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Normal-Pressure Hydrocephalus

Another Treatable "Dementia": Part I

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Learning Objectives: *After reading this article, the participant should be able to:*
1. Describe the clinical presentation of normal-pressure hydrocephalus (NPH).
2. Explain the physiopathology of NPH.
3. Describe the role of the various diagnostic modalities of NPH.

This article is the first of two parts.

Normal-pressure hydrocephalus (NPH) is encountered most often in elderly persons. In this condition, cerebrospinal fluid (CSF) buildup within the ventricles causes them to enlarge, and a variety of clinical symptoms is seen, including gait disturbance, urinary incontinence, and dementia. Because NPH is treatable, it is considered to be a cause of reversible dementia. However, NPH still is largely under- and misdiagnosed, with the result that a significant number of patients who otherwise would have been able to maintain a functional lifestyle end up in nursing homes. The reported incidence ranges from 1% to 10%, with some authors suggesting that as many as 6% of residents of nursing homes may have NPH. Misdiagnosis results from many factors, including failure of clinicians to entertain NPH as a diagnosis, even when patient exhibits all the typical signs and symptoms; or requirement by clinicians that the patient be a "textbook" case before entertaining the diagnosis. Often, reluctance to make the diagnosis stems from concerns about the morbidity of shunting in this patient population. However, as in many other clinical entities, it is crucial to keep this diagnosis in mind and to realize that even patients who have only some of the clinical or radiologic findings associated with NPH may have NPH. These patients will respond to shunting, and therefore they should not be denied that option unless a thorough evaluation is performed and NPH is excluded.

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Historical Notes

In 1965, Adams et al. described a small series of patients with various neurological symptoms, ventricular enlargement, and "normal" CSF pressure as revealed by lumbar puncture who improved in response to shunting. Because of the normal CSF pressure, this syndrome was given the name *normal-pressure hydrocephalus.* NPH was defined as a syndrome of progressive dementia and unsteady gait, with dilatation of the ventricular system and CSF pressure less than 200 mm. Since that time, the syndrome has gained wide recognition, and it now is considered an important element of the differential diagnosis for dementia in elderly persons.

Physiopathology

Some cases of NPH are idiopathic, whereas others are secondary to an insult to the central nevous system. It is thought that these injuries result in scarring of the subarachnoid spaces or the arachnoid villi, leading, in turn, to an extraventricular blockage of the CSF circulation or altered CSF absorption, a process that would explain the increased resistance to CSF absorption regularly found in NPH. With aging, the brain tissue looses its stiffness and becomes more compliant. As CSF outflow is reduced, the ventricles will enlarge. The pressure rises, but to a mild degree, and because

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of the high degree of compliance of the aging brain, pressure stays within the normal range. It is thought that although the CSF pressure as revealed by lumbar puncture registers as "normal," it is higher than expected in that particular patient population.

It also is thought that the progressive ventriculomegaly characteristic of NPH may cause compression of structures adjacent to the ventricles, resulting in the clinical manifestations of the disease. For example, pressure on the frontal lobes and their interconnections may cause dementia and cognitive dysfunction; pressure on the cortical center for bladder and bowel control in the paracentral lobes may cause incontinence; and pressure on the corticospinal "leg fibers" descending lateral to the ventricles may cause gait disturbance, although a subcortical contribution may play a role early on.

Etiology

Approximately 50% of cases of NPH are idiopathic, and no specific etiology can be found. These cases are thought to be secondary to aging of the arachnoid granulations, which leads in turn to decreased CSF absorption. Insults so minor that they were not noticed by the patient may accelerate the process by causing inflammation and scaring of the subarachnoid spaces and villi. Known etiologies of NPH include trauma, subarachnoid hemorrhage, meningitis, previous neurosurgical intervention, and irradiation.

Clinical Findings

Gait Changes

The gait abnormality characteristic of NPH is the earliest and most common finding in patients with this syndrome. The gait disturbance is not uniform and can vary from patient to patient. It may described as shuffling, magnetic or broad based. The steps are shortened in the shuffling gait, while the patient has difficulty raising the legs in the magnetic gait, and the base is widened in the broad based gait. The first two patterns may be seen in combination. The patient has difficulty turning, and families sometimes report that the patient has a tendency to fall backward. The gait disorder represents an alteration of the patient's ability to move smoothly rather than weakness or true imbalance. Sometimes the gait is described as giving the appearance that the patient has forgotten how to walk, and it may be referred to as *gait apraxia.* Excessive activity of the antigravity muscles occurs in NPH, and this activity may prevent smooth gait progression. There is some similarity between the gaits of NPH and Parkinson disease: short stride, slow gait, and difficulty turning. However, in NPH, there is no cogwheel rigidity, no resting tremor, and no response to levodopa. In cerebellar ataxia, other findings are encountered, such as dysarthria, gaze-evoked nystagmus, and appendicular dysmetria. The presence of gait alteration in NPH is the most significant positive clinical prognosticator, possibly because of its relative specificity compared with the other cardinal symptoms.

Cognitive Deficits

Cognitive decline is gradual, usually causing executive dysfunction early in the course of the disease, and it may be difficult to recognize unless specific tests are performed. These deficits may manifest as "psychomotor slowing," verbal dysfluency, and deficits in planning. A variable degree of abulia is manifested by loss of spontaneity and initiative, which have been termed the "abulic traits." These traits can progress to severe akinetic mutism. Rarely, agitation, delusions, and hallucination may be present. On formal mental status testing, nonverbal performance is affected more severely than verbal performance. True aphasia is not seen.

Behavioral disturbances such as agitation and symptoms of depression may be encountered. Hypersomnia occurs in as many as 40% of patients. Somnolence and cognitive impairment are more likely to improve after shunting than are abulia and behavioral disturbances.

Urinary Disturbance

The urinary disturbance of NPH ranges from urinary frequency to urgency to incontinence in advanced cases. Urinary disturbance also can take the form of inability to realize the need to urinate, resembling the incontinence of frontal

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syndromes. The slow gait contributes by preventing the patient with urgency from reaching the toilet on time. Urinary incontinence is present in half of the patients and is nonspecific, with only 33% predictive value for improvement. The differential diagnosis in elderly patients includes a variety of disorders, including benign prostate hypertrophy, pelvic relaxation, and cystitis. Fecal incontinence is rarely present.

Differential Diagnosis

The differential diagnosis of NPH includes a variety of diseases leading to senile dementia, including Alzheimer disease, frontotemporal dementia (Pick disease), Lewy body disease, Parkinson disease (Fig. 1), corticobasal ganglionic degeneration (CBGD), multi-infarct dementia, and depression. In Alzheimer disease, the magnetic gait is not present until the late stages of the disease. In vascular dementia, extensive ischemic changes are seen on MRI. However, cerebrovascular ischemic disease also predisposes patients to NPH. It is important to remember that multiple pathologies may co-exist in elderly patients. We have seen some patients, although few in number, with a dual diagnosis of NPH and dementia. It is important to keep that in mind while discussing therapy with the patient and family.

Diagnostic Testing

Imaging Studies

Diagnosis of NPH is a challenge. Many studies have been published regarding NPH and the predictive values of the various diagnostic tests. However, the range of results reported among studies is wide, and evidence-based recommendations are difficult to make.

CT and MRI. The primary complicating factor encountered by the radiologist is the fact that NPH occurs in elderly people. In this patient population, brain atrophy leads to ventricular enlargement (hydrocephalus ex vacuo) even in patients without NPH. Therefore, radiologists have been trying to pinpoint other features revealed by neuroimaging modalities that will help to diagnose NPH.

On CT scans, these distinguishing features include enlarged temporal horns, enlarged ventricles out of proportion to sulcal enlargement and brain atrophy, and an increased Evans ratio (the ratio of the frontal horns' distance to the width of skull, measured from the inner calvarial table). This ratio may be increased with ex vacuo ventriculomegaly caused by non-NPH dementias. The presence of enlarged sulci has been used as an indicator of ex vacuo ventriculomegaly and as a negative prognosticator. However, more than half of patients with atrophy will respond to shunting. Periventricular lucency, thought to be an indicator of transependymal resorption, has not been shown to correlate consistently with successful shunting.

Other features that are sought on MRI include transependymal resorption, periventricular hyperintensities on T2-weighted MRI, lack of hippocampal atrophy (which is more specific for Alzheimer disease), increased CSF flow through the sylvian aqueduct, and turbulence of CSF flow through the intracerebral channels and foramina.

However, no single criterion has been documented to be reliable in making the diagnosis of NPH with CT or MRI. In our practice, most patients with NPH have had reports stating that they have "ventricular enlargement within the normal range for that age group." Occasionally, the radiologist will add, "however, normal pressure hydrocephalus cannot be ruled out, and clinical correlation is recommended." This lack of specific criteria puts the referring physician at a loss in deciding whether to refer the patient to a specialist.

Cisternography. Cisternography is one of the main tests traditionally used for diagnosing NPH. The technique relies on findings of early and persistent ventricular reflux of radionuclide injected in the lumbar subarachnoid space via a spinal tap. It is thought that because of increased resistance to CSF absorption through the arachnoid granulations, the dye is not absorbed at the convexity as readily as in the normal population or the population with cerebral atrophy. Therefore, it will reflux early on into the ventricular system, where it clears slowly.

Cisternography is far from accurate for making a diagnosis of NPH, however. A normal cisternogram does not rule out NPH, and currently it is thought that this technique is no more sensitive than clinical findings in diagnosing NPH and predicting response to treatment.

Therapeutic Trial of Cerebrospinal Fluid Diversion

A therapeutic trial of CSF diversion is thought to predict response to shunting and the presence of NPH. Two procedures are used most commonly: lumbar puncture (LP) and continuous lumbar drainage.

Lumbar puncture. When LP is chosen, it is performed on an outpatient basis, and the patient is seen 1 to 2 weeks later. The patient's family usually reports that the symptoms improved the same or the following day and then worsened after 1 to 2 weeks, although the symptoms did not return to the same degree of severity that was present before the LP was performed.

The central nervous system will replace the 20 to 30 mL drained via the LP within an hour. On the other hand, the puncture site in the dura will allow CSF to leak into the epidural space for a few days. We ask our patients to maintain their usual activities after the LP, rather than putting them on bed rest with the head of the bed flat for a few hours. The latter step is requested routinely in LPs performed for other purposes, to avoid post-LP headaches.

Alternatively, gait can be analyzed immediately pre- and post-LP. In this method, the patient is asked to walk a fixed distance, e.g., a 25-foot distance marked within the hallway of an outpatient clinic. The patient is asked to walk from one marker to another, turn around, and return. The total 50-foot walk is timed and videotaped. The LP is then performed, with the objective of draining at least 30 mL of CSF. The gait test is repeated immediately. Improvement is expected either immediately or within the first 2 days after the LP.

Continuous lumbar drainage. In continuous lumbar drainage, the patient is admitted, an external lumbar drain is placed, and CSF is drained during a 2- to 3-day period. The patient is assessed for improved clinical findings after the drainage period.

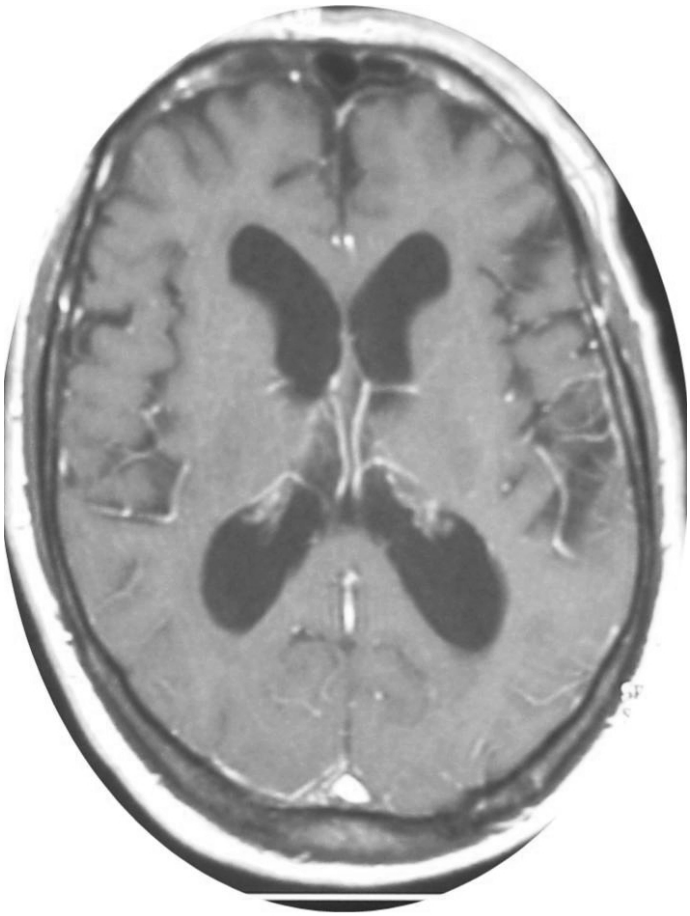

Figure 1. MRI scan of a 78-year-old man who had a severe magnetic gait and was labeled as having Parkinson disease. He eventually became wheelchair-bound. A shunt was inserted, and the patient was walking independently within 3 weeks.

CSF drainage, especially prolonged CSF drainage, is thought by some authors to be a more reliable way of diagnosing NPH, because it replicates shunting. One series by Marmarou et al. demonstrated that CSF drainage was more than 90% accurate in predicting response to shunting. However, these tests may not be conclusive in some patients with long-standing hydrocephalus or aqueductal stenosis. Some series have reported that some patients who do not respond to external drainage will improve with shunting. For that reason, some authors argue that the ultimate therapeutic trial is shunting. Unfortunately, shunting is not an innocuous procedure, and the risk/benefit ratio must be addressed.

During lumbar puncture, resistance to outflow also may be measured. Although resistance to outflow usually is increased in NPH, it does not correlate consistently with response to shunting.

Diagnosis

In some cases, the diagnosis of NPH is straightforward, but in others, it is more subtle and requires a heightened index of suspicion. One of the most common problems is that clinicians seek the typical clinical triad and a radiological report stating the presence of hydrocephalus before investigating further. In our experience and that of others, in numerous patients, only one of the clinical components of the triad may predominate or be the only one present. In addition, some recent work has showed that patients with only gait disturbance or with dementia respond better to shunting than those who have the complete triad, as if early diagnosis of the syndrome carries a better prognosis. Other patients may have ventriculomegaly that is missed by the radiologist or read as normal for their age group, and some patients have ventricles that are not massively enlarged. Because NPH is one of the few reversible causes of dementia, and because of the major financial and social implications of dementia, it is extremely rewarding to the clinician to diagnose these occasionally challenging patients and restore their quality of life.

In our practice, we recommend shunting for patients who present with typical clinical and radiological findings and no other concurrent diagnosis such as Parkinson disease. When the symptoms are not as typical or there are confounding issues, we recommend a therapeutic LP. If the patient improves clinically in response to the LP, then a shunt is placed. If the patient does not improve with a spinal tap, but clinical suspicion is still strong, we recommend prolonged drainage via a lumbar drain.

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1. Headache is a common feature in normal-pressure hydrocephalus (NPH).

   True or False?

2. Imaging is extremely accurate in diagnosing NPH .

   True or False?

3. Parkinson disease is part of the differential diagnosis of NPH.

   True or False?

4. Cisternography is an accurate diagnostic test of NPH.

   True or False?

5. Some authors use drainage of cerebrospinal fluid via lumbar puncture or lumbar drain to diagnose NPH.

   True or False?

6. Urinary incontinence is part of the NPH triad.

   True or False?

7. There are secondary causes of NPH.

   True or False?

8. The presence of microvascular disease does not rule out NPH.

   True or False?

9. All three components of the clinical triad must be present for shunting to provide any therapeutic benefit in treatment of NPH.

   True or False?

10. Hydrocephalus ex vacuo is a term used to describe ventricular enlargement in the presence of brain atrophy.

    True or False?