

Letter to the Editor



On the Potential Benefit of Shunt Surgery in Idiopathic Normal-Pressure Hydrocephalus Patients with Alzheimer's Disease Pathology

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Dear editor,

Many institutions rule out shunt surgery for idiopathic normal-pressure hydrocephalus (INPH) patients with Alzheimer's disease (AD) pathology. However, we believe some INPH patients with AD pathology might benefit from shunt surgery. While some reports suggest AD pathology may not adversely affect improvement after shunt surgery in INPH patients,¹ the predominant position today is that AD pathology will adversely affect shunt surgery outcomes.²⁻⁴ For example, Hamilton et al.³ reported that INPH patients with moderate to severe AD pathology were associated with worse post-shunt outcomes. And Patel et al.⁴ reported INPH patients with high phosphorylated tau/amyloid beta 1-42 ratios showed less improvement following shunt surgery. Based on these studies, Jang et al.⁵ used amyloid positivity on positron emission tomography (PET) to exclude INPH patients for shunt surgery. However, the view that INPH patients with amyloid pathology should not have shunt surgery is likely based on older studies with less reliable methods and shorter follow-ups. We believe further studies are warranted to investigate whether some INPH patients with AD pathology can benefit from shunt surgery.

As an example to illustrate this point, we outline a case of a 79-year-old female INPH patient with AD pathology that showed improvement in one year of follow-ups after shunt surgery. She presented at our institution with progressive memory, gait, and balance impairment. She developed a short-stepped gait and impaired balance without urinary symptoms 18 months earlier, and she recently suffered a few falls. Her husband reported a 10-month gradual decline in her ability to express herself and recent difficulties in carrying out complex tasks. He described her short-term memory as functionally impaired over the past few months and noted she had reduced interest in completing fundamental tasks of daily living. The patient's cognitive function was impaired at the initial examination (Korean Mini-Mental State Examination [K-MMSE] score 22 out of 30 and Clinical Dementia Rating Scale 1). Her apolipoprotein E genotype was $\epsilon 4/\epsilon 3$. Brain magnetic resonance imaging showed communicating hydrocephalus with an Evans' ratio of 0.33 (**Fig. 1A**). She was diagnosed as having INPH according to the consensus criteria of Relkin et al.⁶ ¹⁸F-florbetaben PET imaging showed a high tracer uptake in the frontal cortex, posterior cingulate gyrus, precuneus, and lateral temporal cortex (**Fig. 1B**).

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Conflict of Interest

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She was visually rated as amyloid positive. A lumbar tap was performed to remove 40 mL of cerebrospinal fluid (CSF). Before and after the tap, she was evaluated using the K-MMSE, Timed Up and Go Test (TUG), and INPH Grading Scale (INPHGS). The following criteria were used to decide CSF tap test (CSFTT) response: 1 point or more improvement on the INPHGS, 10% or more improvement in time on the TUG, or 3 points or more improvement on the K-MMSE. She showed improvement using these criteria and was judged as a responder (**Supplementary Tables 1 and 2**). After careful discussion, she underwent shunt surgery. One year after ventriculoperitoneal shunt placement, she showed a marked improvement in gait, and her K-MMSE score also improved to 26. She was confirmed as shunt-responsive definite INPH. A GAITRite system also was used to assess gait. Differences in quantitative gait parameters before the CSFTT and 12 months after the operation were analyzed. She showed more than 20% improvement in gait velocity, step width, stride length, and coefficient of variation (CV) of stride time, and more than 10% improvement in CV of stride length. Additionally, her double-limb support phase decreased by 18.96%.

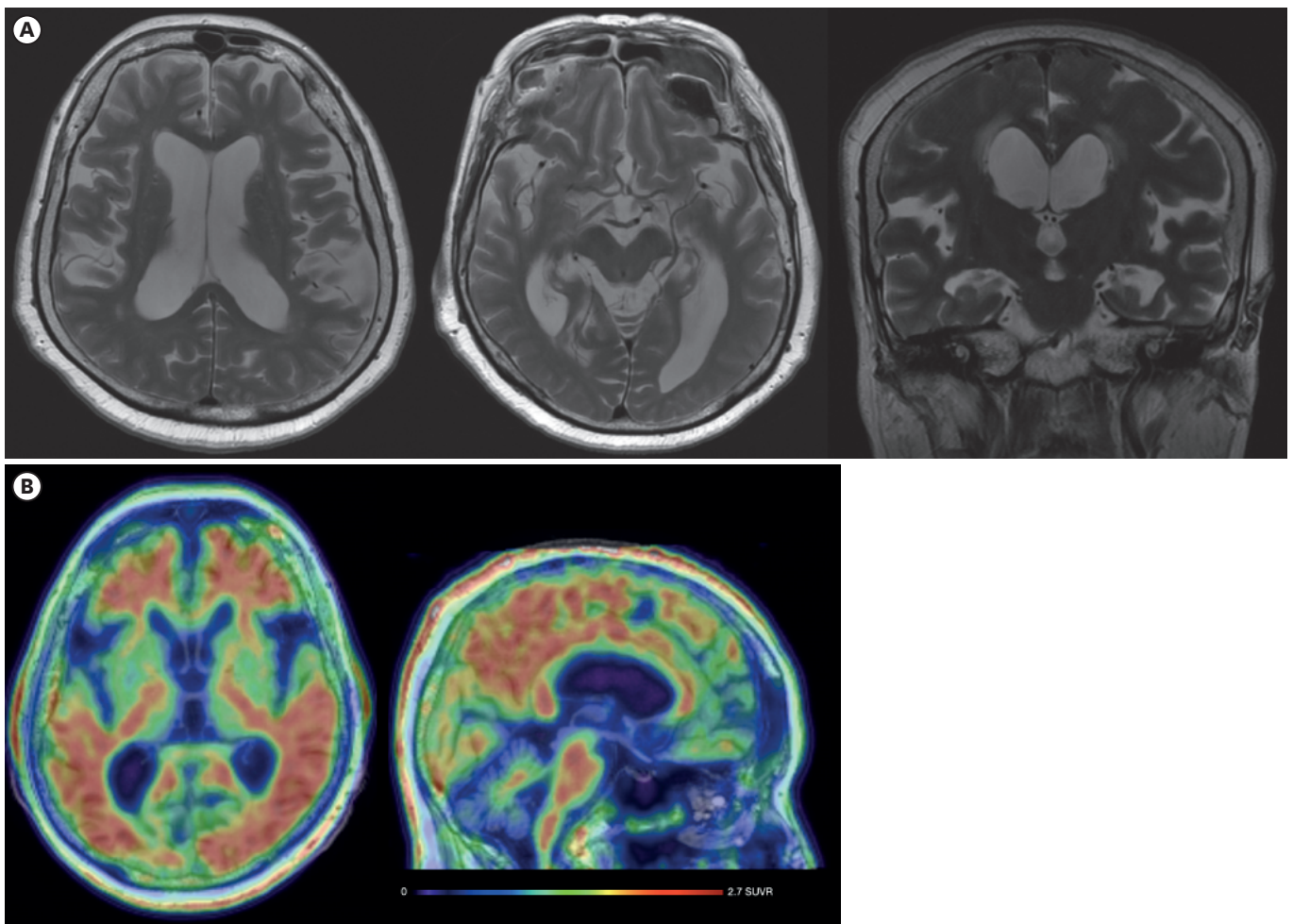


Fig. 1. Preoperative brain magnetic resonance imaging. T2-weighted axial images show lateral ventricular enlargement with cerebrospinal fluid signal void in the cerebral aqueduct. Thinning of the corpus callosum with enlargement of the temporal horns of the lateral ventricles is also demonstrated in the T2-weighted coronal image (A). ^{18}F -florbetaben positron emission tomography imaging shows a high tracer uptake in the frontal cortex, posterior cingulate gyrus, precuneus, and lateral temporal cortex (B).

Author Contributions

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Biopsy to determine amyloid burden is only available during shunt surgery and it involves only a small and specific target area. As amyloid burden is not uniform across brain parenchyma, this method can lead to an inaccurate picture of amyloid burden depending on the area biopsied. Amyloid burden can also be measured with the CSFTT. While CSF biomarkers can measure amyloid pathology, they only indicate the state of amyloid β peptide 42 (A β 42) production and clearance at the time of lumbar puncture, and there can be significant fluctuation in these biomarkers over time.⁷ In addition, both INPH and AD patients have similar low A β 42 levels in CSF.⁸ As a result, CSF biomarkers of amyloid burden have not been helpful in distinguishing between INPH patients with and without AD pathology.⁸ The most recent test of amyloid burden involves amyloid PET. Amyloid PET images show the accumulation of neuritic amyloid plaques over many years.⁷ As a result, amyloid PET has high specificity and sensitivity for detecting amyloid deposition, especially neuritic plaques, in INPH patients.⁵ This suggests amyloid PET would be very useful in assessing amyloid burden relative to shunt surgery outcomes. However, to our knowledge, there has been only 1 study associating amyloid deposition in the brain using PET and clinical improvement following shunt surgery in patients with INPH, but this study had a follow-up time of only 3 months and they did not utilize quantitative gait analysis by an instrument such as GAITRite.²

Analysis of gait is an important component in assessing INPH patients before and after shunt surgery. Previously, the use of standardized clinical tests, such as the TUG test, have proven useful as a complement to visual gait observations.⁹ However, these clinical tests cannot provide a detailed knowledge of various spatiotemporal variables associated with the gait cycle.⁹ Furthermore, such tests are also insufficient in detecting relevant subtle gait abnormalities like changes in gait variability.⁹ The GAITRite electronic walkway is a modern device that can objectively and automatically provide spatiotemporal parameters based on the recorded footfalls.⁹ As a result, a more detailed analysis of gait improvement is possible following shunt surgery in INPH patients. Our INPH patient showed improvement in every GAITRite category, including the important categories of CV of stride time and length. Stride time and stride length variability are related to control of the rhythmic stepping mechanism. Inability to maintain a steady gait with minimal stride-to-stride variations has been closely associated with postural instability and fall risk.¹⁰

Our example illustrates an INPH patient with AD pathology who showed good outcomes following shunt surgery over the course of 1 year. Specifically, quantitative gait measurement improved in all categories, including the important categories of CV of stride time and CV of stride length. Neurological and clinical gait assessments also improved during this relatively long follow-up. Many researchers think shunt surgery in an INPH patient with AD comorbidity likely will not be successful. However, we believe this view should be revisited and reassessed.

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SUPPLEMENTARY MATERIALS

Supplementary Table 1

Results of assessments during CSFTT and in the postoperative follow-up: neuropsychological testing and clinical gait assessment

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Supplementary Table 2

Results of assessments during CSFTT and in the postoperative follow-up: quantitative gait assessment

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