Longstanding overt ventriculomegaly in adults: pitfalls in treatment with endoscopic third ventriculostomy

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Object. The recently described condition of longstanding overt ventriculomegaly in adults (LOVA) has not been defined in terms of the need for intervention, timing of intervention, and ideal treatment. The purpose of this review was to evaluate the role of endoscopic third ventriculostomy (ETV) in the treatment of LOVA.

Methods. Data collected in six patients with LOVA who had undergone ETV were reviewed retrospectively in terms of the definition of treatment success, rates of success, complications, and outcome. All six patients presented with headache disorders. In all patients, triventricular hydrocephalus had been diagnosed as aqueductal stenosis, and head circumference measurements were above the 98th percentile. All six had undergone successful ETV as documented by the free flow of cerebrospinal fluid into the basal cisterns, which remained open throughout the follow-up period. After the procedure, one patient experienced a mild degree of difficulty with short-term memory. Five patients remained symptomatic or had symptoms requiring further treatment 3 months to 3 years after ETV. Four patients received ventriculoperitoneal shunts, and one underwent venous stenting for high intracranial pressure after successful ETV. In two patients in whom aqueductal stenosis had been diagnosed, the sylvian aqueduct was patent after the procedure.

Conclusions. In LOVA patients who present with headaches, ETV may not lead to improvement in the headaches. Despite the presence of triventricular hydrocephalus, closure of the aqueduct may be a secondary phenomenon, and flow through the aqueduct may be reestablished after ETV. If intracranial hypertension persists after successful ETV, its cause may be increased venous sinus pressure.

KEY WORDS • aqueductal stenosis • compensated hydrocephalus • normal-pressure hydrocephalus • endoscopic third ventriculostomy

THE TERM “LOVA” was first used by Oi and colleagues²⁴ to define a condition in young adults with obviously chronic hydrocephalus that had begun before their cranial sutures fused because their head circumference was more than two standard deviations above the 98th percentile. The event causing the hydrocephalus could not be determined in any of the patients, whose hydrocephalus was described as severe. The nomenclature associated with this condition is confusing, and a consensus regarding how and when to treat it is lacking. The purpose of this study was to analyze the results of

ETV in the management of LOVA in terms of its safety and efficacy.

CLINICAL MATERIAL AND METHODS

Between 1992 and 2006, six patients (two males and four females) were identified as having LOVA and underwent ETV as part of their treatment (Table 1). The patients ranged from 16 to 55 years old (mean age 34 years) on first presentation. All patients had clearly macrocephalic head circumferences and longstanding triventricular hydrocephalus. The large head implied that the process leading to the hydrocephalus began before closure of the sutures and most likely began before the age of 2 years. No patient had a history that suggested an initial cause of the hydrocephalus, such as brain tumor, intracranial hemorrhage, or meningitis.

Abbreviations used in this paper: CSF = cerebrospinal fluid; CT = computed tomography; ETV = endoscopic third ventriculostomy; ICP = intracranial pressure; LOVA = longstanding overt ventriculomegaly in adults; MR = magnetic resonance; NPH = normal-pressure hydrocephalus; VP = ventriculoperitoneal.

TABLE 1
Summary of clinical characteristics in six adults with LOV*

Case No.	Age at Dx (yrs), Sex	Presenting Symptoms	First Treatment	Complication	Final Treatment	Follow-Up (yrs)
1	16, F	headache	ETV	short-term memory difficulty	ETV	8
2	22, M	headache	ETV	none	shunt	8
3	26, F	headache	ETV	none	shunt	6
4	55, M	headache, urinary frequency, gait disturbance	ETV	none	shunt	4
5	52, F	headache	ETV	none	shunt	0.5
6	32, F	headache	shunt	shunt infection	venous stent	0.33

* Dx = diagnosis.

Four patients underwent their first imaging study given the sole symptom of headaches. One patient presented at the age of 55 years with severe headaches, gait disturbance, and urinary frequency. In the sixth patient headaches played a role in her presentation, but her course was complicated by an unexpected decline in cognitive performance in high school. Only one patient exhibited the signs and symptoms usually associated with NPH, including gait disturbance and urinary incontinence.¹¹

Five of the six patients underwent ETV at my institution; one was referred after symptoms failed to improve after an ETV performed elsewhere. Five patients underwent ETV as their first procedure. One patient underwent ETV for persistent severe headaches and multiple shunt complications, including infection and failure of the abdomen to absorb CSF. In all patients MR imaging studies showed flow through the stoma. After injecting iodinated myelographic dye into the ventricles through a tapping reservoir, it was apparent in five patients that flow through the stoma was unimpeded: CSF flowed into the basal cisterns and over the convexities (Fig. 1). None of these patients underwent ICP monitoring as part of the workup for hydrocephalus therapy before the first treatment with either ETV (five patients) or ventriculoperitoneal shunt (one patient).

RESULTS

In terms of immediate and long-term CSF flow through the endoscopically created stoma, all procedures were successful. All patients underwent MR imaging studies of CSF flow that confirmed free pulsatile flow through the created stoma. Only one patient, a 16-year-old girl, underwent ETV as the sole procedure. She had presented with morning headaches, declining school performance, and a large head. Magnetic resonance images showed triventricular hydrocephalus. After ETV her headaches resolved, and 48 hours of ICP monitoring via an implanted external ventricular drain showed normal ICP. Four years after treatment, follow-up data in this patient showed no signs of neurological deficit or increased ICP. She reported difficulty with her short-term memory but demonstrated no change in her school performance. This probably permanent but mild difficulty with short-term memory was the only documented complication among patients in this study. Interestingly, late MR imaging studies revealed free CSF flow through the sylvian aqueduct, which had not been present before the ETV.

There were no deaths, and no complications were revealed by general physical or neurological examinations. Five patients underwent ETV as a first procedure. Postoperatively, one of these patients had significantly increased ICP that persisted for 5 days. During hospitalization for this problem, she underwent VP shunt placement despite the free flow of contrast material into the basal cisterns and cortical subarachnoid spaces. Two patients, who had presented with headaches, were symptom free for 18 months and 3 years. Thereafter, they suffered progressively increasing headache disorders refractory to medical management, and they underwent shunting procedures. Despite several admissions for ICP monitoring, headaches remain unrelieved in the three patients who underwent shunting as a salvage procedure.

One patient, who remained symptomatic after a VP shunt had been placed, underwent ETV. Her course was complicated by several infections. The VP shunt was converted to a pleural shunt for failure of the peritoneum to absorb spinal fluid. This patient initially presented with a headache disorder that led to the diagnosis of hydrocephalus and shunt implantation. Her headaches did not respond to adjustment of the programmable shunt valve and documentation of normal ICP during chronic monitoring. The shunt was removed. When her ICP was found to be high after shunt removal, she underwent ETV.^{1,29} Her headaches persisted, and the shunt was reinserted at the request of the patient, who believed that the headaches had worsened after the ETV and shunt removal despite a normal ICP. A second patient who was treated for headaches that persisted after an ETV despite normal CSF flow is discussed next.

ILLUSTRATIVE CASE

History and Examination. This 32-year-old mildly obese woman presented to another center with chronic daily severe headaches. Imaging studies, including CT and MR imaging, showed triventricular hydrocephalus. No flow was seen through the sylvian aqueduct. Initial shunting was complicated by shunt infection and several subsequent revisions. Her abdomen failed to absorb CSF, and an abdominal pseudocyst developed. The shunt was then removed, and an ETV was performed without complications. The patient was discharged but continued to have intractable headaches.

When first evaluated at my institution, the patient was

FIG. 1. Cisternogram demonstrating CSF flow through the stoma created by the ETV.

in significant distress. She had many scalp and abdominal incisions, but results of neurological and general physical examinations were otherwise normal. Magnetic resonance images showed moderate ventriculomegaly and an open sylvian aqueduct (Fig. 2). Magnetic resonance venography revealed bilateral stenosis of the transverse sinuses.

Treatment. The patient underwent insertion of a ventricular access device so that her ICP could be assessed with ease. A transducer was also placed for chronic monitoring of ICP. The next day an iohexol cisternogram showed flow in the aqueduct and rapid spread of the dye into the basal cisterns and subarachnoid spaces. When the patient was awake and erect, her ICP measured 15 to 25 mm Hg. When she was recumbent, a position that she found uncomfortable because of the headaches, her ICP was in the high 20s. While sleeping in the semisitting position, her ICP was frequently between 35 and 40 mm Hg. Her ICP did not change when dexamethasone or acetazolamide was administered.

The patient was offered reimplantation of a lumboperitoneal shunt to manage her condition, a form of pseudotumor cerebri. Due to recent experiences with venous stenting in the context of pseudotumor cerebri, it was also suggested that she undergo retrograde venography together with measurement of dural venous sinus pressure and possible placement of a venous stent (Fig. 3).^{13–15,26,27} The initial pressure differential of 9 mm Hg across the point of constriction of the transverse sinus resolved. Pressure both above and below the stent was 5 mm Hg. Intracranial pressure monitoring after the procedure confirmed that

FIG. 2. Case 6. Magnetic resonance image obtained in a patient treated with ETV for hydrocephalus due to aqueductal stenosis, revealing an open sylvian aqueduct (arrow).

her ICP was normal. The patient was discharged for follow up.

Posttreatment Course. She was readmitted 3 weeks after treatment with continued headaches. Intracranial pressure monitoring was instituted with an implanted ventricular reservoir. On this second admission, her ICP was normal while she was recumbent and when upright.

DISCUSSION

Before the development and popularization of valve-regulated shunts in the 1950s, very few babies with a diagnosis of hydrocephalus received treatment. Most patients died during infancy, and the cognitive outcome of survivors was dismal.^{18–20} Ventricular shunting in babies did not become a routine treatment until the 1960s. At that time, hydrocephalus was difficult to diagnose and only done so in severe cases. Children with large heads but no overt signs of intracranial hypertension were rarely treated because the only way to determine the cause of the megalencephaly was to perform invasive procedures such as air ventriculography or even angiography. In that era, moderate ventriculomegaly would not have been diagnosed in a large percentage of patients. Now in their 40s and 50s, these patients have lived in a compensated state for decades.

In 1973 the first CT unit was installed in the US. Soon thereafter real-time ultrasonography was developed to the point that the anatomy of the lateral ventricles could be defined noninvasively when the anterior fontanel was open. At this point neurosurgeons were faced with a large number of patients with moderate degrees of ventriculomegaly who had received no previous treatment. Potentially effective forms of therapy with shunts were available, however. The issues of how much hydrocephalus is too much and when a shunt would improve outcomes became major subjects for discussion and study.^{30,33} Unfortunately, firm answers to these questions are still not readily available.

FIG. 3. Case 6. *Left:* Angiogram showing stenosis of the right transverse sinus causing a significant pressure gradient. *Right:* Angiogram demonstrating resolution of the pressure gradient after placement of a venous stent.

There is no nomenclatural consensus in terms of patients without shunts but with large ventricles and no overt signs of increased ICP. Neither has the threshold for intervention been defined. Megaloencephaly with ventriculomegaly is almost certainly the substrate for the later development of NPH in the elderly.^{3,5,30} A significant percentage of patients with NPH who have responded to shunting have head circumferences above the 98th percentile. This finding is reassuring when examining potential candidates for the treatment of this condition.³⁻⁵ In this situation, it seems clear that an abnormality in CSF absorption leads to enlarged ventricles and a large head. These findings indicate that the process had begun before the cranial sutures fused in early childhood.

This situation is a chronically compensated state, and for each patient the cost of this compensation must be assessed. If treatment of the hydrocephalus were without risk, all of these patients should undergo shunt placement or ETV.³⁰ The more we seek information regarding risks and benefits, however, the more we realize that intervention does involve significant risks. During infancy and early childhood, the initial shunt insertion is associated with an 8% risk of infection. Fewer than half of the patients who receive a first shunt during childhood have working shunts 2 years later.¹⁶ Patients who undergo shunt placement in childhood have mortality rates of 1% per year, a rate that persists into adulthood.^{7,8,12,21,22} Late deaths have also been reported in patients in whom hydrocephalus is treated with ETV.¹²

This analysis of risk encourages a conservative approach, which entails awaiting the development of NPH in the aging population, overt signs of cognitive or motor deterioration, or signs of increased ICP before recommending intervention. A careful study by authors in Sweden showed results indicating that apparently asymptomatic patients with ventriculomegaly benefited significantly from treatment.¹⁷ The study data provide support for proactive treatment.

The group in the current study represents a broad spectrum of patients with the mildest form of chronically compensated hydrocephalus. A risk-benefit analysis in this group may therefore be the most difficult. At the other end

of the spectrum are patients with severely dilated ventricles, developmental delay, and a grossly abnormal head size. Such patients were the subject of a brief, provocative communication by Lorber²¹ entitled “Is your brain really necessary?,” which specifically featured a CT scan that had been obtained in a mathematics graduate student with massive ventriculomegaly.²¹ For this group of patients, Oi et al.²⁴ coined the term “LOVA” and found that the complication rate associated with shunting in these individuals was low.

The closely related syndrome of hydrocephalus in young and middle-aged adults⁹ relates to children with significant ventriculomegaly, some of whom also have large heads. Some of these patients have previously received shunts and either had the shunt removed or had a failed shunt without that diagnosis being considered important or with it being missed altogether. These patients have presented with subtle symptoms of insidious deterioration in cognitive and motor function. Many have headaches suggestive of mild increases in ICP. These patients challenge the concept that it is possible to have shunt-independent arrest of hydrocephalus and that all of these patients may suffer late deterioration years or decades later.³¹

Aqueductal stenosis is presumed to be the cause of hydrocephalus in a large percentage of patients with hydrocephalus without a clear origin and involving the lateral and third ventricles but not the fourth ventricle. In the context of sex-linked aqueductal stenosis, the aqueduct is closed by an anatomical obstruction. The latter is a genetic disorder found only in boys. The aqueduct is forked and does not allow CSF to pass from the third to the fourth ventricle. The aqueduct can be occluded by ependymitis from infection and by tumors of the tectum of the midbrain.

In animal models such as the HT rat, closure of the aqueduct follows the inward displacement of the temporal horns, leading to secondary closure of the aqueduct and triventricular hydrocephalus.²⁵ This situation also occurs in humans whose aqueduct is opened after a shunt repair.^{2,6,23} In two of the patients (Cases 1 and 6) in the present report, successful internal bypass of the aqueduct by

ETV led to its subsequent opening. I have been unable to find another case report involving opening of the aqueduct after ETV.

If the aqueduct closure is related to a more distal CSF absorptive difficulty, where is the source of that obstruction and what would be the effect of the internal bypass of the aqueduct? The patient in Case 6 provides a clear answer to that question. Her hydrocephalus resulted from congenital stenosis of the transverse sinuses. After the ETV, the aqueduct was shown to be open but ICP did not return to normal. The venous anomalies remained.

This situation is similar to cases of pseudotumor cerebri or the related condition of “normal-volume hydrocephalus,” a term used to refer to infantile hydrocephalus in older patients who become symptomatic at the time of shunt failure without ventriculomegaly.^{10,28} In normal-volume hydrocephalus, the ventricles communicate freely with the cortical subarachnoid space. Patients can be treated using lumboperitoneal shunts.³² Several of the patients treated with these shunts have undergone retrograde venography and showed increased pressure in the dural venous sinuses. This condition has been seen in patients with venous sinus stenosis due to skull base abnormalities such as Crouzon syndrome and achondroplasia. It has been postulated that all pseudotumor cerebri results from high pressure in the dural venous sinuses.¹⁵

Several authors have reported success in treating this condition by using venous stenting techniques.^{13,14,26,27} The patient in Case 6 in the present study had quite high ICP after the ETV. She was found to have bilateral transverse sinus stenosis with a high pressure gradient between the transverse and sigmoid sinuses. A venous stent was placed in this patient, and the pressure gradient resolved. Subsequent ICP monitoring has shown that her ICP is normal when she is either recumbent or upright.

CONCLUSIONS

The study data do not clarify what should be done in the context of seemingly asymptomatic patients with large heads and large ventricles. Neither do they help decide the form that treatment should take, that is, shunting or ETV. Nonetheless, several important conclusions can be derived from this report. In this context, chronic daily headaches are not necessarily caused by increased ICP and may not be ameliorated by intervention. In the absence of overt signs of intracranial hypertension, such as papilledema or increased ICP, headaches may not resolve. Endoscopic third ventriculostomy can be performed with reasonable safety in this patient population and can successfully reestablish normal CSF flow and dynamics. Unless ICP is monitored postoperatively, one cannot assume that it has normalized. If the patient remains symptomatic, further treatment may be needed.

What is the underlying cause of this form of chronic compensated hydrocephalus? Despite the significant degree of ventriculomegaly and large heads, five of the patients in the present study were neurologically normal before their first operation. After the first intervention, all were neurologically normal and independent. The teenager was successful in school, and all five of the adults were independent and employed. Terminal CSF absorption prob-

lems due to high pressure in the dural venous sinuses can lead to abnormalities in CSF flow and cause aqueductal stenosis that is reversible, as it was in two of the patients in this report. In a select group of these patients, ICP dynamics can be normalized by the use of venous stenting.

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