Management of idiopathic normal-pressure hydrocephalus: a multiinstitutional study conducted in Japan

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Object. A cooperative study was undertaken to identify factors that could be used to predict a favorable outcome after extracranial cerebrospinal fluid (CSF) diversion (shunting) in patients with suspected idiopathic normal-pressure hydrocephalus (NPH).

Methods. Questionnaires concerning patients with suspected idiopathic NPH were sent to 14 members of the Committee for Scientific Research on Intractable Hydrocephalus, sponsored by the Ministry of Health and Welfare of Japan. After the questionnaires were returned, a retrospective analysis of the responses was undertaken. To be included in the study, patients had to be 65 years of age or older and had to have undergone surgery between October 1995 and October 1998. Clinical measures included degrees of gait disturbance, dementia, and urinary incontinence as evaluated before, 3 months after, and 3 years after shunt placement. Diagnostic tests in various combinations included lumbar puncture in which CSF was withdrawn; intracranial pressure monitoring; measurements of CSF outflow resistance, level of serum α-1-antichymotrypsin, cerebral arteriovenous differences of oxygen content, and cerebral blood flow; and computed tomography cisternography.

In this study, 120 patients were identified as having idiopathic NPH and these patients underwent placement of shunts. A ventriculoperitoneal shunt with a programmable valve was used in two thirds of the patients. At the end of 3 months (early assessment), there was an 80% overall rate of clinical improvement, which dropped to 73.3% of the 105 patients who could be evaluated at the end of the 3-year study. Of the three variables, gait disturbance was most improved, both at early and late testing periods. Shunt complications occurred in 22 (18.3%) of the patients.

Conclusions. Patients suspected of having idiopathic NPH did not form a homogeneous group, making it difficult to select those who would most likely respond to CSF diversion. Of the diagnostic studies, the most reliable result was improvement in clinical symptoms following a lumbar puncture in which CSF was withdrawn. The use of a programmable valve is recommended because it offers advantages in preventing problems of over- and underdrainage.

Key Words • normal-pressure hydrocephalus • diagnostic criteria • multiinstitutional study

THE clinical triad of gait disturbance, dementia, and urinary incontinence, which is associated with normal CSF pressure measured via lumbar puncture and which subsequently responds to extracranial CSF diversion (shunting), was described by Adams, et al.,1 and by Hakim and Adams in 1965 and is called NPH. Normal-pressure hydrocephalus has subsequently been subdivided into two subcategories, one in which hydrocephalus develops after a known cause, such as a subarachnoid hemorrhage, meningitis, head trauma, or stroke; and another in which no cause can be identified and the disorder is classified as idiopathic. In reality, the diagnosis of idiopathic NPH is accurately made solely in retrospect. Only those patients who respond to shunt placement are classified as having idiopathic NPH, whereas those patients who do not respond are thought to suffer from enlargement of the ventricles due to another cause (such as atrophy of an unknown source, Alzheimer disease,27 Creutzfeldt-Jakob disease,28 orBinswanger disease). Neuroimaging studies are unreliable methods to use in making a definitive diagnosis of idiopathic NPH, and even brain biopsy shows no specific changes that are characteristic of NPH.21 Surprisingly, some individuals in whom brain biopsy has revealed typical features of Alzheimer disease can, on occasion, respond positively to CSF diversion. Various optional tests have been introduced in the hopes of further identifying those patients who would most likely benefit from shunt placement, as there is an appreciable complication rate connected with CSF diversion, but many studies contain relatively few numbers of patients, making it difficult to identify which tests have diagnostic significance.26

In a nation with a rapidly increasing elderly population, such as Japan, the number of patients at risk for the development of idiopathic NPH is becoming proportionately greater. Because idiopathic NPH is a treatable disorder and the best results are obtained when it is treated early, before irreversible changes occur, the Ministry of Health and Welfare of Japan (Chairman: Koreaki Mori, M.D.) conducted a cooperative study from 1996 through 1999 to try to determine the most predictive diagnostic criteria for patients.

Abbreviations used in this paper: CSF = cerebrospinal fluid; ICP = intracranial pressure; NPH = normal-pressure hydrocephalus; VP = ventriculoperitoneal.
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with the suspected diagnosis of idiopathic NPH who would benefit from extracranial CSF diversion.22-24

Clinical Material and Methods

Patient Population

We conducted a retrospective evaluation of patients 65 years and older who were treated between October 1995 and October 1998 for suspected idiopathic NPH. The tentative diagnosis of NPH was formed on the basis of an increasing gait disturbance, dementia, and urinary incontinence associated with computerized tomography and magnetic resonance imaging findings of progressive enlargement of the ventricles.13 Besides the patients’ clinical symptoms and neuroimaging findings, various optional tests such as lumbar puncture, infusion test, ICP monitoring, cisternography, and cerebral blood flow study, were added at many institutions. Patients were excluded from the study population if they had a known predisposing factor for hydrocephalus, such as subarachnoid hemorrhage, meningitis, head injury, or stroke. The patients were evaluated clinically by using the grading system established by the Committee for Scientific Research on Intractable Hydrocephalus in 1996 (Table 1). The cumulative score of the triad of symptoms accompanying NPH was used for determining the severity of NPH. The patients were evaluated prior to shunt placement, 3 months after shunting, and 3 years after shunting. Extracranial CSF diversion was considered effective when the patient’s NPH grade decreased by one or more points. Questionnaires concerning patients meeting the appropriate 14 criteria were sent to members of the research committee; responses to these questionnaires form the data for this study.

The study identified 120 patients who fit the aforementioned criteria and all these patients underwent a shunting operation. The mean age of the patients was 70.2 ± 8.7 years and the male/female ratio was 70:50. The duration from symptom onset to hospital admission was 14.9 ± 14.8 months (range 2–96 months). A VP shunt was inserted in 105 patients (87.5%) and a lumboperitoneal shunt in 15 (12.5%). In 89 (74.2%) of the patients who received shunts a programmable valve was used, and in 31 patients (25.8%) a differential valve was inserted. An antisiphon device was incorporated into the shunting device in 20 patients in whom the shunt had a differential valve and in two patients in whom it had a programmable valve.

Preoperatively, 113 (94.2%) of the patients displayed gait disturbance, 106 (88.3%) dementia, and 92 (76.7%) urinary incontinence.

Results

Three months after shunt placement, 96 patients (80%) showed improvement in one or more grades when compared with their preoperative scores. Among these patients most notable were the frequency and degree of reduction in gait disturbance following shunting in 76 patients (79.2%) compared with improvement in dementia and urinary incontinence in 20 patients (20.8%). During the course of the study, 22 patients (18.3%) sustained shunt-related complications, whereas 19 (15.8%) experienced complications not related to shunting.

At the end of 3 years, there were 105 patients whose NPH could be evaluated and compared with the initial preshunting status. Of this group, sustained improvement was noted in 77 patients (73.3%), no change in 18 (17.1%), further deterioration in seven (6.7%), and death in three patients (2.9%).

Discussion

The high success rate of shunting in our study may be due to precise patient selection and a high prevalence of programmable valves. A randomized multinstitutional clinical trial may be needed to determine the natural history of untreated idiopathic NPH and the long-term outcome of patients who undergo shunt placement.

During the study, 50 patients suspected of suffering from idiopathic NPH (27 men and 23 women with a mean age of 72.1 years; range 59–93 years) underwent diagnostic lumbar puncture with removal of 20 ml or more CSF followed by 3 days of observation. These patients were not included in the original group of 120 because they were recent cases. In this group 30 patients (60%) displayed temporary improvements after CSF removal in the following: gait disturbance in 29 patients (96.7%), dementia in 16 (53.3%), and urinary incontinence in 14 (46.7%). Among this group of 30 patients who showed temporary improvement, 23 patients received shunts after providing their informed consent. After surgery improvement in gait disturbance was found in 21 patients (91.3%), improvement in dementia in eight (34.8%), and improvement in urinary incontinence in 14 patients (60.9%). Twenty patients did not show improvement and none of these persons received shunts. The response to lumbar puncture is thought to be the most useful and practical examination for determining those patients who would benefit from a shunting procedure according to reports in the literature.9,16,28

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
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<tbody>
<tr>
<td>0</td>
<td>normal</td>
</tr>
<tr>
<td>1</td>
<td>unstable, but independent gait</td>
</tr>
<tr>
<td>2</td>
<td>walking w/ one cane</td>
</tr>
<tr>
<td>3</td>
<td>walking w/ two canes or a walker frame</td>
</tr>
<tr>
<td>4</td>
<td>walking not possible</td>
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<tr>
<th>Grade</th>
<th>Definition</th>
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<tbody>
<tr>
<td>0</td>
<td>w/in normal range</td>
</tr>
<tr>
<td>1</td>
<td>no apparent dementia but apathetic</td>
</tr>
<tr>
<td>2</td>
<td>socially dependent but independent at home</td>
</tr>
<tr>
<td>3</td>
<td>partially dependent at home</td>
</tr>
<tr>
<td>4</td>
<td>totally dependent</td>
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<table>
<thead>
<tr>
<th>Grade</th>
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<tbody>
<tr>
<td>0</td>
<td>absent</td>
</tr>
<tr>
<td>1</td>
<td>absent but w/ pollakisuria or urinary urgency</td>
</tr>
<tr>
<td>2</td>
<td>sometimes only at night</td>
</tr>
<tr>
<td>3</td>
<td>sometimes even during the day</td>
</tr>
<tr>
<td>4</td>
<td>frequent</td>
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* Established by the Research Committee on Intractable Hydrocephalus, the Ministry of Health and Welfare of Japan. 1996. The grades of gait disturbance, dementia, and urinary incontinence are summed to obtain the total grade, ranging from 0 to 12.
What Clinical Tests are Useful for Diagnosis of Idiopathic NPH, and Which Patients Will Improve After Shunt Placement?

Optional clinical tests may be necessary to determine atypical idiopathic NPH that is indistinguishable from cerebral atrophy or that show ischemic vascular changes. Various subgroups of patients were given diagnoses according to findings of optional tests in our study. These tests can improve the prediction of the patients with atypical idiopathic NPH who will respond to shunt placement; however, we still have to conduct a randomized controlled clinical study to obtain strong evidence for the usefulness of these tests.

Because CSF diversion carries a significant risk, it would be best to limit surgical intervention to those patients who have a high likelihood of showing a positive response following the procedure. We found that the most important factors in patient selection were the clinical symptoms of gait disturbance, dementia, and urinary incontinence, and that gait disturbance was the most important of these symptoms. Even if patients exhibit dementia and/or urinary incontinence predominately, some will be helped with CSF diversion. Idiopathic NPH may also be associated with Alzheimer or Binswanger disease or even multiple cerebral infarcts, and these are not always contraindications for CSF diversion. In our study, 68 patients with Binswanger disease who were not part of the group of the original 120 patients underwent CSF diversion after obtaining informed consent between 1981 and 1997. Surprisingly, 61 patients (89.7%) showed some improvement following insertion of a VP shunt.

Because no single test is predictive for those patients with suspected idiopathic NPH who will improve following CSF diversion, opinion ranges from therapeutic nihilism to the pragmatic approach of placing a shunt in all patients to see if they will improve, because the diagnosis of idiopathic NPH is only established in those patients who improve after CSF diversion. If the risks for shunting were small, this would be an appropriate approach; however, as that is not the case, we still need diagnostic methods to select those patients who are most likely to benefit from CSF diversion.

From our observations, we propose standard criteria and optional tests for the diagnosis of idiopathic NPH. The standard diagnostic criteria are useful for determining typical idiopathic NPH, and consist of the following: 1) clinical symptoms suggestive of idiopathic NPH; 2) characteristic findings on neuroimaging; and 3) a transient good response to CSF removal by lumbar puncture or continuous lumbar drainage.

Both hydrodynamic and hemodynamic tests are optional. They may be necessary tools to determine atypical idiopathic NPH. Hydrodynamic tests and results consist of the following: 1) ICP monitoring for 24 hours showing a normal or slightly elevated ICP (>15 mm Hg) with high amplitude waves during at least 50% of the recording time; and 2) infusion tests showing an increased CSF flow resistance of greater than 10 mg/ml/min and a pressure volume index of lower than 13 ml. Hemodynamic tests consist of identification of arterial hypertension as a risk factor and cerebral blood flow higher than 20 ml/100 g/min, with impaired vascular response to acetazolamide in the periventricular area.

Which Type of Shunt Valve is Recommended?

From our study we found that, following insertion of a VP shunt to treat idiopathic NPH, there is a narrow window between over- and underdrainage. At present, we recommend that a programmable valve be used because optimal opening pressure differs from one patient to another. It is recommended that, after shunting, the initial opening pressure be set at the same opening pressure selected at the time of lumbar puncture (approximately 100 mm H2O in general), and that this pressure be gradually adjusted upward or downward until the patient’s symptoms improve. Frequent use of either computerized tomography or magnetic resonance imaging should also be performed. In the past in some studies, clinicians who have selected a medium pressure valve may not have lowered the intraventricular pressure adequately and, thus, may have found a higher rate of treatment failure following CSF diversion. Intraventricular pressure should be set a lower range; however, this is more likely to result in a higher incidence of extraxial hematoma formation. To help decrease this risk, it is suggested that an antisiphon device be incorporated in the shunting system to prevent CSF overdrainage. If such an antisiphon device is used, it should be placed in an appropriate position—at least 10 cm below the burr hole—so as not to cause underdrainage of CSF.

Future Study

Future efforts should be directed toward better identification of the pathogenesis of idiopathic NPH, the development of better diagnostic criteria for identifying patients with idiopathic NPH, and long-term follow-up review for those NPH patients treated with CSF diversion. It is also important to develop better shunt systems that can decrease the risk of complications following CSF diversion. The ideal goal would be to identify those factors that cause idiopathic NPH in hopes of eliminating them.

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References

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