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Author(s)	Hashimoto, Hiroaki; Takemoto, Osamu; Nishimoto, Keisuke et al.
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Normal growth curve of choroid plexus in children: implications for assessing hydrocephalus due to choroid plexus hyperplasia

Hiroaki Hashimoto, MD, PhD,^{1,2} Osamu Takemoto, MD, PhD,¹ Keisuke Nishimoto, MD,¹ Gento Moriguchi, MD,¹ Motoki Nakamura, MD,¹ and Yasuyoshi Chiba, MD, PhD¹

¹Department of Neurosurgery, Osaka Women's and Children's Hospital, Izumi, Osaka, Japan; and ²Department of Neurological Diagnosis and Restoration, Graduate School of Medicine, Osaka University, Suita, Osaka, Japan

OBJECTIVE Pediatric hydrocephalus requires evaluation while accounting for growth of the intracranial structures, but information on choroid plexus growth in children is lacking. This study aimed to create normal growth curves for intracranial volume, choroid plexus volume, and lateral ventricles volume. Additionally, the authors aimed to objectively assess the degree of hydrocephalus caused by choroid plexus hyperplasia (CPH) and to examine the impact of surgical procedures.

METHODS This retrospective study analyzed the head CT scans of pediatric patients with minor head trauma treated at Osaka Women's and Children's Hospital between March 2006 and May 2023. The study segmented and calculated intracranial, choroid plexus, and lateral ventricles volumes. The study also calculated the correlation coefficients among these 3 parameters. Patients aged 0 to 10 years were divided into 15 age-related clusters, and mean \pm SD values were calculated for each cluster. Growth curves were created by plotting mean values sequentially. Volume obtained from patients with CPH were z-normalized using mean and SD values and compared.

RESULTS A total of 229 CT scans (94 from females) were analyzed, and positive correlations were observed among intracranial volume, choroid plexus volume, and lateral ventricles volume, with the strongest correlation between the choroid plexus and lateral ventricles volumes. The growth rate of intracranial volume was rapid until approximately 20 months of age, while those of choroid plexus volume and lateral ventricles volume increased rapidly until approximately 1 year of age. Subsequently, choroid plexus volume and lateral ventricles volume plateaued at 1.5 ml and 10 ml, respectively. Three patients with CPH were enrolled and quantitatively evaluated on the basis of the z-normalized volume. Notable abnormal volumes of the choroid plexus (range z-normalized values 24.11–51.17) and lateral ventricles (46.78–122.36) were observed. In 2 patients, improvements in the z-normalized values of intracranial volume and lateral ventricles volume were observed after surgical interventions. Additionally, in 1 patient, choroid plexus volume was reduced by approximately 24% (range z-normalized values 51.17–38.93) after bilateral endoscopic plexus coagulation.

CONCLUSIONS This study provides normal growth curves for intracranial volume, choroid plexus volume, and lateral ventricles volume. Knowledge of these normal values holds the potential for objective assessment of abnormal values associated with hydrocephalus and choroid plexus diseases such as CPH.

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KEYWORDS choroid plexus hyperplasia; choroid plexus volume; growth curves; intracranial volume; lateral ventricles volume; hydrocephalus

HYDROCEPHALUS is a common disorder in both the pediatric and adult neurosurgical fields. The incidence of congenital hydrocephalus in the United States and Canada has been estimated at 68 per 100,000 births.¹ Hydrocephalus has been classically defined as any increase in CSF within the skull² or as active distension

of the ventricular system of the brain resulting from inadequate passage of CSF from its point of production within the cerebral ventricles to its point of absorption into systemic circulation.³ Therefore, there appears to be a close relationship between ventricular size and CSF production. Although recent research has raised doubts about the

ABBREVIATIONS BEC = bilateral endoscopic plexus coagulation; CPH = choroid plexus hyperplasia; EVD = external ventricular drainage; mPGCS = modified Pediatric Glasgow Coma Scale; P1 = patient 1; VAS = ventriculoatrial shunt; VPS = ventriculoperitoneal shunt.

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concept of directed bulk-flow movement of CSF, which involves flow from the choroid plexus into the ventricles and across the arachnoid villi back into the blood,⁴ the choroid plexus is widely recognized as the source of CSF production.⁵ In the neuroscience field, the production and directional flow of CSF have been highlighted along with the glymphatic concept.⁶ In clinical situations, rare cases of choroid plexus papilloma or choroid plexus hyperplasia (CPH) have shown hydrocephalus due to an overproduction of CSF, which is treated with shunt procedures or microsurgical removal.⁷

Normal growth curves related to head circumference are well-established tools used by physicians to assess abnormal growth patterns. Normal growth curves of intracranial volume based on volumetry performed with CT imaging have been reported,⁸ and those of cerebral ventricular volume have been revealed on the basis of volumetry performed with MRI.⁹ Normal thickness of the choroid plexus has been reported in pediatric¹⁰ and adult populations,¹¹ and aging in adult population was associated with increased choroid plexus volume.¹² Recently, the volume of the choroid plexus has been highlighted in diseases such as psychotic spectrum disorder,¹³ Alzheimer disease,¹⁴ multiple sclerosis,¹⁵ stroke,¹⁶ and pediatric autism.¹⁷ However, normal pediatric choroid plexus volume and how it increases in the pediatric population remains unclear.

In this study, we enrolled pediatric patients with minor head trauma who were previously healthy and underwent head CT scans for measurement of intracranial volume, choroid plexus volume, and lateral ventricles volume. We investigated the relationship among these parameters and created growth curves. Additionally, we evaluated the volumes of these parameters in patients with CPH to assess the degree of abnormality and the impact of surgical interventions.

Methods

Patients and Study Setting

In this retrospective study, we enrolled patients who underwent CT imaging for head trauma at Osaka Women's and Children's Hospital between March 2006 and May 2023. Because a significant dose-response relationship was observed between pediatric CT-related radiation exposure and brain cancer,¹⁸ our institution follows guidelines to determine whether CT is performed on children with head trauma.^{19,20} Patients were excluded on the basis of the following criteria: 1) suspicion of abuse, 2) need for craniotomy for decompression within a few days after head injury, 3) cranial depressed fracture requiring a recovery operation, 4) obvious compression and apparent deformation of the lateral ventricles due to hematoma, 5) Ommaya reservoir implantation or drainage surgical procedures, 6) presence of complications such as craniosynostosis, tumor, epilepsy, autism, intracranial arachnoid cyst, chromosomal abnormalities, cardiovascular disease, endocrine disorders, etc., and 7) presence of cavum vergae or cavum septum. Therefore, all subjects were healthy prior to head injury, experiencing only minor trauma, and did not require any surgical interventions.

Multiple follow-up CT scans were conducted in some cases due to medical necessity. However, not all scans were included in the analysis because our primary focus was to determine normal growth curves rather than to correlate growth with head trauma. To select the appropriate scans, we established the following criteria: 1) for patients younger than 1 year with multiple scans taken at different ages (in months), one CT scan was evaluated for each month; 2) for patients older than 1 year with multiple scans taken at different ages (in years), one CT scan was evaluated for each year; and 3) for patients with multiple scans obtained at different ages (in months or years), we evaluated only the scan with the least influence from the head injury.

The Ethics Committee of Osaka Women's and Children's Hospital, Izumi, Japan, provided ethical approval for this study, which was conducted in accordance with the Declaration of Helsinki guidelines for experiments involving humans. Informed consent was obtained using the opt-out method from our center's website because of the retrospective and noninvasive nature of the study.

Data Collection

We conducted a retrospective analysis of CT scans and assessed various medical variables, including sex, age, modified Pediatric Glasgow Coma Scale (mPGCS) score,²¹ and CT findings. For quantitative assessment of intracranial volume, choroid plexus volume, and lateral ventricles volume, DICOM CT data were imported to MATLAB R2020b (MathWorks) and the target areas were segmented manually using the Image Segmenter app in MATLAB (<https://www.mathworks.com/help/images/ref/imagesegmenter-app.html>). Representative segmentation of intracranial volume, choroid plexus volume, and lateral ventricles volume is shown in Supplementary Fig. 1.

The width of each DICOM slice was 5 mm. Choroid plexus observed in the bilateral ventricles and at the foramen of Monro was assessed as a representation of intracranial choroid plexus. The volume of the lateral ventricles was measured as the volume of the bilateral ventricles. These procedures enabled us to calculate the volume (in milliliters) related to the abovementioned parameters, and this method has been used in our other studies.^{22,23}

Statistical Analysis

Categorical data were presented as number (percent). Continuous variables with a normal distribution were presented as mean \pm SD, whereas those with a nonnormal distribution were presented as median with 25%–75% quartiles. Spearman correlation coefficients were calculated to evaluate the correlations among parameters.

To account for the uneven age distribution, we assessed the distribution and defined age-related clusters for adjustment. Mean and 95% CI of the parameters were calculated, and differences between age-related clusters or sexes were compared by assessing overlapping or nonoverlapping CIs. Nonoverlapping CIs were considered an indicator of statistical significance, whereas overlapping CIs were interpreted as indicative of lack of statistical significance.²⁴ Additionally, the unpaired t-test was used to

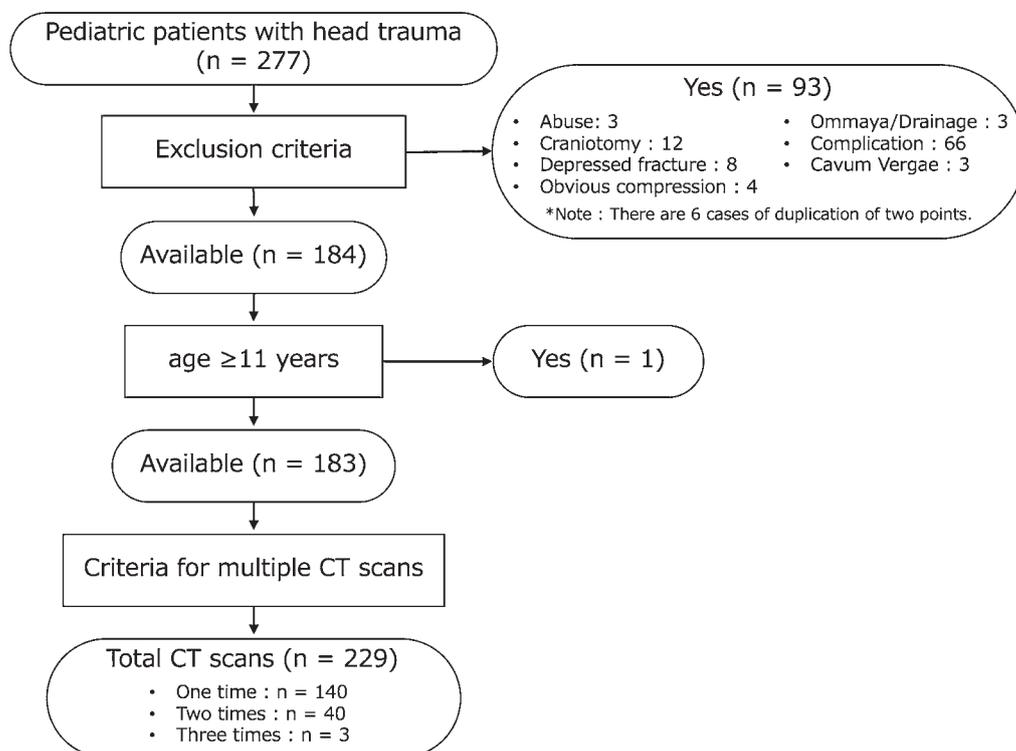


FIG. 1. Patient enrollment and CT scans investigated in this study. This flowchart illustrates the inclusion and exclusion criteria for pediatric patients with head trauma who were investigated in this study. Initially, 277 patients were included, but 93 patients were subsequently excluded. Among the remaining patients, only 1 patient was older than 11 years (specifically 13 years old) and was therefore excluded. Consequently, a total of 183 patients were enrolled. On the basis of our criteria for selecting multiple CT scans, a total of 229 CT scans were obtained for analysis.

compare age-related clusters, and Bonferroni correction was applied for the correction of multiple comparisons. The statistical difference between clusters was considered significant at corrected $p < 0.05$.

The measurements of each parameter were plotted according to months after birth, and the best-fitting logarithmic curves were plotted. Statistical analyses were performed using the Statistical and Machine Learning Toolbox of MATLAB R2020b.

Choroid Plexus Hyperplasia

We collected data from patients with CPH who underwent surgical procedures at our institution between March 2006 and May 2023. The volumes of the parameters were calculated and z-normalized by subtracting the mean values and dividing by the SD of the corresponding age-related clusters.

Data Availability

All data in this study are available from the corresponding author upon reasonable request and after additional ethics approval.

Results

Baseline Characteristics

A total of 277 patients were initially enrolled, but 93

patients were subsequently excluded. Among the remaining 184 patients, 1 patient aged 13 years was excluded as an outlier, resulting in the inclusion of 229 CT scans from 183 patients younger than 10 years of age for evaluation (Fig. 1). Of these CT scans, 94 (41.0%) were obtained from female patients, and the median (range) time interval after birth was 12 (6–43) months. Two CT scans were performed in 40 patients (17 females [42.5%]), and 3 CT scans were performed in 3 patients (0 female [0.0%]).

The majority of the CT scans had an mPGCS value of 15, as observed in 195 scans (85.2%). mPGCS values of 14 were found in 28 scans (12.2%), and values between 9 and 13 were observed in 6 scans (2.6%). Fractures were present in 107 scans (46.7%), including 99 linear fractures (92.5%) and 8 depressed fractures (7.5%). Intracranial bleeding was observed in 67 scans (29.3%), consisting of 33 acute subdural hematomas (49.3%), 26 acute epidural hematomas (38.8%), 13 subarachnoid hemorrhages (19.4%), 3 intracerebral hematomas (4.5%), and 2 intraventricular hemorrhages (3.0%). There were 6 cases of duplicated data points and 2 cases of triplicated data points.

Correlation Analysis

Positive correlations were observed among 3 parameters—intracranial volume, choroid plexus volume, and lateral ventricles volume—in all 3 combinations (Fig. 2). Notably, the correlation coefficient between choroid plexus

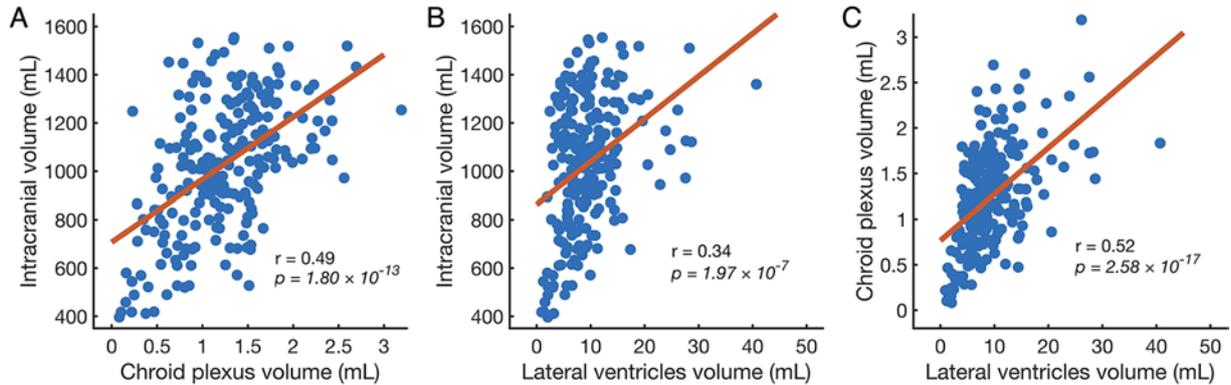


FIG. 2. Correlations between parameters. Scatter plots between intracranial volume and choroid plexus volume (A), intracranial volume and lateral ventricles volume (B), and choroid plexus volume and lateral ventricles volume (C) are presented. The regression lines are indicated as red lines, and *r* represents the correlation coefficients. Figure is available in color online only.

and lateral ventricles volumes reached the highest value, which was significant ($r = 0.52, p = 2.58 \times 10^{-17}$) (Fig. 2C).

Age-Related Clusters

To account for the uneven distribution of the population across different age groups, we categorized the CT scans into 15 age-related clusters: 0 months, 1 month, 2–3 months, 4–5 months, 6–7 months, 8–9 months, 10–11 months, 1 year–1 (i.e., age range 12–17 months), 1 year–2 (i.e., age range 18–23 months), 2 years, 3 years, 4 years, 5–6 years, 7–8 years, and 9–10 years. The number of CT scans performed in each cluster for both males and females is presented in Fig. 3. The population distribution between males and females was uneven due to a higher frequency of CT scans for head trauma in males compared with females.

Sequential Plots of Parameters

The mean values of each cluster, calculated from the total number of CT scans, were plotted sequentially for intracranial volume (Fig. 4A), choroid plexus volume (Fig. 4B), and lateral ventricles volume (Fig. 4C). Intracranial volume consistently increased step-by-step with

each age-related cluster, whereas both choroid plexus and lateral ventricles volume increased until approximately 1 year of age, after which the subsequent rate of increase slowed down. Regarding intracranial volume, the 95% CIs showed almost no overlap among clusters. However, regarding the choroid plexus and lateral ventricles volumes, the 95% CIs after 1 year of age almost showed overlap.

The plots generated from males and females are shown in the lower row of Fig. 4. Except for the error bars for intracranial volume at ages 6–7 months, 8–9 months, and 7–8 years (Fig. 4D), the error bars of the males and females showed overlap in each cluster. We noted that the 95% CIs had negative values due to the small number of included females (Fig. 4E–F). Therefore, in this study, we could not determine any differences between males and females due to the small sample sizes; in the following analyses, we present the results obtained from all CT scans.

We plotted the sequential temporal volume changes observed in each patient who underwent multiple CT scans (Supplementary Fig. 2). We observed an increase in intracranial volume over time. However, some patients showed a decrease in choroid plexus and lateral ventricles volumes.

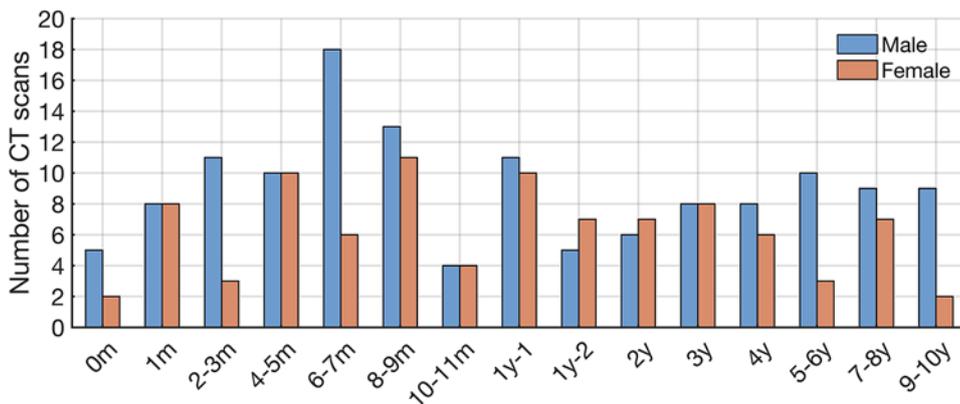


FIG. 3. Distribution of the population based on age-related clusters. Fifteen age-related clusters were defined, ranging from 0 months (*m*) to 9–10 years (*y*). The cluster labeled as *1y-1* corresponds to an age range of 12 to 17 months, and the cluster labeled as *1y-2* corresponds to an age range of 18 to 23 months. Figure is available in color online only.

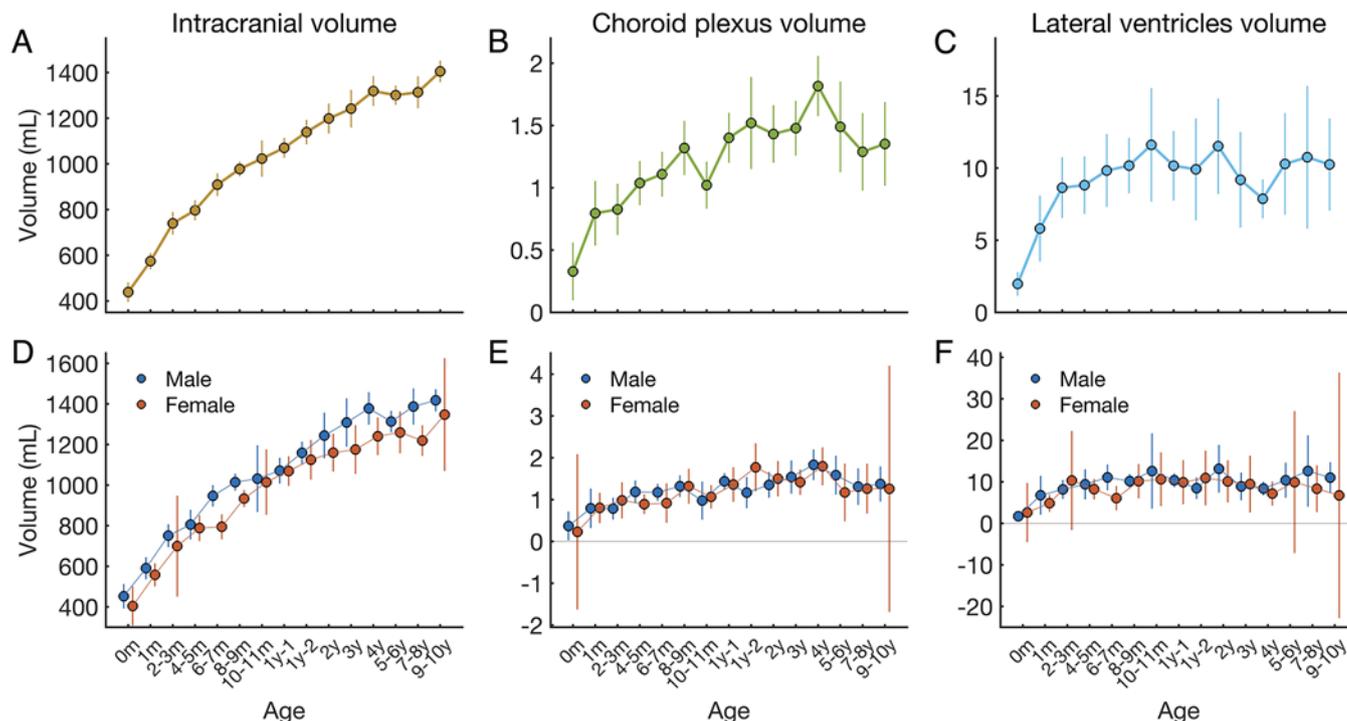


FIG. 4. Sequential plots of mean values. The mean values were calculated for each age-related cluster and sequentially plotted for the 3 parameters. The panels of the upper row were based on all CT scans (A–C), and the panels of the lower row were based on CT scans in males and females (D–F). Error bars indicate 95% CIs. Figure is available in color online only.

Statistical Differences Among Age-Related Clusters

To compare the volumes between two different age-related clusters for each parameter, we performed the unpaired t-test. To account for multiple comparisons, we applied Bonferroni correction by multiplying the obtained p values by 105, which was the total number of combinations [${}_{15}C_2 = (15 \times 14)/2$]. The significant differences in volume, with corrected p values less than 0.05, were presented as a color-scaled matrix (Fig. 5). We observed significant differences in intracranial volume between two different age-related clusters with patients younger than 2 years of age (Fig. 5A). However, except for the combinations of 0 months and the other age-related clusters, we found almost no significant differences between clusters in terms of choroid plexus and lateral ventricles volumes (Fig. 5B–C).

Growth Curve

Scatter plots against age in months were used to generate the best-fitting logarithmic curves: $y = 196.99 \log(x + 1) + 496.60$ for intracranial volume (Fig. 6A), $y = 0.20 \log(x + 1) + 0.71$ for choroid plexus volume (Fig. 6B), and $y = 0.90 \log(x + 1) + 6.90$ for lateral ventricles volume (Fig. 6C). For intracranial volume, the growth rate was faster until approximately 20 months of age and then slowed down after 20 months. However, for choroid plexus and lateral ventricles volume, the growth rate slowed down quickly by approximately 10 months of age.

Cases With CPH

Three cases with CPH were included in this study.

Patient 1. Patient 1 (P1) presented to our department at 3 years 4 months of age with abnormal head enlargement. Head CT revealed hydrocephalus and choroid plexus enlargement. She underwent ventriculoperitoneal shunt (VPS) placement and was diagnosed with trisomy 9p. Follow-up for 16 years showed no complications after VPS placement. The size of the enlarged choroid plexus remained unchanged on CT imaging, leading to the diagnosis of CPH.

Patient 2. Patient 2 (P2) was diagnosed with head enlargement at 4 months after birth and was referred to our department. Head CT imaging revealed hydrocephalus and choroid plexus enlargement. At 5 months of age, she underwent VPS placement. At 1 year of age, she developed refractory ascites and underwent external ventricular drainage (EVD). Daily production of CSF was approximately 2400 ml. One week later, ventriculoatrial shunt (VAS) placement was performed. Staged bilateral plexectomy was conducted between 2 and 4 months later, with pathological examination confirming CPH. The VAS was removed after the procedure. She has been monitored for 8 years without any medical problems.

Patient 3. Patient 3 (P3), with trisomy 9p and partial trisomy 9q, had been under the care of our hospital's department of medical genetics. At 1 year of age, he was referred to our department owing to hydrocephalus. Head CT imaging revealed choroid plexus enlargement, leading to the decision to perform VPS placement combined with bilateral endoscopic plexus coagulation (BEC). Pathological examination confirmed CPH. Supplementary Figure 3 displays CT and MRI scans obtained after the operations,

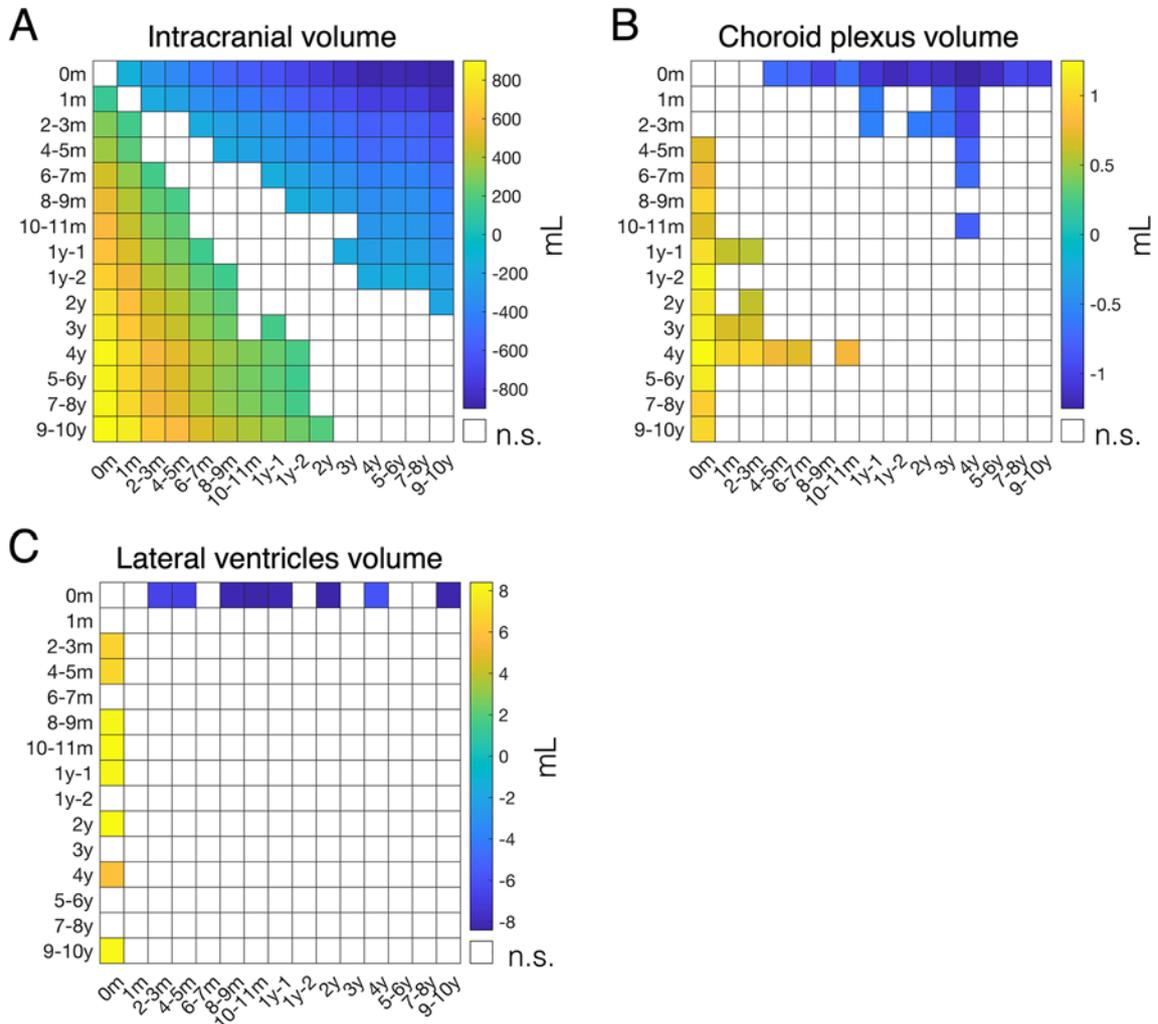


FIG. 5. Color-scaled matrix of significant differences in volume. Differences among the age-related clusters in terms of intracranial volume (A), choroid plexus volume (B), and lateral ventricles volume (C) are presented as a color-scaled matrix. Positive differences, indicating larger volumes in the longitudinal axis compared to the horizontal axis, are colored in *green* to *yellow*. Negative differences, indicating smaller volumes in the longitudinal axis compared to the horizontal axis, are colored in *blue*. Only differences that were significant with corrected *p* values < 0.05 are colored. n.s. = not significant. Figure is available in color online only.

showing similar volumes for the choroid plexus and lateral ventricles. Two weeks later, the patient experienced surgical wound dehiscence and developed meningitis. EVD was performed, and meningitis was treated with antibiotics. The daily production of CSF was approximately 2000 ml. After recovering from meningitis, he was transferred to another hospital, where he underwent one-stage bilateral plexectomy.

Their profiles are summarized in Table 1. The volumes of the parameters were calculated and z-normalized using the mean and SD values obtained from normal age-related clusters (Supplementary Table 1). The results were plotted over the plots calculated from the normal groups (Fig. 7A–C). The z-normalized values of the choroid plexus and lateral ventricles volumes were notably larger than those of intracranial volume.

Specifically, for P2 and P3, the changes in the z-normalized values from the time of initial diagnosis of CPH

to the time of EVD are presented in Figs. 7D–F. The z-normalized values of intracranial volume and lateral ventricles volume decreased. In the case of P3, the z-normalized choroid plexus volume decreased from 51.17 to 38.93 (23.9% decrease) due to BEC.

Discussion

Using CT scans from Japanese pediatric patients with minor head trauma, we generated normal growth curves for intracranial volume, choroid plexus volume, and lateral ventricles volume. Positive correlations were observed among these parameters. The growth rate of intracranial volume was rapid until approximately 20 months of age, while the growth rates of choroid plexus and lateral ventricles volumes slowed down by approximately 1 year of age. Subsequently, the volumes of choroid plexus and lateral ventricles stabilized at around 1.5 ml and 10 ml, respectively. We utilized z-normalization to objectively assess

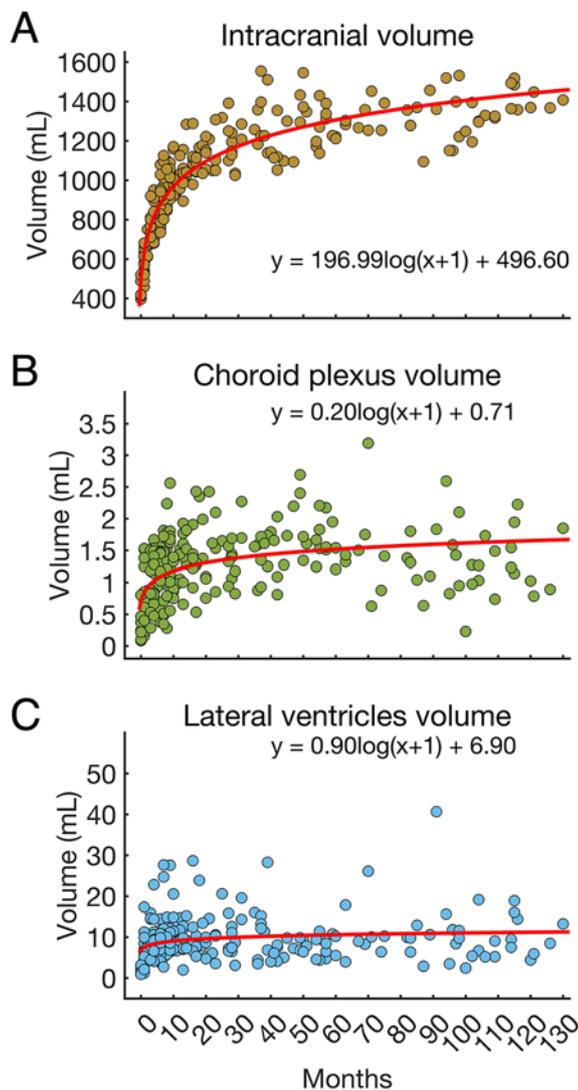


FIG. 6. Scatter plots and growth curves. Scatter plots with age in months along the x-axis are presented for intracranial volume (A), choroid plexus volume (B), and lateral ventricles volume (C). The best-fitting logarithmic curves are indicated as red curves. Figure is available in color online only.

hydrocephalus caused by CPH and its impact of surgical procedures.

Although MRI is commonly used to assess the volume of the ventricles⁹ or choroid plexus,^{13–17,25–27} we chose to utilize CT imaging in our evaluation. The border between the choroid plexus and ventricle wall is more clearly defined with MRI, while it appears less distinct with CT imaging (Supplementary Figs. 1 and 3). Consequently, MRI is considered the superior method for choroid plexus assessment. However, obtaining head MRI from healthy children without underlying conditions can be challenging. Hence, we utilized CT scans from pediatric patients with minor head trauma and no pre-existing health issues. The volumes calculated from the CT scans of P3 showed similar values to those obtained from MRI (Supplementary Fig. 3). A previous MRI study reported a mean choroid plexus volume

TABLE 1. Clinical profiles of the patients with CPH

Patient No.	Sex	Age at Diagnosis of CPH	Preop Intracranial Vol (z.v.)	Preop Choroid Plexus Vol (z.v.)	Preop Lateral Ventricles Vol (z.v.)	1st Procedure	Complications	Further Procedures	Daily CSF Production (ml)	Definitive Procedure	Genetic Diagnosis
P1	F	3 yrs 4 mos	1687.8 ml (2.89)	17.3 ml (38.67)	386.9 ml (60.83)	VPS	No				Trisomy 9p
P2	F	5 mos	1430.5 ml (6.75)	10.2 ml (24.11)	530.1 ml (122.36)	VPS	Ascites	EVD, VAS	2400	SBP	
P3	M	1 yr 1 mo	1522.4 ml (4.75)	23.9 ml (51.17)	257.6 ml (46.78)	BEC + VPS	SWD + meningitis	EVD	2000	OSBP	Trisomy 9p + partial trisomy 9q

OSBP = one-stage bilateral plexectomy; SBP = staged bilateral plexectomy; SWD = surgical wound dehiscence; z.v. = z-normalized value.

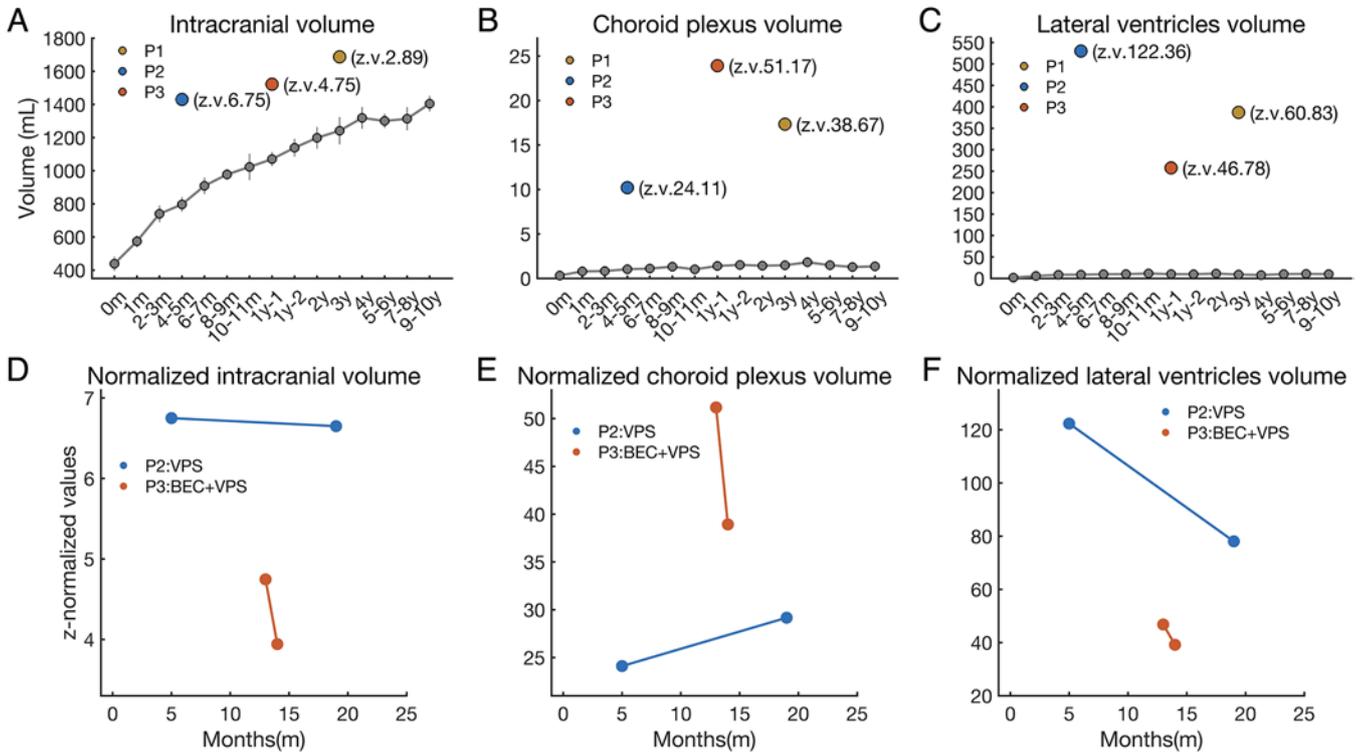


FIG. 7. Results from cases with CPH. Volumes calculated from the patients with CPH for each parameter are presented in the upper row (A–C), with plots and lines calculated from normal age-related clusters indicated in gray, similar to the upper panels of Fig. 3. The changes of the z-normalized values of P2 and P3 for each parameter are presented in the lower row (D–F). z.v. = z-normalized value. Figure is available in color online only.

of approximately 1.2 ml in adult control groups,¹⁶ which aligns with our findings. Moreover, because only one evaluator (H.H.) segmented the choroid plexus, there was consistency in our measurements. Additionally, a previous MRI study indicated that the 50th percentile of ventricular volume after 1 year of age was approximately 10 ml, with rapid growth occurring in the 1st year of life.⁹ This is consistent with our results. Although we used CT scans with a 5-mm slice width and had concerns about lower resolution, a previous CT study that employed a slice width of 2 mm or less reported normal pediatric growth curves for intracranial volume,⁸ similar to our findings. These consistencies between previous findings and our results validate our methodology and outcomes. However, it is important to note that the use of CT is a limitation of this study.

Posttraumatic hydrocephalus, with an incidence ranging from 0.7% to 50%, can develop after a brain injury.^{28,29} In Supplementary Fig. 2, we show a temporal reduction in choroid plexus and lateral ventricles volumes. This led us to suspect that the initially enlarged ventricles after head injury might return to a normal state. Previous studies have reported a positive correlation between choroid plexus and lateral ventricles volumes,^{13,17,27} as we also found. However, the causal relationship between these volumes remains unclear. Although it is natural for a large volume of choroid plexus to induce a large volume of the lateral ventricles in patients with CPH, larger ventricles could potentially overestimate choroid plexus volume. Because the choroid plexus is a soft tissue, its size is likely to vary depending

on the size of the ventricles. Consequently, cases with larger lateral ventricles, possibly due to head trauma, exhibited larger choroid plexus volumes. In this study, we assumed that minor head trauma had no impact on the growth of the intracranial structures. Further research is needed to explore this relationship. It is important to acknowledge that the inclusion of patients with head trauma is a significant limitation of this study.

We categorized the pediatric patients into age-related clusters and calculated volumes within each cluster. Mean and SD values were obtained for each cluster (Supplementary Table 1), and these were used to calculate z-normalized values. A z-normalization approach is commonly used to compare groups with different baseline values, such as with electroencephalogram-related frequency analysis.³⁰ In the field of pediatric neurosurgery, because the baseline values of intracranial volume vary among patients of different ages, we found that z-normalization was useful for comparing volumes across different age groups. Adult studies have assessed variability in head size. For example, choroid plexus volume was corrected for intracranial volume,¹² and the 2-dimensional Evans index has been used to evaluate normal pressure hydrocephalus. However, the limitations of the Evans index have been noted,^{31,32} and the importance of 3-dimensional assessment has been emphasized.⁹ Our study provides normal volume values, which are 3-dimensional data and have the potential to enable assessment of pediatric hydrocephalus while accounting for the growth of intracranial structures. Specifically, because we demon-

strated the rapid rate of growth of the choroid plexus and lateral ventricles until 1 year of age, we believe that accounting for normal growth is essential to the assessment of pediatric hydrocephalus in patients younger than 1 year.

Although there are no established radiological criteria for defining the dimensions of a normal choroid plexus or CPH,^{7,33} thereby resulting in subjective diagnoses, we aimed to provide an objective assessment of CPH. In the case of P1, although the actual intracranial volume was the highest among the 3 patients, its z-normalized value was the lowest. In the case of P2, the z-normalized choroid plexus volume increased due to growth after VPS treatment, while the z-normalized intracranial volume and lateral ventricles volume improved. In the case of P3, BEC was added to VPS treatment, resulting in a reduction of approximately 24% in z-normalized choroid plexus volume and improvement in z-normalized intracranial volume and lateral ventricles volume. These changes likely reflected the effect of VPS or BEC. Our findings have the potential to provide an objective assessment of abnormal volumes in hydrocephalus or choroid plexus disorders, such as CPH, choroid plexus papilloma, and choroid plexus carcinoma. However, further studies are needed to demonstrate the usefulness of our normal growth curves for objective assessment of the effects of surgery.

Our findings indicate that the choroid plexus exhibits rapid growth until 1 year of age, reaching a volume of approximately 1.5 ml. After this point, it reaches a plateau. Interestingly, a previous study reported a different trend, with choroid plexus volume decreasing between the ages of 5 and 10 years and then stabilizing.¹⁷ Furthermore, the calculated mean choroid plexus volume in the adult control groups was approximately 1.2 ml,¹⁶ and it has been noted that choroid plexus volume increases with age after 50 years.¹² These findings suggest that the growth rate of choroid plexus volume is rapid until approximately 1 year of age, averaging 1.5 ml, followed by a decrease to an average of 1.2 ml and subsequent stabilization. Additionally, there may be a resurgence in the growth of choroid plexus volume after the age of 50 years.

CPH is a rare pediatric disorder characterized by the overproduction of CSF. Trisomy 9p and tetrasomy 9p have been associated with CPH, as genes on chromosome 9p are likely involved in the regulation of choroid plexus growth.³³ In our study, 2 of 3 patients in our study showed trisomy 9p. Although VPS placement is the initial treatment for most cases, nearly all CPH patients experience complications such as refractory ascites, often necessitating additional procedures such as BEC or choroid plexus removal.⁷ CSF production exceeding 2000 ml daily has been reported,^{7,34–36} and it has been suggested that hydrocephalus caused by villous hyperplasia of the choroid plexus can be resolved with a VAS if CSF production does not exceed 1000 ml/day.³⁷ In our study, 1 patient was successfully treated with VPS placement alone, while the other 2 patients with daily CSF production exceeding 2000 ml experienced complications. One of these patients developed meningitis, which is known to decrease CSF absorption due to an inflammatory response.²⁹ This may have worsened the patient's hydrocephalus and increased the daily drained CSF volume. Considering the challenges that we

encountered with VPS-related complications in CPH patients, it is crucial for neurosurgeons to identify factors that render VPS ineffective for CPH-related hydrocephalus.

Although our study did not reveal significant differences between males and females, it is important to acknowledge that our sample size, especially for females, may have been insufficient to detect sex-related differences. The proportion of females in our study was approximately 40%, which could be lower than the proportion of males due to the enrollment of children with head trauma. A previous study that investigated head injury in individuals aged 15 to 79 years reported that females consisted of only 23% of the study population.³⁸ These findings suggest that males have a higher incidence rate of head trauma compared with females in both pediatric and adult populations. However, previous studies that evaluated adult or pediatric ventricular volume reported no significant effect of sex¹² or slightly lower ventricular volumes in females compared with males.⁹ Therefore, it is possible that there may be no statistical differences in the growth of intracranial volume, choroid plexus volume, and lateral ventricles volume between sexes.

Our study had a few additional limitations. First, we were unable to collect data on low-birth-weight infants, which could have influenced the growth curves presented in our study. Secondly, our study included data from only Japanese children, so there is a possibility that racial differences may have impacted our results. However, because our findings were consistent with those from other populations,^{9,16} we believe that these differences can be disregarded. Lastly, our study provided only results for children as old as 10 years of age, and the growth curves for children older than 10 years are still unknown.

Conclusions

Our study, conducted on Japanese pediatric patients with minor head trauma, provides normal growth curves for intracranial volume, choroid plexus volume, and lateral ventricles volume. Choroid plexus volume and lateral ventricles volume demonstrated rapid increases until 1 year of age, reaching approximately 1.5 ml and 10 ml, respectively, and plateauing thereafter. Using z-normalization, we demonstrated the potential for objective assessment of hydrocephalus severity in CPH patients and the evaluation of surgical intervention effectiveness. Our findings contribute to the objective evaluation of hydrocephalus and choroid plexus-related disorders while considering the growth patterns of children. Objective assessments have the potential to unveil factors associated with complications after CPH surgical procedures, providing crucial insights for neurosurgeons planning interventions for CPH patients.

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Disclosures

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

Author Contributions

Conception and design: Hashimoto, Chiba. Acquisition of data: all authors. Analysis and interpretation of data: Hashimoto. Drafting the article: Hashimoto. Critically revising the article: Hashimoto,

Chiba. Reviewed submitted version of manuscript: Hashimoto, Chiba. Approved the final version of the manuscript on behalf of all authors: Hashimoto. Statistical analysis: Hashimoto. Administrative/technical/material support: Hashimoto, Takemoto, Chiba. Study supervision: Takemoto, Chiba.

Supplemental Information

Online-Only Content

Supplemental material is available with the online version of the article.

Supplementary Figures and Table. <https://thejns.org/doi/suppl/10.3171/2023.7.PEDS23218>.

Data Availability

All data in this study are available from the corresponding author upon reasonable request and after additional ethics approval.

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Correspondence

Hiroaki Hashimoto: Osaka Women's and Children's Hospital, Izumi, Osaka, Japan. h-hash@wch.opho.jp; h-hashimoto@ndr.med.osaka-u.ac.jp.