Clinical Neurology and Neurosurgery 183 (2019) 105366

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

The surgical results of endoscopic third ventriculostomy in long-standing overt ventriculomegaly in adults with papilledema

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ARTICLE INFO

Keywords:
Longstanding overt ventriculomegaly in adults
LOVA
Papilledema
Endoscopic third ventriculostomy
Hydrocephalus

ABSTRACT

Objective: Longstanding overt vetriculomegaly in adults (LOVA) is a type of chronic hydrocephalus presumed to begin during infancy, which manifests in adults after a long and slow clinical course. Only a quite small number of LOVA case series have been published, controversies regarding optimal management still exist. The authors describe a series of symptomatic LOVA patients with papilledema treated successfully using endoscopic third ventriculostomy (ETV) at a single institution.

Patients and methods: In the past 7 years, 4 LOVA patients with papilledema were surgically treated using ETV. Clinical features and neuroimaging of all patients were carefully reviewed retrospectively. Changes of the third ventricle transverse diameter, Evan's ratio, frontal occipital horn ratio after operation were measured.

Result: There were two males and two females, with a mean age of 24 (21–29) on first presentation. Presentation symptoms were visual problems (4 cases), headaches (3 cases), hemidysesthesia(1 case), and poor mobility(1 cases). Papilledema and increased intracranial pressure were identified in all 4 cases. The mean follow-up period of this series was 5 years (range 4–6 years). All patients reported improved vision function 3 months and experienced other symptom relief accompanying with normalized intracranial pressure after ETV and did not require any further surgical intervention.

Conclusions: Endoscopic third ventriculostomy provides an effective treatment for LOVA patients with papilledema, which can improve the symptoms of LOVA and relive papilledema. The fundoscopy is of great value in making decisions related to surgical intervention for LOVA patients.

1. Introduction

Long-standing overt ventriculomegaly in adults (LOVA) is an entity of progressive hydrocephalus firstly defined by Oi and colleagues in 2000. [1] In general, patients with LOVA have developed progressive symptoms of hydrocephalus before their cranial sutures fused, which resulted in their head circumference more than two standard deviations above the 98th percentile. Supratentorial ventriculomegaly and macrocephaly are well-known characteristics of LOVA, however, the underlying mechanism causing this phenomenon remains unclear. It is hypothesized that congenital stenosis of the aqueduct is the aetiopathogenic mechanism [1] and endoscopic third ventriculostomy (ETV) is recommended as one optional treatment for LOVA patients [1–3]. In spite of this, the diagnostic criteria and management strategy of this condition continue to be a topic of debate in the literature [2,4].

The clinical symptoms of LOVA which previously be reported in the literature [1,5] include macrocephaly with or without subnormal intelligence quotient(IQ), headache, dementia, gait disturbance, visual symptoms, urinary incontinence, vegetative state, kinetic mutism, apathetic consciousness and parkinsonism. The above mentioned symptoms are useful in establishing a diagnosis, however, most of them are of less value in choosing treatment for LOVA patients whose pathophysiological process is typically slow and progressive in nature. Moreover, loss in brain parenchyma plasticity makes it is difficult to predict the surgical outcomes of LOVA, no matter which surgical procedure is applied.

Papilledema is considered to be one of the most important signs of hydrocephalus and a critical determinant of the management strategy. [6–10] However, there are quite few reports about papilledema in LOVA patients and its role in treatment strategy. This case series collates outcome data from LOVA patients with papilledema treated using endoscopic third ventriculostomy (ETV) at our institution. It was a preliminary study to analyze the effect of ETV in improving symptoms, especially papilledema of LOVA patients.

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https://doi.org/10.1016/j.clineuro.2019.05.014
Received 25 February 2019; Received in revised form 9 May 2019; Accepted 13 May 2019
Available online 14 May 2019
0303-8467/

Table 1
Clinical and radiological criteria used to confirm the diagnosis of LOVA (adapted from Oi[1]et al).

1. Clinical symptoms including headaches, visual deterioration, diplopia, gait disturbance, imbalance,subnormal IQ, dementia, vegetative state, akinetic mutism, psychological disturbance
2. marocephaly (head circumference > 98th percentile in adulthood male 53.8 cm; female 52.9 cm).
3. Neuroimageing findings: triventriculomegaly involving the lateral and third ventricles, with cortical sulcal effacement and expanded or destruction of the sella turcica as evidence of long-standing ventriculomegaly
4. Absence of a secondary cause for aqueductal stenosis in adulthood (e.g. previous meningitis, subarachnoid heamorrhage, traumatic brain injury)

2. Material and methods

2.1. Clinical features

Between 2012 and 2018, there were altogether 72 patients with hydrocephalus were treated with ETV in our institution. 4 patients among them were identified as having LOVA by virtue of all patients meeting the clinical and radiological criteria (Table 1) for LOVA established by Oi et al. [1]. Following the pre-operative workups for hydrocephalus patients in our institution, visual acuity inspection, fundus color photography and lumber puncture with manometry of ICP preoperatively were carried out in all patients. None of these patients underwent ICP monitoring as part of the workup for hydrocephalus therapy before treatment. Data regarding age, gender and onset of symptoms, clinical examination and radiological findings at the time of diagnosis, visual acuity, fundus photography, and intraoperative videos, complications related to the surgical procedure, postoperative outcome, and time to the latest follow-up were carefully retrospectively reviewed. The study was approved by medical research ethics committee of The First Affiliated Hospital of Nanchang University and adheres to Declaration of Helsinki. All patients' questions were answered, and informed consents were obtained for the procedures.

2.2. Treatments

Since aqueduct stenosis and intracranial hypertension were identified in all cases preoperatively (Table 2), ETV was chosen as the treatment in the first instance. None of the patients underwent the insertion of cerebrospinal fluid (CSF) diversion devices before ETV. The ETV procedures underwent using the same standardized operative technique, outlined by Al-Jumaily et al. [11]. The single burr hole was located in the mid-pupillary line just 1 cm anterior to the coronal suture. A stoma in the floor of third ventricle was created using a figure-of eight balloon under visualization of rigid endoscopes. If present, any secondary membrane in the prepontine cistern was opened. All operations were performed by the senior author (Donghai Li) via a rigid 0° endoscope (Karl Storz GmbH& Co, Tuttlingen, Gemany).

2.3. Neuroimaging studies

The morphology of hydrocephalus was assessed in the image workstation, according to the third ventricle transverse diameter, Evan's ratio, frontal occipital horn ratio (FOHR). Postoperative data were recorded at the last follow-up.

3. Results

3.1. Preoperative findings

Table 3 depicts the demographics, presenting symptoms and outcomes for the 4 cases of LOVA treated at our institution from 2012 to 2018. There were two males and two females, with a mean age of 24(21–29) on first presentation. No patient had a history that suggested an initial cause of the hydrocephalus, such as brain tumor, intracranial hemorrhage, or meningitis. All patients had clearly macrocephalic head circumferences with the mean number of 58.5 cm (56–62 cm). Presentation symptoms were visual problems (4 cases), headaches (3 cases), hemidysesthesia (1 case), and poor mobility (1 case). Papilledema and intracranial hypertension were demonstrated in all 4 cases. The ICP ranges from 200 to 400 mmH_20, with mean of 285 mmH_20. Radiological images showed triventriculomegaly, aqueduct stenosis in all patients (Table 2). A pathological sella turcica was observed in all patients. It was enlarged in 2 cases and destroyed (Fig. 1) in 3 cases.

3.2. Outcome

All patients reported either improvement or halt of progression in their presenting symptoms. All patients reported improved vision function and did not require any

further intervention, three of them demonstrated papilledema disappearance 3 months after operation. The papilledema of the other patient improved 3 months after ETV, which completely recovered 1 year after ETV (Fig. 1). The intracranial pressure of all the patients were within the normal range (mean 160 mm H_20) 3 months after ETV. The mean follow-up period was 4 years (4 years to 6 years). All cases were shunt free at the last follow-up.

3.3. Postoperative complications

No surgical mortality or permanent complications occurred. One patient experienced meningitis two days after operation, which resolved with antibiotics. Most of the patients were discharged one week after operation. None of the patients died until the last follow-up.

3.4. Neuroimaging findings

Pre-and post-operative MRI findings are listed in Talbe2. The transverse diameter of the third ventricle were reduced from mean 15.4 to11.5 mm.The Evan's ratio were reduced from mean 0.41 to 0.37. The FOHR exhibited a reduction. The sulcal effacement were improved after

Table 2
Neuroimaging findings of 4 LOVA patients associated with papilledema.

Case	Extent of hydrocephalus						Other findings
	V3 transverse diameter(mm)		Evan's ratio		Frontal and occipital horn ratio		
	Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op	
1	13.6	9.8	0.41	0.37	0.63	0.50	Aqueduct stenosis, triventriculomegaly, destroyed sella turcica
2	15.4	10.6	0.38	0.34	0.56	0.49	Aqueduct stenosis, triventriculomegaly, expanded sella turcica, sulcal effacement
3	17.2	14.2	0.45	0.42	0.51	0.48	Aqueduct stenosis, triventriculomegaly, destroyed sella turcica, sulcal effacement
4	15.2	11.3	0.40	0.36	0.53	0.49	Aqueduct stenosis, triventriculomegaly, expanded sella turcica,
mean	15.4	11.5	0.41	0.37	0.56	0.49	

Table 3
Case series of 4 patients diagnosed with LOVA and treated with ETV. Outcome were reviewed at 3 months and subsequently between 6 months- 6 years post-operatively.

Case	Gender	Presenting symptoms	Age at presentation	Head circumference	Pre-op Papilledema	Pre-op ICP mmH20 (mean 285)	Operative complications	Post-op(3 months after ETV) ICP mmH20 (mean 160)	Outcome at 3 months	Outcome beyond 3 months
1	M	Hemidysesthesia, blurred vision, Headaches	21	56cm	Yes	290	No	150	Hemidysesthesia improved, vision improved, No papilledema	6 years: no deterioration
2	F	Decreased vision, Headaches,	24	59cm	Yes	250	No	160	Reduced headache frequency, improved papilledema	5 years: No headache, No papilledema
3	M	Vision impairment, Headaches,	22	62 cm	Yes	400	No	175	Vision improved, Reduced headache frequency, No papilledema	5 years: normal vision, no headaches
4	F	Poor mobility and blurred vision	29	57cm	Yes	200	meningitis	155	Improved mobility and vision, No papilledema	4 years: Improved mobility and vision

surgery both in case 2 and case 3.

4. Discussion

All the 4 patients in present study meets the diagnosis criteria established by Oi et al. [1] which includes radiological and clinical criterion. The age of symptom onset of LOVA is from 21 to 29 in our case series. In 2016, after reviewing all the reports on LOVA, Ved et al [3] found the onset of LOVA can occur at any stage in adulthood and there is no clear- cut differences in patient sex. Early diagnosis and treatment may help to maximize the effect of surgical intervention to halt the disease process. Nevertheless, the various, indistinguishable, “arrest” symptoms and non –specific signs make early recognize and diagnosis of LOVA still be a big challenge.

The onset symptom of LOVA is of great diversity. Besides the common features such as headaches and imbalance [11]. Other cognitive and psychological problems such as decline in memory, dementia, sub-normal IQs, anxiety and disinhibition has also been reported in LOVA [5 [11,12]. Quite interesting, all of patients (100%) complained visual problems at presentation after excluding primary ophthalmology problems in our series, which is an indirect proof of intracranial hypertension. In 2017, Guillermo et al. [2], pointed out the diagnostic criterion proposed by Oi mixed symptoms and clinical signs, which should be clear differentiated. In fact, macrocephaly is the only sign in Oi’s diagnosis criterion. There is lack of attention to the importance of papilledema, which is one of the important signs of hydrocephalus. According to Ibanez-Botella's report [2], which is the largest case series (including 27 LOVA patients) by far, blurred vison and papilledema was demonstrated in 7 (25.9%) patients, unfortunately, there was no outcome details about the papilledema after ETV. In Ved’s report, only one (7.1%) of the 14 patients complained diplopia, but information about whether existence of papilledema cannot be confirmed in all cases [3]. In Al-Jumaily’s report, visual obscuration is found in 8 patients (40%), still no result of the fundus examination [11]. From the result of our series, it is obviously that the neglected papilledema seems to be a more common sign in LOVA patients than previously believed. We are not explaining that papilledema should be considered as the second sign in diagnosis criterion of LOVA, but its value should not be underestimated when choose the appropriate pre-operative workup in LOVA.

Overt lateral and third ventricle enlargement is one typical neuroimaging finding of LOVA, which is identified in all our cases. Simultaneous lumbar puncture indicated raised ICP in all cases. Ventirculomegaly may result from a number of conditions [13], such as loss of brain substance after trauma, compliant brain accommodating an increase volume of CSF without raised ICP, altered CSF dynamics making non-compliant brain enlarge. However, when ventriculomegly is long-standing, brain viscoelastic properties and the pressure- volume relationship may be altered such that ventricles remain expanded even when ICP is normal [14,15]. The relationship between ventricle size and ICP is poorly understood [9].Thus, it is difficult to make clear definite ICP value with no use of measurement in patient with ventriculomegly. Hyareh [16] stated that discus opticus edema occurs mechanically when ICP rises within the confined skull cavity. Previous report described the clinical implications of papilledema in adults with ventriculomegly [9]. Even the absence of papilledema could be a false-negative sign of raised ICP, the presence of papilledema is the most useful indicator for preoperative confirmation of intracranial hypertension [17]. This can also be reflected the coherence result of ICP value and papilledema in our study both preoperatively and postoperatively.

Since the introduction of LOVA, it represents just a small group of idiopathic hydrocephalus patients. The unique pathophysiological, chronological changing in brain parenchyma and diversity of symptoms make its surgical outcome difficult to predict. Most previous reports advocated surgery for symptomatic cases of LOVA. However, the debate

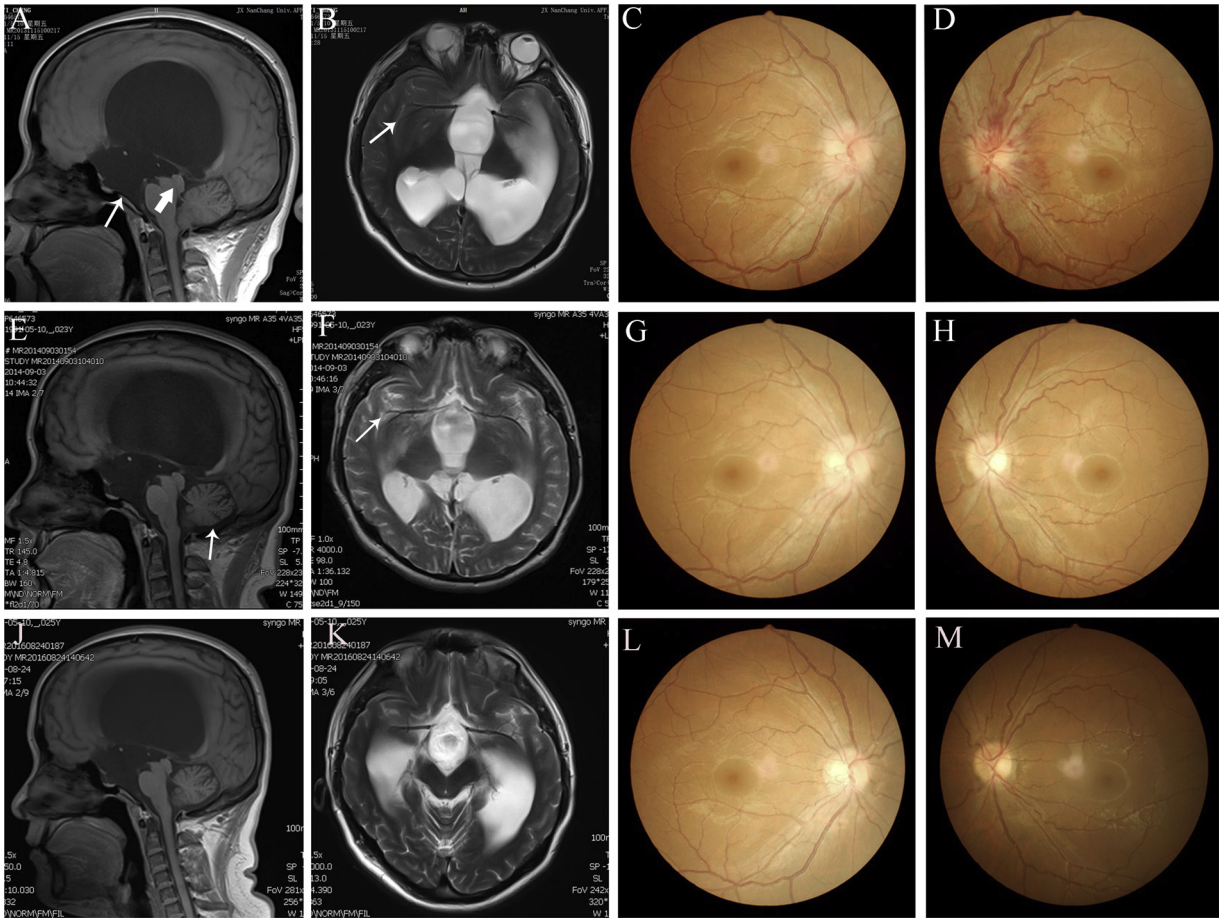

Fig. 1. Radiological and Fundus photography of LOVA patients with preoperative papilledema. (Case 3). A. Preoperative T1 sagittal MR image, the small arrow indicates the destroyed sellar turcica, the big arrow indicates the stenosis of sylvian aqueduct. B: Preoperative T2 axial MR image shows the triventriculomegaly, the arrow indicates the sulcal effacement in the Sylivan fissure. C and D: Sever optic disc edema (papilledema) is manifested before operation. E: The post-operative (1 year) T1 sagittal MR image, the arrow indicates the enlarged subarachnoid space in posterior fossa. F. The post-operative (1 year) T2 axial MR image indicates the reappearance of sulci, the arrow showed the sylvian fissure. G and H: the papilledema has improved 3 months after ETV.J and K: MRI images 3 years after ETV. L and M: the picture of optic disc 18 months after ETV.

between ETV versus CSF shunt diversion has lasted over a decade [1,18–22]. In the present series, we demonstrated that the symptoms, papilledema and intracranial hypertension of patients had improved 3 months after ETV, meanwhile the neuroimaging findings showed both the transvers diameter of third ventricle and FOHR ratio reduced after ETV.

It is deem that congenital stenosis of the aqueduct of Sylvius as aetiopathogenic mechanism, therefore, recommended endoscopic third ventriculostomy (ETV) as the treatment of choice for LOVA [1]. In our present series, stenosis of aqueduct is identified in all cases. Al-jumaily et al. [11] retrospectively analysis 20 cases of LOVA, 90% patients had improvement and 80% had improvement in balance after ETV. In 2016, Ronak et al. [3] reported 14 cases of LOVA treated by ETV, all patients (100%) reported improvement or halt of the progression in presenting symptoms 3 months post-operatively. Similar to majority previous studies in the literature [11,12,23], all (100%) the LOVA patients in this series achieve post-operative clinical improvement in symptoms and papilledema after ETV. Despite the above impressive outcomes after ETV, other works report less promising results. Rekate [4] published his experience in six cases treated endoscopically, in which only one patient had a positive ETV outcome at 4-year-follow-up, other patients required a secondary procedure for persistent symptoms: shunt insertion, repeat ETV or venous stenting. Furthermore, studies have presented patients in whom ETV did not facilitate objective improvement in cognitive or neuropsychological tests [11].

Due to the enormous craniocerebral disproportion [21,22], shunt therapy in LOVA is associated with a high risk of over-drainage and its sequela(subdural hygroma or hematoma, silt ventricle). High infection (and thus revision) rates for shunt devices is another drawbacks of shunt procedure for LOVA. However, in an study including 23 LOVA patients, 82% patient demonstrated clinical improvement after gravitational shunt insertion and the author recommend gravitational shunt insertion are a viable alternative to ETV in the management of LOVA [21]. In addition, Ono reported a case of LOVA who failed after initial ETV achieved improvement in memory after secondary pressure programmable vale VP shunt [20]. The above data highlighted the importance of continued follow-up whatever intervention is implemented.

This study has some limitations. First, it is a retrospective study with quite small case number. Just like the statement of Al-jumaily, “the LOVA condition becomes less frequent with newer generations of hydrocephalic children having their condition recognized sooner with subsequent early and effective management of their hydrocephalus”. Second, there is no other assessment to evaluate the ETV success rate except papilledema obliteration, clinical symptoms improvement and postoperative ICP manometry. Third, ICP recording was not used both in diagnosis and in the subsequent assessment of the treatment results. The importance role of ICP recording has already been highlighted by Rekate [4] and Horachajadsa [25].A comparative study between LOVA patients with papilledema and without papilledema is yet to be completed, such work could highlight the neglected value of papilledema

and provide useful data to aid therapeutic decision-making for LOVA patients.

5. Conclusion

Based on our results, we believe that endoscopic third ventriculostomy provides an effective treatment for LOVA patients with papilledema, which can improve the symptoms of LOVA and relive papilledema. Papilledema may probably be a more common sign encountered in LOVA patients than previously reported. The fundoscopy is of great value in making decisions related to surgical intervention for LOVA patients.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Disclosure

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

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