

Review

□ Idiopathic normal pressure hydrocephalus: review of a curable disease

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SUMMARY: Idiopathic normal pressure hydrocephalus is, generally, a communication hydrocephalus of intriguing pathophysiology, characterized by classical clinical triad described by Adams and Hakim, gait disturbance, dementia and urinary incontinence, in addition to ventricular dilation visible by brain imaging and normal cerebrospinal fluid pressure during lumbar puncture. The disease, is defined as a clinicopathological condition related to the insufficient capacity to absorb cerebrospinal fluid, but the exact mechanism of the development of the clinical symptoms is not known. It is a chronic disorder affecting the elderly, reaching 0.2% in the age group of 70 to 79 years, and 5.9% for age 80 years and older. Idiopathic normal pressure hydrocephalus has been estimated to account for up to 10% of cases of dementia and is significant because it is treatable by ventriculoperitoneal shunting. Despite differences in disease etiology, several brain disorders in the elderly share dementia as a common clinical feature. The treatment for the majority of these disorders is merely symptomatic and does not modify the course of illness. Symptoms of idiopathic normal pressure hydrocephalus are the only ones that can be modified if they are recognized in time and treated appropriately. Clinicians play a paramount role in the identification of patients who should be evaluated for possible idiopathic normal pressure hydrocephalus and patients who can improve with shunt surgery. With contemporary diagnostic tests and treatment with adjustable valves, the benefit to risk ratio of shunt surgery is highly favourable. The introduction of programmable valves has dramatically lowered the need for shunt revisions and most complications can be handled by modifying the shunt setting.

KEY WORDS: Dementia, Elderly, Idiopathic normal pressure hydrocephalus.

□ INTRODUCTION

Idiopathic normal pressure hydrocephalus is a syndrome generally found in elderly and is the most common form of hydrocephalus in adults. The disease, first described in 1965 by Hakim and Adams, is defined as a clinicopathological condition related to the insufficient capacity to absorb CSF, but the exact mechanism of the development of the clinical

symptoms is not known(1). The prevalence of iNPH is age related, reaching 0.2% in the age group of 70 to 79 years, and 5,9% for age 80 years and older(13). Patients develop a syndrome characterized by communicating hydrocephalus with dilated cerebral ventricles, impaired gait, cognition and urinary control (urgency and incontinence). The CSF pressure checked at a diagnostic LP is normal. Normal pressure hydrocephalus is usually described

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LIST OF ACRONYMS AND ABBREVIATIONS: AD = Alzheimer Disease; CDT = Clock Drawing Test; CSF = CerebroSpinal Fluid; CT = Computerized Tomography; DESH = Disproportionately Enlarged Subarachnoid space Hydrocephalus; ICP = IntraCranial Pressure; iNPH = idiopathic Normal Pressure Hydrocephalus; LP = Lumbar Puncture; MMSE = Mini-Mental State Examination; MRI = Magnetic Resonance Imaging; PD = Parkinson Disease; PM 47 = Progressive Matrices 47; VP = VentriculoPeritoneal shunt; SVE = Subcortical Vascular Encephalopathy; TMT = Trail Making Test.

as idiopathic, although it can be secondarily present in several disorders and conditions such as subarachnoid hemorrhage, infection, head trauma, cerebral tumors and in patients who have undergone an intracranial neurosurgical procedure.

The disease remains one of the most controversial neuropathological entities both in regards to its diagnosis and its proper clinical management. iNPH symptoms are not pathognomonic and may also be present in vascular dementia, AD, and PD, among many other less common diseases⁽¹⁴⁾.

The only effective treatment for iNPH is CSF shunt, usually configured between the lateral ventricle and the peritoneum, the VP shunt⁽¹⁸⁾.

The diagnosis of iNPH is based on a patient's clinical status, the natural history of the disease, imaging findings and clinical response to specific diagnostic procedure.

iNPH should be suspected in elderly patients presenting with unexplained, symmetric gait distur-

bance, which is the primary symptom of iNPH. Findings include difficulty with transitional movements, gait initiation failure, shuffling gait and poor foot clearance. Although dementia and incontinence are frequently present, the complete triad is not needed to suspect the disorder.

Neuroimaging with either CT or MRI is required for the diagnosis of iNPH; however, MRI is preferable. CT scanning of the brain is useful if MRI is unavailable. MRI T2-weighted images are especially helpful.

As ventricular enlargement occurs with other dementias and to an extent with normal aging, a ratio of maximum width of the frontal horns of the lateral ventricles and the maximal internal diameter of the skull, known as the Evans index, of > 0.3 has been proposed to correlate with iNPH⁽²⁸⁾ (Figure 1).

A further important role of neuroimaging is to assess for hydrocephalus with ventriculosulcal disproportion that is a disproportionate widening of the ventricles in comparison to the cerebral sulci. Japanese researchers have described this as DESH^(9,12,13). A coronal section at the level of the posterior commissure reveals a narrow subarachnoid space surrounding the outer surface of the brain (a "tigh convexity) and narrow medial cisterns (Figure 2).

Clinical presentation and neuroimaging abnormalities suspecting for iNPH are usually not sufficient to recommend shunt surgery. Predictive tests to determine the likelihood of surgery responsiveness are suggested. Subtraction tests used to raise the prognostic accuracy are the spinal tap test and the continuous spinal drainage. Infusion testing for assessment of CSF hydrodynamics is commonly used in Europe to diagnose iNPH and rarely in Canada and United States.

The spinal tap test consists with the removal of 30 to 70 mL of CSF with lumbar puncture. The CSF subtraction can be repeated for two or three consecutive days. The continuous spinal drainage of 150 to 200 mL of CSF per day for 2 to 7 days is conducted with an external lumbar drainage.

These tests are considered to be positive if the number of steps taken in a 10 meters gait test, and the time needed to walk 10 meters, are reduced by at least 20% and psychometric tests show an improvement of

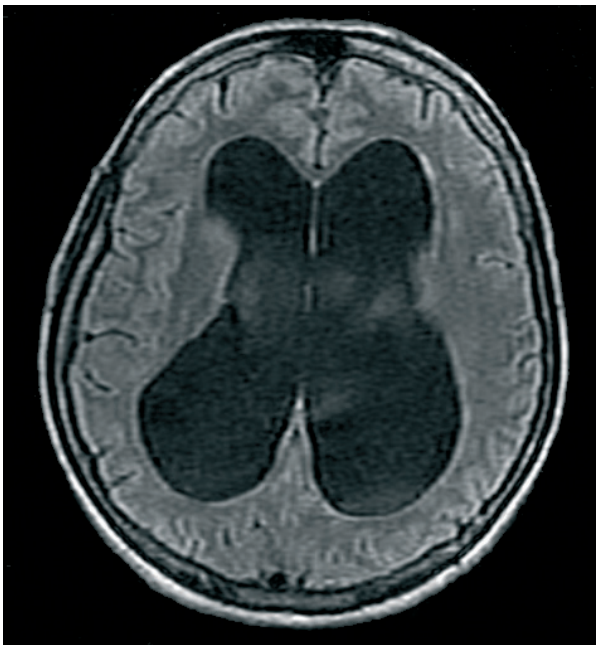


Figure 1. Evans' Index is the ratio of maximum width of the frontal horns of the lateral ventricles and the maximal internal diameter of the skull. Ratio is > 0.38 .

at least 10%. The CSF infusion test involves infusing Ringer lactate via one spinal needle while simultaneously recording CFS pressure via a second spinal needle. Several methods for infusion testing exist but one of the most consistent findings in iNPH research is that the patients have an increased resistance to CSF outflow (Rout)^(15,23).

Finally long-term recording of ICP for 24 to 72 hours has been used as a diagnostic test for iNPH for 40 years. Such techniques are not recommended for routine use currently. Elderly patients with obstructive hydrocephalus may present with symptoms of iNPH. In such cases diagnostic ICP measurement via intracranial methods should be considered to submit patients to third endoscopic ventriculostomy (Figure 3 and 4).

Aims. The purpose of the Authors was to define the iNPH as clinical entity and to suggest a diagnostic and therapeutic method to manage it, evaluating the actual context of scientific literature and own experience based on a multidisciplinary collaboration.

□ MATERIALS AND METHODS

This article is based on a selective review of literature, including current guidelines, carefully selected review article published in English since 2001, and original article retrieved by a PubMed search.

□ DISCUSSION AND CONCLUSION

According to Hakim and Adam's hypothesis, iNPH occurs when CSF absorption is decreased resulting in increased chronic intracranial pressure. Over time, ventricular enlargement occurs as a compensatory

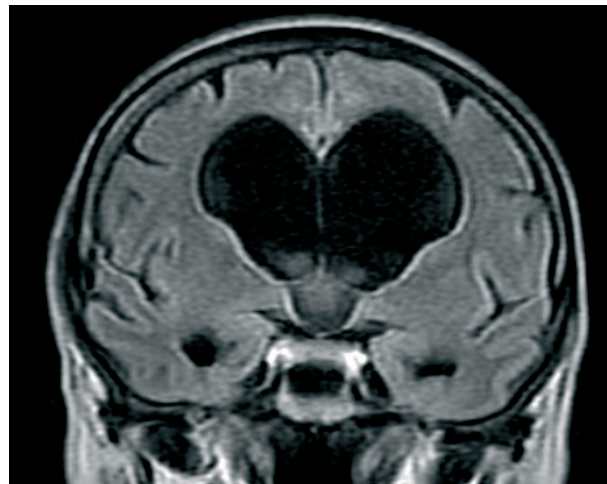


Figure 2. Coronal section at the level of the posterior commissure reveals a narrow subarachnoid space surrounding the outer surface of the brain (a "tight convexity") and narrow medial cisterns.

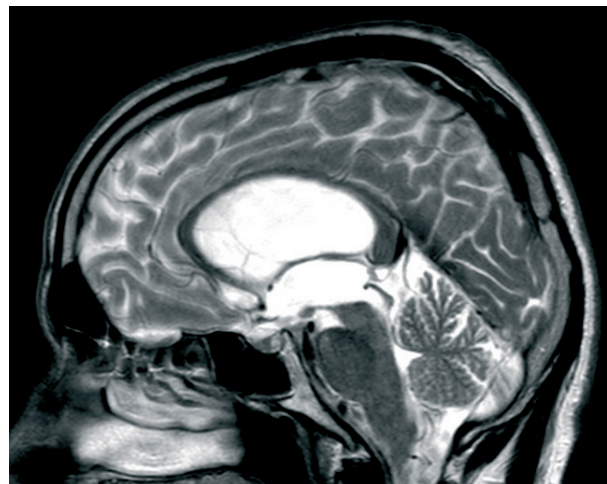


Figure 3. Sagittal T2 MRI shows obstructive hydrocephalus.

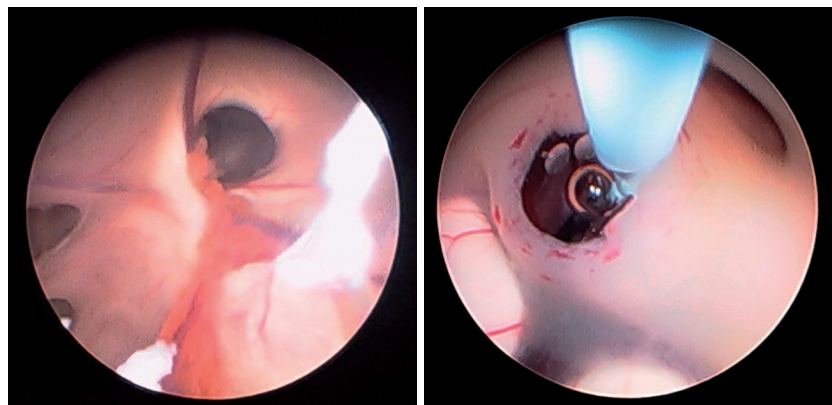


Figure 4. Endoscopic third ventriculostomy phases.

Characteristics	Clinical Findings
Step frequency in gait test (10 m)	Number of steps > of 13; duration > 10 "
Step breadth	Distance between toes > 1 foot length
Step length	Distance < 1 foot length
Turn on yourself	> 4 to 6 steps
Bipedal gait	Correction of foot position > 25% of steps

Table 1. Features of gait impairment in iNPH.

mechanism. This results in a new intracranial pressure steady state. As a modification, CSF flow is directed more toward the Virchow-Robin spaces into brain parenchyma. Parenchymal changes occur resulting in tissue compression and deep white matter ischemia, hallmarked by myelin pallor.

Idiopathic normal-pressure hydrocephalus is characterized by a combination of clinical and radiological findings arising in adulthood. The cardinal symptoms of iNPH are gait impairment, dementia, and urinary incontinence. Imaging studies of the brain reveal ventriculomegaly without any marked degree of cortical atrophy.

However, these symptoms are not pathognomonic and may also be present in vascular dementia, AD, PD, among many other less common diseases⁽¹⁴⁾.

Impairments of gait and balance are typically the first symptoms to be noticed and may be very mild at the outset. They are also the most likely to improve after CSF shunting, with a probability of more than 85%⁽¹¹⁾. Patients may initially complain of dizziness, difficulty walking on a slope or stairs, and difficulty getting up from or sitting down on a chair. As the disease progresses, the patient's gait deteriorates markedly, becoming broad-based, slow, short-stepped, and glue-footed (a gait disturbance of the abasia-astasia type). Table 1 describe characteristics of gait impairment in iNPH.

Some patients with iNPH present with mild cognitive impairment rather than dementia. The major cognitive impairments in patients with iNPH are frontal lobe symptoms, such as psychomotor slowing and impairment of attention, working memory, verbal fluency and executive function. The cognitive and behavioral disturbances accompanying iNPH have been commonly described as "fronto-subcortical dementia"^(19,26). iNPH patients failed on attentional tasks which may reflect a deficit in cognitive flexibility, similar to patients with frontal lobe excision and patients with fronto-subcortical dementia

such as Parkinson's disease^(20,21), and unlike patients with Alzheimer Disease in which frontal functions are spared⁽²²⁾.

To assess the cognitive impairments in iNPH numerous neuropsychological assessment were used, investigating different cognitive domains to evaluate the effects of CSF shunt surgery on cognitive dysfunction^(8,24).

The MMSE is widely used to screen for cognitive impairment in adults providing a global score of cognitive ability.

Abstract reasoning was assessed by "Raven's coloured progressive matrices PM 47"⁽⁶⁾. PM 47 are a multiple choice intelligence tests and in each test item, the subject is asked to identify the missing item that completes a pattern.

To assess focused and divided attention visual search tasks were used. These tests were used to assess the ability to detect a target element embedded in a series of distractor elements. It predicts both response time and error rates. Visual Search Task⁽²⁵⁾ is an attention test that requires some selectivity, as all stimuli are irrelevant except the ones designated as target. In TMT⁽¹⁰⁾, all numbered circles are to be regarded as "noise" except the number that the subject is searching for. The Stroop Color-Word Test⁽⁴⁾ was used to assess the selective attention and the sensitivity to interference.

Digit span forward/backward⁽¹⁷⁾ was used to assess verbal short-term memory and verbal working-memory. Sequences of digits increasing in number are orally presented and the subject has to either repeat it in the original (forward) or the reversed order (backward). Spatial span backward/forward was used to assess visuospatial short-term memory and visuospatial working-memory. To evaluate visuoconstructional abilities the CDT⁽⁵⁾ were administered. This test required participants to draw the contour, numbers, hands, and center of the clock. In the prose memory test⁽²⁵⁾ the patient is asked to

Disease	Atypical INPH features	Common features with iNPH
Cortical Dementia		
<i>Alzheimer's disease</i>	Focal cortical deficits; appearance of gait problems when dementia is severe	Dementia without gait impairment is very rare
<i>Fronto-Temporal dementia</i>	Personality change, psychiatric abnormalities; disinhibition, impulsiveness, irritability, emotional lability, aphasia, no motor disturbance, incontinence is very rare	
Subcortical Dementia		
<i>Lewy-Body Dementia</i>	Visual hallucinations, delusions, markedly fluctuating cognitive function	Gait impairment and dementia
<i>Parkinson's disease and vascular parkinsonism</i>	Rest tremor, unilateral onset; speed of movement can be increased with the aid of external stimuli (this is not the case in NPH). The patient cannot simulate walking and bicycle-riding while supine; no broad-based gait with externally rotated feet; mildly reduced step height, markedly reduced arm swing, markedly stooped posture, autonomic dysfunction	Hypokinetic gait, tremor (40%) in iNPH
<i>Progressive supranuclear palsy</i>	Pseudobulbar palsy, supranuclear upward gaze paresis	Frontal brain signs, impaired executive function, gait disturbance
<i>Corticobasal degeneration</i>	Rigor, asymmetrical symptoms, alienlimb phenomenon, apraxia, supranuclear upward gaze paresis, cortical sensory deficits, severe loss of postural control	
<i>AIDS-dementia complex</i>	Positive HIV serology	Psychomotor slowing, impairment of memory and concentration, gait impairment due to HIV myelopathy
<i>Age-related depression</i>	Depressive thought content because of frequently comorbid vascular dementia, sometimes other features as well	Pseudodementia, neuropsychological test findings very similar to those seen in NPH
Mixed Dementia		
<i>Vascular Dementia</i>	Asymmetrical (sometimes transient) symptoms, possibly correlated with lesions seen in imaging studies	Thought disorder, impaired executive function

Table 2. Dementia differential diagnostic criteria.

recall a short passage of prose read by the examiner. The verbal fluency test was used to evaluate executive functions and the ability to generate words fluently in a phonemic format (Phonemic Fluency Test)⁽⁶⁾ or from overlearned concepts (Semantic Fluency Test)⁽⁷⁾.

Several studies report that patients with iNPH are impaired in various aspects of cognition involving both 'frontal' executive functions and 'posterior cortical' functions and report that after shunt operation, cognitive impairment improves but marked improvement in cognitive functions is less frequent than that of the gait disorder. Table 2

described the main features for differential diagnosis between dementias.

Urinary urgency and frequency are the most common urinary symptoms and may occur with or without incontinence. Patients are usually aware of the urinary urge and are concerned about their incontinence. Because bladder symptoms are very common among elderly, other causes are frequently present in patients with suspected iNPH.

The presence of commorbidities doesn't exclude the possibility of iNPH. However commorbidities do influence the prognosis after shunt surgery.

Distinguishing dilated ventricles due to cerebral

atrophy from iNPH is sometimes difficult. Typical findings of iNPH include disproportionate widening of the ventricles in comparison to the cerebral sulci. Changes in the signal characteristics of periventricular tissue must be interpreted with caution. SVE may cause changes quite similar to those seen in iNPH as a result of transependymal CSF diapedesis. Periventricular white matter lesions immediately adjacent to the ventricular wall are considered to reflect fluid movement from ventricles into the parenchyma, but white matter lesions that are more peripheral or more diffuse and confluent are more likely to represent ischemic changes.

Moreover, Evans' index detected on neuroimaging is only a rough marker for ventriculomegaly, and thus, there has been recent debate of its accuracy and reliability in iNPH diagnosis⁽²⁷⁾. A recent new Evans index is proposed by M.K. Beyer et al.⁽³⁾ resulting that it cannot be applied to separate healthy elderly controls from patients with AD due to low sensitivity, but may separate separate healthy elderly controls from iNPH patients with high sensitivity. When applying the proposed cut-offs for Evans index in men and women aged 65-84 years (0.34-0.37), they differentiated between iNPH and CTR with a sensitivity of 80%. In iNPH, the Sylvian fissures are often widened out of proportion to the cortical sulci, which are flattened. This feature could suggest a block of CSF flow over the cerebral convexity to the arachnoid granulations.

The international guidelines recommend tests of CSF hydrodynamics (tap test, external lumbar drainage and infusion testing) to demonstrate either that the patient has the potential to respond to shunt surgery or that the patient has abnormal CSF hydrodynamics that are consistent with hydrocephalus^(2,11,18,23).

External lumbar drainage involves continuous CSF drainage and requires hospitalization. This procedure is said to be accurate, with both a high positive-predictive value and a high negative-predictive value. The most frequent serious complication of external lumbar drainage is bacterial meningitis, seen in 2% to 3% of patients. Because the possibilities of this complication and the need for hospitalization, in our unit we prefer to use tap test to check the possibility for surgery.

The tap test, also known as the large volume LP, should be done with an 18 or 20 gauge spinal needle, usually removing 30 ml to 50 ml of CSF. The interval between the LP and the formal follow up examination is usually between 3 and 6 hours with 10-meters gait

test and neuropsychological exams. The patient does not have to stay supine after the LP, and usually headache and nausea after LP are uncommon in the iNPH population. The CSF subtraction can be repeated for two or three consecutive days.

The absence of response to CSF removal does not exclude shunt responsiveness because the tap test is specific (range of 50% to 100% in various studies), rather than sensitive (range of 50% to 80%).

We perform lumbar infusion test when tap test is not significant in the patients with high iNPH still clinical suspect. Kahlon et al. have found the false negative predictions in the operated patients are much higher (58%) with the tap test than with lumbar infusion test (16%)^(15,16).

Shunt surgery is treatment of the most cases of iNPH, in only few iNPH patients third endoscopic ventriculostomy is appropriate. The purpose of shunt is to divert CSF from craniospinal CSF space to another anatomic space where CSF can be reabsorbed. The most common configuration is VP shunt.

Two types of shunt valves are widely used: shunt with a fixed-valve opening pressure and programmable shunts with variable valve opening pressure that can be changed via an external magnetic programming device. No evidence supports the use of one specific make or model of shunt over another. We prefer use programmable shunts with variable valve opening pressure to manage eventually shunt's serious complication, such as subdural effusion or hematoma. Adjustable valves offer the advantage of being able to lower the pressure setting incrementally until symptoms improve and to raise the pressure setting if flow-pressure symptoms or complications emerge.

The introduction of programmable valves has dramatically lowered the need for shunt revisions and most complications can be handled by modifying the shunt setting⁽²⁹⁾.

In meantime, however, improved diagnostic and therapeutic methods, have raised clinical successful into the range of 70% to 90%, and the risk benefits analyses have shown beyond any doubt that surgery for iNPH is far better than conservative treatment or the natural course.

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