Ventriculoperitoneal (VP) shunt surgery is a common treatment for hydrocephalus. In many pediatric neurosurgical centers, shunt surgery is one of most frequently performed operations. Although endoscopic procedures can be substituted for shunt procedures in certain situations, VP shunt surgery is often the preferred treatment for hydrocephalus, especially for patients with infantile hydrocephalus. However, shunting procedures are plagued with various complications. Acute surgical complications include catheter-related intracerebral hemorrhage, intraventricular hemorrhage (IVH), and catheter malposition. In the later postoperative period, shunt malfunction, infection, catheter migration, bowel perforation, catheter exposure, and CSF overdrainage can ensue. Obviously, VP shunt surgery is a simple surgical procedure; however, the complications associated with the procedure can cause problems for neurosurgeons and their patients.

In certain situations, uncommon complications can occur after shunting procedures. We encountered several patients with noteworthy complications over the last 10 years: specifically, multifocal intraparenchymal hemorrhages (MIPH) after shunt surgery. MIPH differs from diffuse lesions, which are usually observed after VP shunt surgery.

Multifocal intraparenchymal hemorrhages after ventriculoperitoneal shunt surgery in infants

Clinical article

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Object. Ventriculoperitoneal (VP) shunt surgery is the most common treatment for hydrocephalus. In certain situations, uncommon complications can occur after shunting procedures. The authors undertook this study to analyze the clinical characteristics of pediatric patients who developed multifocal intraparenchymal hemorrhages (MIPHS) as a complication of shunt surgery. The authors also analyzed the risk factors for MIPH in a large cohort of patients with hydrocephalus.

Methods. This study included all pediatric patients (age < 18 years) who underwent VP shunt surgery at the authors’ institution between January 2001 and December 2012. During this period, 507 VP shunt operations were performed in 330 patients. Four of these patients were subsequently diagnosed as having MIPH. The authors analyzed the clinical characteristics of these patients in comparison with those of the entire group of shunt-treated patients.

Results. The incidence of MIPH was 1.2% (4 of 330 cases) for all pediatric patients who underwent VP shunt placement but 2.9% (4 of 140 cases) for infants less than 1 year old. When the analysis was limited to patients whose corrected age was less than 3 months, the incidence was 5.3% (4 of 76 cases). Of the 4 patients with MIPH, 2 were male and 2 were female. Their median age at surgery was 54 days (range 25–127 days), and in all 4 cases, the patients’ corrected age was less than 1 month. Three patients were preterm infants, whereas one patient was full-term. None of these patients had a prior history of intracranial surgery (including CSF diversion procedures). All showed severe hydrocephalus during the preoperative period. Their clinical courses as patients with MIPH were comparatively favorable, despite the radiological findings.

Conclusions. MIPH is a rare but not negligible complication of VP shunt surgery. This complication might be a unique phenomenon in infants, especially young, preterm infants with severe hydrocephalus. Moreover, the absence of previous intracranial procedures might be one of the risk factors for this complication. The rapid alteration of brain conditions in the setting of immaturity might cause MIPH. To prevent this complication, the authors recommend that pressure settings of programmable valves should be gradually adapted to the target pressure.

Key Words • hemorrhage • hydrocephalus • infant • multifocal • preterm • shunt
rect catheter-related brain injury. These patients developed delayed-onset multifocal bleeding after shunt surgery. Typically, the bleeding was not related to proximal catheter positions. More importantly, MIPH developed only in young infants, which presents certain etiological associations.

In this study, we analyzed the incidence of MIPH as well as the characteristics and clinical courses of patients with MIPH. We also analyzed the risk factors associated with MIPH in a large cohort of patients with hydrocephalus.

**Methods**

This study included all pediatric patients (age < 18 years) who underwent VP shunt surgery between January 2001 and December 2012 at Seoul National University Children’s Hospital. During this period, 507 VP shunt operations were performed in 330 patients. We excluded subduroperitoneal, ventriculosubgaleal, and lumboperitoneal shunt surgeries.

Under the approval of the institutional review board of the Seoul National University Hospital, we performed a retrospective review of the medical records and radiological images of these 330 patients. We analyzed the situations of initial VP shunt surgery, excluding all shunt revisions. The median patient age at the time of initial VP shunt placement was 1 year (mean 3.7 years, range 0–18 years). Fifty-five patients (16.7%) were born prematurely. The male/female ratio was 1.31 (187:143). The most common etiology of hydrocephalus was brain tumor, followed by infantile posthemorrhagic hydrocephalus. A summary of the demographic characteristics of the 330 patients is presented in Table 1.

All patients had follow-up assessments more than 6 months after surgery, including ultrasonography, CT, or MRI. All patients were examined at least once using brain ultrasonography, CT, or MRI within 1 month after the operation. If unexpected findings including hemorrhage were observed via ultrasonography, then the subsequent CT or MRI was checked to confirm the lesion.

MIPH was defined as having the following characteristics. 1) A new intraparenchymal hemorrhage was documented via postoperative CT or MRI (not only ultrasonography) at any follow-up assessment. 2) The hemorrhage was multifocal (that is, developing in 3 or more distinct sites in the brain parenchyma). 3) The hemorrhagic site was distant from the proximal shunt catheter. 4) No underlying lesion (for example, tumor or vascular malformation) was found at the site of hemorrhage. 5) The patients did not have documented coagulopathy (that is, a preoperative international normalized ratio [INR] > 1.20 or thrombocytopenia [platelet count < 150 × 10^9/μl]). We excluded pure postoperative IVH because this condition is usually caused by a catheter puncture of the ventricular walls.

Of the 330 patients, 22 had new intracranial bleeding after their initial shunt operation, including subdural hemorrhage (SDH), epidural hemorrhage (EDH), subarachnoid hemorrhage (SAH), intraparenchymal hemorrhage or IVH. Twelve patients showed pure SDH, EDH, SAH, or IVH without parenchymal hemorrhage. Of the 10 patients with parenchymal hemorrhage, 4 showed parenchymal hemorrhage around the proximal catheter and 2 patients had underlying lesions at hemorrhagic sites (infarction and brain tumor); we therefore excluded these 6 patients. According to the proposed criteria, we ultimately identified 4 patients with MIPH after the shunting operation (Fig. 1). These patients had unremarkable laboratory findings regarding bleeding tendency.

We compared the clinical characteristics of the 4 patients who had MIPH (e.g., sex, age at operation, etiol-
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Fig. 1. A schematic diagram of the cases analyzed in this study. ICH = intracranial hemorrhage.

The results of immediate postoperative brain ultrasonography were unremarkable. One month after the surgery, a follow-up CT scan showed a somewhat resolved state of MIPH with subdural hygroma (Fig. 2B and C). She

Illustrative Cases

Case 1. This female infant underwent VP shunt surgery at the age of 62 days for congenital hydrocephalus that was detected in utero at 27 weeks’ gestational age (GA). She was born at 34 weeks’ GA via an emergency cesarean section due to preterm labor. Her birth weight was 2870 g. A CT scan of her brain showed severe ventriculomegaly and aqueductal stenosis (Fig. 2A). Progressive hydrocephalus was detected, and a subsequent VP shunt operation was performed at the corrected age of 22 days. The results of her preoperative laboratory tests were unremarkable. The opening pressure at ventricular puncture was 2.9 mm Hg. (There seemed to be an error during measurement, because she had bulging fontanel and showed a rapid increase of head circumference.) A PS Medical flow-controlled low-pressure valve (Medtronic) was implanted. The proximal catheter was inserted at the right parietooccipital point (PO point).
was asymptomatic, and the hemorrhages were resolved according to the follow-up images, without specific treatment. Two months later, however, the shunt device was removed and revised due to shunt infection. Five years after the initial operation, MRI showed a resolved hemorrhage and subdural hygroma; however, some hemorrhagic lesions had calcified (Fig. 2D). The patient is currently 11 years old; she is healthy and has shown successful school performance.

Case 2. This male infant was born at 23 weeks’ GA to a 34-year-old woman via an unplanned vaginal delivery due to premature labor. His birth weight was 620 g. Because of his extreme preterm age, he had many medical problems: patent ductus arteriosus, bronchopulmonary dysplasia, germinal matrix hemorrhage (GMH) and IVH. According to Papile’s classification, the GMH was Grade II. The GMH and IVH were fully absorbed without a CSF drainage procedure of any kind. However, a progressively increasing head circumference and ventriculomegaly were detected from a physical examination and brain CT scan (Fig. 3A). When the infant was 127 days old (corrected age, 12 days), a VP shunt operation was performed. No evidence of coagulopathy or thrombocytopenia was observed in the preoperative laboratory studies. The opening pressure was 18.4 mm Hg. The ventricular catheter was inserted at the right Kocher’s point. A Strata programmable valve (Medtronic) was installed with a 1.0 performance level. The immediate postoperative CT scan was not remarkable (Fig. 3B). The next day, the infant developed seizures and projectile vomiting. A follow-up CT scan revealed MIPH with subdural fluid collection (Fig. 3C and D). The valve performance level was adjusted to 2.0, and a conservatively treatment was provided. The hemorrhage was absorbed with improvement of the subdural hygroma. The patient is currently 6 years old. Although he has mild cerebral palsy, he can perform normal daily activities with little caregiver assistance. No shunt revision surgery has been performed as of this writing.

Case 3. This male infant was born via vaginal delivery at 29 weeks’ GA (birth weight 1430 g). Hydrocephalus was diagnosed prenatally at 6 months’ GA. After birth, brain ultrasonography showed GMH with IVH (Papile’s classification Grade II). Although the IVH fully resolved, the hydrocephalus gradually progressed (Fig. 4A). Shunt placement was performed when the infant was 46 days old. The opening pressure was 11.0 mm Hg. The ventricular catheter was inserted at the right Kocher’s point. A Strata programmable valve was inserted with a 1.5 performance level. The immediate postoperative CT scan did not reveal specific findings. A high fever occurred 5 days later, and CSF tapping was attempted through a reservoir in order to exclude infection. Because the CSF sample was remarkably bloody, another CT study was performed in order to check for brain hemorrhage. This study revealed MIPH (Fig. 4B and C). The shunt device was removed because shunt infection was confirmed. Since then, several shunt revisions have been performed due to shunt infection or malfunction. Follow-up imaging
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demonstrated resolution of the MIPH (Fig. 4D). The patient is currently 6 years old, and he is regularly evaluated due to intractable seizures and developmental delays.

**Case 4.** This female infant was delivered at full term. Hydrocephalus was diagnosed prenatally. An MRI study performed immediately after birth did not show an obvious brain lesion other than severe ventriculomegaly (Fig. 5A). The infant’s head circumference increased from 34.5 cm to 42.8 cm (over the 97th percentile) over 22 days. Therefore, a VP shunt operation was performed when she was 25 days old. The opening pressure was 8.8 mm Hg. The proximal catheter was inserted at the right Koecher’s point. A Strata programmable valve was implanted with a 0.5 performance level. We did not have any immediate postoperative images for this patient. However, a CT scan performed 2 days after the operation showed MIPH with remarkable IVH (Fig. 5B and C). The hematoma gradually resolved over the follow-up period (Fig. 5D). She continues to be evaluated regularly and currently (10 months after surgery) has no significant clinical problems. Her shunt device is not causing any problems.

**Clinical Characteristics of Patients With MIPH**

The incidence of MIPH was 1.2% (4 of 330 cases) for all pediatric ages but 2.9% (4 of 140 cases) for infants less than 1 year in our patient cohort. When we limited analysis to cases involving patients less than 3 months of corrected age, the incidence was 5.3% (4 of 76 cases).

![Fig. 5. Case 4. A: Preoperative T2-weighted axial MR image showing severe hydrocephalus without aqueductal stenosis or a mass-like lesion. The MRI study revealed no abnormality other than ventriculomegaly. B and C: Postoperative CT images (obtained 2 days after the operation) showing MIPH with IVH. D: T2-weighted axial MR image from the most recent follow-up imaging study, performed 8 months after surgery, showing hemorrhage resolution.](image)

All patients with MIPH (n = 4) were infants. The median age of these patients at surgery was 54 days (range 25–127 days). Interestingly, in all 4 cases, the corrected ages of the patients were less than 1 month. We analyzed our data based on a corrected age of 3 months, and this age was significant (p = 0.003, Fisher’s exact test). Furthermore, 3 of the patients with MIPH were born prematurely (3 cases in 55 preterm births), whereas only 1 patient with MIPH was born full term (1 case in 275 full-term births). Preterm birth was significantly associated with the occurrence of MIPH (p = 0.016, Fisher’s exact test). Another important commonality was that no patient with MIPH had a prior history of intracranial surgery, including CSF diversion procedure (such as craniotomy, extraventricular drainage, or shunt placement). The absence of previous intracranial surgery was also significant (p = 0.011, Fisher’s exact test). Sex was not associated with MIPH development (2 patients were male, and 2 were female). These results are displayed in Table 1.

Moreover, the 4 patients with MIPH had another similarity. All had severe preoperative hydrocephalus. The mean frontal and occipital horn ratio in the MIPH patient group was 0.72 ± 0.06 (range 0.68–0.80), whereas the mean frontal and occipital horn ratio in the patients without MIPH was 0.52 ± 0.12 (range 0.22–0.94). The difference in ventricular size between these 2 groups was statistically significant (p = 0.004, Mann-Whitney U-test).

Another similarity was that the MIPH showed delayed occurrences. In the 3 cases in which immediate postoperative imaging studies were available for evaluation, they showed no evidence of hemorrhage. (No postoperative imaging study was performed in Case 4 until 2 days after surgery. Therefore we do not know whether an immediate hemorrhage occurred in this patient.) As for the etiology of hydrocephalus in the patients with MIPH, 1 full-term patient had congenital hydrocephalus of unknown etiology. (No evidence existed for aqueductal stenosis or an MRI mass.) One preterm patient had severe hydrocephalus with aqueductal stenosis, and 2 preterm patients had postnatal IVH and infantile posthemorrhagic hydrocephalus. Two of the patients with MIPH had comorbid anomalies: The patient in Case 1 had agenesis of the corpus callosum, and the patient in Case 2 had patent ductus arteriosus and bronchopulmonary dysplasia. Table 2 displays the characteristics of these patients.

**Discussion**

Intracranial bleeding after CSF shunt surgery is a well-recognized complication. Many studies have noted that intracranial bleeding develops along the path of the ventricular catheter. Thus, direct surgical injury during ventricular catheter placement is the primary cause of the bleeding after shunt surgery. This catheter-related bleeding might be caused by injuries to the ependymal vessels and choroid plexus after repeated attempts at perforation of the ventricles or the inadequate placement of the catheter within the brain parenchyma. However, MIPH differs from previously reported intracranial bleeding types after shunt surgery. In particular, MIPH
TABLE 2: Summary of clinical characteristics of 4 patients with MIPH*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age at Op (corrected age)</th>
<th>GA (wks+days)</th>
<th>Birth Weight (g)</th>
<th>Primary Cause of HCP</th>
<th>FOR</th>
<th>Coexisting Anomaly</th>
<th>Preop Lab Findings (no. plts, INR)</th>
<th>Opening Pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>62 days (22 days)</td>
<td>34+2</td>
<td>2870</td>
<td>congenital aqueductal stenosis</td>
<td>0.80</td>
<td>agenesis of corpus callosum</td>
<td>162 × 10^3, 1.05</td>
<td>2.9</td>
</tr>
<tr>
<td>2</td>
<td>127 days (12 days)</td>
<td>23+4</td>
<td>620</td>
<td>IPHH</td>
<td>0.72</td>
<td>PDA, BPD</td>
<td>305 × 10^3, 1.02</td>
<td>18.4</td>
</tr>
<tr>
<td>3</td>
<td>46 days (PMA 35 wks)</td>
<td>29+0</td>
<td>1430</td>
<td>IPHH</td>
<td>0.68</td>
<td>none</td>
<td>288 × 10^3, 1.05</td>
<td>11.0</td>
</tr>
<tr>
<td>4</td>
<td>25 days (21 days)</td>
<td>39+3</td>
<td>3490</td>
<td>unknown etiology</td>
<td>0.68</td>
<td>none</td>
<td>278 × 10^3, 1.12</td>
<td>8.8</td>
</tr>
</tbody>
</table>

* BPD = bronchopulmonary dysplasia; FOR = frontal and occipital horn ratio; HCP = hydrocephalus; INR = international normalized ratio; IPHH = infantile posthemorrhagic hydrocephalus; PDA = patent ductus arteriosus; plts = platelets; PMA = postmenstrual age.

...develops in irrelevant areas of the ventricular catheter, thereby indicating that the hemorrhage is not directly related to a surgical injury.

MIPH is a rare occurrence. We found that the incidence of MIPH was 2.9% among infants. The incidence was higher (5.3%) when the patients’ corrected age was limited to less than 3 months. We found several clinical and epidemiological characteristics associated with MIPH. All of our cases involved young infants, and we believe that MIPH is likely to be a phenomenon unique to young infants. In addition, we found that prematurity was also a meaningful risk factor for MIPH. Remarkably, the patients who were treated with previous intracranial surgeries (for example, tumor surgery or placement of an external ventricular drain) did not develop MIPH. Ventriculoperitoneal shunt surgery was the initial intracranial procedure among patients with MIPH, and this factor also showed a statistically significant relationship with the development of MIPH. In addition, the patients with MIPH in our study had larger ventricles during the preoperative period than the patients without MIPH. The frontal and occipital horn ratio is a simple and reliable measure of ventricular size in children with hydrocephalus, and a value greater than 0.55 denotes severe hydrocephalus. All of the patients with MIPH reported on here had frontal and occipital horn ratios greater than 0.68; therefore, we hypothesize that severe hydrocephalus is associated with this complication. Based on these findings, we presume that young, premature infants with severe hydrocephalus who have not been treated with an intracranial procedure are a high-risk group for MIPH.

Moreover, a meaningful amount of time occurred between the operation and the hemorrhage among patients with MIPH. A delayed onset of several days might be a characteristic finding; this result also supports the hypothesis that MIPH has an etiological mechanism unlike typical catheter-related intracranial hemorrhages that develop immediately after catheter placement. Furthermore, the hemorrhagic locations of patients with MIPH also showed disparate features. MIPH primarily occurred in the periventricular white matter and was occasionally accompanied by subependymal hemorrhage or IVH. The caudate nucleus and the floor of the lateral ventricle were relatively spared.

Recently, Okazaki et al. reported on 2 patients with multiple hemorrhages after shunting procedures. These patients had characteristics similar to those of our patients. They were young infants (35 and 69 days of age) and showed a delayed onset of hemorrhage. Furthermore, the locations of hemorrhages were the periventricular white matter and subependymal areas. The clinical course of these cases was benign, similar to that of our cases.

The cause of MIPH is not known for certain. A previous case report suggested that the remnant germinal matrix layer related to congenital anomalies might be harmed by ischemic damage, and delayed GMH might be caused by the reduction of intracranial pressure after VP shunt placement. We agree with this theory to a degree. However, not all MIPH patients in our study had a congenital anomaly. Furthermore, typical GMH among premature infants primarily occurs in the caudate nucleus, the floor of the lateral ventricle, and the caudothalamic groove, in which germinal matrix is abundant. Thus, there may be a possibility that previously reported cases were also cases of MIPH rather than delayed GMH. We assume that this phenomenon occurs when a sudden environmental transition takes place in the immature but rapidly growing brains of infants. In particular, we suspect that the premature brain vasculature might cause MIPH, given that MIPH was related to age and prematurity. We hypothesize that the increase of cerebral perfusion pressure after shunt surgery occurs in proportion to the decrease of intracranial pressure. The delicate vasculature in the premature brain might not be able to tolerate the change in pressure (arterial hypothesis). We also presume that, after VP shunt surgery, the abrupt change of the venous flow in the periventricular areas where the medullary veins are located causes MIPH. This explanation is interrelated with the premature vessels (venous hypothesis). Moreover, unrecognized bleeding diatheses that may not be detected by routine coagulation evaluation (for example, platelet function disorder, factor XIII deficiency, vitamin K deficiency, and Von Willebrand disease) should be considered when unexplained multifocal bleeding develops.

The clinical course of patients with MIPH is not dismal, contrary to their terrible radiological findings. In all of our cases the hemorrhages were naturally absorbed, and they did not cause any neurological deficit except for seizure in Case 3. Even in this one case, there was no clear evidence that the epileptogenic focus was an area of hemorrhage. Moreover, shunt malfunction (note that shunt infection caused the shunt revision in our study) was not
directly related to MIPH, although a remarkable IVH was found in 2 patients. Given that patients who suffer parenchymal hemorrhages might be more likely to have tissue loss or calcification at the hemorrhagic site, MIPH might have an adverse effect on the developing brain. However, whether MIPH negatively affected the brain development of our patients is unclear.

To prevent MIPH, more gradual decompression of the intracranial pressure should be attempted in patients in the high-risk group (as mentioned above, those who are young infants, premature, with severe hydrocephalus, and without previous intracranial surgery histories) to accommodate to their altered brain condition over time. Thus, a programmable valve should be set to the highest pressure level for the initial postoperative period, and the setting should then gradually be decreased to the targeted value. This method might prevent abrupt pressure changes in immature brains. Otherwise, a high-pressure valve with fixed resistance might also be helpful to prevent MIPH. For high-risk patients, gradual adaptation of a programmable valve or application of a high-pressure valve with fixed resistance can be recommended.

Conclusions

Our study investigated specific characteristics of MIPH and similarities among patients and found an incidence of 2.9% in shunt-treated infants. MIPH is a rare but not negligible complication of VP shunt surgery. This complication might be a unique phenomenon among infants, especially young infants with severe hydrocephalus and without a history of intracranial surgery, including CSF diversion procedures. The rapid alteration of the brain combined with the prematurity of the brain’s vasculature might cause MIPH. To prevent this complication, the gradual and slow change of a programmable pressure-setting valve or a high-pressure valve with fixed resistance is advised in high-risk patients.

Disclosure

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Author contributions to the study and manuscript preparation include the following. Conception and design: Phi, Choi. Acquisition of data: Choi. Analysis and interpretation of data: Phi, Choi. Drafting the article: Choi. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Phi. Statistical analysis: Phi, Choi. Administrative/technical/material support: Choi, Kim, Wang, Cheon. Study supervision: Phi, Kim, Wang, Lee, Cheon.

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