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Endoscopic third ventriculostomy for the management of children with cerebrospinal fluid disorders, ventriculomegaly, and associated Chiari I malformation

Amparo Saenz *, Rory J. Piper, Dominic Thompson, M Zubair Tahir

Department of Paediatric Neurosurgery, Great Ormond Street Hospital for Children NHS Trust, Great Ormond Street, London, WC1N 3JH, UK

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ABSTRACT

Objectives: Our objective was to review the outcomes of children with CIM and associated cerebrospinal fluid (CSF) disorders and ventriculomegaly undergoing endoscopic third ventriculostomy (ETV) as a primary intervention.

Materials and methods: A retrospective, single-center, observational cohort study was conducted of consecutive children with CIM with associated CSF disorders and ventriculomegaly treated first by ETV between January 2014 and December 2020.

Results: Raised intracranial pressure symptoms were the most frequent in ten patients, followed by posterior fossa and syrinx symptoms in three cases. One patient had a later stoma closure and required a shunt insertion. The success rate of the ETV in the cohort was 92% (11/12). There was no surgical mortality in our series. No other complications were reported. The median herniation of the tonsils was not statistically different in the pre vs. post-operative MRI (1.14 vs. 0.94, $p=0.1$). However, the median Evan's index (0.4 vs. 0.36, $p<0.01$) and the median diameter of the third ventricle (1.35 vs. 0.76, $p<0.01$) were statistically different between the two measurements. The preoperative length of the syrinx did not change significantly compared with the post-operative (5 vs. 1; $p=0.052$); nevertheless, the median transverse diameter of the syrinx did improve significantly after the surgery (0.75 vs. 0.32, $p=0.03$).

Conclusions: Our study supports ETV's safety and effectiveness for managing children with CSF disorders, ventriculomegaly, and associated CIM

1. Introduction

Chiari I malformation (CIM) is a structural abnormality characterized by the herniation of the cerebellar tonsils through the foramen magnum.[1] However, CIM should not be considered a single diagnostic entity but rather herniation of the hindbrain should be considered as a consequence of different pathophysiological processes.[2] Cerebrospinal fluid (CSF) disturbances are among the most frequently described etiologies for tonsillar ectopia.[3]

Overt hydrocephalus is present in 6.5–9.6% of patients with CIM and there is a general consensus within the literature that the hydrocephalus should be treated before foramen magnum decompression (FMD). However, more subtle disorders of CSF circulation may accompany CIM and might also benefit from intracranial pressure-directed therapy.[2]

The treatment of patients co-presenting with CIM and CSF disorders is another point of contention. Whilst it could be argued that FMD may relieve outflow obstruction at the foramen magnum and consequently resolve the hydrocephalus, a reasonable body of evidence implies that preoperative hydrocephalus is associated with CSF complications following FMD surgery.[1,4] This forms, in part, the basis for the recommendation for primary CSF diversion before consideration of FMD.[2,5] Furthermore, there have been a number of studies that suggest that primary CSF diversion in CIM could avoid the need for FMD in the future.[6]

In the literature, there are cohort studies analyzing the long-term outcomes of endoscopic third ventriculostomy (ETV) in CIM with overt hydrocephalus.[3,6] However, these two studies were in adult or mixed adult and pediatric patients and the pathophysiology behind CIM in adults and pediatric patients differs significantly.

Our objective, therefore, was to investigate the outcomes of children

* Corresponding author. Dir.: Great Ormond Street, London, WC1N 3JH, UK.
E-mail addresses: amparo_saenz@hotmail.com, amparo.saenz@gosh.nhs.uk (A. Saenz).

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with CIM and associated CSF disorders and ventriculomegaly undergoing ETV as the primary intervention.

2. Materials and methods

2.1. Patient population

A retrospective, single-center, observational cohort study of consecutive children with CIM and associated ventriculomegaly treated first by ETV was conducted. Patients were identified from the operative logs at Great Ormond Street Hospital between January 2014 and December 2020. Exclusion criteria included the presence of aqueduct stenosis, any other type of posterior fossa malformation other than CIM, prior FMD, prior ventriculoperitoneal shunt (VPS), incomplete pre-or post-operative magnetic resonance imaging (MRI) and/or completion of less than six months of follow up.

Although not an essential morphological feature of CIM,[2] to remain consistent with existing literature, the diagnosis of CIM was defined as a tonsillar herniation greater than 5 mm below the foramen magnum on sagittal MRI. Ventriculomegaly was confirmed if Evan's index was >0.3 on axial MRI.

2.2. Preoperative symptoms

Based on data from the clinical records, the children were divided into two groups depending on their preoperative symptoms:

- Group 1: Raised intracranial pressure (ICP) symptoms - headache, vomiting, papilledema, hyporeactivity, and macrocrania;
- Group 2: Posterior fossa or syrinx-related symptoms, occipital and tussive headache, neck pain, dysphagia, sleep apnoea, and acute respiratory arrest, dysesthesia, paraesthesia, dissociated sensory loss and upper limbs weakness.

2.3. Clinical outcomes

Clinical outcomes were determined after reviewing the patient's clinical record. A good outcome was defined as a complete resolution of all the symptoms. The success of the ETV was defined as an absence of need for a second surgery to treat existing or emerging symptoms during the follow-up phase. This subsequent surgeries could include the need for VPS insertion, re-do of the ETV, or FMD surgery.

2.4. Imaging

Patients routinely underwent T1-and T2-weighted MRI studies of the brain and spine before and after ETV. The degree of tonsillar herniation was measured below the basion-opisthion line. The Evan's index and the transverse diameter of the third ventricle were also recorded. Other findings recorded were the presence of a syrinx, the length of the syrinx (measured by the number of vertebral bodies), the maximum diameter of the syrinx, and the morphology of the syrinx (uni- or multi-loculated).

2.5. Statistical analysis

Continuous data were presented as the median and interquartile range (IQ) and categorical data were presented as absolute frequency, due to the sample size. After checking the assumptions, we used the Wilcoxon Signed Rank test to compare the pre-and postoperative continuous data. Significance was set at $p < 0.05$. The STATA MP 14 (StataCorp, 4905 Lakeway Dr. College Station, TX 77845, USA) software was used to analyze the results.

3. Results

3.1. Demographics

Fourteen children were identified who co-presented with CIM and ventriculomegaly and who underwent ETV at our center. After excluding two patients because of incomplete MRI studies, our cohort comprised of 12 children. The median age at ETV was seven years (IQR 3–10.5), and eight patients were male. Two children had previously been diagnosed with sagittal synostosis. The median follow-up was 25 months (IQR 11–36).

3.2. Preoperative symptoms

All clinical variables are summarised in Table 1. Symptoms of raised ICP (Group 1) were the most frequent symptoms, presenting in 10 patients (two cases with papilledema). Three children had symptoms caused by posterior fossa and syrinx (Group 2).

3.3. Clinical outcomes

There was no surgical mortality or complications in this cohort. The overall success rate of the ETV in this cohort was 92% (11/12) (Fig. 2).

For patients belonging to Group 1, all 10 patients who had symptoms

Table 1

Patient	Age in years	Gender	Group 1 symptoms	Group 2 symptoms	Tonsillar herniation in cm	III ventricle diameter in cm	Syrinx	Final outcome	Follow-up in months
1	10	M	Headaches	–	1.06	0.86	No	A	26
2	3	M	Macrocrania	–	1.90	1.1	Yes	A	19
3	3	M	–	Hand weakness	1.49	1.27	No	A	36
4	6	F	Headaches	–	0.66	1.51	Yes	A	26
5	11	M	Papilledema	Cough occipital headaches	2.32	1.26	No	A	8
6	10	M	Headaches/Vomits	–	1.50	1.51	No	A	8
7	13	F	–	Cough occipital headaches and Dissociated sensory loss	1.07	1.38	Yes	A	6
8	8	M	Headaches/Vomits	–	1.43	1.13	Yes	S	14
9	<1	F	Macrocrania	–	1.11	1.12	No	A	24
10	15	F	Headache	–	0.76	1.53	Yes	A	60
11	3	M	Headache/Macrocrania	–	1.17	1.68	Yes	A	36
12	2	F	Headache/ Macrocrania/ Papilledema	–	0.62	1.80	Yes	S -VP shunt	72

M: Male.
F: Female.
A: Asymptomatic.
S: Symptomatic.
VP: Ventriculoperitoneal.

of raised ICP improved immediately after the surgery. One of these 10 patient presented two months after surgery with recurrent symptoms of raised ICP and an MRI showed closure of the stoma. For this patient, a VPS was inserted.

The three patients in Group 2 had a good outcome and resolution of symptoms after the ETV and remained asymptomatic at the end of the follow-up.

3.4. Imaging outcomes

The MRI measurements and statistical analyses are summarised in Table 2. For the entire cohort, the median herniation of the cerebellar tonsils was 1.14 cm (IQR 0.91–1.49) below the basion–opisthion line and the median preoperative Evan's index was 0.4 (IQR 0.34–0.43), and the median transverse diameter of the third ventricle was 1.35 cm (IQR 1.12–1.52). Seven patients had a syrinx shown on preoperative MRI, with a median length of five body levels (IQR 1–18) and a median maximum transverse diameter of 0.75 cm (IQR 0.34–1.12). Two of the seven children with a syrinx were uniloculated, and five were multiloculated.

11/12 patients had evidence of tonsillar ectopia evident on postoperative MRI. The median herniation of the cerebellar tonsils was 0.94 cm (IQR 0.73–1.53) below the basion–opisthion line. The median herniation of the tonsils was not statistically different in the pre vs. postoperative MRI (1.14 vs. 0.94, $p = 0.1$) (Fig. 1). The median postoperative Evan's index was 0.36 (0.31–0.39), and the median transverse diameter of the third ventricle was 0.76 cm (0.63-0.95). Both the Evan's index (0.4 vs. 0.36, $p < 0.01$) and the diameter of the third ventricle (1.35 vs. 0.76, $p < 0.01$) were statistically different between pre and postoperative measurements (Fig. 2).

A syrinx completely resolved in one patient (Fig. 3) and decreased in size in six patients. The median length of the syrinx after the ETV was one body level (IQR 0–4), and the median transverse diameter was 0.32 cm (IQR 0–0.46). Two of the six children who had a persisting syrinx were uniloculated, and four were multiloculated. The preoperative length of the syrinx did not change significantly compared with the postoperative (5 vs. 1, $p = 0.052$). The median transverse diameter of the syrinx did improve significantly after the surgery (0.75 vs. 0.32, $p = 0.03$) (Fig. 4).

4. Discussion

The relationship between hydrocephalus and CIM was first described by Chiari in his original monograph [7] in 1987, where he made the following statement: *"I have had the impression that the extension of the tonsils and medial sides of the inferior lobes probably always is the result of chronic and very early onset of cerebral hydrocephalus."* In the case of overt hydrocephalus, most authors believe hydrocephalus results from impaired CSF circulation in the outlets of the fourth ventricle.[8–10] Whilst overt hydrocephalus occurs in a relative minority of CIM patients, disordered CSF circulation may be more prevalent than previously believed.[2] Despite the uncertainty of the pathogenesis of hydrocephalus in CIM, it has been suggested that the first line of treatment should be CSF diversion, either through VPS insertion or ETV.[11,12] ETV has recently gained widespread acceptance as a durable alternative for VPS placement in obstructive hydrocephalus, with a success rate between 80 and 90% and low complication rate.[13–16] The reduction in the size of the prepontine space in patients with CIM has been considered a limiting factor for a successful ETV. In our literature review, however, at least 46 cases of CIM and overt hydrocephalus were treated with ETV without any major complications, suggesting that ETV is a safe procedure to perform despite the small size of the prepontine space.

Table 2

Measurement	Pre-ETV	Post-ETV	*P* value
Presence of Chiari I (absolute frequency)	12/12	11/12	
Degree of tonsillar herniation in cm (median and IQ range)	1.14 (0.91–1.49)	0.94 (0.73–1.53)	0.1
Evan's index (median and IQ range)	0.4 (0.34–0.43)	0.36 (0.31–0.39)	0.005
Diameter III ventricle in cm (median and IQ range)	1.35 (1.12–1.52)	0.76 (0.63–0.95)	0.003
Presence of syrinx (absolute frequency)	7/12	6/12	
Length of the syrinx in body levels (median and IQ range)	5 (1–18)	1 (0–4)	0.052
Transverse diameter of the syrinx in cm (median and IQ range)	0.75 (0.34–1.12)	0.32 (0–0.46)	0.03

IQ: Interquartile.
ETV: Endoscopic third ventriculostomy.

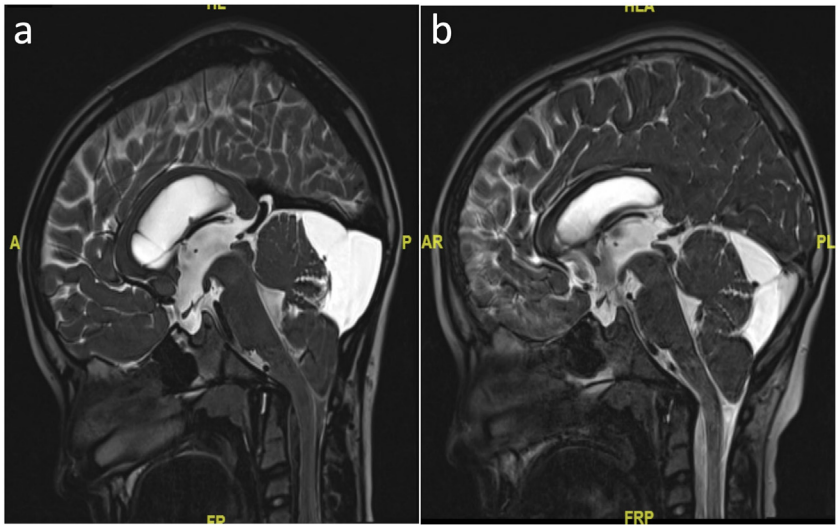

Fig. 1. Magnetic Resonance Image (MRI) showing the third ventricle stoma and posterior fossa anatomy after surgery. a) Preoperative sagittal T2 sequence MRI showing a crowded posterior fossa and distended III ventricle. b) Postoperative sagittal T2 sequence MRI showing a patent stoma and flow in the floor of the III ventricle after endoscopic third ventriculostomy and relaxed posterior fossa. However, the herniation of the tonsils did not change significantly.

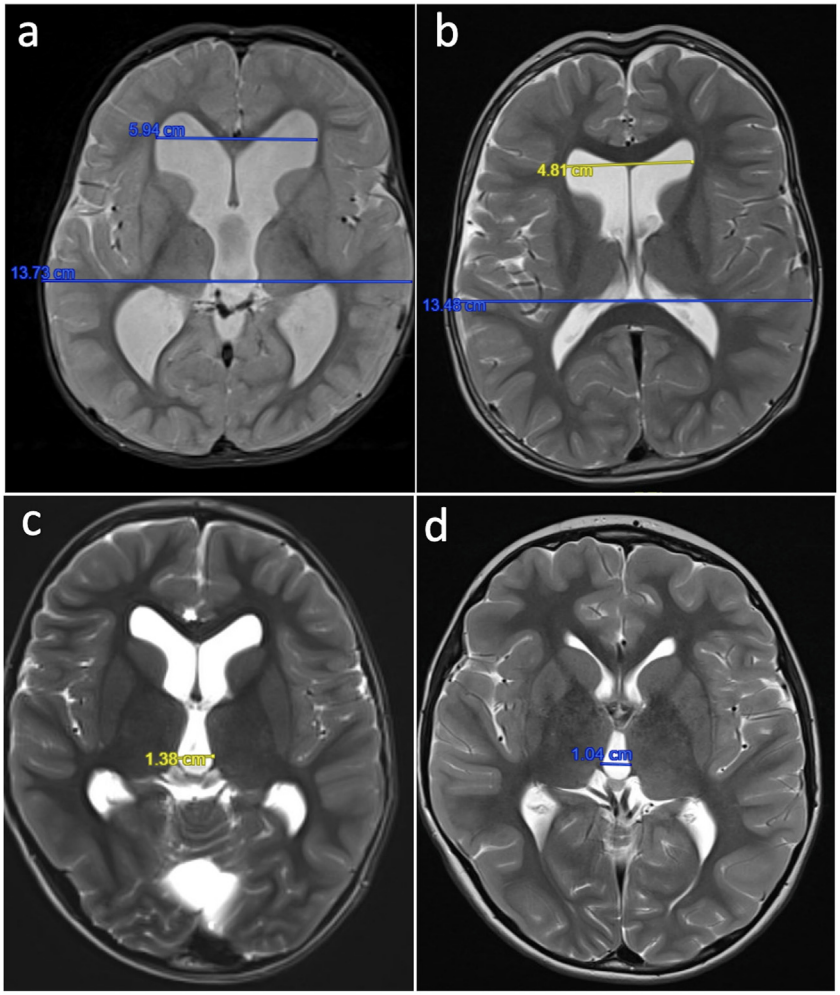

Fig. 2. Magnetic Resonance Image (MRI) shows the ventricular system change after surgery. a) Preoperative axial T2 sequence MRI showing ventricle measurements for Evan's index. b) Postoperative axial T2 sequence MRI showing ventricle measurements for Evan's index. c) Preoperative axial T2 sequence MRI showing III ventricle measurement. d) Postoperative axial T2 sequence MRI showing III ventricle measurement.

The reported success rate for ETV in patients with CIM and ventriculomegaly is 40/46 (86%) (Table 3). The largest pediatric cohort with CMI treated with ETV was by Massimisi et al[17] 2011 and included 11 pediatric patients and five adults. The limitation of this article resides in the fact that the conclusions were drawn from a mixed population of pediatric and adult patients where the pathophysiology and management of CSF disorders, especially in the presence of CIM, differs significantly. Nevertheless, all of the patients had a postoperative improvement in their symptoms. For those with a pre-operative syrinx, 3/6 patients resolved, 2/6 improved, and 1/6 remained stable. Two cases required a redo ETV for obstruction of the stoma.

Hayhurst et al[6] presented 16 patients (mean age 31.9 years) with CIM and hydrocephalus, 15/16 had resolution of symptoms related to high ICP, while 6/16 patients required subsequent FMD to treat symptoms associated with posterior fossa syndrome. The syrinx improved in 4/6, resolved in 1/6, and remained stable in 1/6 patients. The third-largest series was presented by Wu et al[18] with 10 cases (mean age 28.14 years) with a success rate of 80% (8/10) and two patients requiring a second surgery, one of them an FMD. Lastly, a series by Deq et al[19] reported data from five patients (mean age 29.6 years), four of whom had a postoperative improvement in symptoms whilst one patient required a revision of the ETV.

In contrast to Hayhurst[6] et al's findings, in our series there was no distinction between symptomatology improvement in patients with symptoms related to raised ICP or posterior fossa syndrome. None of the patients required FMD after the ETV. However, only three patients presented originally with posterior fossa, so the initial number was too small to draw strong conclusions.

In terms of syrinx improvement, 1/7 patient had complete resolution of their syrinx, whilst the rest (6/7) had reduction in the length and transverse diameter of the syrinx. Previous reports[6,17] have shown a higher rate of complete resolution of the syrinx compared to ours. Nevertheless, the definition they used for the resolution of the syrinx is unclear.

Tonsillar ectopia was improved in one case after ETV and, even though an improvement in the descent of the tonsils was seen (1.14 cm vs. 0.94 cm), it was not statistically significant. On the other hand, the diameter of the third ventricle and lateral ventricles did improve after the surgery. Wu et al[18] found similar results, reporting a reduction of the mean transverse diameter of the third ventricle from 12.79 mm preoperatively to 6.34 mm postoperatively ($p = 0.0035$).

Since no complications were recorded in our cohort, our data supports the suggestion that ETV is a safe procedure to treat CSF disorders in patients with ventriculomegaly and CIM. We also found that there is no need to have an improvement in the tonsillar herniation to have a successful resolution of the symptoms. However, a reduction in the ventricle's size should be expected after a successful ETV. In terms of the syrinx and syrinx-associated symptoms, improvement of the symptoms should

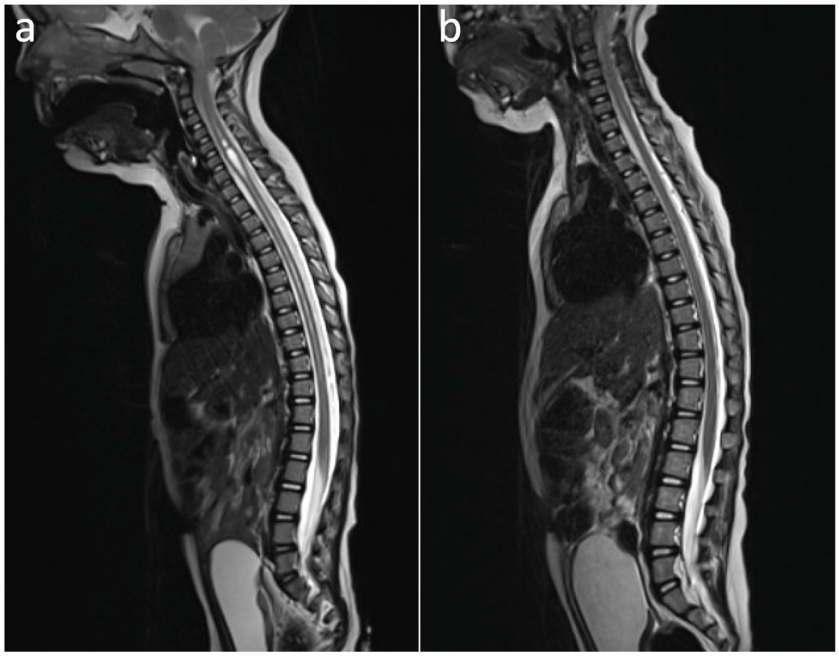

Fig. 3. Magnetic Resonance Image (MRI) showing the resolution of the syrinx after surgery. a) Preoperative sagittal T2 sequence MRI showing tonsillar ectopia and extensive multiloculated syrinx. b) Postoperative sagittal T2 sequence MRI showing complete resolution of the syrinx.

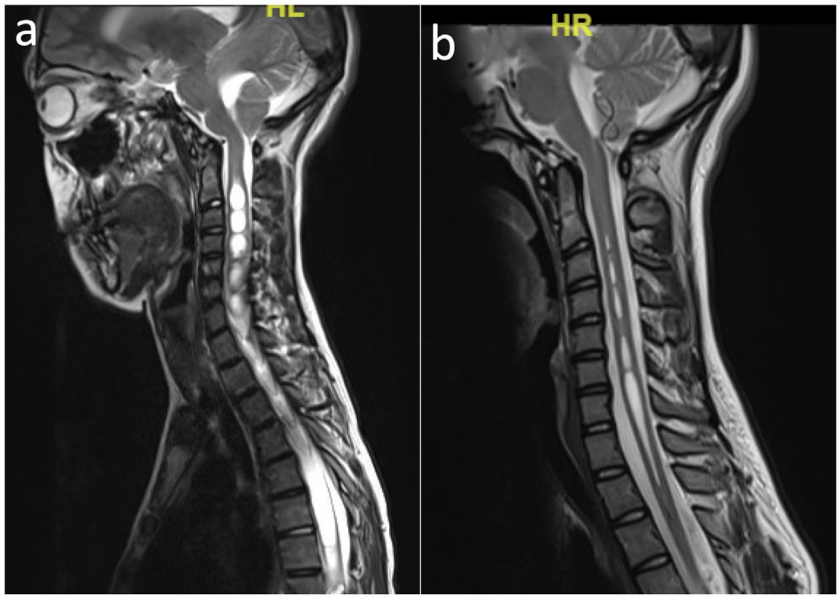

Fig. 4. Magnetic Resonance Image (MRI) showing partial resolution of the syrinx after surgery. a) Preoperative sagittal T2 sequence MRI showing tonsillar ectopia and extensive multiloculated syrinx. b) Postoperative sagittal T2 sequence MRI showing improvement of the tonsillar ectopia and partial resolution of the syrinx, especially reduction on the transverse diameter of the syrinx.

Table 3
Review of the literature and current series.

Author	Year	Number of patients	Mean age	Success rate	Follow up in months
Decq et al.	2001	5	29.6 years	5/5	Mean 50.39
Hayhurst et al.	2008	16	31.9 years	15/16	Mean 42
Massimi et al.	2011	15	15.06 years	15/15	Mean 35
Yiping Wu et al.	2015	10	28.14 years	8/10	Mean 92
Current series	2022	12	7 years	11/12	Median 25

be accomplished, even without the complete disappearance of the syrinx. Main changes should be expected in the syrinx maximum transverse diameter.

Finally, since all of our patients presented control MRIs during follow-up, we can confirm that treatment failure (stoma closure) was always accompanied by recurrence of symptoms.

The main limitation of this study is the small number of patients included. However, since patients with CIM and associated CSF disorders and ventriculomegaly are infrequent, this cohort series helps to enlarge the already existing pool of case series published in the literature. Nonetheless, our conclusions need to be validated using a larger number of patients.

5. Conclusion

Our study provisionally supports the safety and effectiveness for managing children with concurrent CSF disorders, ventriculomegaly and CIM using ETV. Further and larger studies are required to corroborate this finding.

Credit authorship statement

Amparo Saenz, MD, Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Roles/Writing - original draft; Writing - review & editing.Pipper Rory, MD, Conceptualization; Data curation, Writing - review & editing, Thompson Dominic, MD, Supervision; Validation; Visualization, Tahir Zubair, MD, Roles/Writing - original draft; Supervision; Validation; Visualization.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abbreviation list

(CIM): Chiari I malformation
(CSF): Cerebrospinal fluid
(FMD): Foramen magnum decompression
(ICP): Intracranial pressure
(MRI): Magnetic resonance imaging
(VPS): Ventriculoperitoneal shunt
(ETV): Endoscopic third ventriculostomy
(IQ): Interquartile range