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Subdural hematoma prevalence and long-term developmental outcomes in patients with benign expansion of the subarachnoid spaces

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OBJECTIVE Benign expansion of the subarachnoid spaces (BESS) is a condition seen in macrocephalic infants. BESS is associated with mild developmental delays which tend to resolve within a few years. It is accepted that patients with BESS are at increased risk of spontaneous subdural hematomas (SDHs), although the exact pathophysiology is not well understood. The prevalence of spontaneous SDH in BESS patients is poorly defined, with only a few large single-center series published. In this study the authors aimed to better define BESS prevalence and developmental outcomes through the longitudinal review of a large cohort of BESS patients.

METHODS A large retrospective review was performed at a single institution from 1995 to 2020 for patients 2 years of age or younger with a diagnosis of BESS by neurology or neurosurgery and head circumference > 85th percentile. Demographic data, head circumference, presence of developmental delay, occurrence of SDH, and need for surgery were extracted from patient charts. The subarachnoid space (SAS) size was measured from the available MR images, and the sizes of those who did and did not develop SDH were compared.

RESULTS Free text search revealed BESS mentioned within the medical records of 1410 of 2.6 million patients. After exclusion criteria, 480 patients remained eligible for the study. Thirty-two percent (n = 154) of patients were diagnosed with developmental delay, most commonly gross motor delay (53%). Gross motor delay resolved in 86% of patients at a mean age of 22.2 months. The prevalence of spontaneous SDH in this BESS population over a period of 25 years was 8.1%. There was no significant association between SAS size and SDH formation.

CONCLUSIONS This study represents results for one of the largest cohorts of patients with BESS at a single institution. Gross motor delay was the most common developmental delay diagnosed, and a majority of patients had resolution of their delay. These data support that children with BESS have a higher prevalence of SDH than the general pediatric population, although SAS size was not significantly associated with SDH development.

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KEYWORDS benign expansion of the subarachnoid spaces; benign external hydrocephalus; cerebrospinal fluid; subdural hematoma; motor development; head circumference; trauma

BENIGN expansion of the subarachnoid spaces (BESS) is a common condition seen by pediatric neurologists and neurosurgeons in macrocephalic infants, with an incidence of 0.4 per 1000 live births in term infants.[1,2] Also known as benign external hydrocephalus (BEH), the condition is characterized by a rapid increase in head circumference within the first 12 months of life. On imaging, these infants typically have enlarged subarachnoid space (SAS), particularly over the bilateral frontal lobes, with normal to mildly enlarged lateral ventricles on neuroimaging (Fig. 1).[2–5] While the macrocrania often persists to adulthood, the enlargement of the extra-axial fluid spaces typically resolves by 2–3 years of age.[5–7] Although the pathophysiology of BESS remains unknown, several investigators suggest that a delay in maturation of the arachnoid villi results in an inability to absorb CSF. CSF accumulates in the SAS until the arachnoid villi mature at around 18 months of age.[3–6]

ABBREVIATIONS ASD = autism spectrum disorder; BEH = benign external hydrocephalus; BESS = benign expansion of the subarachnoid spaces; NAT = nonaccidental trauma; SAS = subarachnoid space; SDH = subdural hematoma.

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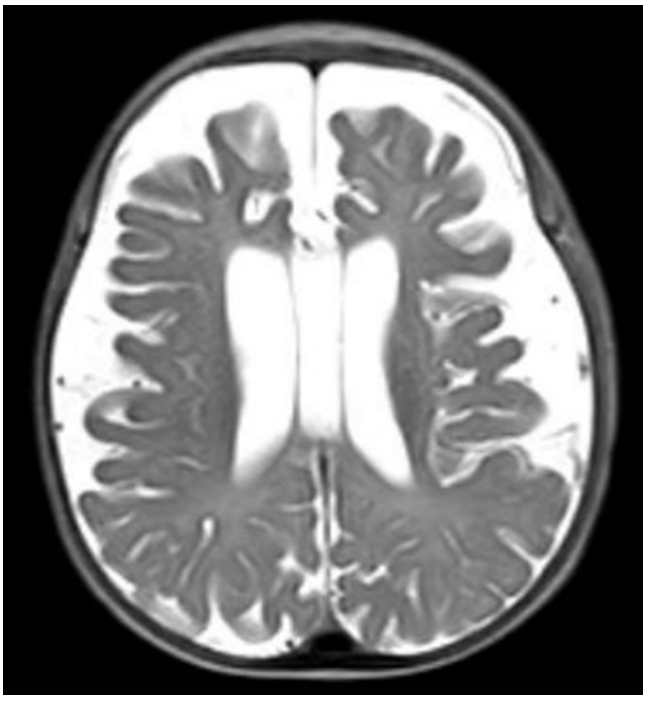

FIG. 1. Axial T2-weighted MR image of an infant with BESS. There is enlargement of the SAS, specifically along the bilateral frontal lobes. Patients may or may not have mild ventriculomegaly as well.

BESS is frequently associated with mild developmental delay, particularly gross motor and speech/language delay.[3–5,8,9] In a prior retrospective study of 99 patients with BESS, the majority of motor delays resolved within the 13-month follow-up period.[9] While these delays were thought to resolve in the first few years of life, recent long-term studies have challenged this assumption. One study documented subtle motor deficits on long-term follow-up, while other studies have documented subtle neurocognitive difficulties persisting into adolescence.[9–11]

BESS is thought to be a risk factor for subdural hematoma (SDH) formation with or without minor trauma. It is hypothesized that this is due to the enlarged SAS leading to stretching of bridging veins. As a result, these infants may be more prone to injury after even minor trauma.[12] In the general population, the incidence of SDH in infants younger than 2 years is 13–16.5 cases per 100,000 infants.[13–15] In infants with BESS, the prevalence of spontaneous SDHs, defined as onset of SDH without a known inciting event, has been estimated between 4% and 5.8%,[9,16] although this number is poorly defined, with only a few large single-center studies published. In this study we aimed to better define this prevalence and developmental outcomes through the longitudinal review of a large cohort of BESS patients treated at a single institution. To our knowledge, this is the largest published cohort of BESS patients followed over a long term.

Methods

A retrospective review was performed at a single institution from 1995 to 2020. The institutional review board designated the study as exempt (HUM00170641). The electronic medical record was queried using the Electronic Medical Record Search Engine (EMERSE)[17] for all patients for the term "benign external hydrocephalus" or "benign expansion of the subarachnoid spaces." Patients were included if they were seen by neurology or neurosurgery to confirm the diagnosis, were diagnosed at 2 years of age or younger, had neuroimaging available, and had a head circumference > 85th percentile for corrected age. Patients were excluded if they were not diagnosed with BEH or BESS, had not seen a neurologist or neurosurgeon, or lacked cranial imaging. Ninety-nine patients seen between 1997 and 2002 were previously reported.[9] Patient demographics, head circumference, developmental delay, length of follow-up, occurrence of SDH, comorbidities, need for surgery, and imaging findings were extracted from the medical record. Follow-up visits included routine pediatrician, neuropsychological/neurodevelopmental, and neurology/neurosurgery clinic visits but did not include other subspecialty visits as such visits would be less likely to record developmental outcomes over time. Developmental delay and autism spectrum disorder (ASD) diagnosis were recorded if the diagnosis was confirmed with documented neuropsychiatric testing. All MR images were reviewed by one of two board-certified neuroradiologists. SAS size was defined as the largest distance between the brain and inner cortex of the skull along either frontal lobe and then graded in accordance with the prior published classification by Tucker et al.,[16] who described a 3-point scale to grade SAS size: < 5-mm depth of the SAS is BESS grade 0, 5–9 mm is grade 1, and ≥ 10 mm is grade 2.[16]

Statistical Analysis

IBM SPSS Statistics for Macintosh version 27.0 (IBM Corp.) was used for statistical analysis. A Pearson chi-square test was used to determine if there was a significant relationship between the SAS size grade and SDH formation. In addition, a one-way ANOVA was used to determine if SAS size differed between patients who did and did not develop SDH. A Tukey post hoc analysis was applied to the one-way ANOVA.

Results

Over 2.6 million patients' medical records were queried retrospectively from a single institution between 1995 and 2020 (Fig. 2). Of those, 1410 patients had BEH or BESS mentioned within their charts. When patients with incomplete records were excluded (318 patients did not have cranial imaging or clinical notes and 309 were not seen by neurology or neurosurgery), 783 patients were included in initial review of the medical record. The medical records of these patients were reviewed in detail. Ultimately, 480 patients were included in this cohort, after the exclusion of patients with a head circumference < 85th percentile (n = 170), patients diagnosed when older than 2 years (n = 55), and patients whose notes specified that they had "no diagnosis of BESS or BEH" (n = 78).

Demographics

There were 480 patients included in this study. Of

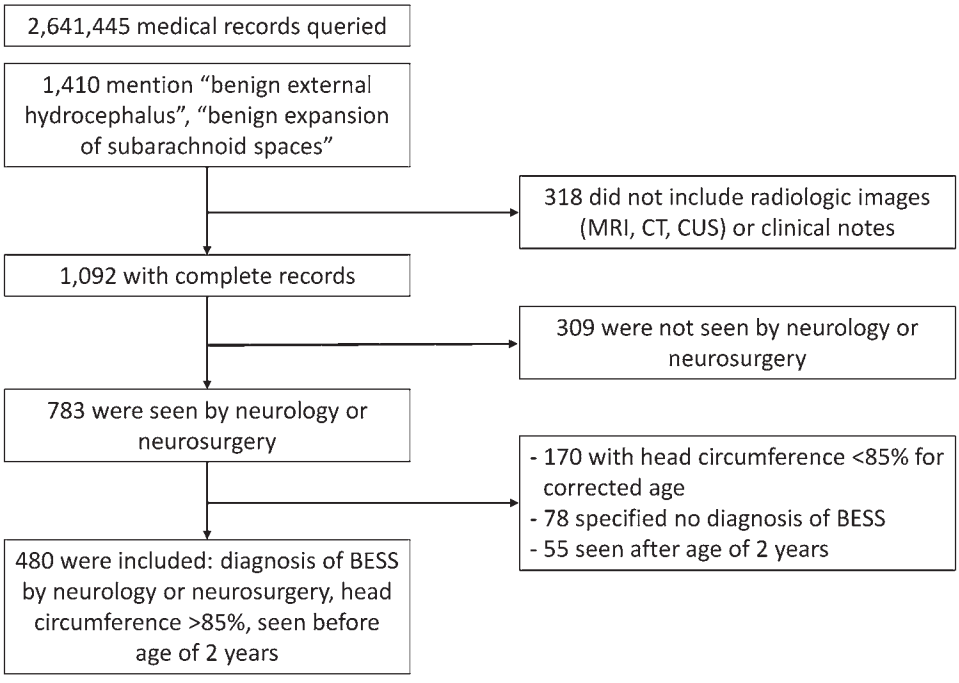

FIG. 2. BESS was mentioned in the medical records of 1410 patients. We excluded 318 patients due to incomplete charts and an additional 309 were not seen by neurology or neurosurgery. Ultimately, 480 patients were included in this study. CUS = cranial ultrasound.

these, 65% (n = 314) were male. The mean age at diagnosis was 9.1 months, ranging from 0.8 months to 24 months. In total, 360 patients (75%) were seen by neurosurgery. The vast majority, 89% (n = 428), were seen in an outpatient setting, while the remainder were seen for the first time as an inpatient or in the emergency department. Approximately 89% (n = 429) were referred by their pediatrician for evaluation. The majority of patients were evaluated due to macrocrania (Table 1). The average length of follow-up was 4.1 years (0 to 23.3 ± 4.9 years). A majority of patients, 62%, were seen before 2010 (Fig. 3).

Developmental Delay

Clinicians demonstrated concern for developmental delay in 32% (n = 154) of patients based on history and physical examination performed at the initial neurological evaluation, which was then confirmed with further neuropsychiatric testing at a separate visit. All patients with developmental delay were referred to the state-based early intervention service. Eighty-two of these patients were reported to have gross motor delay, 52 had global delay, and 20 had speech/language delay. When looking specifically at children with gross motor delay, 71 (86%) had resolution of their delay at a mean age of 22.2 months (± 10.8 months). Twenty-three patients (4.8%) were diagnosed with ASD during their follow-up.

TABLE 1. Reason for patient evaluation by neurology and neurosurgery

Reason for Evaluation	No. of Pts (n = 480)
Macrocrania	350
Craniofacial anomaly	30
SDH	30
Developmental delay	18
Seizures	14
Other	38

Pt = patient.

SDH in Study Patients

A total of 58 patients (12%) were found to have an SDH during their clinical course. Out of the total population, we found that 8.13% (n = 39) of patients with BESS developed a spontaneous SDH. Eleven patients were seen prior to diagnosis of their SDH, and their characteristics are detailed in Table 2. Seven patients (12%) were found to have an SDH thought to be due to nonaccidental trauma (NAT) as confirmed by skeletal survey, presence of retinal hemorrhages, or social work notes and investigation by the Child Protection Team. About 75% of patients with spontaneous SDHs underwent an NAT workup, as mentioned previously, which was negative. The remainder of SDHs (n = 12, 20%) were due to trauma.

Nine patients underwent surgery for their SDH, with a total of 12 operations (Table 3). The most common surgery was burr hole drainage of the SDH (n = 6), followed by subdural to peritoneal shunts (n = 5), and ICP monitor placement (n = 1).

SAS Size and SDH Formation

Of the 480 patients included in the study, 187 children had MR images of the brain available for review. The av-

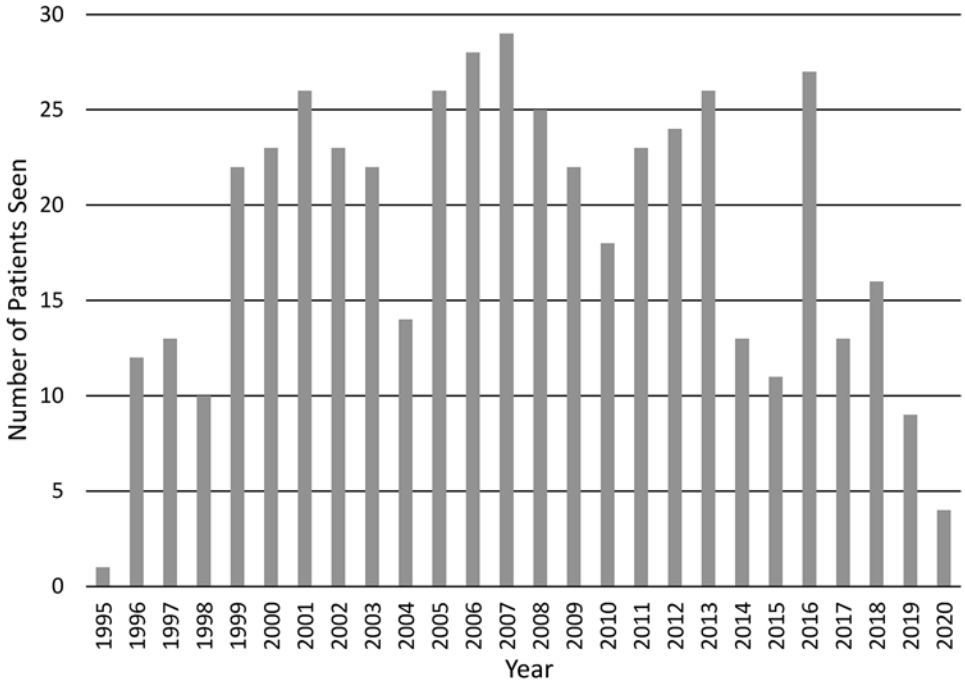

FIG. 3. Number of BESS patients seen by neurology and neurosurgery by year. A majority of patients were seen before 2010.

erage size of the SAS was 5.8 mm (± 2.3 mm). A majority of patients, 64.7%, had a grade 1 SAS. About 39% had ventriculomegaly as defined by the reading neuroradiologist. Using the grading system, there was not a significant association between SAS grade and prevalence of SDH ($p = 0.1$). SAS size was not significantly different between patients with and those without SDH formation ($p = 0.4$).

Discussion

In this retrospective study of 480 patients with BESS, followed for an average of 4.08 years, we assessed and reported the long-term developmental outcomes of patients with BESS and prevalence of SDHs.

Developmental Delay

In our study, clinicians expressed concern for developmental delay during initial consultation in 32% of patients. Gross motor delay was the most common developmental delay in our cohort, which is consistent with prior studies.[3–5,8,9] One explanation that has been offered for gross motor delay in these infants is that a relatively massive head is more difficult to balance and support until a time of more advanced neuromuscular development.[5,9,18] Investigators who conducted recent long-term studies have asserted that motor delays persist longer than previously reported.[9–11] More recently, in a study by Zahl and colleagues of 133 BESS patients, around 6% had a persistent

TABLE 2. Detailed descriptions of the 11 patients seen in the neurology or neurosurgery clinic prior to SDH formation

Pt No.	Age at Dx (mos)	Time to SDH (mos)	SDH Discovery	Surgery
1	8	0	Incidental on routine imaging	No
2	7	12	Incidental on routine imaging	No
3	9	16	Trauma	No
4	6	16	Incidental on routine imaging	Yes, burr hole evacuation
5	7	0	Incidental on routine imaging	No
6	5	26	Minor trauma	No
7	13	1	Incidental on routine imaging	No
8	11	3	Incidental on routine imaging	No
9	10	0.5	Minor trauma	No
10	4	4	Minor trauma	No
11	7	0.5	Minor trauma	No

Dx = diagnosis.

TABLE 3. Detailed descriptions of the 9 BESS patients who underwent surgery for SDH

Pt No.	Age (mos)	SDH Cause	Surgery
1	2	NAT	Subdural to peritoneal shunt
2	6	Spontaneous	Burr holes
3	5	NAT	Bilat subdural to peritoneal shunts
4	7	Spontaneous	Burr holes
5	21	Spontaneous	Burr holes followed by subdural to peritoneal shunt
6	3	Trauma	ICP monitor placement due to trauma
7	5	NAT	Burr holes
8	15	Trauma	Burr holes twice followed by subdural to peritoneal shunt
9	12	Spontaneous	Bilat subdural to peritoneal shunts

motor impairment/clumsiness at long-term follow-up.[11] This study by Zahl et al. included only patients with a head circumference > 97.5th percentile and relied on patient or parent report of physical impairment. By including only patients with a head circumference > 97.5th percentile, these data may be biased toward the most severe cases. Additionally, by relying on patient and parent report of symptoms, confirmation bias may come into effect whereby parents who expect their children to display developmental delay are more likely to interpret behaviors as mild developmental delay. It should be noted that detection bias may play a role in the elevated rates of developmental delay, as infants with macrocrania and developmental delay are more likely to undergo cranial imaging. Using clinician evaluation to determine resolution, we found that 86% of patients with gross motor delay had resolution at a mean age of 22.2 months. Our study lends further support to these findings in that most, but not all, patients had resolution of their gross motor delay.

Interestingly, 23 patients (4.8%) were diagnosed with ASD at some point during their follow-up. This is more than double the US prevalence of ASD, which is 1.8%.[19] This association has been previously noted by Zahl and others.[11] Children with ASD commonly have macrocrania, with a recent study showing an increase in extra-axial fluid on MRI in infants who would go on to develop ASD.[20] In their case-control study, Shen et al.[20] found that patients with ASD had significantly more extra-axial CSF than controls, which contributed to their macrocrania. These authors suggest that the macrocephaly in patients with ASD may be due to CSF accumulation and stagnation within the SAS.[20] This could imply a common genetic origin between macrocephaly and ASD. Other studies have shown that children with BESS perform below their peers in school, indicating the presence of subtle neurocognitive difficulties that persist into adolescence.[9,10] Caution should be taken when interpreting these results, as detection bias may be influencing the diagnosis of mild ASD in these children. This bias is twofold: parents and pediatricians are likely to monitor children with a diagnosis of BESS more closely for developmental delay, and children with neurocognitive problems are more likely to undergo imaging.

SDH Prevalence

In our population, 12% of patients were found to have SDHs during their clinical course. Eleven patients with BESS were seen prior to developing an SDH. Of these SDHs, 39 were without NAT or other significant trauma. Prior case series have reported lower incidences of SDH in this population, which may have been due to the length of follow-up in this study; the mean follow-up of 4.1 years is more than 3 times the prior follow-up durations.[9,16] Although patients with BESS are more likely to develop an SDH, very few of them require surgical intervention. Only 15.5% of patients with SDH in our study underwent surgery, most commonly burr hole drainage or subdural to peritoneal shunts.

The pathophysiology of increased risk of SDH formation is not well understood. The current hypothesis states that the increased width of the SAS stretches the bridging veins and predisposes them to rupture.[21] This hypothesis is supported by Papasian and Frim's mathematical model of the intracranial space.[12] Even though these patients are at increased risk of SDH formation with or without trauma, it is essential to perform a thorough trauma and NAT workup.[6,16,21,22]

Given the larger prevalence of SDH formation in the BESS population compared to the general pediatric population, we looked for an association between SAS grade and risk of SDH formation. In our cohort, there was no statistically significant difference in SAS grade and SDH development. The SAS grading system as described by Tucker et al.[16] was used for consistency. The data on SAS size and development of SDH are mixed. In their study of 311 patients with BESS, Tucker and others found there was a very significant association between the prevalence of SDHs and the grade of SAS. There was also a significant difference in prevalence of SDHs between patients with and without BESS. In Tucker et al.'s study, head circumference data were only available in 139 patients, raising the possibility that patients with other forms of enlarged extracerebral spaces, such as brain atrophy, were included in that study.[16] Our study only included patients with a head circumference > 85th percentile to avoid inclusion of patients with brain atrophy and normocephalic infants. Our findings are more consistent with those of Fingarson and others,[23] who found no statistically significant association between enlarged SAS (> 4 mm) and SDH formation in infants who had a minor fall. Regardless of grading system, we found there was no significant difference in SAS grade in patients with and those without SDHs. Our data support an association between BESS and increased prevalence of SDHs, but not an association between SAS grade and SDH formation.

Study Limitations

There are several important limitations that should be considered when interpreting the results of this retrospective study. There are no specific *International Classifica-*

tion of Diseases, 9th or *10th Revision*, codes for BESS, which limited our search to free text searches. Many patients had incomplete data and were excluded from analysis. Follow-up data were obtained from routine pediatric clinic visits as well as neuropsychological and neurodevelopmental visits. Routine visits without cranial imaging may miss asymptomatic SDH formation. It is possible that patients who were deemed more at risk for neurological difficulties were more likely to undergo follow-up and therefore have complete medical records, introducing a selection bias toward serious cases in our series. We only included patients who were seen by neurology and neurosurgery as they were more likely to have an accurate diagnosis of BESS and an interpretation of the neuroimaging in the appropriate clinical context. There is a lack of uniform criteria for BESS diagnosis: 1410 patients had mention of BESS in their charts, and only 480 met inclusion criteria for this study. As reported above, the number of patients with BESS who are seen by neurology and neurosurgery is decreasing over time. Therefore, excluding recent patients not seen by neurology or neurosurgery may exclude an important part of the population. We only included patients with a head circumference > 85th percentile in order to exclude enlarged SAS due to brain atrophy. Including only patients with macrocephaly is common in the BESS literature; in fact, other groups have been even more strict and used a cutoff of the 97.5th percentile.[2,9,11,16] This cutoff does exclude a portion of the population with BESS and a normal head circumference, which may bias the results toward the more severe end of the clinical spectrum. Additionally, we only included patients with MR images of the brain available for SAS size measurement, which introduces additional selection bias toward patients who needed additional cranial imaging.

Conclusions

This is the largest retrospective study to our knowledge examining long-term outcomes and SDH formation in pediatric patients with BESS. Thirty-two percent of patients had any type of developmental delay on presentation. Gross motor delay was the most common developmental delay diagnosed, and a majority of these patients had resolution of their delay at a mean age of 22.2 months. We found a larger prevalence of spontaneous SDH formation in this population than previously reported, 8.1%. There was no significant association between SAS size or grade and SDH formation.

References

1. Wiig US, Zahl SM, Egge A, Helseth E, Wester K. Epidemiology of benign external hydrocephalus in Norway—a population-based study. *Pediatr Neurol*. 2017;73:36-41.
2. Zahl SM, Egge A, Helseth E, Wester K. Clinical, radiological, and demographic details of benign external hydrocephalus: a population-based study. *Pediatr Neurol*. 2019;96:53-57.
3. Hussain ZB, Hussain AB, Mitchell P. Extra-axial cerebrospinal fluid spaces in children with benign external hydrocephalus: a case-control study. *Neuroradiol J*. 2017;30(5):410-417.
4. Marino MA, Morabito R, Vinci S, et al. Benign external hydrocephalus in infants. A single centre experience and literature review. *Neuroradiol J*. 2014;27(2):245-250.
5. Zahl SM, Egge A, Helseth E, Wester K. Benign external hydrocephalus: a review, with emphasis on management. *Neurosurg Rev*. 2011;34(4):417-432.
6. Ghosh PS, Ghosh D. Subdural hematoma in infants without accidental or nonaccidental injury: benign external hydrocephalus, a risk factor. *Clin Pediatr (Phila)*. 2011;50(10):897-903.
7. Williams CA, Dagli A, Battaglia A. Genetic disorders associated with macrocephaly. *Am J Med Genet A*. 2008;146A(15):2023-2037.
8. Haws ME, Linscott L, Thomas C, Orscheln E, Radhakrishnan R, Kline-Fath B. A retrospective analysis of the utility of head computed tomography and/or magnetic resonance imaging in the management of benign macrocrania. *J Pediatr*. 2017;182:283-289.e1.
9. Yew AY, Maher CO, Muraszko KM, Garton HJ. Long-term health status in benign external hydrocephalus. *Pediatr Neurosurg*. 2011;47(1):1-6.
10. Mikkelsen R, Rødevand LN, Wiig US, et al. Neurocognitive and psychosocial function in children with benign external hydrocephalus (BEH)-a long-term follow-up study. *Childs Nerv Syst*. 2017;33(1):91-99.
11. Zahl SM, Egge A, Helseth E, Skarbø AB, Wester K. Quality of life and physician-reported developmental, cognitive, and social problems in children with benign external hydrocephalus-long-term follow-up. *Childs Nerv Syst*. 2019;35(2):245-250.
12. Papasian NC, Frim DM. A theoretical model of benign external hydrocephalus that predicts a predisposition towards extra-axial hemorrhage after minor head trauma. *Pediatr Neurosurg*. 2000;33(4):188-193.
13. Högberg U, Andersson J, Squier W, et al. Epidemiology of subdural haemorrhage during infancy: a population-based register study. *PLoS One*. 2018;13(10):e0206340.
14. Jayawant S, Rawlinson A, Gibbon F, et al. Subdural haemorrhages in infants: population based study. *BMJ*. 1998;317(7172):1558-1561.
15. Hobbs C, Childs AM, Wynne J, Livingston J, Seal A. Subdural haematoma and effusion in infancy: an epidemiological study. *Arch Dis Child*. 2005;90(9):952-955.
16. Tucker J, Choudhary AK, Piatt J. Macrocephaly in infancy: benign enlargement of the subarachnoid spaces and subdural collections. *J Neurosurg Pediatr*. 2016;18(1):16-20.
17. Hanauer DA, Mei Q, Law J, Khanna R, Zheng K. Supporting information retrieval from electronic health records: a report of University of Michigan's nine-year experience in developing and using the Electronic Medical Record Search Engine (EMERSE). *J Biomed Inform*. 2015;55:290-300.
18. Neveling EA, Truex RC Jr. External obstructive hydrocephalus: a study of clinical and developmental aspects in ten children. *J Neurosurg Nurs*. 1983;15(4):255-260.
19. Maenner MJ, Shaw KA, Baio J, et al. Prevalence of autism spectrum disorder among children aged 8 years—Autism and Developmental Disabilities Monitoring Network, 11 sites, United States, 2016. *MMWR Surveill Summ*. 2020;69(4)(SS-4):1-12.
20. Shen MD, Nordahl CW, Li DD, et al. Extra-axial cerebrospinal fluid in high-risk and normal-risk children with autism aged 2-4 years: a case-control study. *Lancet Psychiatry*. 2018;5(11):895-904.
21. McNeely PD, Atkinson JD, Saigal G, O'Gorman AM, Farmer JP. Subdural hematomas in infants with benign enlargement of the subarachnoid spaces are not pathognomonic for child abuse. *AJNR Am J Neuroradiol*. 2006;27(8):1725-1728.
22. Hansen JB, Frazier T, Moffatt M, Zinkus T, Anderst JD. Evaluations for abuse in young children with subdural hemorrhages: findings based on symptom severity and benign enlargement of the subarachnoid spaces. *J Neurosurg Pediatr*. 2018;21(1):31-37.

23. Fingarson AK, Ryan ME, McLone SG, Bregman C, Flaherty EG. Enlarged subarachnoid spaces and intracranial hemorrhage in children with accidental head trauma. *J Neurosurg Pediatr.* 2017;19(2):254-258.

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: Maher, Holste. Acquisition of data: Holste, Ibrahim, Parmar. Analysis and interpretation of data: Holste, Ibrahim. Drafting the article: Holste, Wieland, Saleh, Garton. Critically revising the article: Maher, Holste, Wieland, Saleh, Garton. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Maher. Statistical analysis: Holste.

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