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ORIGINAL ARTICLE

Proposed radiological score for the evaluation of isolated fourth ventricle treated by endoscopic aqueductoplasty

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Abstract

Purpose Evidence supporting the effectiveness of endoscopic aqueductoplasty (EA) for the treatment of isolated fourth ventricle (IFV) is limited to small surgical series of cases. Additionally, studies adopted different radiological outcome criteria, which makes it difficult to compare outcomes accurately. Thus, we aimed to develop a radiological score (RS) as an alternative assessment method for EA.

Methods The cases of 20 consecutive pediatric patients harboring IFV and treated by EA were retrospectively reviewed. Clinical data and pre- and 1-year postoperative brain images were analyzed. The RS was based on the enlargement of the fourth ventricle and deformation of the cerebellum and brainstem. After randomization, three experts, blinded to patient outcomes, analyzed the brain images and established a consensus for the values of the score. Outcomes were validated by comparing the maximum anteroposterior distance of the fourth ventricle using the RS, pediatric functional status score, and clinical symptoms.

Results The RS was strongly correlated with the anteroposterior distance of the fourth ventricle (Pearson's coefficient = 0.78), and the mean RS dropped from 6.15 to 3.90 ($p < 0.001$) 1 year after EA. Upward extension ($p = 0.021$) and brainstem deformation ($p = 0.010$) were the most significant improved features. There was agreement among RS and symptom improvement in 16 children (80%) and the pediatric functional status score in 14 children (70%).

Conclusion In this study, the proposed radiological score proved to be an accurate tool for the evaluation of IFV treatment with EA.

Keywords Hydrocephalus · Cerebral aqueductoplasty · Treatment success · Neuroendoscopy

Introduction

Isolated fourth ventricle (IFV) primarily affects children with hydrocephalus when inflammatory processes obstruct the entry and exit paths of the cerebrospinal fluid (CSF) through the fourth ventricle. Additionally, the continuous production of CSF in this cavity leads to its progressive growth, with the compression and deformation of the brainstem and cerebellum, which result in the clinical symptoms [9, 11, 16, 18, 28].

In several reports, endoscopic aqueductoplasty (EA) has been recommended as the best option to treat the IFV due to its lower potential for bleeding compared with the posterior fossa craniotomy and lower complication rates compared with the fourth ventricular shunts. Furthermore, EA allows for a pressure balance between the supra- and infratentorial ventricular compartments [4–8, 14, 15, 22, 24, 25, 27].

Although the main radiological features of IFV, such as herniation through the tentorial notch, dilatation of the lateral recesses, and flattening of the floor of the fourth ventricle with involvement of the prepontine cistern and cerebellum compression, have been described in previous studies; heterogeneous morphometric criteria were adopted to radiologically assess outcomes, thereby precluding accurate comparisons of outcomes across studies [1, 10, 13, 15, 24, 25, 28].

We hypothesized that a study of the deformation of the neural structures in the posterior fossa and their relationship with fourth ventricle enlargement might improve the knowledge of the morphological and clinical characteristics in

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relation to clinical outcomes. Hence, the purpose of this study was to develop a radiological score (RS) that could become a standardized method to assess treatment outcomes in cases of IFV.

Methods

Patients and eligibility criteria

Following the Ethics Committee approval of the study at the Federal University of Minas Gerais, Vila da Serra Hospital and Biocor Institute, Brazil, we identified all pediatric patients who underwent neuroendoscopic treatment for IFV between January 2006 and December 2017.

The EA alone or with the placement of a multiperforated catheter was indicated in cases of clinical symptoms of fourth ventricle enlargement with radiological evidence of cerebral aqueduct obliteration. Children who had dilatation of the fourth ventricle without the obstruction of the cerebral aqueduct and those with Dandy-Walker syndrome were excluded.

Endoscopic technique

All operations were performed under general anesthesia by two different endoscopic approaches. If the supratentorial ventricular system was large enough to allow neuroendoscopic navigation, a precoronal approach was selected; in all other cases, a suboccipital approach was considered appropriate. A rigid neuroendoscope (Aesculap AG or Karl Storz, Tuttlingen, Germany) was used in all cases. Fogarty catheter (N° 3) or a monopolar used as a stylet was used to open the membrane and release the aqueduct obstruction. In some cases, the balloon was gently insufflated in order to optimize the overture. A multiperforated catheter was inserted parallel to the neuroendoscope by the same burr hole, and the tip was guided into the aqueduct with the aid of the endoscope.

Selection of data

All computed tomography or magnetic resonance images performed immediately before and 12 months after surgery were obtained, and the RS was applied. Demographic data, etiology of IFV, preoperative symptoms, and postoperative complications were considered. The Brazilian version of the pediatric functional status score was applied before and 12 months after the procedure, based on data from the medical records and follow-up. This score was developed by Pollack et al. [17] and cross-culturally adapted to the Brazilian population by Bastos et al. [3] in which six functional domains such as mental status, sensory, communication, motor functioning, feeding, and respiratory status are assessed.

Construct validity of RS

The RS system was created based on the extension of fourth ventricle enlargement and the degree of deformation exhibited by the midbrain, pons, medulla oblongata, and cerebellum, ranging from 0 to 12 (Table 1). The pons and medulla oblongata were evaluated simultaneously as both these structures form the floor of the fourth ventricle. Brain images in midsagittal and axial views with visualization of the lateral recesses were selected. Four anatomical points were identified in the midsagittal section, namely, the *tuberculum sellae*, *basion*, anterior limit of the falcotentorial junction, and torcular region. From these landmarks, three lines were drawn to evaluate the extent of ventricular growth and the degree of cerebellar deformation (Fig. 1).

For the extent criterion, one point was assigned for each direction of the dilation of the fourth ventricle, i.e., if it exceeded lines 1 to 2 (upper extent), lines 3 to 4 (lower extent), and dilation of at least one of the lateral recesses (lateral extent) (Fig. 1). Neural deformation was graded from 0 (absent) to 3 (severe). Deformation of the midbrain was defined as mild when only the *tectum mesencephali* was affected, moderate if the tectum and tegmentum were affected, and severe if the midbrain exhibited a membranous appearance (Fig. 2). The deformation of the pons and medulla oblongata was classified as mild if there was a curvature in the ventricular floor without cisternal alterations, moderate if there was an additional reduction in the prepontine cistern, and severe if there was cistern effacement. Twining's line (lines 1–4) (Figs. 1 and 3) was previously used to evaluate the fourth ventricle position. In this study, it was described as cerebellum deformation [2, 12]. The midpoint line (number 5) was considered the normal posterior limit of the fourth ventricle. If the posterior limit of the fourth ventricle was between points 5 and 6, the deformation of the cerebellum was considered mild, and if it was between 6 and 4, it was defined as moderate. If there was no visible cerebellar parenchyma between points 6 and 4, the deformation of the cerebellum was classified as severe (Fig. 3).

Table 1 Radiological score for isolated fourth ventricle

Criteria	Features				Value
Fourth ventricle extent	Yes	No			
Upward	1	0			1
Downward	1	0			1
Lateral	1	0			1
Deformation	Absent	Mild	Moderate	Severe	
Mesencephalon	0	1	2	3	3
Pons/medulla oblongata	0	1	2	3	3
Cerebellum	0	1	2	3	3
					12

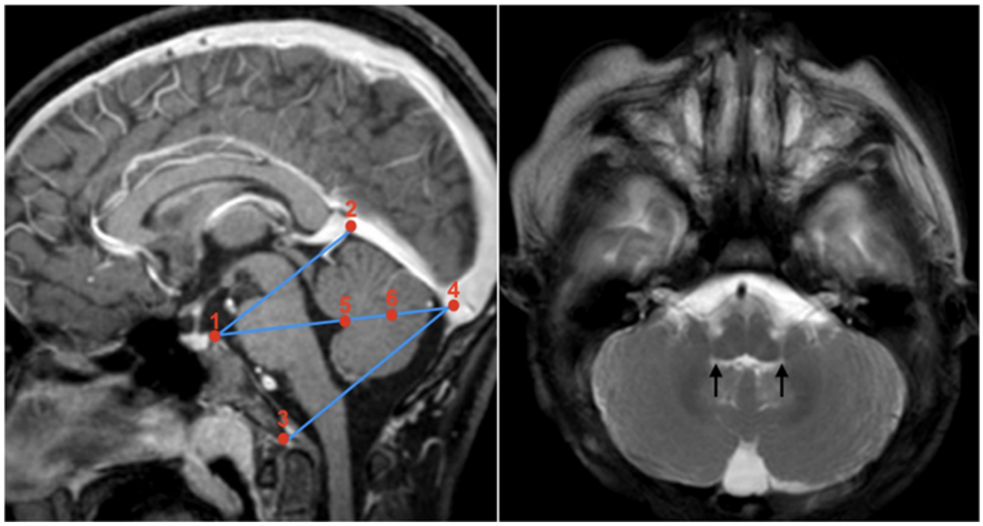

Fig. 1 (Left) Midsagittal T1 image with contrast of the brain in a normal infant, demonstrating the six points and three linear landmarks of RS. (1) Tuberculum sellae, (2) anterior falcotentorial limit, (3) basion, (4) torcula, (5) midpoint of Twining's line, and (6) midpoint between (5) and torcula (4). (Right) Axial T2 without contrast demonstrating the normal lateral recesses (double black arrow)

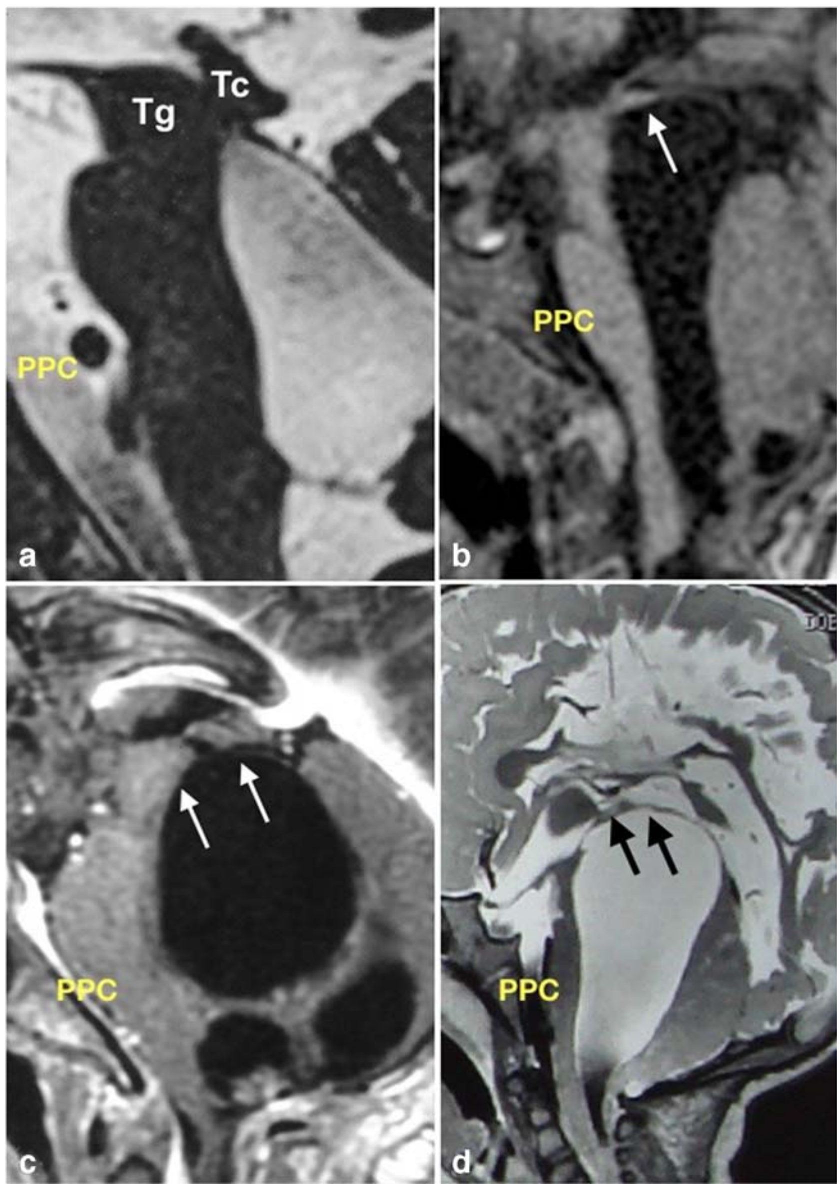

Fig. 2 Midsagittal magnetic resonance imaging of the brain and different patterns of brainstem distortions developed as a result of isolated fourth ventricle. **a** The normal shape of the midbrain and mild distortion of the pons and medulla; Tg, tegmentum mesencephalon; Tc, tectum mesencephalon; PPC, prepontine cistern. **b** Mild distortion of the midbrain with tectum distortion (small white arrow) and moderate distortion of the pons and medulla with cistern patency. **c** Moderate distortion of the midbrain tectum and tegmentum (double thick white arrows) and severe distortion of the pons and medulla with effacement of the cistern. **d** Severe distortion, upward dislocation, and membranous shape of the mesencephalon (double black arrows) and severe distortion of the pons and medulla oblongata with effacement of cistern

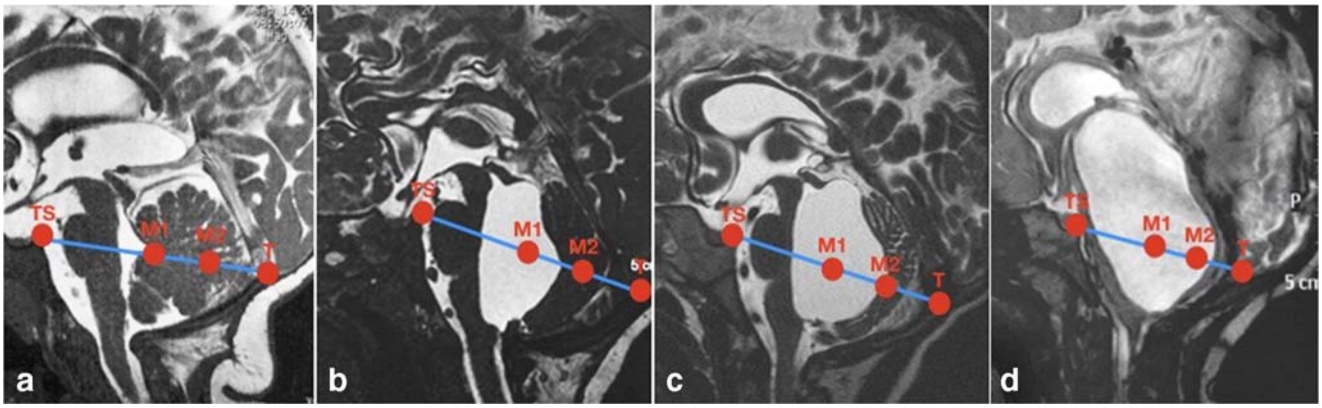

Fig. 3 Midsagittal magnetic resonance imaging of the brain and different patterns of cerebellum distortions developed as a result of isolated fourth ventricle. **a** The normal shape of the cerebellum; TS, Tuberculum sellae; T, torcula; M1, midpoint of Twining's line; M2, three fourths of Twinning's line. **b** Mild distortion of the cerebellum. **c** Moderate distortion of the cerebellum. **d** Severe distortion of the cerebellum

For each patient, a sagittal cut and an axial cut were selected as the representative pre- and postoperative images. These images, in addition to those of two children without IFV, were compiled, randomly distributed, and printed without patient identification data. Thus, the RS was applied to a total of 42 images.

The three experts, two radiologists and one neurosurgeon all with at least 10 years of experience, who were blinded from patient names and outcomes analyzed the images. After the first independent analysis, the three experts jointly decided on the score for each examination.

Concurrent validity

The maximum anteroposterior distance of the fourth ventricle was measured using the Osirix MD ANVISA® (Pixmeo SARL, Switzerland) software. The midsagittal section of the magnetic resonance images in Digital Imaging and Communications in Medicine format was selected. The RS obtained by the group of experts were compared for the same examinations. A 12.56-mm distance was used as a cutoff point for the normal width of the fourth ventricle as estimated by Sari et al. [23]

Content validity of RS

The content validity of the RS was obtained comparing the preoperative values and those at the 12-month postoperative follow-up. Complete morphological recovery was considered if the final score was equal or less than 12.56-mm considered normal. Partial recovery was considered if the final score remained higher than the normal value and no recovery if the score increased after EA. The correlation among improvement of RS, clinical symptoms, and pediatric functional status score was assessed.

Statistical methods

The software used to analyze the data was SPSS ver. 20 (IBM, Armonk, NY, USA), Minitab 16 Statistical Software (Minitab, PA, USA), and Microsoft Excel 2010 (Microsoft Corporation, Redmond, WA, USA). Pearson's correlation was used to evaluate the relationship between RS and the anteroposterior distance of the fourth ventricle. After performing a linear regression and using analysis of variance, a receiver operating characteristic (ROC) curve was obtained to evaluate the RS considering the normal anteroposterior distance of the fourth ventricle.

Results

Patient characteristics

During the observation period, an endoscopic procedure was performed in 20 pediatric patients and a multiperforated catheter was inserted into an IFV in 16 cases according to the intraoperative decision of the neurosurgeon. There were nine girls and eleven boys with ages ranging from 5 months to 10 years of age (mean 4.8 years; median 4.1 years).

The IFV etiologies were previous ventricular hemorrhage of prematurity in three patients and intraventricular hemorrhage associated with ventriculitis in nine children. One child had congenital encephalitis by herpes simplex. Five children were born with myelomeningocele and presented symptoms of IFV after ventriculitis. Two additional children developed IFV after treatment of a tumor: one with ganglioglioma of the fourth ventricle and one with choroid plexus papilloma of the fourth ventricle associated with ventriculitis (Table 2).

Table 2 Patient characteristics

Patient no.	Sex/age (months)	Etiology	Clinical presentation	EA	Complications	FSS Pre/pos	RS Pre/pos	Clinical course
1	M/27	IVH, V	Vomiting, ataxia	SO		12/9	11/9	Complete reversion
2	F/98	IVH, V	Vomiting, dysphagia, sleep apnea	SO[c]		12/8	8/6	Complete reversion
3	F/16	MMC, V	Ataxia, dysphagia	SO		9/9	6/5	No improvement
4	F/40	IVH	Tetraparesis, opisthotonus, dysphagia, coma	ST		29/10	11/7	Partial reversion, dysphagia[p]
5	M/5	IVH, V	Macrocrania	ST[c]		11/8	3/0	Complete reversion
6	M/24	IVH	Ataxia, dysphagia	ST[c]		13/8	4/2	Complete reversion
7	M/5	MMC, V	Ataxia, motor regression	ST		11/9	6/1	Partial reversion, ataxia[p]
8	M/24	MMC, V	Dysphagia, motor regression	ST[c]		12/8	4/2	Complete reversion
9	M/84	IVH	Vomiting, motor regression, dysphagia	ST		11/8	4/3	Partial reversion, dysphagia[p]
10	M/72	PT	Dysphagia	ST[c]		27/17	3/3	No improvement
11	M/48	IVH, V	Opisthotonus , coma	ST[c]		14/8	7/5	Complete reversion
12	M/51	IVH, V	Headache, irritability	ST[c]	Transient ophthalmoparesis	7/6	7/0	Complete reversion
13	M/84	IVH, V	Headache, vomiting	ST[c]		8/6	6/4	Complete reversion
14	M/84	IVH, V	Irritability	ST[c]		10/10	6/3	Complete reversion
15	F/50	IVH, V	Headache, vomiting	ST[c]	Transient ophthalmoparesis	7/7	5/9	Complete reversion
16	F/120	V	Ataxia	ST[c]	Transient ophthalmoparesis	19/12	7/7	Complete reversion
17	F/28	MMC, V	Vomiting, opisthotonus	ST[c]		20/9	10/8	Complete reversion
18	F/17	IVH, V	Headache	ST[c]		10/10	2/1	Complete reversion
19	F/108	MMC , V	Headache, opisthotonus	SO[c]		17/13	5/0	Complete reversion
20	F/108	PT , V	Nystagmus, ataxia	SO[c]	Transient ophthalmoparesis	9/8	8/3	Partial reversion, nystagmus, ataxia[p]

EA, endoscopic aqueductoplasty; *FSS*, pediatric functional status score; *IVH*, prematurity and intraventricular hemorrhage; *MMC*, myelomeningocele; *RS*, radiological score; *PT*, post tumor resection; *SO*, suboccipital approach; *ST*, supratentorial approach; *V*, ventriculitis

[c] Multiperforated catheter was used

[p] Persistent symptom

Presenting clinical symptoms

Clinical presentation included dysphagia (n = 7), ataxia (n = 6), vomiting (n = 6), headache (n = 5), opisthotonos (n = 4), motor regression (n = 3), depressed consciousness (n = 2), sleep apnea (n = 1), nystagmus (n = 1), and tetraparesis (n = 1) (Table 2).

Validation of RS

A strong correlation was observed between RS and the anteroposterior distance of the fourth ventricle (Pearson's coefficient was 0.789; p < 0.001). Linear regression was performed with the values obtained, and a ROC curve was plotted; the area under the curve was 0.953. The cutoff value for a normal score was two points (Fig. 4).

Twelve months after the neuroendoscopic procedure, there was a significant improvement in the RS and a reduction in its mean value (p < 0.001), with a greater impact on the size of the fourth ventricle (p = 0.021), midbrain deformation (p = 0.010), and pons/medulla oblongata deformation (p = 0.001). There was no difference in cerebellar deformation (p = 0.214) (Table 3).

Complete morphological recovery was achieved in five cases, partial recovery was obtained in 12 cases, and stability was observed in two cases. In one case, the RS was worse at the 12-month follow-up (Table 2 and Fig. 5).

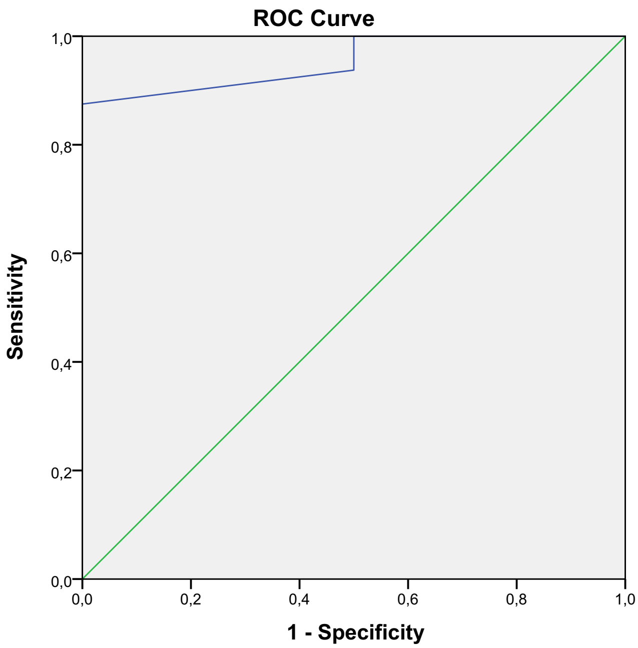

Fig. 4 ROC curve. The ROC curve plots the sensitivity (true positive rate) against 1-specificity (false positive rate) for the consecutive cutoffs of the RS. The concordance (c) statistic is equivalent to the area under the ROC curve and equals 0.953

Clinical outcome and radiological score

There was an agreement between RS and symptom improvement in 16 children (80%) and with the pediatric functional status score in 14 children (70%). The pediatric functional status score significantly improved in the domains mental state ($p = 0.015$), communication ($p = 0.001$), motor function ($p < 0.001$), and feeding ($p = 0.003$), with the total mean score improving from 12.95 to 9.15 ($p < 0.001$). This means that the functional status improved of moderate to mild dysfunction 1 year after the endoscopic procedure. Four patients had no change in the functional scale. Complete improvement of symptoms was observed in 14 patients. Persistence of dysphagia was observed in two patients, ataxia in three patients, and nystagmus in one patient. There were no deaths or worsening of symptoms during the study period (Table 2).

Table 3 Radiological score before and 1 year after endoscopic aqueductoplasty

Criteria	Mean score		*p* value
	Preoperative	Postoperative	
Fourth ventricle extension	2.00	1.30	0.002
Upward	0.65	0.40	0.021
Downward	0.60	0.40	0.163
Lateral	0.75	0.50	0.056
Deformation	4.20	2.60	0.001
Mesencephalon	1.20	0.60	0.010
Pons/medulla oblongata	1.90	1.10	0.001
Cerebellum	1.10	0.90	0.214
Sum	6.15	3.90	< 0.001

Discussion

Scoring systems are increasingly being developed for various diseases with the objective of improving the evaluation of severity and assessing the efficacy of therapeutic modalities [19, 26]. In the field of pediatric neurosurgery, further research is needed to better understand uncommon and challenging conditions such as IFV. Thus, the present study provides an overview of the morphological features of IFV after EA and confirms the different radiological and clinical presentations of IFV.

Although the anteroposterior distance of the fourth ventricle is a unique measurement studied in normal pediatric brain imaging by Sari et al. [23], some research studies have reported other morphometric parameters such as fourth ventricle volumetry, pons and cisternal width, laterolateral distance, and fourth ventricle indexes as radiological outcomes which makes comparisons difficult [1, 13, 24]. Hence, the high correlation observed between the RS and the anteroposterior width of the fourth ventricle supports the use of this scoring system as a valid radiological outcome assessment, and the combination of recognizable landmarks in two representative brain images allows the application of this method even by non-experts.

The simultaneous assessment of ventricular dilation and neural deformation showed that cerebellar deformation persisted ($p = 0.214$), even with the reduction in the size of the fourth ventricle in most patients. This result shows that the morphology of the cerebellum, unlike that of the brainstem, tends to not recover even after the hypertension of the fourth ventricle has ceased. This phenomenon might be related to the intrinsic biomechanical differences of the cerebellum, leading to its early deformation during ventricular expansion, and making the deformation persisting for a longer period compared with the brainstem. Another possible explanation is the influence of the hemorrhagic and infectious lesions that cause IFV. These lesions might alter the composition and consistency of the neural tissue and affect brain turgor, thereby reducing the ability of the brain to morphologically recover. This concept was postulated by Rekate who referred to the intrinsic resistance of the brain under deformation forces [21]. Thus, some studies have argued that a complete morphological recovery of the fourth ventricle should not be the objective of IFV treatment [25, 28, 29].

Significant improvement was observed in the deformation of the pons and medulla oblongata, suggesting that the clinical and functional improvement exhibited by children

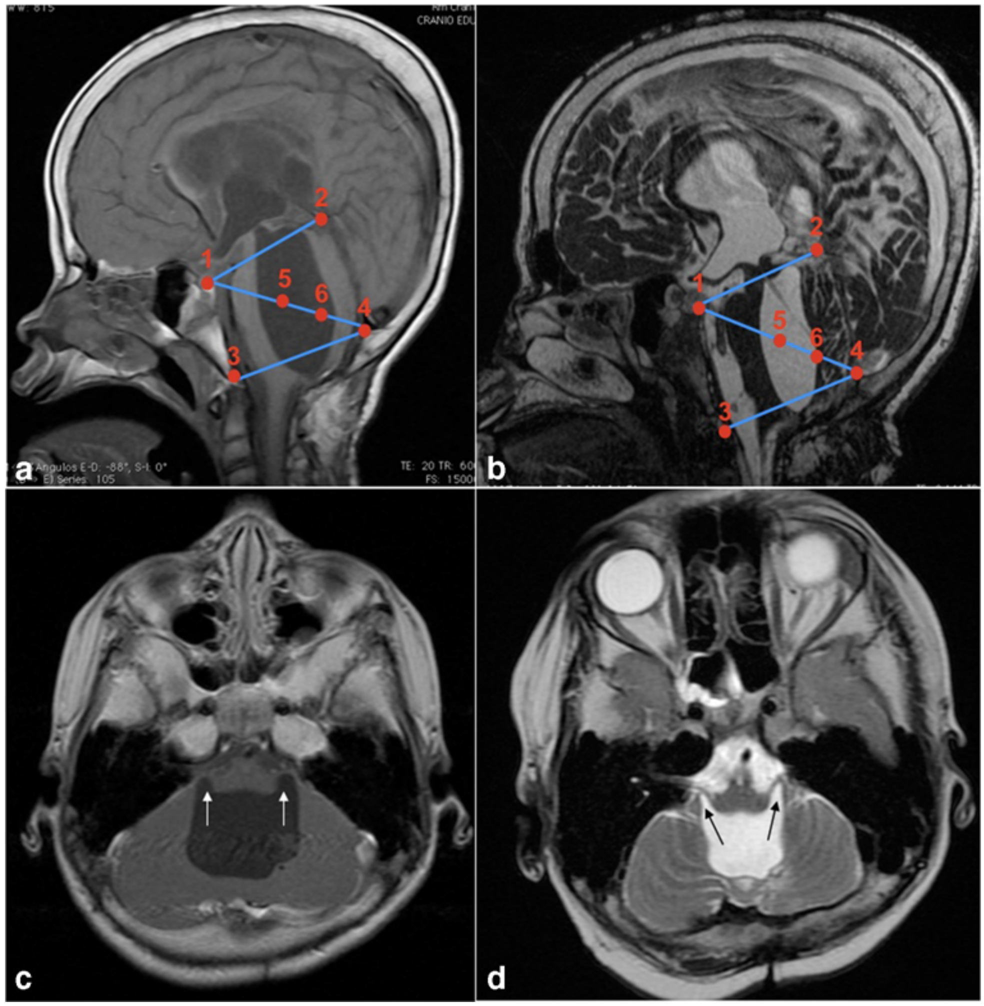

Fig. 5 Images of RS applied to the same child (patient number 20, Table 2) before and after EA. **a** and **c** (preoperative period) scored as 8 (fourth ventricle extent = 3, midbrain = 1, pons/medulla = 2, cerebellum = 2). **b** and **d** (postoperative period) scored as 3 (fourth ventricle extent = 1, midbrain = 0, pons/medulla = 0, and cerebellum = 2)

during the postoperative period is related to the decompression of the floor of the fourth ventricle. Previous studies have reported this pattern of improvement also. Signs of increased pressure inside the ventricular cavity are a decrease in the size of the prepontine cistern and anterior displacement of the brainstem [28].

Raouf et al. conducted a case series with 13 children who underwent EA using an infratentorial approach to treat IFV and found a flattening of the posterior aspect of the brainstem and the effacement of the prepontine cistern in all patients during the preoperative period [20]. These observations were corroborated in a case series of 19 children receiving neuroendoscopic treatment for IFV, in which the volume of the fourth ventricle and the thicknesses of the pons and prepontine cistern were measured using the Osirix® software. The mean volume reduction was 21.1 ml, and the thicknesses of the pons and prepontine cistern increased by 0.3 cm and 0.1 cm, respectively. However, another study suggested that cerebellar deformation impairs the accuracy of ventricular volume measurements [28]. Udayakumaram et al. performed craniotomies and posterior fossa shunting of the fourth ventricle and observed an increase in the prepontine cistern with a reduction in ventricular size as criteria for radiological improvement [28]. In addition to these findings, the present study showed a reversal in mesencephalic deformation. Other studies have yet to quantify this finding. A relationship was found between clinical improvement and the morphologies of the neural and ventricular contents of the posterior fossa in most cases as well as among the functional domains evaluated by the pediatric functional status score, with significant improvements in the mental state, communication, motor function, and diet. Previous studies have observed radiological as well as clinical improvements after EA, despite not having performed a functional evaluation [4, 5, 13, 15, 24].

Some limitations of this study were the retrospective collection of clinical data and the small sample of patients. Given the low occurrence rates of this disease, it is difficult to generalize the clinical outcomes. Nevertheless, this study should provide a basis for a broader, multicenter, prospective study using a similar methodology including functional and morphological evaluations to promote the classification of this disease in the future.

Conclusions

We developed a novel and practical method, the RS, to assess IFV. The findings of this study indicate that the RS is an accurate instrument to evaluate IFV and demonstrate a good correlation between RS and clinical outcome.

Author contributions Conception and design: Furtado, Giannetti. Acquisition of data: Furtado. Analysis and interpretations of data: Furtado, Giannetti. Drafting the article: Furtado. Critically revising the article: Furtado, Giannetti, Costa Val Filho. Reviewed the submitted version of the manuscript: Furtado. Statistical analysis: Furtado. Administrative/technical/material support: Furtado. Study supervision: Giannetti, Costa Val Filho

Compliance with ethical standards

Conflict of interest 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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