The Triad of Idiopathic Normal-Pressure Hydrocephalus A Clinical Practice Case Report

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Abstract

An 89-year-old white male presented with memory impairment, slowness in responsiveness, and frequent falls over a two-year duration. Six months earlier, the patient was believed to have had a "dementia with parkinsonian features," but showed no response to incrementing doses of both donepezil and carbidopa-levodopa. Urinary urgency was believed to have been due to prostate hypertrophy. A head CT with contrast revealed moderate ventriculomegaly in the setting of mild diffuse cortical atrophy. A diagnosis of idiopathic normal-pressure hydrocephalus (INPH) was made.

Introduction

The ubiquitous nature of cognitive, gait, and urinary problems in the elderly makes the diagnosis of a unitary process to explain all three dysfunctions difficult, if not illogical. Since the 1960s, however, it has been realized that a small number of adults (particularly those over 70, with equal frequency in both sexes) have a triad of slowness of thought processes (bradyphrenia), a magnetic gait (decreased foot-to-floor clearance), and urinary frequency, if not incontinence. Brain-imaging studies in these patients reveal large ventricles without obstruction. No identifiable precipitant of the hydrocephalus is identified. In this context, the diagnosis of INPH (idiopathic normal-pressure hydrocephalus) can be made. The great challenge for the clinician is to appreciate that, while dementia is more commonly associated with Alzheimer's disease, slowness of gait is more commonly associated with Parkinson's disease, and urinary incontinence is more commonly related to prostatic disease. However, the combination of these features—dementia, gait disorder, and incontinence—mandates a consideration of the diagnosis of INPH. It is also increasingly recognized that INPH can exist with only one or two of the triad components.

Case presentation

An 89-year-old white male presented with a two-year history of worsening cognitive problems and "frozen walking." The problem in thinking was described by the patient as difficulty concentrating and just "some slowing down because I'm getting old." Family members of this retired engineer describe him as listless, though showing no clear evidence of depression. The problem of cognition took the patient to a psychiatrist and neuropsychologist, who found him to have some mild impairment in immediate and delayed auditory memory and mild decrease in executive functioning. Clinical depression was not diagnosed. Learning, language, orientation, and other dimensions of memory were in tact. There was a suspicion of early Alzheimer's disease, and the patient was begun on donepezil. However, no improvement in his mental state was noted after one year, despite dose increments to maximal levels. The drug was then tapered off without difficulty.

Around one year ago, the family began to notice an increase in falls that had occurred rarely before that time. The patient had a long history of osteoarthritis and complained of lumbar and bilateral hip pain. Non-steroidal anti-inflammatory drugs (NSAIDs) improved the pain, but did not change the rate of falling that had reached monthly levels by the time of this evaluation. The patient states he had difficulty "getting the motor running," which the daughter translated as a kind of freezing while stepping in an increasingly slow manner. The exact cause for the falls was not clear, as the patient noted no pain on falling backwards six months ago, the time of a comprehensive physical exam by the patient's family physician (FP).

That doctor believed the patient had some parkinsonian features, despite no evidence of a tremor, and so began the patient on carbidopa-levodopa. The dementia was felt to be mild and "not definitively Alzheimer's," but perhaps related to cortical atrophy noted on an initial head CT obtained by the psychiatrist. Thyroid studies proved normal. Mild to moderate bilateral carotid atherosclerosis was noted on ultrasonography, but no stroke was apparent based on history, physical exam, or a new head CT.

Neurological consultation followed six months later, after increasing doses of carbidopa-levodopa showed no effect on the "stiffness of gait" on re-evaluation by the FP.

Neurological evaluation revealed the following:

The patient seemed mildly disheveled and showed some urine stains in the anterior groin area of his pants. There was psychomotor slowing, decreased accuracy in number placement on drawing a clock face and a Mini-Mental Status Exam score of 25. Cranial nerves were normal, full sensation and strength was evident, and all reflexes were normal, except for the presence of a positive sucking and snout. Bradykinesia with diffuse, mild rigidity of limbs and mild retropulsive tendency with a somewhat wide stance was evident; gait was shuffling and magnetic, but symmetrical; and there was no involuntary motion or ataxia.

Discussion

Part 1

In analyzing a case of this type, the crux of the matter is apparent: This is a patient who falls "outside the ordinary" in the areas of geriatric dementia and movement disorders. On the other hand, lack of a response to donepezil does not mean the patient does not have Alzheimer's disease (AD). The absence of striking memory deficits, along with largely in tact orientation, naming, and visuospatial skills, supports the fact the patient does not have AD. Because there are some memory deficits and attentional issues, however, AD must still be considered; a more detailed analysis, such as more focused hippocampal imaging via brain MRI and positron emission tomography (PET) scans, cerebral spinal fluid (CSF) analysis for beta-amyloid1-42 and tau proteins might well be helpful in ruling out AD. One would also argue for a more detailed depression inventory via added neuropsychological testing, such as the Minnesota Multiphasic Personality Inventory (MMPI). Pseudodementia with a covert depression would be a concern. This senior is not on side-effect-laden medication, which rules out that common cause of impaired cognition.

Beyond the possibilities of masked or atypical presentations for mental status aberrations is the issue of his bradykinesia, rigidity, postural instability, and absence of tremor. Indeed, this could be Parkinson's disease, but the lack of response to carbidopa-levodopa strongly argues against it. Dementia due to PD often occurs late in the disease, so that prior to the carbidopa-levodopa failure, a PD dementia was a consideration. Vascular Parkinsonism is not suggested, based on the symmetrical exam and a CT that reveals no infarction. Binswanger's disease is ruled out with a CT that shows no significant white matter disease that is the signature finding of that vasculopathy. Such a "lacunar state" could induce a short-stepped gait and subcortical dementia. Although the axial difficulties in the absence of tremor are very consistent with progressive supranuclear palsy, the absence of eye movement limitations effectively rules out that diagnosis. Additionally, there is no history of dementia pugilistica or evidence of this condition on the imaging study results. Corticobasilar degeneration and multisystem atrophy, both of which can reveal such Parkinsonism, are not suggested, based upon the absence of more striking higher cortical dysfunction noted in the former and autonomic difficulties classically found in the latter [1-3].

Certainly, an 89-year-old could have an orthopedic condition to explain the gait disorder, but in this patient, the lack of an antalgic gait argues against a painful arthropathy as the cause for falling. A cervical myelopathy is not suggested on exam. Neurogenic claudication typical of spinal stenosis is not implicated, but such a lumbar condition is not ruled out. There is no large-fiber, neuropathy/steppage gait problem such as that seen in Vitamin B12 deficiency or in neurosyphilis. The latter disorder, incredibly diverse phenomenologically, cannot be ruled out completely at this point.

What may be indifference to incontinence is disturbing in this case, because it implies there may be advancing deficits in judgment characteristic of a frontal lobe or subfrontal derangement. In this regard, prostatism cannot easily explain the condition.

Additional Workup

Brain MRI: moderate diffuse ventriculomegaly, mild cortical atrophy (both worse compared to the first head CT performed one year ago), no infarct, some periventricular demyelination that may be age related, aqueductal flow void and no hippocampal atrophy (Figures 1 and 2).
VDRL (serum): negative.
Lumbar CT: no evidence for spinal stenosis.
Urodynamics: hyperactive bladder.
Neuropsychological testing: progressive frontal lobe region disease, with no depression and significant worsening in attentiveness and judgment; minor immediate and delayed memory errors, unchanged from initial testing.

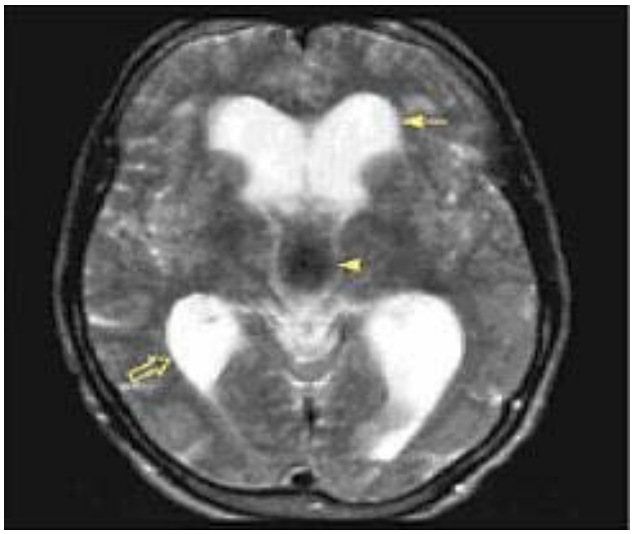

Figure 1. Idiopathic normal-pressure hydrocephalus. Note moderately enlarged ventricles (arrows show dilated frontal and posterior horns); normal volume of brain parenchyma; hypointensity in the third ventricle signifies turbulent flow of CSF.

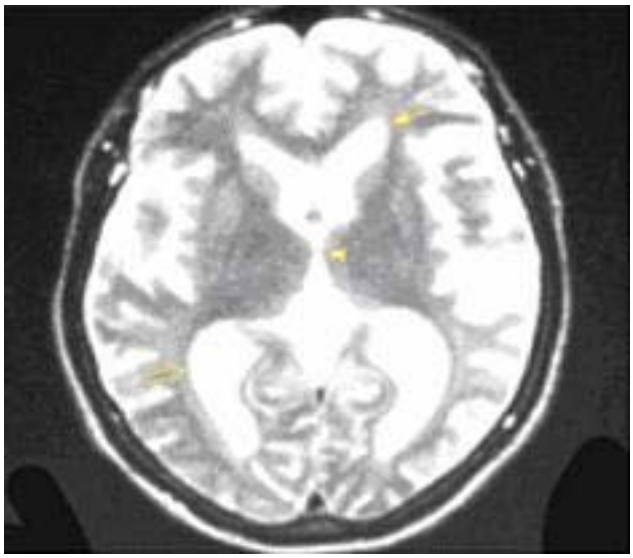

Figure 2. Advanced Alzheimer's disease. Mildly enlarged ventricles; brain tissue atrophy characterized by increased white rippling around the periphery of the cortex, signifying an increased volume of CSF in subarachnoid space around atrophic brain.

Part 2

The lead diagnosis is now idiopathic normal-pressure hydrocephalus. The patient has the triad of dementia, gait dysfunction, and incontinence with evidence for disease progression over two years [1,4,5]. His "cortical reserve" may have lessened the impact on cognition. Typically, obliviousness to incontinence appears in advanced dementia patients, but the apparent anosognosia regarding incontinence can occur with any cognitive deficit. Stretching of more central frontal lobe-white matter fibers explains the impact not only on thinking, but also on gait and continence in INPH patients.

Whereas the diagnosis, based upon clinical and lab results, is most consistent with INPH, it is reasonable at this time to review in greater detail the imaging studies used to confirm this diagnosis.

The Evans index is a measure reflecting ventricular size to cranial diameter [6]. In this case, it would be expected that it is greater than 0.3, which formally confirms ventriculomegaly. This can be helpful when there is significant cerebral atrophy or megalencephaly.

The periventricular halo noted on MRI in this patient has been associated with leukoareosis seen in hydrocephalus, including that of INPH [1]. However, like the aqueductal flow void (arising from a signal artifact created by hyperdynamic CSF flow through the cerebral aqueduct) also noted in this case, the INPH diagnosis is supported, but not confirmed, via these findings [7].

Likewise, although SPECT, PET, and nuclear cisternography may be abnormal in INPH, 100- percent certainty regarding INPH cannot be made, based on such studies [1]. Therefore, the neurological diagnostic work-up does not require them. Nuclear cisternography may be abnormal and is sometimes helpful in diagnosing INPH.

The critical question at this point is: Given the great likelihood of INPH in this patient, will a ventriculoperitoneal or ventriculoatrial shunt be effective in reducing the signs and symptoms of the condition? In this patient, as in most, a less-than-severe dementia is a good prognostic feature. Predominant gait difficulty with mild or absent dementia is a good prognostic sign for shunt success. Age alone is not a strong argument against shunting. It has been reported that the best indicator for shunt responsiveness was the presence of the complete triad, with those showing a 61.2-percent rate of improvement in all three and a 35.4-percent complication rate, mostly reversible and typically including subdural hygroma, subdural hematoma, or shunt infection [8].

Beyond the clinical presentation, ways to predict a positive response to shunting include a large volume lumbar tap test (Assess the gait prior to the tap, remove 30cc of CSF, and then quickly re-assess for gait improvement, though guidelines argue not to exclude candidates based on a negative tap test) and external lumbar drainage (ELD) (48-72 hours of 10cc/hr CSF drainage in a special monitored setting, during which gait is frequently re-evaluated to confirm ongoing efficacy of a shunt). ELD is helpful in identifying patients who would more likely benefit from a shunt and who have a negative tap test, i.e., a substantial subgroup improves with ELD and not with the tap test [9,10].

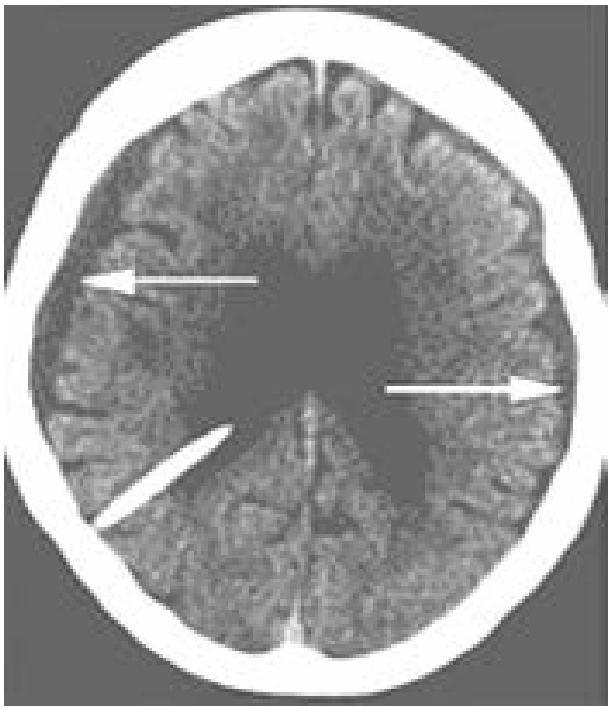

Figure 3. Bilateral subdural hygromas. After placement of a ventriculoperitoneal shunt for INPH.

Opening pressure (OP) determination in INPH is similar to those found in normals (122mm + 34mm H2O) though the range is somewhat wider in INPH.11 CSF OP measurement may be most useful in identifying hydrocephalic conditions (such as secondary hydrocephalus due to a subarachnoid hemorrhage or aqueductal stenosis) other than INPH, particularly when the OP is elevated above 245mm. OP determinations have mostly diagnostic value in suggesting a non-communicating hydrocephalus [1]. Once defined in INPH levels, however, CSF OP does not influence prognosis significantly. Similarly, the value of CSF Ro or impedance of flow offered by the CSF absorption pathways is not clearly helpful in shunt responsiveness predictions [9].

Finally, this patient had high flow velocities through the aqueduct. Despite this characteristic INPH result, no statistically significant relationship between an aqueductal flow void sign and responsiveness to shunting has been consistently reported [12]. After a positive gait response to the lumbar tap test, the patient underwent ventriculoperitoneal shunting without perioperative complications. Starting one week after shunting, CT scans revealed diminishing ventricular size to normal. The patient showed significant clinical improvement—mental improvement occurring earlier than the restoration of proper gait without falls and urinary control.

The triad of gait disturbance, dementia, and urinary urgency is kind of pathognomonic for INPH and should alert the physician for such a diagnosis. The normal CSF OP and the presence of hydrocephalus in brain imaging is confirmatory diagnosis for INPH.

Cognitive impairment is usually mild and subcortical. Urinary incontinence usually is present only in advanced cases. Gait disorder is the first clinical sign to appear in patients with INPH. Identifying and treating patients at this early stage, before the emergence of cognitive impairment or urinary incontinence, result in good outcome.

INPH is a treatable disorder, especially when treatment is started early in the course of the disease.

References

1. Relkin N, Marmarou A, Klinge P, Bergsneider M, Black PM. Diagnosing idiopathic normal-pressure hydrocephalus. Neurosurgery. 2005 Sep;57(3 Suppl):S4-16.

2. Knutsson E, Lying-Tunell U. Gait apraxia in normal-pressure hydrocephalus: Patterns of movement and muscle activation. Neurology. 1985 Feb;35(2):155-60.

3. Boon AJ, Tans JT, Delwel EJ, Egeler-Peerdeman SM, Hanlo PW, Wurzer HA, Hermans J. Dutch Normal-pressure hydrocephalus study: The role of cerebrovascular disease. J Neurosurg. 1999 Feb;90(2):221-6.

4. Adams RD, Fisher CM, Hakim S, Ojemann RG, Sweet WH. Symptomatic occult hydrocephalus with "normal" cerebrospinal-fluid pressure. A treatable syndrome. N Engl J Med. 1965 Jul 15;273:117-26.

5. Hakim S, Adams RD. The special clinical problem of symptomatic hydrocephalus with normal cerebrospinal fluid pressure: Observations on cerebrospinal fluid hydrodynamics. J Neurol Sci. 1965 Jul-Aug;2(4):307-27.

6. Evans WA. An encephalographic ratio for estimating ventricular and cerebral atrophy. Arch Neurol Psychiatry 1942; 47:931-937.

7. Dixon GR, Friedman JA, Luetmer PH, Quast LM, McClelland RL, Petersen RC, Maher CO, Ebersold MJ. Use of cerebrospinal fluid flow rates measured by phase-contrast MR to predict outcome of ventriculoperitoneal shunting for idiopathic normal-pressure hydrocephalus. Mayo Clin Proc. 2002 Jun;77(6):509-14.

8. Black PM. Idiopathic normal-pressure hydrocephalus. Results of shunting in 62 patients. J Neurosurg. 1980 Mar;52(3):371-7.

9. Kahlon B, Sundbarg G, Rehncrona S. Comparison between the lumbar infusion and CSF tap tests to predict outcome after shunt surgery in suspected normal pressure hydrocephalus. J Neurol Neurosurg Psychiatry. 2002 Dec;73(6):721-6.

10. Walchenbach R, Geiger E, Thomeer RT, Vanneste JA. The value of temporary external lumbar CSF drainage in predicting the outcome of shunting on normal pressure hydrocephalus. J Neurol Neurosurg Psychiatry. 2002 Apr;72(4):503-6.

11. Bono F, Lupo MR, Serra P, Cantafio C, Lucisano A, Lavano A, Fera F, Pardatscher K, Quattrone A. Obesity does not induce abnormal CSF pressure in subjects with normal cerebral MR venography. Neurology. 2002 Nov 26;59(10):1641-3.

12. Bradley WG Jr, Scalzo D, Queralt J, Nitz WN, Atkinson DJ, Wong P. Normal-pressure hydrocephalus: Evaluation with cerebrospinal fluid flow measurements at MR imaging. Radiology. 1996 Feb;198(2):523-9.