Normal pressure hydrocephalus treated with ventriculoperitoneal shunt

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■ Cite as: *CMAJ* 2023 January 23;195:E115-9. doi: 10.1503/cmaj.221027

A 79-year-old college-educated woman was referred to our geriatric medicine clinic because of rapidly progressive cognitive and functional impairment. Two years earlier, a large dural-based extra-axial petroclival meningioma with stable mass effect on her left pons had been discovered, which had been managed nonsurgically with radiation treatment. After radiation, the patient developed mild short-term memory impairment, which remained stable. She lived at home with her husband and was able to function independently with respect to instrumental activities of daily living. Vascular risk factors included well-controlled hypertension and dyslipidemia, and she took acetylsalicylic acid, amlodipine, candesartan, hydrochlorothiazide, ezetimibe, rosuvastatin, cholecalciferol and latanoprost eyedrops and used a fluticasone inhaler. She had no family history of a movement or neurocognitive disorder.

When we reviewed her as an outpatient, she had a 9-month history of gait dysfunction with increasing frequency of falls, which required her to use a 4-wheeled walker. About 6 months after the start of the gait disturbance, her cognitive impairment became more pronounced, and she developed worsening of chronic urinary urge incontinence, necessitating the use of incontinence pads. She had become dependent on others for many of her basic and instrumental activities of daily living. Her Montreal Cognitive Assessment score was 8/30, indicative of severe dementia owing to impaired visuospatial or executive function, delayed recall, language and orientation. On neurologic examination, she had frontal release signs, was imbalanced and had a slowed and mildly wide-based gait, but with no shuffling. Otherwise, there was no sign of parkinsonism or cerebellar dysfunction and we found no other focal neurologic deficit.

Ten days earlier, the patient had undergone a computed tomography (CT) scan because she had fallen. The CT scan showed ventricular prominence out of proportion with sulcal prominence. At our assessment, given the evidence of cognitive decline, gait disturbance and incontinence, as well as the results of the recent CT brain scan, we diagnosed normal pressure hydrocephalus (NPH). Because of the patient's substantial functional decline and impaired mobility, we admitted her to the geriatric medicine inpatient unit to expedite diagnostic testing, consult with neurology and neurosurgery and manage her.

Key points

- Normal pressure hydrocephalus is a form of adult hydrocephalus with ventriculomegaly in the absence of any structural blockage of the cerebrospinal fluid circulation.
- Normal pressure hydrocephalus is a partially reversible cause of dementia, manifesting with a triad of cognitive impairment, gait disturbance and urinary incontinence.
- A detailed cognitive assessment, neurologic examination and brain imaging is necessary to exclude alternative causes and confirm the diagnosis.
- High-volume lumbar puncture with pre- and postprocedure gait assessment is recommended as a confirmatory test before a decision is made regarding therapeutic interventions such as shunting.

We ordered serum basic and extended electrolytes, kidney and liver function tests, thyroid function tests, vitamin B_{12} and infectious (i.e., HIV, viral hepatitis B and C, syphilis) workups, and the results of all were normal. A magnetic resonance imaging (MRI) brain scan showed classical features of NPH with ventriculomegaly out of proportion to sulcal enlargement (Figure 1), a disproportionately enlarged subarachnoid space hydrocephalus and tightening of the callosal angle (Figure 2), which were not seen on previous scans.

We performed a high-volume lumbar puncture, after which the patient's gait improved substantially. The Timed Up and Go test improved from more than 3 minutes pre-tap to 32 seconds after removal of 30–40 mL of cerebrospinal fluid (CSF). As a result, we inserted a ventriculoperitoneal shunt, and her gait and subjective cognitive function improved while she was in hospital.

One month after surgery, the patient developed redness around the abdominal incision site and was noted to have a distal ventriculoperitoneal shunt malfunction due to coiling of the peritoneal catheter. She was therefore readmitted and underwent shunt revision surgery at the peritoneal site with no complications.

Twelve months after shunt insertion, the patient's Montreal Cognitive Assessment score was 23/30 (points lost mainly for delayed recall and language), she no longer required a gait aid

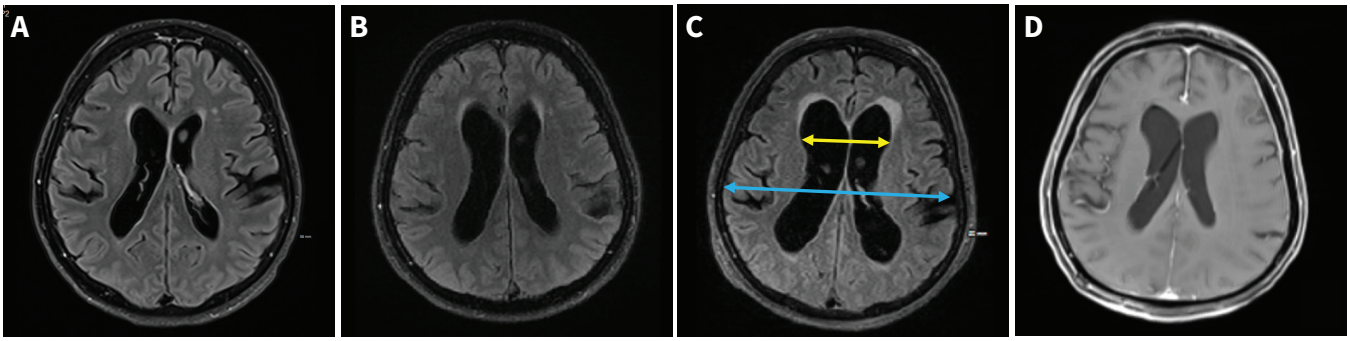

Figure 1: Serial axial magnetic resonance imaging scans of the brain of a 79-year-old woman, from 2 years before diagnosis of normal pressure hydrocephalus to 6 months after shunting. (A–C) Axial T_2 fluid-attenuated inversion recovery (FLAIR) sequences; (D) T_1 postcontrast gadolinium image (no FLAIR sequence is available 6 mo after shunting). Axial images show gradual enlargement of lateral ventricles over 2 years when the patient's Evans index increased from < 0.3 (A and B) to 0.38. The Evans index is defined as the ratio of the maximal width of the frontal horns (yellow arrow) to the maximum inner skull diameter (blue arrow) (C). Ventricle size significantly decreased after shunt insertion (D).

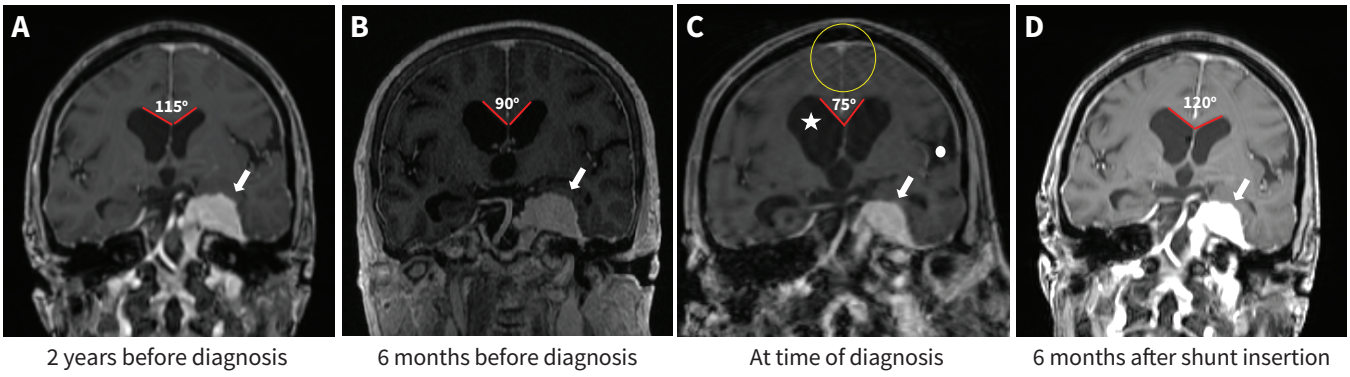

Figure 2: Serial coronal magnetic resonance imaging scans of the brain of a 79-year-old woman, from 2 years before diagnosis of normal pressure hydrocephalus (NPH) to 6 months after shunting. (A–D) Coronal T_1 after contrast gadolinium sequences. In coronal images, disproportionately enlarged subarachnoid-space hydrocephalus (DESH) is present at the time of NPH diagnosis (C), reflecting the combination of ventriculomegaly (white star), Sylvian fissure widening (white circle), and cortical crowding with tight high-convexity effacement at the vertex (inside yellow circle) owing to disproportionality between the superior and inferior cerebrospinal fluid spaces (there is some motion artifact). Changes related to DESH are not seen 6 months before diagnosis and appear to be resolving 6 months after shunt insertion. A gradual narrowing in callosal angle is noted from 115°, 2 years before NPH diagnosis (A), to 75° at the time of NPH diagnosis (C). After shunting, the callosal angle widened again to about 120° (D). Coronal sequences show a large extra-axial, homogeneously enhancing left petroclival meningioma, which remained the same size over 2.5 years.

and her incontinence was much improved. She was independent for all basic and most instrumental activities of daily living. One year after shunting, her cognitive performance test functional score had improved from 3.9/5.6 to 4.6/5.6.

Discussion

Normal pressure hydrocephalus is a communicating form of adult hydrocephalus with resultant ventriculomegaly in the absence of any structural blockage of the cerebrospinal fluid circulation. Little consensus exists regarding the diagnostic criteria for NPH, which makes it poorly recognized and leads to a wide range of incidence rates. Its prevalence increases from 0.2% in people aged 70–79 years to 6% in those older than 80 years (although this is likely to be underestimated), with no difference between men and women.[1]

Normal pressure hydrocephalus presents clinically with cognitive impairment, gait disturbance and urinary incontinence, although the complete triad is not always seen.[2] Other disorders can present with all or some of these features and should be considered carefully (Table 1).

As in our patient, gait disturbance is typically the first symptom and is characterized by a short-stepped magnetic or glue-footed gait and difficulty initiating movements, resulting in postural instability and falls.[2,3] Cognitive impairment usually develops later and involves multidomain subcortical and frontal features such as difficulties with psychomotor processing, attention, concentration and executive function.[3] At early stages, urinary symptoms are usually urgency and nocturia, which evolve to frontal lobe incontinence and detrusor overactivity seen in almost all people with NPH.[4]

Table 1 (part 1 of 2): Differential diagnoses for normal pressure hydrocephalus, their key clinical and distinguishing diagnostic features

Differential diagnosis	NPH triad			Other key clinical features	Distinguishing imaging or investigational features
	Progressive dementia	Gait disturbance	Urinary incontinence		
Alzheimer disease	+++	+	+	• Early amnesia • Aphasia, anomia, apraxia • Behavioural and mood disorders	• Hydrocephalus ex vacuo • Medial temporal lobe atrophy • Temporoparietal cortical atrophy
Vascular dementia	+++	++	–	• Vascular risk factors and events • Post-stroke dementia • Gait base is narrower and more closely resembles the parkinsonian gait	• Hydrocephalus ex vacuo • Prominent microvascular changes • Evidence of stroke
Dementia with Lewy bodies	+++	++	+	• Parkinsonian signs • Fluctuating cognitive status • Psychosis (i.e., visual hallucinations) • RBD	• Hydrocephalus ex vacuo (cortical atrophy)
Parkinson disease dementia	++	+++	+	• Parkinsonian signs • Nonmotor features (RBD, constipation, mood disorders, hyposmia)	• Hydrocephalus ex vacuo (cortical atrophy)
Progressive supranuclear palsy	++	+++	+	• Supranuclear ophthalmoplegia • Axial rigidity • Early falls • Dysphagia, dysarthria	• Midbrain atrophy (hummingbird sign)
Multiple system atrophy	+	++	+++	• Parkinsonian or cerebellar signs • Dysautonomia (orthostasis, impotence, constipation) • Inspiratory stridor • RBD	• Putaminal atrophy • Disproportionate atrophy of the cerebellum and brain stem • Loss of pontocerebellar fibres (hot cross bun sign)
Corticobasal syndrome	+++	++	+	• Asymmetric parkinsonism • Limb dystonia • Limb myoclonus • Alien limb phenomena • Asymmetric cortical sensory loss	• Hydrocephalus ex vacuo • Asymmetric cortical atrophy • Atrophy of the corpus callosum or basal ganglia
Autoimmune encephalitis	+++	+	–	• Various neurologic manifestations depending on the autoantibody (sleep disorders, seizure, movement disorder, neuropsychiatric symptoms, etc.)	• Abnormal EEG, CSF and autoimmune serum markers • Signal hyperintensities in MRI in affected brain regions
Infectious encephalitis	+++	+	–	• Infectious prodrome or symptoms (e.g., headache, fever, malaise) • Meningismus • Behavioural abnormalities • Focal neurologic deficits • Seizure	• Abnormal CSF markers • Signal hyperintensities in MRI in affected brain regions or brain abscess
Prion disease (i.e., Creutzfeldt–Jakob disease)	+++	+++	–	• Behavioural abnormalities (e.g., apathy, mutism, catatonia) • Aphasia, apraxia • Myoclonus • Cerebellar manifestations • Extrapyramidal and pyramidal signs	• Abnormal EEG and CSF markers • Signal hyperintensities in MRI (caudate nucleus, cortical ribboning)

Table 1 (part 2 of 2): Differential diagnoses for normal pressure hydrocephalus, their key clinical and distinguishing diagnostic features

Differential diagnoses	NPH triad			Other key clinical features	Distinguishing imaging or investigational features
	Progressive dementia	Gait disturbance	Urinary incontinence		
Musculoskeletal disorders	–	++	+/–	• Limited range of motion • Radicular pain • Back or joint pain	• Abnormal spine or pelvis imaging (e.g., degenerative disc, herniated disc, osteoarthritis) • Normal brain imaging
Peripheral neuropathy	–	++	–	• Sensory ataxia • Sensory deficits	• Abnormal electrodiagnostic studies • Normal imaging

Note: CSF = cerebrospinal fluid, EEG = electroencephalogram, MRI = magnetic resonance imaging, NPH = normal pressure hydrocephalus, RBD = rapid eye movement sleep behaviour disorder.

There are conventional morphological parameters in both CT and MRI scans to confirm dilation of the ventricles. Evans index is a widely used indicator for ventriculomegaly, defined as the ratio of the maximum width of the frontal horn of the lateral ventricle divided by the maximum width of the cranial cavity, measured at the same axial level. An Evans index of more than 0.31 highly suggests the presence of hydrocephalus.[5] More recently, disproportionately enlarged subarachnoid-space hydrocephalus, visualized as narrowed medial subarachnoid spaces at the high convexity on coronal MRI, has been described as another indicator of NPH, which takes into account the unevenly enlarged ventricles and sylvian fissures compared with the extent of background cerebral atrophy.[5]

Normal pressure hydrocephalus gradually progresses over time. This deterioration is only partially reversible at later stages. Therefore, early diagnosis is important and a ventricular shunt should be inserted early.[6] Because of the lack of a gold standard for diagnosing NPH, the invasive nature of the treatment and its considerable failure rate, a high-volume lumbar puncture or a lumbar drain before surgery is usually performed as a preliminary measure of the patient's likely response to shunting. The patient's gait function is assessed with a Timed Up and Go test and compared before and 30–60 minutes after removal of 30–50 mL of CSF. Our patient demonstrated significant improvement in gait speed after a high-volume tap, which has an excellent positive predictive value of more than 90%.[7] Conversely, high-volume CSF tap has been shown to have a limited negative predictive value of less than 60%, as several patients who show no response to removal of high-volume CSF later improve with surgery.[7] Continuous CSF drainage via a temporary catheter in the lumbar space is another assessment method with sensitivity of 60%–100% and specificity of 80%–100% to predict subsequent response to shunting.[8]

Complications occur in more than one-third of the patients in whom a shunt is inserted. Most are temporary or correctable, and include shunt overdrainage, intracranial infection, seizures, intracerebral hemorrhage from catheter insertion, mechanical shunt failures or blocked shunts.[9]

In 1 case series, half of patients with NPH required shunt revision surgery over 6 years of follow-up owing to shunt malfunction,[10] as in our patient. Shunting resulted in symptoms improvement in 59% (range 24%–100%) of patients, and 29% (range 10%–100%) experienced prolonged sustained effect, with the most benefit for gait dysfunction.[9] Cognitive impairment, particularly if it is moderate to severe, is least likely to improve.[9] A systematic review and meta-analysis showed that global cognition, learning capacity, memory and psychomotor speed benefit the most from shunting, but executive functioning does not usually improve.[11] Visuospatial and executive functions substantially improved in our patient after shunting, while her memory deficit remained persistent, possibly because of her baseline short-term memory impairment, arising from radiation therapy, mild Alzheimer disease or both.

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Competing interests: Shirley Huang is a member of the Canadian Geriatric Society. No other competing interests were declared.

This article has been peer reviewed.

The authors have obtained patient consent.

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Contributors: All of the authors contributed to the conception and design of the work. Seyed-Mohammad Fereshtehnejad and Mitchell Nicholls drafted the manuscript. All of the authors revised the manuscript critically for important intellectual content, gave final approval of the version to be published and agreed to be accountable for all aspects of the work. Seyed-Mohammad Fereshtehnejad and Mitchell Nicholls are co–first authors.

Acknowledgement: The authors thank the patient and her family.

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