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Hydrocephalus and epileptic seizures

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Abstract Is there an association between shunted hydrocephalus and the development of epileptic seizures? To answer this question a retrospective review of the medical records of 197 patients with shunted hydrocephalus was undertaken. In this series 17% of patients with hydrocephalus developed seizures. No correlation was found between the occurrence of epileptic seizures and a shunt malfunction, the number of shunts placed, the age of the patient at the initial shunt procedure or the location of the shunt. Patients with hydrocephalus who had significant

cognitive delay or significant motor disability were significantly more likely to develop seizures than patients who did not. The findings of this review support the hypothesis that the occurrence of seizures in children with hydrocephalus is related to an underlying diffuse encephalopathy and not to the hydrocephalus or to procedures related to the treatment of this disorder.

Key words Seizures · Hydrocephalus · Childhood

Introduction

Epilepsy and hydrocephalus are common pediatric neurological problems. Epilepsy has a prevalence rate of 4.3–9.3 cases per 1000 children in the population. Its etiologies are diverse, being divided into idiopathic and symptomatic. The prognosis is variable depending on the cause.

Hydrocephalus has a prevalence rate of 1–3 cases per 1000 children in the population. Its etiologies are also diverse and divided into idiopathic or symptomatic. Epileptic seizures have been noted to have occurred in this group of patients. This paper examines the question of whether having hydrocephalus significantly increases the risk of having epileptic seizures.

Patients and methods

This study was a retrospective chart review. To be included in this review, the patient had to have had their initial shunting procedure

done at the Children's Hospital of Eastern Ontario. Follow-up data for at least 2 years after the procedure had to be available. Patients with a prior history of seizure disorder or a degenerative brain disorder were excluded. Patients were consecutively entered into this study.

The chart reviews were all done by the same person (D. L. K.). Data collected from the charts included the patient's age in years at the time of surgery; age at the time of the first shunting procedure; total number of shunting procedures done per patient; location of the shunts; etiology of hydrocephalus; and type of hydrocephalus based upon imaging studies. The patient's intellect level and clinical state were based on the patient's last visit to the neurosurgical clinic. If seizures had occurred, the type of seizures, etiology of seizures, frequency of seizures and possible seizure etiologies were recorded.

The data were coded and entered into a computerized data base. A cross-check of the individual entry data was done to assure that data had been correctly entered. The patient study population was divided into a seizure-free group and a group with seizures. The difference between group means for ages of initial shunting procedure, age of shunting procedures and mean number of shunts per patients was examined with the aid of the Student *t*-test. The Chi-square method was used for the remainder of the intergroup comparisons. The SSPC-pc statistical package was used for the analysis [15]. Significance was taken as $P > 0.05$.

Results

In all, 197 (117 male and 80 female) patients met the criteria for entry on this study, 118 (60%) of whom had obstructive or noncommunicating hydrocephalus. The mean age at the time of the review was 7 years. The mean age at first shunt insertion was 1.5 years; 138 patients (68%) had their first shunt inserted prior to the age of 6 months; 150 patients (76%), before the age of 1 year, and 167 patients (80%), before the age of 2 years.

The shunt was inserted in the right parietal region in 130 patients (66%) and the left parietal region in 32 patients (16%). Twelve patients (6%) had multiple shunts in place. In 24 patients (12%) lumboperitoneal shunts were in place.

Etiologies of the hydrocephalus were diverse, 71 patients (36%) having no identified cause for their hydrocephalus. Hydrocephalus was associated with a spinal dysraphic state in 87 patients (45%), and in 22 patients (11%), with a neoplastic lesion. Twelve patients (6%) developed hydrocephalus following a perinatal intracranial bleed. Four patients (2%) developed hydrocephalus as a complication of a postnatal central nervous system infection.

There were 102 patients (52%) who were intellectually normal, while 18 patients (9%) had a significant learning disorder requiring a specialized learning program within the regular classroom setting. A further 14% were felt to have borderline intellectual abilities. Twenty patients (10%) had a mild degree of mental retardation, 16 patients (8%), a moderate degree of mental retardation, and 13 (7%), a severe degree of mental retardation.

Examination of the central nervous system was normal in 85 patients (43%). Eighteen patients (9%) had mild diffuse nonspecific soft signs. Hemiplegia was noted in 12 patients (6%). Six patients (3%) were noted to have spastic quadriplegia. Ten patients (5%) were noted to have spastic diplegia. Four patients (2%) had double hemiplegia. Six patients (3%) had cranial nerve dysfunction. Fifty-nine patients (30%) were noted to have had significant flaccid diplegia.

There were 33 patients (17%) who had had at least one epileptic seizure. Seizures did not occur at the time of acute obstruction of cerebrospinal fluid or at the time of shunt malfunction in any of the patients during the time period of this study. Twelve patients (37%) had had only a single seizure. Seven (20%) had approximately one seizure per year. Three (10%) had a seizure approximately once every 6 months. One (3%) had a seizure approximately once every 3 months. Ten (30%) had seizures more frequently than once per month.

Seizures were classified as partial in type in 14 (43%) patients, while 13 patients (40%) had generalized seizures; 6 patients (17%) had multiple seizure types.

The mean age at the first seizure was 1.35 years. Seventeen patients (51%) who were going to have seizures had had their first seizure during the 1st year of life; 25 patients (75%) who were going to develop seizures had their first

Table 1 A comparison of patients with hydrocephalus who developed seizures with those who did not

| Variable | Patient without seizures (n=164) | Patient with seizures (n=33) |
|------------------------------------|----------------------------------|------------------------------|
| Male-to-female ratio | 1.75:1.0 | 1.41:1.0 |
| Mean age at time of survey (years) | 7.6±4.8 | 7.0±4.8 |
| Mean age of original shunt (years) | 1.7±3.4 | 1.2±3.0 |
| Mean number of shunts/patient | 1.7±1.5 | 2.2±1.9 |
| Type of hydrocephalus | | |
| Communicating | 37% | 54% |
| Obstructive | 63% | 55% |
| Etiology of hydrocephalus | | |
| Idiopathic | 35% | 35% |
| Perinatal bleed | 5% | 9% |
| Infection | 1% | 3% |
| Tumor | 14% | 0% |
| Spinal dysraphism | 44% | 53% |
| Location of shunt | | |
| Right parietal | 66% | 64% |
| Left parietal | 14% | 24% |
| Multiple | 13% | 6% |
| Lumboperitoneal | 5% | 6% |
| Intellectual status* | | |
| Normal | 56% | 27% |
| Learning disorder | 8% | 15% |
| Borderline | 14% | 12% |
| Mild mental retardation | 10% | 12% |
| Moderate mental retardation | 8% | 9% |
| Severe mental retardation | 4% | 24% |
| Neurological examination* | | |
| Normal | 43% | 35% |
| Diffuse soft signs | 9% | 10% |
| Hemiplegia | 3% | 23% |
| Spastic quadraplegia | 2% | 10% |
| Spastic diplegia | 4% | 7% |
| Double hemiplegia | 4% | 3% |
| Abnormal cranial nerves | 3% | 0% |
| Flaccid diplegia | 35% | 7% |

* $P > 0.05$

seizure prior to 2 years of age; 30 patients (90%) who were going to develop seizures had done so by the age of 3 years.

The clinical features of the patients who had epileptic seizures can be found in Table 1. When the group of patients who had both hydrocephalus and epileptic seizures was compared with the group who did not, the only clinical variables that differed significantly were intellectual status and abnormalities found on examination of the central nervous system.

Discussion

Seizures occurred in 17% of patients in this series. This frequency is significantly greater than would have been ex-

pected on the basis of incidence figures for seizure occurrence in this age group. This suggests that patients with hydrocephalus are at a greater risk of having or developing a seizure disorder than the general population. The reason for this risk is unclear. None of our patients had seizures attributable to acute obstruction of cerebrospinal fluid; nor was there an association between occurrence of seizures and the number of shunt revision or the position of the shunt. The higher number of children with hydrocephalus associated with intellectual or motor impairment suggests that the increased risk of seizures in this group was due to underlying brain abnormalities. These findings were similar to the gradually emerging consensus in the medical literature.

Hosking [7] reported that 30% of children with hydrocephalus had developed seizures. This was based on a retrospective analysis of 200 hydrocephalic children followed over a 5-year period. In this series 100 children had hydrocephalus associated with spina bifida; the remainder had developed hydrocephalus secondary to either meningitis or neonatal intracranial hemorrhage. The frequency of seizures did not differ between these two groups in this series. Ten patients (5 in each group) each had a seizure related to a blocked shunt. The number of shunt revisions and prior history of meningitis were significantly correlated with the occurrence of a seizure.

Lorber et al. [11] retrospectively reviewed 315 children with shunted hydrocephalus (198 with congenital and 117 with acquired hydrocephalus). Children with hydrocephalus associated with spina bifida were excluded. Particular attention was paid to the time of the convulsions. Four patients with congenital hydrocephalus had seizures prior to the shunting procedure. Fifteen (12%) had seizures secondary to an infection or a blocked shunt. Thirty-three percent of their patients had seizures without any clearly identified reason. Among the patients with hydrocephalus associated with a structural central nervous system lesion, 49% had seizures. The authors concluded that epilepsy was more common in patients with physical or mental disabilities rather than being related to the shunt.

In the series reported by Blaauw [1], 34% of 323 children with hydrocephalus developed epileptic seizures. The etiologies of the hydrocephalus included bacterial meningitis, intrauterine infections, perinatal hemorrhage, and association with spina bifida. Seizures were significantly more frequent in the postbacterial meningitis group and significantly less frequent in patients in whom the hydrocephalus was associated with spina bifida. The number of shunt revisions was not a significant factor in the development of seizures. Shunt infections were significantly correlated with the risk of late occurrence of seizures. No relationship between shunt malfunction and the occurrence of seizures was found.

Copeland et al. [2] found that 19 of their 91 patients with hydrocephalus developed postoperative seizures. The etiologies of the hydrocephalus included neoplasm in 37 cases, aqueductal stenosis in 11 cases, and communi-

cating hydrocephalus in 27 cases; the etiology was unknown in 3 cases. The mean age of patients at the time of the review was 27.4 years (range 1–78 years), with a mean follow-up period of 30 months. He found that the risk of developing a seizure was significantly increased if there was a history of shunt infection. Because of his observation that when seizures did occur they involved the body side contralateral to the shunting procedure, he felt that the shunting procedure played a part in the development of seizures. No correlation with the etiology of the hydrocephalus was found. Fifty-eight percent of the patients had their first seizure within the first month after the shunting procedure. The actual risk of developing a seizure following the shunting procedure was 18% in 1st year, 5% in the 2nd year, and 3% in the 3rd year.

Dan and Wade [4] retrospectively reviewed the medical records of 207 patients with ventricular shunts in place. The minimum follow-up period was 2 years. The mean age was 38.2 years (extending from the neonatal period to 70 years of age). Seventeen patients (9.4%) had convulsions. The underlying etiology of the hydrocephalus did not predict which patients were at risk for the development of seizures. In their series 24.2% patients who had a shunt revision had seizures, as against 5.9% patients who did not require a shunt revision. When they compared the site of shunt insertion and the development of seizures, they found that 10 of 168 patients who had undergone a posterior parietal shunt procedure had seizures, as opposed to 6 of 11 patients who had shunts placed in the frontal region.

Of the 93 patients with shunted hydrocephalus in the series reported by Venes and Deuser [18], 5 developed seizures following the procedure and 24 had seizures prior to the shunting procedure. No correlation was found between the site of the shunt and development of seizures.

Leggate et al. [10] published a retrospective review of 56 hydrocephalic patients, 16 (16%) of whom developed seizures.

In a retrospective study Faillace and Canady [5] reported on 15 patients with hydrocephalus who had a seizure at the time of shunt malfunction. In 8 patients there had been no past history of seizures. These 15 patients represented 2% of all patients with hydrocephalus requiring revision of the shunt because of a shunt malfunction during the 3-year period covered by the review.

Saukkonen et al. [14] retrospectively reviewed the records of 168 shunt-treated hydrocephalic children. There were 80 patients (47.6%) who had had seizures: 37 (22%) patients had seizures prior to the initial shunting procedure, and 43 (25.6%), after the original shunting procedure. No significant correlation between seizure occurrence and etiology of the hydrocephalus was found. Six patients (14%) had seizures within the first 6 months after the shunt placement; 11 patients (25%) had a seizure within the 1st year, and 17 (39.5%) patients had a seizure within 2 years. The remaining 26 patients (60.5%) who had seizures had them within 2–15 years of the initial shunting procedure.

In a series of 346 patients with meningomyelocele and shunted hydrocephalus Hack et al. [6] reported that 51 patients developed seizures. These 51 patients had a total of 129 admissions for a possible shunt malfunction. Nine patients (9%) were having a seizure at the time of admission. These patients also had other evidence of a shunt malfunction. The authors concluded that seizures alone were not an adequate predictor of a shunt malfunction.

Noetzel et al. [12] retrospectively reviewed 68 patients with congenital hydrocephalus not associated with meningomyelocele: 33 (48.5%) of these patients had seizures. Acute shunt malfunction and high fever were very infrequently noted to be associated with seizure onset. Risk factors identified included mental retardation and the presence on cranial tomography of cortical malformation. Nonsignificant risk factors included the total number of shunt revisions, infections, seizure type, family history of nonfebrile seizures, and age at time of original shunt insertion.

Talwar et al. [17] reviewed the medical records 81 children followed at a multidisciplinary meningomyelocele clinic. Seventeen patients (21%) developed seizures; 2 patients had seizures in the neonatal period; 3 patients had seizures associated with acute intracranial hemorrhage during the ventriculoperitoneal shunt revision; and 14 patients (17.3%) had recurrent seizures. Other pathology of the central nervous system was present that could account for the development of seizures in 12 of the children. This included past stroke, cerebral malformations and post-cardiac arrest hypoxic ischemic encephalopathy.

In a retrospective review of 817 children with shunted hydrocephalus reported by Johnson et al. [9], 308 children (38%) had epilepsy. These included 181 children (22%) who had their first seizure after the initial insertion of the shunt. The location of the shunt placed did not correlate with the occurrence of seizures. Seizures were significantly more likely to occur if the hydrocephalus was related to cerebral trauma, infections of the nervous system, or perinatal intracranial bleeding. Sixteen of 544 (2.9%) visits to the emergency room for seizures resulted in a shunt revision, and 16 of 1831 (0.9%) shunt revisions were associated with a seizure.

Piatt et al. [13] retrospectively reviewed 464 patients with hydrocephalus to determine the prevalence of epilepsy amongst this group of patients and to identify risk factors for the development of seizures. The definition of epilepsy employed by the authors was the occurrence of epileptic seizures that required the administration of antiepileptic drugs to control them. Survival curves were used, the end-point being the initiation of medications. The follow-up period was 66 months. Twelve percent of patients had epilepsy at the time when their hydrocephalus was diagnosed. Each year after the insertion of the shunt, the risk of developing epilepsy was 2%. By 10 years after the initial shunt placement, 33% of the patients had developed epilepsy. The cause of the hydrocephalus was found to correlate strongly with the risk of developing seizures. There was no correlation between age of the patient at the time of the initial shunt, the placement of the shunt, the number of shunt revisions or a history of shunt infection and risk of developing seizures.

The few reported series of electrographic findings in hydrocephalus have shown a variety of associated abnormalities [2, 8, 12, 16, 17]. In the patients with hydrocephalus and seizures, all studies have shown a significantly higher rate of epileptic abnormalities than in the group of hydrocephalic children who did not develop seizures. In the latter group, either diffuse or focal nonspecific slowing of background activity was common.

In summary, epileptic seizures are not an uncommon occurrence in children with shunted hydrocephalus. No correlation has been found between either the number of shunt revisions nor the site of placement of the shunt and the risk that a child with hydrocephalus will develop epilepsy. Hydrocephalic children with mental or physical disability from whatever cause are more likely to develop seizures. The findings of our study and those derived from the literature review suggest that the occurrence of a seizure at the time of acute shunt malfunction is uncommon. The most likely explanation for the development of seizures in this group of patients is the presence of associated malformations of the cerebral cortex.

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EDITORIAL COMMENT

The authors have retrospectively reviewed a consecutive series of 197 patients with hydrocephalus in order to identify variables associated with seizure development. Patients were excluded if they had a seizure disorder prior to the onset of hydrocephalus. All shunts were placed in a parietal location except for 12% of patients who had lumboperitoneal shunts; 17% of the patients developed seizures. There was no correlation between shunt malfunction, number of shunts, shunt location, or age at initial shunt placement. There was a statistically significant difference in intellect and neurologic status between the groups. The group

who developed seizures had a worse intellectual status and a worse neurologic status than the group without seizures. The authors conclude that it is not the hydrocephalus or shunt-related factors that cause seizures. They believe that associated malformations of the cerebral cortex are probably related to the development of seizure.

This study shares many of the pitfalls of other retrospective case reviews. A significant correlation is identified, and this is valuable; however, this then can lead to speculation. The authors found a statistically significant difference in intellect and neurologic status between hydroce-

phalic patients who developed seizures and those who did not. The authors then speculate that malformations of the cerebral cortex are the likely cause. It is also possible to conclude that the seizure disorder itself led to worse intellect and neurologic status. Analysis of MRI or PET data between the two groups in a blinded fashion could perhaps yield some support for the authors' conclusion.

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