, challenges in interpreting the anatomy of deeper structures especially the posterior fossa, and adjusting to the still unfamiliar imaging planes. It is a non-invasive, cost-effective, and radiation-free modality that allows multiplanar real-time imaging and can be also be used intra-operatively to confirm adequate membrane fenestration in cases of multiloculated hydrocephalus, among other applications. Operator dependence and comfort remains the main limitation. In its current form, however, ultrasound as a diagnostic modality is used in conjunction with CT and MRI to evaluate children with hydrocephalus, but remains a very helpful surveillance and screening tool [16].

Fig. 1 Coronal transfontanelle ultrasound image demonstrating lateral ventricles, choroid plexus, third ventricle as well parafalcine sulcal and gyral markings

The use of duplex-Doppler flow indices in newborns is a valuable diagnostic adjunct, especially when used in conjunction with lateral ventricle size and altered brain parenchyma echogenicity [17]. In hypoxic-ischemic encephalopathy, color Doppler indices are valuable in early detection as well as predicting severity and outcome [17]. Doppler flow indices can be measured over the anterior cerebral artery (ACA), middle cerebral artery (MCA), basilar artery (BA), or the internal carotid artery (ICA) and include the resistance index (RI) and pulsatility index (PI). The indices are calculated using acquired blood flow parameters such as the systolic velocity (V_s) and the diastolic velocity (V_d) [18].

Pathological conditions of the neonatal brain where ultrasound-based flow velocities of the cerebral arteries may be used include brain hemorrhage, hydrocephalus, brain edema, brain death, and hypoxic-ischemic brain injury [19]. Age-related normal flow velocities also need to be considered when interpreting these values. Doppler flow indices also appear to have a poorer correlation with absolute ICP, in the context of TBI, but may serve as a useful screening tool in the emergency setting [20–24].

CT scan

CT scans are most commonly used in assessing hydrocephalus in the acute setting, as it is a fast, reliable technique which is available in most centers with a neurosurgery service. It is also very helpful in children due to the short duration of the test, limiting the need for sedation. There is however concern with the repeated use of CT scans in pediatric hydrocephalus patients, as the potential for long-term harmful effects of repeated exposure to ionizing radiation have been described [16]. To this end, low-dose CT protocols which have been developed to reduce the cumulative dose of radiation have been described [16].

In the early phases of meningitis, the CT findings can be quite subtle. A contrast-enhanced CT scan may show the beginnings of meningeal enhancement or exudate deposition in the ventricles or basal cisterns, which may become more accentuated in later stages of the disease (Fig. 2). Measurement of ventricular size, both the lateral and third ventricles, using various indices is also possible on CT scan [25].

CT scans are more reliable than MRI for ventricular catheter tip localization, but do not provide sufficient anatomical detail when planning is required for specific procedures, e.g., endoscopic third ventriculostomy (ETV) [16, 25].

MRI scan

Magnetic resonance imaging (MRI) is the imaging modality of choice when evaluating pediatric hydrocephalus [25]. It provides exquisite detail of the ventricular morphology, brain parenchyma, vasculature, and cisternal anatomy. The additional benefit of specific MRI sequences allows for assessment of features like periventricular edema, CSF volume in the cortical subarachnoid spaces, patency of the cerebral aqueduct, and morphology of the third ventricle, and the use of CINE MRI allows assessment of CSF flow. The surveillance of ventricular size, identification of the underlying etiology of hydrocephalus, assessment for ETV stoma patency, and assessment of parenchymal changes and pericerebral spaces among others make imaging assessment of treatment outcomes possible [16].

Fig. 2 Axial CT scan showing mixed density multiloculated collections in the left lateral ventricle

Multiplanar imaging contributes significantly to surgical planning and is a requisite for adjuncts like neuronavigation [26].

Steady-state T2 images are important for assessing membranes in the ventricles or cisternal spaces and are especially relevant when planning surgery for cystic lesions or complex, multiloculated hydrocephalus [16].

MR angiogram (MRA)—raised ICP in infants with hydrocephalus may lead to significant decreases in cerebral blood flow (CBF). Increased apparent diffusion coefficient (ADC) values may be found on diffusion weighted MR imaging, especially in the periventricular white matter and is usually suggestive of interstitial edema without cytotoxic edema. MRA can be used to measure the volume flow in the ICAs and the BA, and is a non-invasive technique to investigate flow changes in patients [16, 25].

Cine MRI—this technique can be used to acquire information on CSF dynamics using cardiac gated computer-aided modeling. It provides information on "to and fro" CSF flow velocity as well as direction during a single cardiac cycle with specially designed flow-sensitive gradient echo (GRE) sequences [25].

Diffusion-weighted imaging (DWI) has an important role in diagnosing intracranial infection [27]. In neonates where the brain has a higher water content and the immune and cardiovascular systems are immature, differentiating between ischemic and infectious lesions remains difficult. DWI together with anatomical location of the lesion, i.e., watershed areas, may assist in making the diagnosis of intracranial infection. Reduced diffusion with an apparent diffusion coefficient (ADC) lower than that of cortical gray matter has been described as consistent with intracranial empyema, particularly in the subdural space. This is likely due to the viscosity of the collection and is thus useful in differentiating reactive subdural effusion (SDE) from empyema [28, 29].

Surgical management of PIH

The presence of infection in the CSF usually requires a temporizing measure to divert CSF and also allows sampling to perform a cell count and culture. The choice of antibiotic may initially include broader-spectrum agents to cover for the commonly identified organisms, but should be tailored to the specific infective organism as soon as this is identified. The temporizing measures can continue for days to weeks, as required. Once the cell count is appropriate and the infection fully treated, the decision to proceed to a permanent treatment option can be made (Table 1).

The optimal time to implant a V/P shunt, especially where there is evidence of previous infection, is usually based on CSF and serum marker levels and trends, aiming to achieve CSF sterility after an appropriate response to parenteral antibiotic therapy. The decision regarding when CSF is sufficiently sterile in order to define optimal ventriculoperitoneal shunt (VPS) infection treatment practice remains a difficult issue, mostly due to a lack of controlled clinical studies [30, 31]. The duration of antibiotic therapy requires a minimum of 10–14 days, but varies widely between institutions depending on, among other factors, the specific causative organism [32, 33]. Regarding the CSF profile, a recent study suggested a preference towards utilizing a leukocyte count $< 20 \times 10^9$/L, irrespective of CSF protein levels [34], while another study described a CSF protein level of > 100 mg/dL prior to shunt re-insertion as associated with shunt re-infection [31], with CSF glucose and globulin levels appearing to be less relevant in this context. The practice of managing CSF shunt infection appeared to vary significantly depending on the volume of VPS surgery performed as well as geographical location [34]; however, the combination of clinical presentation suggestive of CNS infection with a CSF profile of leukocytosis ($> 20 \times 10^9$/L), neutrophil count > 10%, low glucose and high protein levels, and elevated serum C-reactive protein (CRP) and procalcitonin levels are considered indicative of VPS infection [34, 35]. Additional markers which may be useful in detecting CSF infection include, lactate, cytokine, and globulin levels [5, 34, 36].

Temporizing measures

Ventricular taps

Ventricular taps may be performed when there is acute CSF infection of intraventricular hemorrhage in neonates. These have been advocated as temporizing measures, performed usually once or twice to remove protein or blood from the ventricles. The volume of CSF removed is usually enough to

Table 1 Surgical management of PIH

Treatment option	Permanent/temporizing/either	Advantage	Disadvantage
Ventricular tap	Temporizing	Useful in treating raised ICP	Limited time span for use, usually only 2–3 times
External ventricular drain (EVD)	Temporizing	Useful in treating raised ICP Allows repeat sampling of CSF	High complication rate Requires routine replacement
Ventriculosubgaleal shunt	Temporizing	Useful in treating raised ICP Allows for the patient to be more mobile	Limited time span for use
Ventriculoperitoneal shunt (VPS)	Permanent	Allows for treatment of raised ICP	Complication rate still unacceptably high
Neuroendoscopic techniques			
ETV	Permanent	Allows patient to be shunt free, if successful	Indicated mostly in triventricular hydrocephalus
ETV and CPC	Permanent	Improved success rate in refractory hydrocephalus	Requires specific equipment, i.e., flexible endoscope and extensive choroid plexus obliteration
Septosotomy	Permanent	Allows access to both lateral ventricle by communicating them	May require more than 1 burrhole in some instances
Foraminoplasty	Permanent	May allow communication between lateral and third ventricles	May be complicated by forniceal injury and memory impairment
Aqueductoplasty	Permanent	Allows communication between the third and fourth ventricle and may	May be complicated by gaze palsy
Membrane fenestration	Permanent	Allows communication of the ventricular system	High reclosure and recurrence rate
Endoscopic assisted catheter insertion or removal	Permanent	Allows direct visualization for catheter placement and removal, especially where the ventricular anatomy is abnormal	Not useful where ventricles are small
Endoscopic lavage	Temporary	Allows removal of exudate and debris in the ventricle with improved shunt survival	Shunt insertion is still required

leave the anterior fontanelle soft and flat, or approximately 10 mL/kg per ventricular tap [1, 37]. While repeated ventricular taps have not been shown to have any significant effect on the need for a V/P shunt, there is also an associated risk of secondary infection with this procedure. Ventricular taps should therefore be used only as a temporizing measure to control raised ICP before a permanent CSF diversion procedure is possible [38].

External ventricular drain

Where ventricular taps or LPs have not been successful as standalone temporizing measures in hydrocephalus, insertion of an external ventricular drain (EVD) is the next temporizing measure. EVDs are usually inserted into the frontal horn of the lateral ventricle, always under strict aseptic conditions. The distal end should be tunneled subcutaneously at least 5 cm away from the insertion site, and firmly secured. EVD not only provides a rapid reduction of intracranial pressure but also provides a therapeutic test to assess whether CSF diversion will help the child. The duration of EVD drainage and protocol for sampling CSF, therapeutic drainage, and measurement of ICP as a marker of dependence and ready for CSF diversion may vary institutionally, but should follow broad guidelines [37, 39, 40]. The overall complication rate for EVD is around 26%, with varying rates of infection described [34, 40].

Ventriculosubgaleal shunt

Ventriculosubgaleal shunt (VSGS) insertion involves placement of a ventricular catheter, usually into the frontal horn of the lateral ventricle with the distal end implanted in the subgaleal space and secured via right angle connector. The elasticity, avascularity, and absorptive capacity of the subgaleal space make it an attractive option as a temporizing measure in the treatment of hydrocephalus.

The subgaleal pocket should be carefully dissected to ensure the correct plane is identified and made large enough to collect an adequate volume of CSF from the ventricles. Slits in the distal catheter end inserted in a subgaleal pocket may also offer some mechanical resistance to outflow [41, 42].

Because the subgaleal tissue is not affected by the limitations imposed by the blood–brain barrier and due to its shorter length and simplicity, the VSGS offers a sensible treatment option for associated infectious processes [41].

The described length of survival of the VSGS is on average of 37.4 days, but may be a viable option for up to 3 months. The most important detail of the procedure in our experience is the careful and watertight closure of the neonatal scalp [41, 42].

With persistent hydrocephalus assessed clinically and radiologically, and once the CSF is clear or the weight of the child has improved, the VSGS should be removed and a VPS inserted; however, if the hydrocephalus appears to have arrested, the VSGS may be left in place and removed electively [43]. A high infection rate in the neonatal population when VSGS has been used has been described in infants with post-hemorrhagic hydrocephalus [43].

Neuroendoscopic ventricular lavage

This technique represents a method of evacuating the inflammatory debris and pus in the ventricles. This clearance of debris may have a positive impact on shunt survival, as the increased protein content in CSF during PIH is thought to a factor in shunt blockage and malfunction [4]. The technique involves accessing the ipsilateral ventricle thought to have the larger debris load via a precoronal burrhole. The endoscope is introduced into the ipsilateral ventricle, and endoscopic lavage is commenced with body temperature warmed lactate-free Ringer solution. The solution is introduced via a gravity-set infusion through the inflow port of the endoscope trochar. The outflow port allows passive outflow of the exudate containing fluid. The separate inflow and outflow ports enable effective irrigation of the ventricle; this is important to maintain ICP within and normal range. Additional pus or debris can be aspirated via a 10-mL syringe, which may be

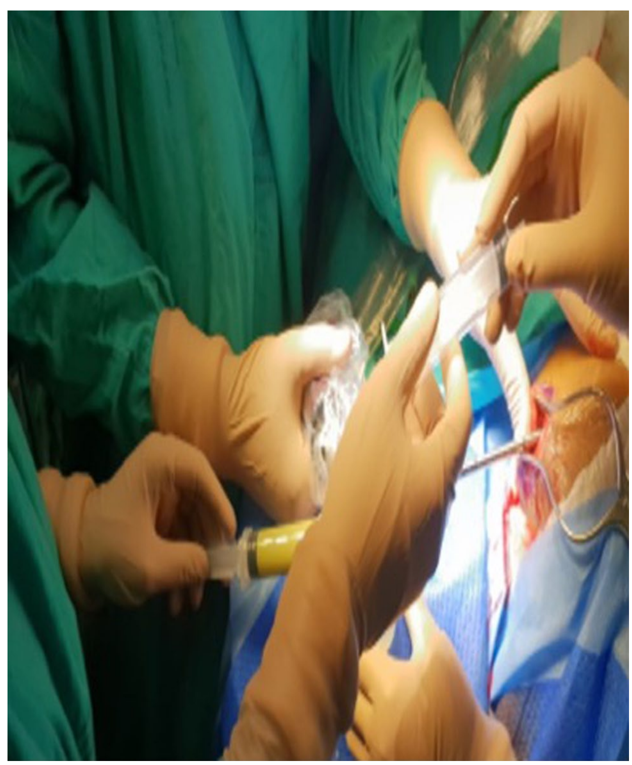

Fig. 3 Ultrasound-guided endoscopic lavage, aspiration of debris and fenestration of multiloculated hydrocephalus

attached to a fine bore nasogastric tube, as the endoscope tip is brought close to the debris. Additionally, a septostomy can be performed to allow access to the contralateral ventricle and repeat the procedure. The lavage should be continued until the CSF becomes clear (Fig. 3). After removal of the endoscope, an EVD or ventricular access device may be left in situ. A watertight closure is imperative [44, 45].

Permanent measures

Ventriculoperitoneal shunts

The decision-making paradigm in postinfectious hydrocephalus is a complex one. The options to treat in the context of acute infection or where the conditions for VPS insertion are not yet optimized have been discussed above. Where the hydrocephalus is deemed to be communicating and the CSF is clear, insertion of a VPS is the treatment option suggested [5]. In cases of obstructive or triventricular hydrocephalus, ETV should strongly be considered; however, the success rate of this procedure in the context of PIH is poor [4, 5].

Once the decision has been made to insert a VPS, there is a wide spectrum of options available regarding VPS hardware. These options range from flow to pressure regulated valves, programmable vs non-programmable valves, gravitational valves, the size and profile of the valve, and whether the catheter is antibiotic impregnated or not [46, 47]. The use of antibiotic-impregnated shunts as a first option in patients of all ages in the UK was an important finding in order to reduce the risk, harm, and cost associated with shunt infection [48]. While the evidence does support insertion of an antibiotic impregnated shunt as the first shunt inserted [47, 48], the cost factor also has to be included into the decision-making curve. This issue is perhaps even more relevant issue in regions where the condition is more prevalent [6]. There are also several technical issues related to the most appropriate insertion site, i.e., frontal vs occipital or whether adjunctive tools are required to optimize ventricular catheter placement [49, 50]. Detailed discussions of these issues fall outside the scope of this article.

Perhaps the most important detail for optimizing outcome from VPS surgery is compliance with a carefully formulated institutional protocol, incorporating the broader guidelines and modified for the particular geographical context. The complication rate of VPS insertion in the context of PIH is also considered to be higher than in other causes of hydrocephalus [5].

Neuroendoscopy

While *ETV* is a well-established surgical treatment option in triventricular or obstructive hydrocephalus, the success rate in hydrocephalus secondary to infection has been reported to be markedly lower at around 55.9–56.4% [7, 51, 52].

Scarring of the ependyma, turbid CSF, distorted ventricular anatomy, thickening of the third ventricle floor, and septations in the ventricular and cisternal spaces make endoscopic surgery in PIH difficulties encountered in PIH, and influence the intention to treat in these cases. The use of ETV as the ab initio choice of treatment in PIH has been considered, with most arguments favoring this approach described in the context of tuberculous meningitis [53, 54]. Poor results from ETV in the context of PIH have largely favored the use of VPS as a preferred first treatment option, especially in neonates [5, 7, 55]. Defining the outcome after an ETV can also be challenging, given the subtlety of clinical findings and limited sensitivity of radiological features [56].

The options for neuroendoscopic surgery in PIH are considerable and include ETV alone or combined with choroid plexus coagulation (CPC), endoscopic septostomy, foraminoplasty, aqueductoplasty, membrane fenestration, endoscopic guidance for ventricular catheter insertion, or removal and endoscopic lavage [4, 5, 57].

While the description of combining *ETV with CPC* as a treatment option for hydrocephalus has been around for a while [58], the use of this procedure in the context of refractory hydrocephalus cases, was largely re-invigorated by work done in Uganda on neonates with various etiologies of hydrocephalus [7, 59]. The combination of ETV and CPC in the PIH group of this study demonstrated less benefit when compared to results in the overall cohort [59]. Results from groups performing ETV and CPC in North America, appeared to be less promising [55].

Endoscopic septostomy provides an option that has good benefit with less associated risk. The indications for this procedure should be carefully chosen, and they are usually considered in the context of an isolated lateral ventricle, usually due to obstruction at the foramen of Monro or septum pellucidum cyst [44, 60, 61]. The septostomy may decrease the number of ventricular catheters required. A *foraminoplasty* is also an option, but carries the additional risk of injury to the fornix, adjacent veins, or hypothalamus [60]. The optimal entry point and trajectory for performing this procedure using a rigid endoscope is still unclear, but can be performed through a standard precoronal burrhole, using Kocher's point, providing the additional benefit of being able to perform an ETV using the same approach [62].

Endoscopic aqueductoplasty is a described technique to treat hydrocephalus due to aqueduct stenosis or an entrapped fourth ventricle [63]. The risk of injury to the peri-aqueductal gray matter resulting in disturbances of conjugate vision or trochlear nerve palsy should always be considered and preempted. The additional endoscopic placement of a stent across the aqueduct to maintain patency has been recommended [64].

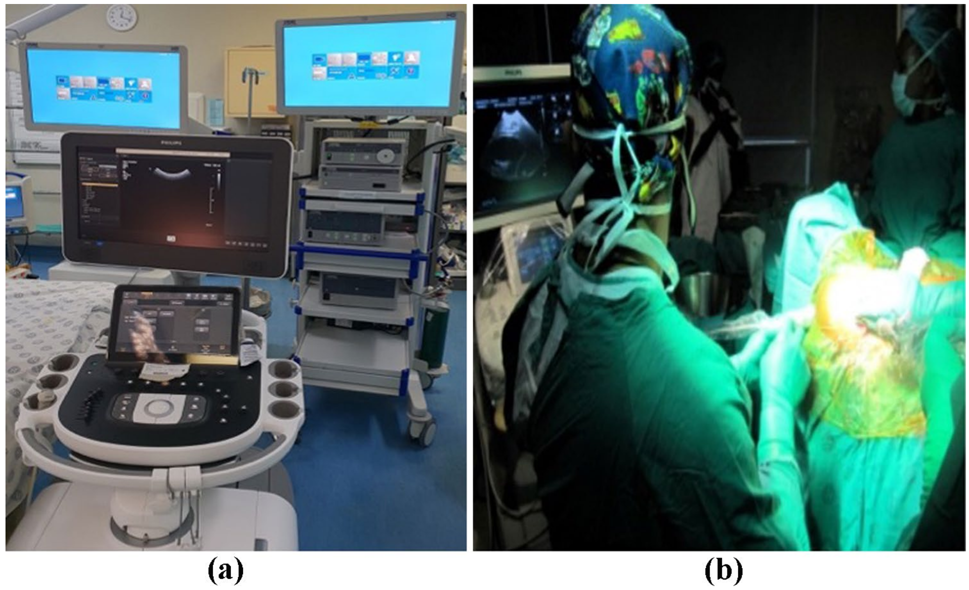

Fig. 4 **a** Ergonomic layout showing positions of the ultrasound machine during ultrasound-guided endoscopic procedures, **b** Surgeon position during endoscopic procedure with intra-operative ultrasound guidance

Endoscopic membrane fenestration in the management of complex or multiloculated hydrocephalus has been widely described as the preferred surgical treatment option [57, 65–67]. The distorted ventricular anatomy and scarring of the ependymal walls make the procedure technically quite challenging. The goal of the surgery is to communicate as many of the compartments as possible, ideally into a single communicating ventricular system, which requires insertion of a single ventricular catheter. The success rate of ETV alone or in combination with CPC in multiloculated hydrocephalus is poor [68].

Endoscopy-assisted ventricular catheter insertion or removal is a useful technique especially in cases where the ventricular anatomy is distorted or where the ventricular catheter tip is thought to be tethered by choroid plexus or fibrotic tissue. Endoscopy-guided insertion of the ventricular catheter to ensure that it is optimally placed to drain the various fenestrated locules is a very useful adjunct [57, 69, 70]. The use of neuronavigation to guide the entry point and initial trajectory of the endoscope has been advocated, but the CSF shift encountered after entry in to the cyst cavity limits the usefulness of this adjunctive tool [26, 71].

Neuroendoscopic ventricular lavage represents a method of evacuating the inflammatory debris and pus in the ventricles. It is a temporizing measure and has been described more extensively under this section above.

Adjuncts to neuroendoscopic techniques

Adjuncts in the use of neuroendoscopy to treat post-infectious or multiloculated hydrocephalus, which include the use of neuronavigation and intra-operative imaging, have increasingly become a standard of care.

Navigation to plan the entry point of the endoscope as well as the initial trajectory of the endoscope is valuable in refining operative planning and intraoperative orientation [26]. A study from 2009 described the additional benefit of using the navigation probe tip as the first fenestration tool, it also found that the CSF volume shifts were not a problem [72]. A subsequent study, however, described the combined use of intraoperative MRI combined with neuronavigation

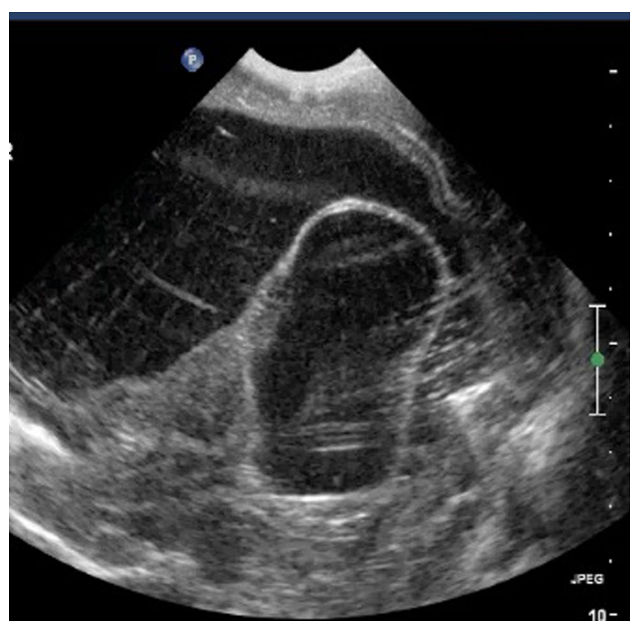

Fig. 5 Sagittal ultrasound ventriculography image demonstrating isolated cystic lesion in the lateral ventricle, showing endoscope tip in the inferior aspct, prior to endoscopic fenestration

as helpful in redefining targets and documenting CSF and brain shift [73]. The use of intraoperative ultrasound to guide neuroendoscopic procedures (Fig. 4a, b) especially for fenestration of loculations and cysts has been described as very useful in providing real-time guidance of the scope, detecting blood vessels, and confirming adequate membrane fenestration (Fig. 5) [15, 74, 75].

Outcomes

PIH contributes significantly to the overall types and numbers of hydrocephalus [4, 6]. In PIH, perhaps more so than in any other condition in neurosurgery, patient selection plays an important role in outcome, a significant difference in functional outcome between the shunt-treated and non-shunt-treated patients. Infants with PIH who were treated endoscopically were also more likely to have had a less severe inflammatory brain insult. Of the patients treated successfully for PIH who survived more than 5 years, more than a third appear to be severely disabled from the initial infection, as determined by their ability to independently perform basic activities of daily living [7]. The outcome of the disease process relates to the extent of the parenchymal injury and the treatment of raised intracranial pressure due to hydrocephalus that commonly complicates its course [7, 12].

Conclusion

The surgical treatment of PIH remains a challenging prospect for pediatric neurosurgeons. Despite the early promise of advances in the VPS technology and endoscopic techniques, the outcome in this group of patients remains unsatisfactory. Multiloculated hydrocephalus as a complication of the inflammatory process in PIH represents a further obstacle in the management algorithm. While there are various endoscopic options in this group, timeous placement of the appropriate VPS is still the pillar of management.

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Declarations

Conflict of interest The authors have no conflict of interest to declare.

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