REVIEW ARTICLE

Idiopathic Normal-Pressure Hydrocephalus

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IDIOPATHIC NORMAL-PRESSURE HYDROCEPHALUS IS A SYNDROME OF IMpaired gait and balance, urinary urgency or incontinence, cognitive impairment, and enlarged cerebral ventricles (ventriculomegaly) that usually occurs in persons older than 60 years of age (Fig. 1). It is typically treated by surgical implantation of a cerebrospinal fluid (CSF) shunt.[2] The first description of normal-pressure hydrocephalus, published in the *Journal* 60 years ago,[2] was based on the doctoral thesis of the Colombian neurosurgeon Salomon Hakim.[3] Subsequent work showed that intracranial pressure waveforms and compliance were abnormal. However, the use of normal pressure refers to normal or minimally elevated CSF pressure measurements obtained during lumbar puncture or ventriculostomy placement in the context of enlarged ventricles.

There are two categories of normal-pressure hydrocephalus: idiopathic and secondary. Both are forms of communicating hydrocephalus, meaning that there is no obstruction to the flow of spinal fluid within the ventricular system, and they have similar signs and symptoms. Secondary normal-pressure hydrocephalus can develop at any age as a consequence of intracranial hemorrhage, head trauma, infection, or treatment for a brain tumor or other brain disorders. In contrast, the idiopathic form develops later in life and without any known cause. Because the idiopathic form of normal-pressure hydrocephalus is more common and more challenging to diagnose than the secondary form, it has been the subject of most studies and is the focus of this review.

Early descriptions of idiopathic normal-pressure hydrocephalus as a surgically treatable form of dementia were followed by a surge of enthusiasm in the 1960s and 1970s for diagnosing and treating the disorder. However, subsequent reports of minimal or only transient improvement, high rates of treatment-related complications, coexisting conditions mimicking idiopathic normal-pressure hydrocephalus, and limited knowledge of the pathophysiology of the disorder prompted skepticism regarding its existence as a clinical entity and its response to treatment.[4,5] A 2013 survey showed that nearly 350 neurologists and neurosurgeons were divided on the efficacy of shunt surgery in treating idiopathic normal-pressure hydrocephalus.[6] In our view, four misconceptions about the disorder persist: it is rare or does not exist, diagnostic tests are risky or not useful, the risks of shunt surgery outweigh the benefits, and improvements after shunt surgery are transient or not clinically meaningful.

PATHOPHYSIOLOGY

Questions regarding the mechanisms underlying the symptoms of idiopathic normal-pressure hydrocephalus and the increase in ventricular size, despite the absence of an apparent obstruction to CSF flow and normal intracranial pressure, have persisted since the initial description of the disorder. Hyperlipidemia, hypertension, diabetes, obesity, alcohol use disorder, and other risk factors have been tentatively associated with idiopathic normal-pressure hydrocephalus, but the

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CME

KEY POINTS

IDIOPATHIC NORMAL-PRESSURE HYDROCEPHALUS

- Idiopathic normal-pressure hydrocephalus is a progressive neurologic disorder that usually occurs after the age of 60 years and is characterized by enlarged cerebral ventricles, gait and balance difficulty, incontinence, and cognitive impairment.
- Each symptom of idiopathic normal-pressure hydrocephalus has an extensive differential diagnosis. A thorough history taking and neurologic examination are recommended, with computed tomography or magnetic resonance imaging of the brain and, if indicated, treatment of any contributing disorders.
- Prognostic tests to determine the likelihood of improvement after cerebrospinal fluid (CSF) shunt surgery are supported by clinical guidelines.
- Surgical implantation of a CSF shunt with a programmable valve is a safe and durable treatment for idiopathic normal-pressure hydrocephalus that can ameliorate symptoms, improve quality of life, and decrease mortality.

underlying pathophysiological relationships are unknown.[1,7] It seems unlikely that the symptoms of idiopathic normal-pressure hydrocephalus are caused simply by the stretching of nerve fibers surrounding the enlarged lateral ventricles because the symptoms can abate rapidly after CSF drainage, despite a decrease in ventricular size of less than 15%.[8] Furthermore, many patients with ventricular enlargement are asymptomatic. Increased intracranial pressure pulse amplitude, white-matter abnormalities, decreased cerebral blood flow, abnormal cerebrovascular reactivity, abnormal neural network activity, and decreased CSF movement through the subarachnoid and paravascular spaces of the brain glymphatic pathway (a system for CSF circulation through the subarachnoid, paravascular, and interstitial spaces of the brain) have been observed in idiopathic normal-pressure hydrocephalus, but causative roles have not been established.[9,10]

Reports of familial idiopathic normal-pressure hydrocephalus have described pedigrees with autosomal dominant transmission. A study of one such family revealed a germline variant in *CFAP43* (the gene encoding cilia- and flagella-associated protein 43) as a possible cause of familial idiopathic normal-pressure hydrocephalus.[11] CFAP43 is important for the normal development and function of motile cilia, and homozygous Cfap43 deletion in mice causes abnormalities in motile cilia structure and communicating hydrocephalus. Deletions in *CWH43* have been identified in 15% of patients with idiopathic normal-pressure hydrocephalus.[12] *CWH43* modifies the lipid anchor of glycosylphosphatidylinositol (GPI)ñ anchored proteins. Mice carrying an idiopathic normal-pressure hydrocephalusñassociated *Cwh43* mutation have enlarged ventricles, gait and balance abnormalities, and a decreased number of ventricular motile cilia. A 2024 Finnish genome-wide association study identified six genomic regions significantly associated with idiopathic normal-pressure hydrocephalus, although the role of these loci in the disorder is not known.[13]

EPIDEMIOLOGY

Idiopathic normal-pressure hydrocephalus occurs primarily after the age of 60 years, and its prevalence increases with age, with no apparent difference according to sex. The features of possible idiopathic normal-pressure hydrocephalus, as defined in published guidelines (i.e., ventriculomegaly and clinical findings consistent with idiopathic normal-pressure hydrocephalus but without prognostic testing for possible improvement after shunt surgery), have been used for population-based epidemiologic studies.[14,15] The pooled prevalence of possible idiopathic normal-pressure hydrocephalus among persons older than 65 years of age was 1.3% in a systematic review of these studies.[16] A Swedish study that incorporated symptoms, neurologic examination findings, and brain imaging showed that the prevalence of possible idiopathic normal-pressure hydrocephalus was 1.5% (1500 cases per 100,000 persons) at the age of 70 years.[17] In a longitudinal prospective study of a Japanese community-based cohort followed from the age of 70 years to 86 years, the prevalence of possible idiopathic normal-pressure hydrocephalus was 7.7%.[18]

There is evidence that idiopathic normal-pressure hydrocephalus may be underdiagnosed and undertreated. For example, from 2004 to 2011,

the incidence of shunt surgery for idiopathic normal-pressure hydrocephalus in Sweden was only 2.2 procedures per 100,000 persons per year (0.0022%),[19] and in a U.S. inpatient sample, only approximately 6600 shunt procedures for idiopathic normal-pressure hydrocephalus were performed annually.[20] In contrast, approximately 15% of patients in memory clinics and 14% of nursing home residents have possible idiopathic normal-pressure hydrocephalus according to two surveys, and other cases are probably not diagnosed.[21,22]

IMAGING

Although ventricular enlargement is a key feature of idiopathic normal-pressure hydrocephalus, this finding alone is nonspecific, occurring in many conditions, including brain volume loss with aging. The ventriculomegaly of idiopathic normal-pressure hydrocephalus is often described as "out of proportion to brain atrophy," which is a subjective assessment. The Evans ratio and the callosal angle (Fig. 2A) are quantitative screening tools for idiopathic normal-pressure hydrocephalus but do not reliably predict the response to shunt surgery.[23] Sulcal effacement at the brain vertex, accompanied by focal sulcal dilatation elsewhere (Fig. 2A), has a positive predictive value of 77% for shunt responsiveness but a negative predictive value of only 25%.[26] A scoring system, the Radscale, retrospectively differentiated preoperative brain scans from patients with idiopathic normal-pressure hydrocephalus who had a response to shunt surgery from scans obtained from asymptomatic controls, but this finding requires prospective validation.[27]

Thus, no single imaging finding reliably distinguishes between patients with idiopathic normal-pressure hydrocephalus who will have a response to shunting and those who will not have a response.[19] Clinical guidelines do not support the use of radionuclide cisternography for diagnosis, although it has been used for that purpose in the past.[14,15] Periventricular white-matter hyperintensities are common in the age group affected by idiopathic normal-pressure hydrocephalus, and their presence does not rule out the disorder.[28,29] An obstruction of the flow of CSF should be ruled out with the use of computed tomography (CT) or magnetic resonance imaging (MRI). The presence of an obstruction signifies that hydrocephalus is obstructive and not communicating and is therefore not consistent with idiopathic normal-pressure hydrocephalus. Cine MRI to view CSF flow through the cerebral aqueduct or balanced steady-stateñfree

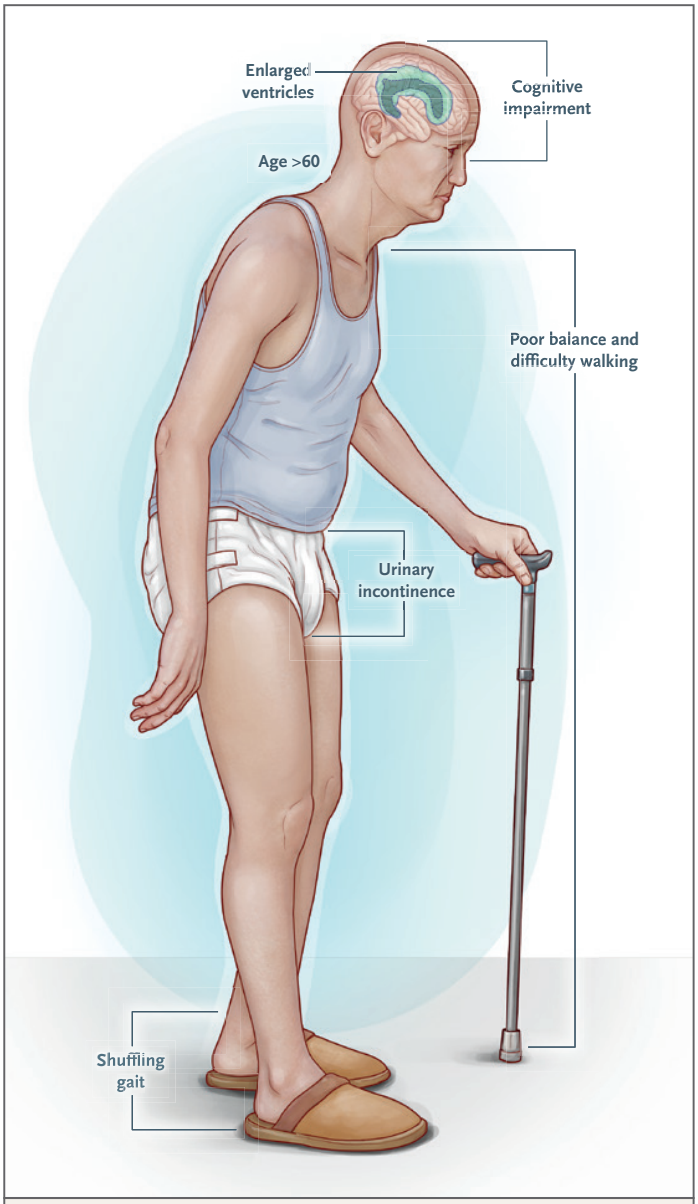

Figure 1. Signs and Symptoms of Idiopathic Normal-Pressure Hydrocephalus (NPH).

The typical signs and symptoms of idiopathic NPH are shown. In a retrospective study involving 418 patients with shunt-responsive idiopathic NPH, 96% of the patients had gait difficulty, 76% had cognitive impairment, and 75% had urinary urgency or incontinence.[1] Approximately 63% of the patients in this cohort had the full triad of gait difficulty, urinary incontinence or urgency, and cognitive impairment.

precession pulse-sequence MRI to identify sites of anatomical obstruction are sensitive techniques that can be used for this purpose. Lumbar puncture is not recommended when obstructive hydrocephalus is present because of the risk of cerebral herniation.

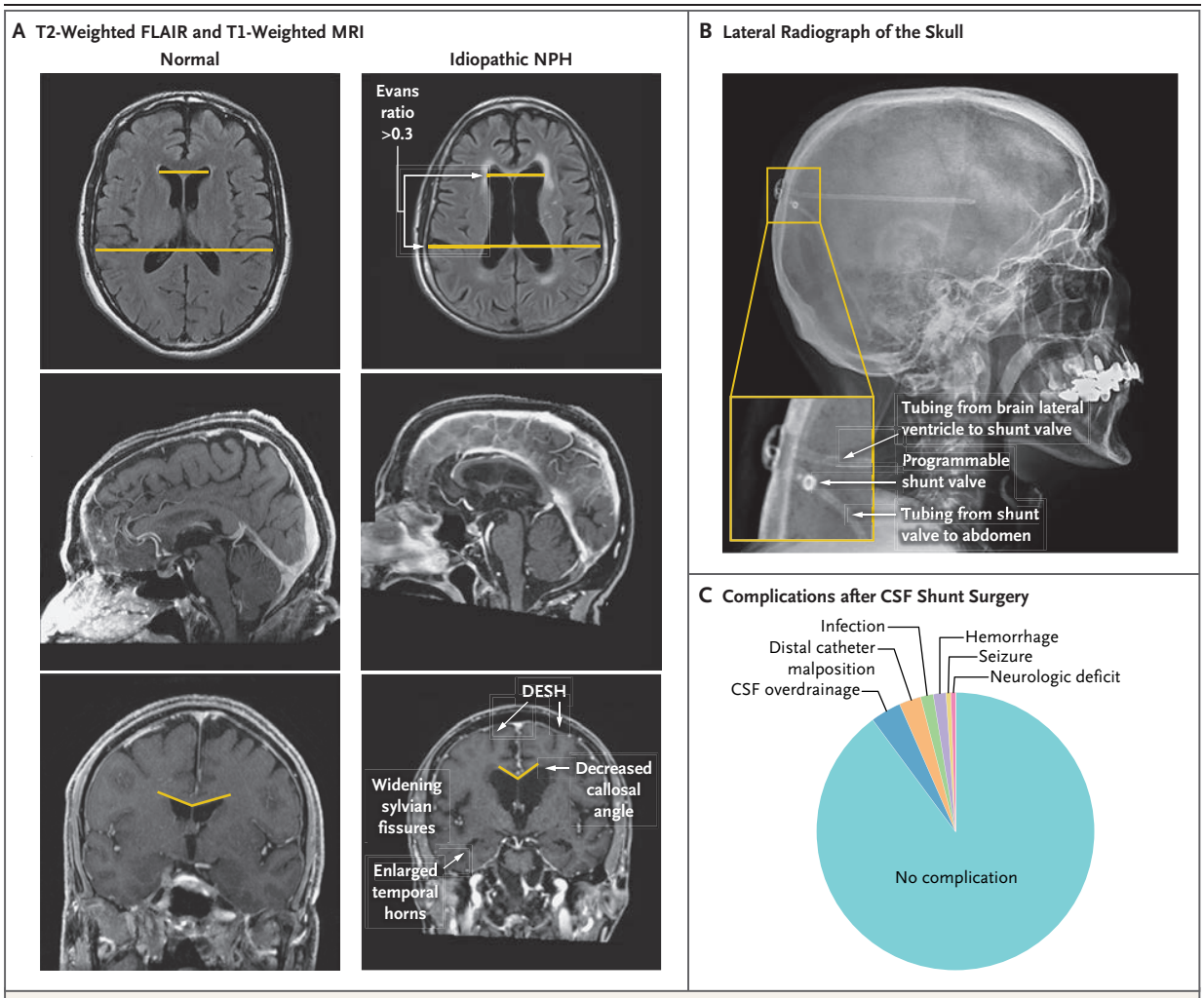

Figure 2. Imaging Features of Idiopathic NPH, Programmable Cerebrospinal Fluid (CSF) Shunt Surgery, and Surgical Risks.

Panel A shows T2-weighted fluid-attenuated inversion recovery (FLAIR; top row of images) and T1-weighted (middle and bottom rows) magnetic resonance imaging (MRI) in a 73-year-old man with no evidence of idiopathic NPH (left side of the panel) and a 71-year-old woman with shunt-responsive idiopathic NPH (right side of the panel). Three imaging features that are characteristic of idiopathic NPH on brain computed tomographic (CT) or MRI studies are shown. The top two images show the Evans ratio, calculated as the frontal horn span (upper yellow line) divided by the widest dimension of the inner table of the skull in the same image slice. An Evans ratio exceeding 0.3 is characteristic of idiopathic NPH. The middle images show enlargement of the third ventricle and cerebral aqueduct in idiopathic NPH. The characteristic findings in the lower images are a callosal angle less than 90 with sulcal effacement at the vertex and enlarged sylvian fissures (disproportionately enlarged subarachnoid space hydrocephalus [DESH]), as well as enlarged temporal horns. The callosal angle is measured in the coronal plane at a line intersecting the posterior commissure and perpendicular to the anterior posterior commissure. It becomes more acute as the corpus callosum impinges on the falx with enlargement of the ventricles. The lateral radiograph of the skull in Panel B shows an occipital ventriculoperitoneal shunt placed for the treatment of idiopathic NPH. The inset shows the programmable shunt valve. The pie chart in Panel C shows the types of complications after CSF shunt surgery for idiopathic NPH at five centers with expertise in managing the disorder. More than 91% of patients had no complications. The data shown in the chart, which are based on reports from a single multicenter study that did not provide mean percentages of patients with complications or confidence intervals, may not be generalizable.[24,25]

CLINICAL PRESENTATION

Symptoms of idiopathic normal-pressure hydrocephalus develop insidiously over a period of months to years.[17] The characteristic triad of gait or balance difficulty, urinary urgency or incontinence, and cognitive impairment (Fig. 1) has an extensive differential diagnosis (Table 1).[30,31] Signs and symptoms of elevated intracranial pressure, such as severe headaches or papilledema, are not present in idiopathic normal-pressure hydrocephalus. Guidelines for diagnosing the disorder recommend obtaining a thorough history, performing a neurologic examination, and ordering brain imaging, as mentioned above; identifying and treating coexisting conditions such as parkinsonism, Alzheimer s disease, or other disorders that may contribute to the patient s symptoms; and performing prognostic tests (described below) to determine whether improvement after shunt surgery is likely.[14,15]

Although the full symptom triad is present in only two thirds of affected patients, impaired gait and balance occur in more than 90% of patients.[32] The gait and balance impairments involve difficulty integrating motor and sensory input and executing normal gait patterns and postural reflexes.[33,34] The appearance of the gait can be distinguished from the gait that characterizes cerebellar disorders and sensory ataxia but may be difficult to distinguish from the short-stepped parkinsonian gait. The gait in patients with normal-pressure hydrocephalus is often wide-based and unstable, with decreased step height and stride length and may incorporate a degree of shuffling. Patients may have difficulty standing from a sitting position without using their arms to push off from a chair or other support, may be unable to easily initiate walking, or may tend to freeze midstride during walking. Instability while turning is common, as are falls. Gait velocity is slow (typically ≤1 m per second),[24,33,34] but leg strength, sensation, and reflexes are normal. Spasticity, hyperreflexia, Romberg s sign, and neurogenic claudication are not typical findings (Table 1).[24,33-35]

The cognitive symptoms of idiopathic normal-pressure hydrocephalus, which include difficulty with short-term memory and activities of daily living, can resemble those of neurodegenerative dementia (Table 1). Remote memory is usually preserved. Inability to recognize family members, marked personality change, delirium, and hallucinations are not typical.[33,34] Neuropsychological testing shows a frontalñsubcortical pattern of decline, with impaired processing speed and executive function but also with memory impairment that benefits from cues and with preserved naming and fluency ó a pattern of findings that is generally not characteristic of Alzheimer s dementia. However, this pattern of impairment may overlap with other disorders (Table 1).[33,34] Dementia without gait impairment is uncommon in idiopathic normal-pressure hydrocephalus, and detailed testing for dementia may be warranted before consideration of shunt surgery in such cases.

The urinary dysfunction of idiopathic normal-pressure hydrocephalus includes urgency and difficulty inhibiting bladder emptying due to detrusor overactivity.[36] It can be distinguished from the urinary hesitancy and incomplete bladder emptying caused by prostatic hypertrophy in men, as well as the stress incontinence caused by pelvic-floor disorders in women (Table 1). Fecal incontinence has been reported in patients with idiopathic normal-pressure hydrocephalus, but it has been an uncommon finding, and other potential causes should be explored if it is present.[37]

In some persons, brain imaging shows enlarged cerebral ventricles and effacement of the sulci at the vertex, findings that are consistent with idiopathic normal-pressure hydrocephalus, in the absence of symptoms.[38] Prognostic testing for idiopathic normal-pressure hydrocephalus (described below) and shunt surgery are not indicated in such persons. In a prospective series of asymptomatic persons with these findings, however, symptoms of idiopathic normal-pressure hydrocephalus developed in approximately 52% of patients within 3 years, and follow-up is therefore advisable. If symptoms develop later, testing can then be performed.[38]

PROGNOSTIC TESTS FOR TREATMENT RESPONSE

Because there are no reliable markers for a definite diagnosis of idiopathic normal-pressure hydrocephalus, guidelines recommend tests that assess the physiology of CSF circulation or the clinical response to CSF drainage in order to determine whether improvement after shunt surgery

Table 1. Findings Suggestive of Idiopathic Normal-Pressure Hydrocephalus (NPH) or Other Disorders and Differential Diagnosis.

Category	Findings Suggesting Idiopathic NPH	Findings Suggesting Other Disorders	Differential Diagnosis
Gait	Gait initiation failure Short steps Stuttering steps Shuffling with poor foot clearance Festination Falls while walking Low gait velocity (<1 m/sec) Multistep turns Difficulty getting in or out of seats or up from the floor Limited walking distance Normal strength and sensation despite abnormal gait pattern	Step length asymmetry Focal motor weakness Pain, antalgic gait, or guarding Spasticity, hyperreflexia, or clonus Muscle fasciculations Paresthesias Impaired sensation in the feet Romberg s sign Parkinsonian tremor Rigidity Claudication Dyspnea on exertion Normal gait velocity and gait pattern	Stroke Radiculopathy Osteoarthritis of hips or knees Lumbosacral spine arthritis Myelopathy Spinal central canal stenosis Neuropathy Myopathy Parkinsonism Peripheral vascular disease Cardiopulmonary disease Asymptomatic ventriculomegaly Medication side effects
Balance	Falling with turns Retropulsion while seated or standing Inability to maintain stance with push or pull test Unexplained falls	Romberg s sign Paresthesias Nystagmus Cerebellar ataxia Dysmetria, dysdiadochokinesia, dysarthria Movement-provoked vertigo Normal balance	Neuropathy Vestibular dysfunction Cerebellar stroke or degeneration Orthostatic hypotension Subacute combined degeneration Alcohol use disorder Asymptomatic ventriculomegaly Medication side effects
Bladder control	Urinary urgency Urinary frequency Difficulty inhibiting bladder emptying Spontaneous bladder emptying without warning	Lack of urinary urge or sensation Stress incontinence (e.g., loss of urine with coughing) Urinary retention Urinary hesitation Incomplete bladder emptying Slow urinary stream Dysuria	Myelopathy Pelvic organ prolapse (e.g., cystocele) Urinary outlet obstruction Prostatic hypertrophy Sequelae of urologic or gynecologic surgery Urinary tract infection Medication side effects
Cognition	Nonamnestic memory impairment (benefits from cues or clues) Slowed processing speed Impaired executive functioning Apathy or lack of motivation	Dementia with minimal or no gait impairment Amnestic memory impairment Delirium, hallucinations, delusions Impaired naming Aphasia Agnosia Anhedonia Normal neuropsychological testing	Alzheimer s dementia Parkinson s disease Lewy body dementia Vascular cognitive impairment Severe depression with pseudodementia Vitamin B_{12} deficiency Hypothyroidism Asymptomatic ventriculomegaly Medication side effects
General examination		Sleep intrusions Gasping, observed apneas during sleep Acting out dreams Parkinsonian tremor Hypophonic speech Vertical gaze impairment Syncope or near syncope Absent or diminished pedal pulses Visual impairment	Sleep apnea Rapid-eye-movement sleep behavior disorder Dysautonomia Parkinsonism Lewy body dementia Cardiac dysrhythmia Peripheral vascular disease Cataracts, retinopathy, macular degeneration, glaucoma Medication side effects

is likely.[14,15,39,40] Lumbar infusion testing (which involves the infusion of Ringer s lactate and the simultaneous recording of CSF pressure) assesses CSF volumeñpressure relationships and CSF outflow resistance to predict shunt responsiveness. The positive predictive value of infusion testing is 80%, but it fails to predict improvement after shunt surgery in 15 to 20% of patients.[39,41] Abnormally increased intracranial pressure pulsatility (pulse pressure of ≥4 mm Hg), as assessed by intracranial pressure monitoring, predicts shunt responsiveness with an accuracy similar to that of infusion testing, although it is not a widely used measure.[42]

Evaluation of the response to temporary drainage of a large volume of CSF is a common approach to prognostic testing. A lumbar puncture that removes 30 to 50 ml of CSF can be performed in the outpatient setting. The positive predictive value of this test for shunt responsiveness, based on improvement in gait, as described below, is approximately 90%, but the negative predictive value is only approximately 20%.[39,43] Thus, the absence of improvement after a large-volume lumbar puncture does not rule out idiopathic normal-pressure hydrocephalus. Prolonged lumbar drainage, which involves hospital admission and insertion of a lumbar intrathecal catheter for 24 to 72 hours for continuous CSF drainage, has approximately 90% specificity and sensitivity for shunt responsiveness.[32,44] The main complication of this approach is meningitis, which occurs in 1 to 2% of patients.[24,40,44]

It is advisable to accurately and quantitatively assess gait and balance shortly before and within several hours after CSF removal. Subsequent monitoring of gait for 24 to 48 hours may show delayed improvement.[32] Typical assessments include a timed 10-m walk, the timed up-and-go test (in which the patient stands up from a chair, ambulates 10 feet, turns around, and returns to sit in the chair), and the Tinetti performance-oriented mobility assessment, which measures transitions between sitting and standing, standing balance, turning, and gait characteristics. Patient and caregiver impressions of changes in symptoms can be sought but should not be a substitute for formal evaluations.

A European multicenter study in which 115 patients who were selected on the basis of clinical presentation and imaging underwent infusion testing, high-volume CSF removal by lumbar puncture, and shunt surgery showed improvement in 84% of the patients 12 months after surgery, regardless of the test results.[39] However, neither international nor Japanese guidelines recommend proceeding to shunt surgery without prognostic testing because testing to select patients for shunt surgery greatly increases the likelihood of improvement.[14,15,45] It is unclear whether patients with signs and symptoms of idiopathic normal-pressure hydrocephalus who do not have improvement after shunt surgery have reached a stage of the disorder in which it no longer responds to treatment or whether they have other disorders underlying their symptoms.

Results of standard CSF analysis in patients with idiopathic normal-pressure hydrocephalus are normal. The use of CSF biomarkers to determine whether patients will have a response to shunt surgery currently has limited value. The ratio of phosphorylated tau 181 to amyloid beta (Aβ) 1-42 may help to identify concurrent Alzheimer s disease in patients with idiopathic normal-pressure hydrocephalus, but it is not useful for identifying idiopathic normal-pressure hydrocephalus itself and is not used alone to predict the response to shunt surgery.[46] The evaluation and treatment of patients who have both idiopathic normal-pressure hydrocephalus and Alzheimer s disease is complex. A decrease in the dementia caused by Alzheimer s disease would not be expected after shunt surgery. Improvement in gait and balance has the potential to reduce falls, although the risk of wandering behavior could be increased. Continence may also improve. Careful discussion of the goals of care and the risks and benefits of shunt surgery with the patient and family is recommended.

TREATMENT

Currently, the most effective treatment for idiopathic normal-pressure hydrocephalus is surgical implantation of a CSF shunt. A 2024 Cochrane review of four randomized, placebo-controlled trials of shunt surgery for idiopathic normal-pressure hydrocephalus showed that gait velocity increased by 30% on average, and disability was reduced, with approximately 1 in 3 patients becoming functionally independent within the first 6 months after surgery, when compared with patients who did not have a shunt or who had programmable CSF shunts that were in inactive mode to create a placebo condition.[47] The same review called the evidence for an effect on cognitive function unclear. A 2025 multicenter, double-blind, randomized, placebo-controlled trial involving 99 participants provided convincing evidence of the effectiveness of CSF shunt surgery in patients with idiopathic normal-pressure hydrocephalus who were selected on the basis of gait-velocity improvement with CSF drainage. At 3 months after surgery, participants who were randomly assigned to an open-shunt valve setting showed a statistically significant and clinically meaningful improvement in gait velocity (0.23 m per second) as compared with no change

(0.03 m per second) in participants who were assigned to a placebo valve setting with a high opening pressure that precluded drainage. In total, 75% of the patients assigned to an open-shunt valve setting had improved gait velocity at 3 months. Participants with open shunts also had fewer falls and had changes in tertiary measures of cognition, quality of life, and functional independence that were suggestive of benefit but did not reach statistical significance. Subdural hematomas, some of which required surgical intervention, occurred in 12% of the open-shunt group and 2% of the placebo group.[48]

Ventriculoperitoneal, ventriculoatrial, and lumboperitoneal shunt systems have similar efficacy.[49] In a single small trial involving patients with idiopathic normal-pressure hydrocephalus that assessed endoscopic third ventriculostomy to divert CSF from the third ventricle directly into the subarachnoid space, the results regarding the effectiveness of endoscopic third ventriculostomy as compared with shunting were considered to be inconclusive.[50] Although acetazolamide has occasionally been used to reduce CSF production, data from randomized, controlled trials showing its effectiveness are lacking.

The prevailing practice has been to use programmable magnetic shunt valves that can be adjusted noninvasively to regulate the amount of CSF drainage (Fig. 2B). Patients may benefit from follow-up assessments of the clinical response and, when indicated, a change in the shunt valve setting to decrease symptoms of idiopathic normal-pressure hydrocephalus as much as possible while avoiding signs and symptoms of CSF overdrainage, such as positional or tussive headaches, muffled hearing, or subdural fluid collections. The setting of most programmable magnetic shunt valves can be inadvertently altered by strong external magnetic fields such as those involved in MRI examinations, and verification or correction of the valve setting is recommended after MRI of any part of the body. A change in ventricular size may not be apparent on CT or MRI of the brain unless careful volumetric measurements are made, because decreases in ventricular volume after shunt placement are usually small in patients with idiopathic normal-pressure hydrocephalus.

The most common serious complications of shunt surgery are infection, brain injury from catheter misplacement, and subdural hematoma. Careful patient selection, the use of programmable shunt valves, improvements in surgical technique such as neuronavigation, laparoscopic peritoneal catheter placement, and infection prevention measures have been used to reduce the frequency of these problems. A study involving 193 patients at five centers that treated large numbers of patients with idiopathic normal-pressure hydrocephalus showed that over a period of 1 year, more than 91% of the patients who underwent shunt surgery had no complications, and 6% had major complications that required an extended hospital stay or further surgery (Fig. 2C).[24] In the United States, the incidence of reoperation after shunt surgery (not restricted to idiopathic normal-pressure hydrocephalus) among adults 55 years of age or older is 32.4%, indicating that outcomes may be better at centers with expertise in managing idiopathic normal-pressure hydrocephalus.[24,25,48]

Sustained symptom abatement after shunt surgery has been reported for approximately 90% of patients with idiopathic normal-pressure hydrocephalus.[7,24,45] One report cited improvement in more than 90% of patients at 3 months and in more than 75% of patients at 4 years after shunt surgery.[45] Functional decline over time occurred primarily in patients older than 80 years of age. Treatment of idiopathic normal-pressure hydrocephalus is generally cost-effective and is associated with improvement in quality of life during the 5 years after surgery for most patients.[51]

Delays in the diagnosis and treatment of idiopathic normal-pressure hydrocephalus may be disadvantageous. In a Swedish cohort, patients whose shunt surgery was unavoidably delayed by more than 6 months for reasons unrelated to their health had substantial worsening of their symptoms by the time of shunt surgery and less improvement afterward than patients who underwent surgery within 3 months after diagnosis.[52] After 6 years of follow-up for the same cohort, mortality among the patients whose surgery was delayed by more than 6 months was 2.6 times as high as that among those who underwent surgery sooner.[53]

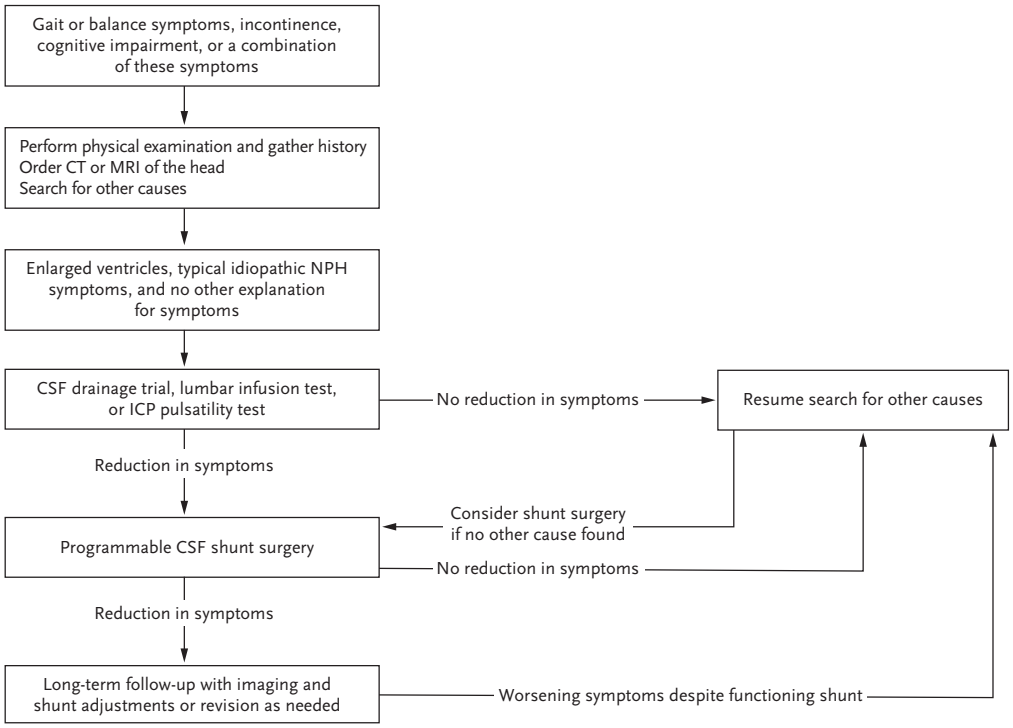

Figure 3. A Diagnostic and Treatment Algorithm for Idiopathic NPH.
The algorithm is based on clinical guidelines.[14,15] ICP denotes intracranial pressure.

If symptoms of idiopathic normal-pressure hydrocephalus return after initial abatement, appropriate interventions include adjustment of the shunt valve setting to increase CSF drainage, evaluation for possible shunt malfunction (estimated to occur in approximately 13% of patients over a 17-year period), and a search for coexisting disorders that may have developed after shunt placement.[7,54] A diagnostic and treatment algorithm for idiopathic normal-pressure hydrocephalus that we have developed on the basis of clinical guidelines is shown in Figure 3.[14,15]

FUTURE DIRECTIONS

Research on the glymphatic circulation of the brain, the functioning of the choroid plexus, brain water transport, and genetic propensities may help to elucidate the cause and pathophysiology of idiopathic normal-pressure hydrocephalus.[55-57] Efforts are under way to develop new surgical approaches and medications that reduce ventricular size by decreasing CSF production or increasing CSF drainage.[58,59]

In summary, idiopathic normal-pressure hydrocephalus is a common, frequently undiagnosed disorder affecting gait, cognition, and urinary continence that can cause disability in persons older than 60 years of age. An approach to management that includes differential diagnosis, prognostic testing, treatment with shunt surgery when appropriate, and longitudinal follow-up can result in favorable outcomes.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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