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Case Report

A Case Report Of Idiopathic Normal Pressure Hydrocephalus And Review Of The Diagnostic Approaches.

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Abstract

This report depicts a 56-year-old female with a triad of symptoms that was diagnosed and treated for Idiopathic Normal Pressure Hydrocephalus (iNPH). Her story is unlike many cases due to both her young age and the significant improvement after a large-volume lumbar puncture with 30 milliliters of cerebrospinal fluid removed. Both her gait and cognition significantly improved after the large volume spinal tap, including a 15-foot gait test with a walker and a Montreal Cognitive Assessment (MOCA) test. These tests were done before the lumbar puncture, 1 hour after, and 11 hours after the therapeutic spinal tap. This case illustrates the clinical approach to evaluating, diagnosing, and managing Idiopathic Normal Pressure Hydrocephalus (iNPH). It also reviews essential diagnostic procedures, emphasizing their roles in confirming the diagnosis, predicting treatment outcomes, and ruling out differential diagnoses to ultimately improve patient care.

Keywords: Idiopathic normal pressure hydrocephalus, symptom triad, CSF, DESH, Evans Index, callosal angle, shunting.

INTRODUCTION

Normal pressure hydrocephalus is a treatable condition characterized by an abnormal buildup of cerebrospinal fluid (CSF) in the brain, causing cardinal symptoms of urinary incontinence, cognitive impairment, and gait disturbance. NPH can be classified as either idiopathic or secondary. Idiopathic NPH has no identifiable cause, whereas secondary NPH may result from causes such as subarachnoid hemorrhage, brain trauma, or meningitis. The existence of iNPH has been debated, primarily due to the co-occurrence and overlapping symptoms with neurodegenerative conditions like Alzheimer's disease (AD), making diagnosis difficult [1]. iNPH typically affects older patients, with an average age of onset around 70 years [2]. Studies have found a similar prevalence of iNPH and AD of up to 3% in patients who are over 65 years old [3], which suggests that older patients can present with both diseases at the same time by chance. Despite these challenges, other measures, such as the clinical history, presenting symptoms, and the CSF tap test, can help in identifying iNPH. In this article, we present a patient who, despite being younger than the average age of onset for iNPH, exhibited classic features of this condition. The patient showed significant improvement with a large-volume lumbar puncture and was referred for a ventriculoperitoneal shunt. We will highlight the importance of considering iNPH even in younger patients despite its rarity in those under 65, emphasize the need for early diagnosis to avoid treatment delays, and review acute treatment approaches.

CASE PRESENTATION

The patient is a 56-year-old right-handed female with a past medical history of hypertension, type 2 diabetes mellitus, obesity, migraines, sleep apnea, and stage 3 chronic kidney disease who was being evaluated for confusion for the past month.

During her stay in the hospital, she was alert; however, she was only self-oriented and believed she was in the clinic to check her blood glucose. She did not ambulate or void, and when questioned, she simply stated that she just "doesn't want to." The patient did not think there was any reason for her to be at the hospital and was a poor historian.

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The patient's daughter was able to supply her medical history. Per the daughter who has been the patient's caregiver for the past year, the patient has been slowly declining in normal daily activities for the past two years. She has had problems cooking and going to the bathroom. However, for the past month, her confusion has been becoming much worse; beginning a couple of weeks ago, they would have a conversation, and the next day, the patient would completely forget the conversation.

The patient's incontinence has been worse for the past year; however, at her baseline, she notices she leaks or is unable to make it to the bathroom in time and can go to the bathroom and clean herself. The patient also has been receiving physical therapy at home for the past year due to some walking issues which her daughter was unable to clarify. She required support from her daughter for walking even within her house. She has not walked for about six weeks, as it was getting more difficult for the daughter to help move the patient.

Upon examination, the patient was, at times, uncooperative, and alert and oriented x1. On examination of mental status, she believed that Barack Obama was president and took time to explain where she was born and where she grew up. The patient was able to identify the hospital and her age when given choices. The patient's language was intact with normal repetition, naming, comprehension, and reading, although slowly. Her cranial nerve exams were unremarkable with normal extraocular movements and no nystagmus. Motor exam of her extremities revealed normal muscle bulk, tone, and strength. Normal symmetric reflexes were found in the upper and lower extremities, with a positive grasp sign on the right; the Babinski reflex was negative bilaterally. Her gait was apraxic and magnetic.

NEUROIMAGING

Image 1. Head MRI Transverse Axis T2 FLAIR Sequence.

Image 2. Head MRI Coronal Axis.

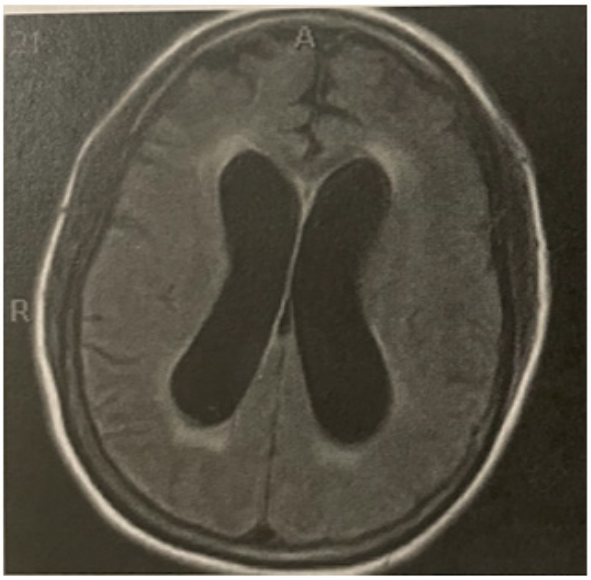

Image 3. Head MRI Coronal Axis, with Callosal Angle Measured.

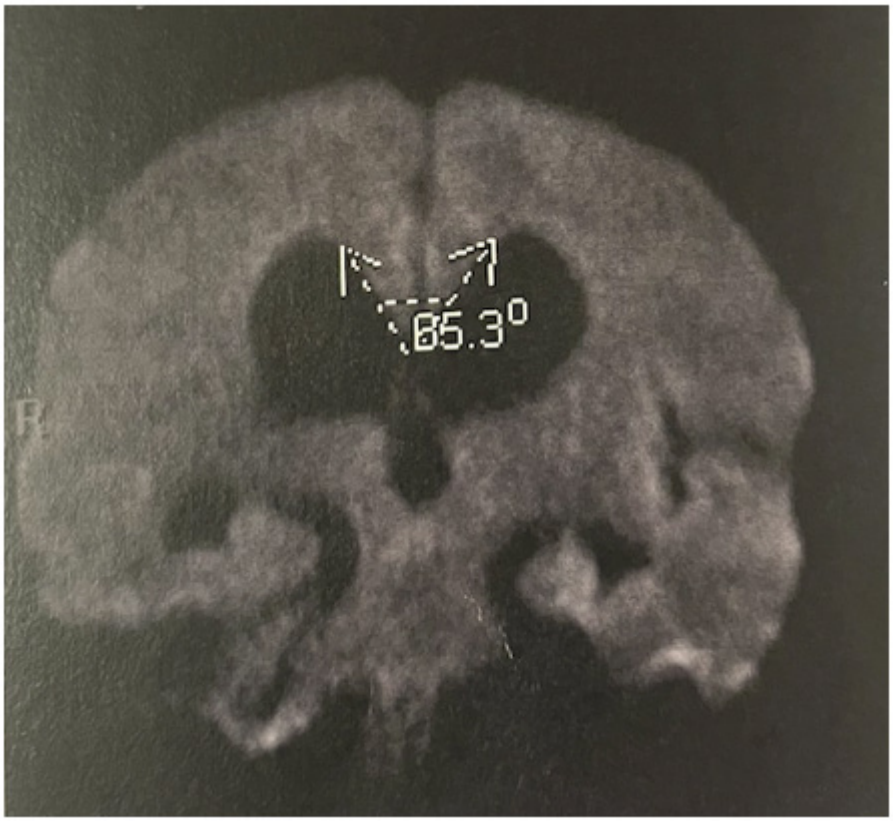

Image 4. Head CT Transverse Axis, with Lateral Ventricle Measurements.

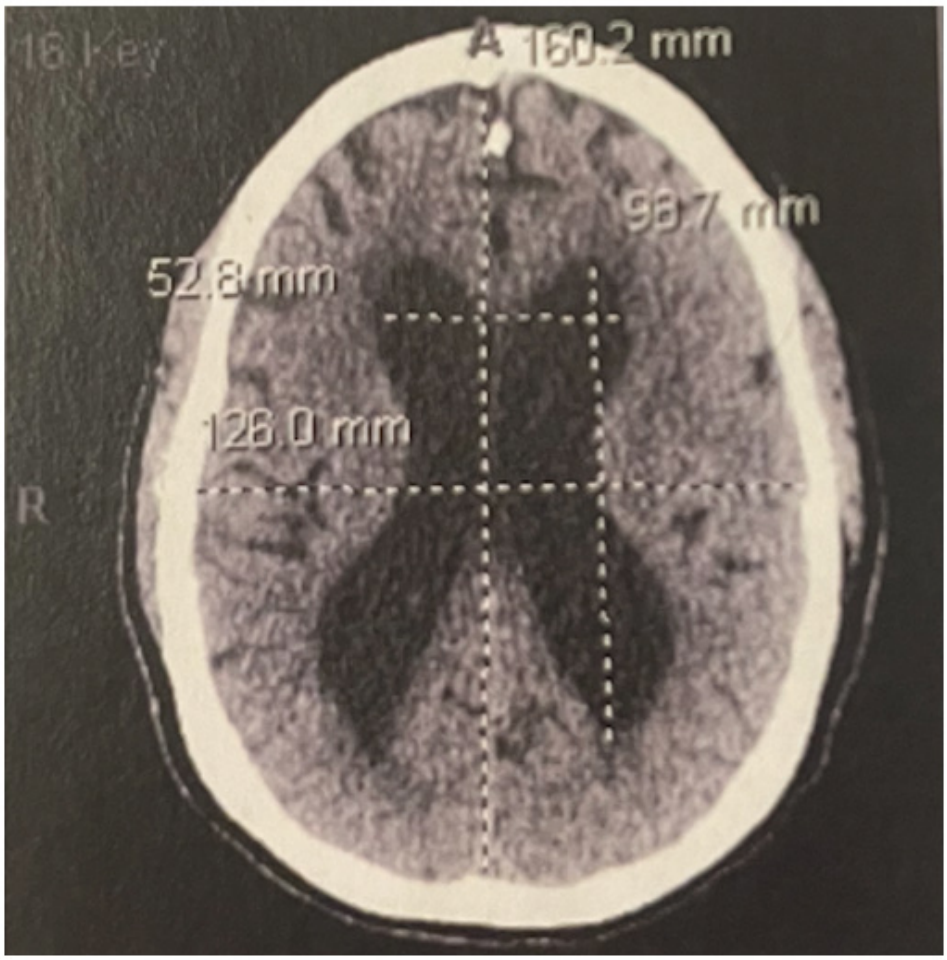

IMAGE FINDINGS

1. Ventriculomegaly increased Evans index >0.3: 52.8/126mm= 0.42
2. Increased ALVI (anteroposterior diameter of the lateral ventricle index) >0.5: 98.7/160.2= 0.61
3. Widening of the temporal horns of the lateral ventricles >6 mm not accounted for by hippocampal atrophy: 10.8
4. Acute callosal angle (less than 90 degrees): 65.3
5. Upward bowing of the corpus callosum: mildly
6. Dilated Sylvian fissures and insular cisterns: yes
7. Effacement of the sulci and subarachnoid spaces at the vertex and medial/parafalcine region: yes
8. Cingulate sulcus sign: posterior half of cingulate sulcus is narrower than the anterior half: n/a
9. Focal/isolated dilation of individual sulci over the medial surface or convexity (sometimes called transport sulci)

MANAGEMENT

The clinical diagnosis with her clinical and neuroimaging findings is most consistent with iNPH. The next step we did was to perform a large-volume lumbar puncture to remove 30-50 milliliters of CSF. In order to gauge the patient's improvement, a Montreal Cognitive Assessment (MOCA) test and a gait test were administered before the large-volume lumbar puncture, one hour status post procedure, and the next day (11 hours status post procedure). The gait test involved walking approximately 15 feet with a walker, observing the gait, and recording the time it took her to walk this distance.

Before the lumbar puncture, the patient's MOCA score was 1/30, and her time to walk 15 feet was 86 seconds. The patient's gait was magnetic. She would often push the walker too far from her body and more with her right arm, which would cause her to turn more to the left. The patient had a much difficult time turning around and needed some help from the nurse to keep her balance. She became very tired and wanted to quit towards the end of her walk.

30 milliliters of CSF were removed during the lumbar puncture. The opening pressure of the spinal tap could not be measured because the patient was uncooperative. One-hour status post lumbar puncture, the patient's MOCA score was 7 out of 30, and her time to walk 15 feet was 45 seconds. The patient's gait was much faster and more normal. She was able to lift her feet off the floor higher compared to the previous attempt. The patient was walking straight and did not take as many steps when turning around. The patient did not ask or require a nurse to help guide her and was able to always keep the walker close to her.

After 11 hours (the next day), status post lumbar puncture, the patient's MOCA score was 11 out of 30, and her time to walk 15 feet was 44 seconds. The patient's family was at the bedside before evaluating the patient and discussed how they noticed cognitive improvement from yesterday, as the patient was talking more and "made more sense." Her gait was very similar to the previous test but slightly faster.

Finally, neurosurgery was consulted and updated on the patient's presentation and examinations. Neurosurgery agreed to place a ventriculoperitoneal shunt. She was transferred to neurosurgery and a ventriculoperitoneal shunt was performed. The patient's cognitive function and gait returned to normal during follow-up one month after surgery. He did not have any more urine incontinence.

CASE PRESENTATION TIMELINE

Last 2 years	Last 1 year	Last 6 weeks	Last 1 month	Post spinal tap	Post-surgery
Problems cooking, urge urine incontinence	Worsened urine incontinence, problems walking	Not walking even at home	Intermittent confusion, frank memory impairment	Significant improvement in MOCA score, Significant improvement in walking	Cognition and gait returned to normal. No urine incontinence.

DISCUSSION

Clinical Features of Normal Pressure Hydrocephalus

To initiate the investigation of Normal Pressure Hydrocephalus (NPH), it is crucial to understand the clinical features. This will allow a high index of suspicion and consequently contribute to many patients' improvement rather than exploring an incorrect diagnosis that could be detrimental to the patient's health. NPH's primary three characteristics are cognitive impairment, progressive gait impairment, and urinary urgency or incontinence, known as the Hakim-Adams Triad [2].

However, the triadic symptoms are nonspecific and not all NPH patients present with all three features, complicating diagnosis. The most common symptoms are urinary incontinence and gait impairment. Cognitive impairment is more subtle and a later clinical feature. Our patient was admitted to the hospital due to her altered mental status, which could have easily been mistaken for neurodegeneration, sepsis, or an iatrogenic effect. However, with further examination, it could be seen that

the patient had the complete triad. NPH typically occurs in geriatric patients and often overlaps with age-related confusion and Alzheimer's disease (AD) [1,2]. However, this age association aids in differentiation; younger patients (such as the 56-year-old patient presented here) are less likely to have dementia, as Alzheimer's prevalence almost doubles every 5 years after the age of 65, thus pointing more towards cognitive impairment as a result of NPH [4]. The diagnosis of NPH in this patient was strengthened by the co-existence of the classical clinical triad.

Although the patient's age is unusually young, her dramatic improvement with a large-volume lumbar puncture is actually quite uncommon. Many studies disagree whether large-volume lumbar punctures help depict NPH or if it is a good indicator for treatment, while others state that it could help the patient's gait impairment [5,6]. One hour following the removal of 30 milliliters of CSF, her MOCA score improved, from being unable to answer almost every question to understanding and answering 7 out of 30 questions. Eventually, after one day, her score improved to 11 out of 30. Her gait showed similar improvements. The speed at which she was able to walk significantly improved one hour after the lumbar puncture, with it now taking the patient about half of the time to walk the same distance. Although progress slowed the day following the lumbar puncture, this was an important improvement, as being less bed-bound decreases the risk of comorbidities developing. Moreover, the ability to ambulate greatly improves overall quality of life.

An important factor to also evaluate is if large-volume lumbar punctures is a good indicator for treatment, when should it be done and when should the MOCA and gait test be performed. There is also a lack of studies that help depict the best time to perform tests as in our case, improvement was significant on day 2. Although our patient had an overall excellent response to the lumbar puncture, where both her cognitive impairment and gait improved very rapidly and then somewhat plateaued, we were unable to see this unless her MOCA and gait was repeated consistently. One studied showed increased sensitivity after the seventh day of a large-volume lumbar puncture [7].

IMPORTANT RADIOLOGICAL FEATURES AND THEIR SIGNIFICANCE

Ventriculomegaly

One crucial component to ensure the correct diagnosis of NPH is to understand the radiological features of the unique ventriculomegaly that can be seen. As mentioned previously, it can at times be difficult to differentiate between iNPH and other neurodegenerative diseases, as well as overlap in the same patient [1,8]. To correctly determine the diagnosis, it is pivotal to understand the Evans Index, Callosal angle, and DESH (Disproportionately Enlarged Subarachnoid-space Hydrocephalus) Criteria. It is pivotal to understand the influence these radiological findings have on your diagnosis and plan of action.

The Evans Index is a ratio that can be seen on the transverse axis of the brain by measuring the maximal width of the frontal horns over the maximal inner skull diameter [9]. A valve of greater than 0.3 highly suggests hydrocephalus. While the Callosal angle is the angle between the two lateral ventricles on the coronal slice, a value of 63 degrees was found by studies to be the best indicator that a patient has hydrocephalus [10]. Both features can be calculated on any coronal MRI for a patient suspected of having NPH. However, these findings are not specific and must be used in conjunction with the DESH pattern and clinical features to make a diagnosis.

The DESH pattern can be seen in NPH, as imaging shows sulci crowding superiorly near the vertex and inferiorly near the Sylvian fissure due to enlarged CSF spaces, and this pattern is currently being used in Japanese diagnostic guidelines. DESH is a good radiological indicator of increased CSF pressure in the cerebral sulci, or outside of the ventricular system. Many studies also found DESH to be predictive of shunt-response in patients with iNPH [11,12]. A previous study used a DESH index where a 3D T1-weighted MRI would be obtained to calculate the combined total volume of the ventricles, Sylvian fissure, and basal cistern to divide by the high-convexity part of the subarachnoid space volume. This calculation provided a sensitivity and specificity of 95.0% and 91.5%, respectively [13]. Imaging like this may be more specific and sensitive than the others and could have a lot of benefits; however, it is important not to solely depend on this metric. One downside is that not every facility has the resources to calculate the DESH as an index. Due to those limited resources, it is also key to apply the main purpose of DESH when viewing imaging as was done in our iNPH patient. It is important to treat the patient's symptoms and not solely the CT or MRI findings, as there are many cases where a patient has NPH without these radiologic features and vice versa [14]. Another basis to not overly depend on the DESH pattern or other radiologic indexes as even if the patient has iNPH, these are not one of the predictors of a successful surgery, and more should be done to determine the treatment plan for the patient [12,15].

As seen in **Image 1** in our patient, there is crowding of the anterior sulci that could have possibly explained the patient's grasp reflex, as pressure on the frontal lobe can translate to possible primitive reflexes in the physical examination. In **Image 2**, the DESH pattern is apparent as the ventricles are enlarged and there is crowding both in the superior sulci and the sulci near the Sylvian fissure, causing effacement. It is also apparent that the Sylvian fissures were enlarged when compared to the average 56-year-old female brain MRI. These

DESH patterns can be seen both in the coronal and transverse views with no cerebral atrophy. **Image 3** depicts the Callosal angle of 65.3 degrees, which would suggest NPH rather than other causes of enlarged ventricles. Finally, the Evans Index can be calculated with **Image 4** with 52.8/126 with an index equaling 0.42. The combination of radiological features along with her clinical clues allowed a high index of suspicion for iNPH, thus prompting further investigation to determine if the patient had any predictors that would indicate that surgery would be the best course of action.

Abnormal Cerebrospinal Fluid Flow Dynamics

Another radiological feature that helps guide us is depicting a picture of the abnormal CSF flow dynamics. Unlike obstructive hydrocephalus, where CSF is unable to flow throughout the ventricular system, NPH has issues with overproduction or blockage of CSF. This creates an imbalance in the CSF flow, which can at times be seen on CT or MRI, as well be depicted with Radionuclide Cisternography.

Although it can be seen in all the images, **Images 1 and 2** best illustrate the abnormal CSF flow not only due to the already mentioned ventriculomegaly, but also the changes outside the ventricles. NPH can be seen on the outer surface of the brain as the sulci are narrowed due to the increased pressure [16]. This is an effect of the abnormal flow dynamics, which results in a somewhat opposite effect of hydrocephalus ex vacuo. This can be understood as the head has a finite amount of space, and if there is too much CSF, there is less room for the brain matter itself. In hydrocephalus ex vacuo, the primary problem is that there is less brain matter, which causes increased CSF to be produced to compensate.

Finally, a Radionuclide Cisternography can also be used to understand the particular flow abnormality in each patient. This is strongly correlated to the DESH pattern; however, it also allows for a possible view of causes of secondary NPH by allowing visualization of possible structural or functional abnormalities [17].

Predictors of Successful Surgeries

While pharmacologic treatments have been explored, surgical shunt placement remains the most effective treatment option for iNPH patients [18,19]. The presence of diagnostic markers can be used as predictors of successful shunt placement.

For example, patients with early-stage iNPH with mild symptoms and a disease duration of less than one year were more likely to show positive outcomes after surgery [20]. Similarly, another study found that shorter durations of gait disturbances were a good predictor of gait improvement post-surgery [21].

Tap tests or large-volume lumbar punctures are commonly used to gauge candidacy for shunt placement. Removing a large volume of CSF mimics the effects of a shunt, and a resultant improvement in symptoms has been shown to be a strong predictor of shunt success [22]. However, tap tests have low negative predictive value, and therefore, negative tap tests do not rule out the benefit of shunt placement [23].

Lumbar drainage, a more invasive procedure in which CSF is removed constantly over a course of two to three days via a catheter, is an alternative to tap tests and provides a better mimic of a shunt. Similar to tap tests, improvement in symptoms following lumbar drainage has been shown to provide great positive predictive value while providing low negative predictive value [24].

Imaging markers such as DESH and a callosal angle less than 90 degrees are often used as markers to diagnose NPH. However, these markers alone have not been shown to be predictors of successful surgery [25].

Overall, the best predictors of successful surgery have been shown to be a combination of imaging, procedural, and clinical symptoms. Patients who present with early onset NPH, with relatively mild and short duration of symptoms, with DESH and a narrow callosal angle on imaging, and with a positive tap test or lumbar drainage have been shown to have the best outcomes post-surgery [26].

Following these predictors, our patient was chosen as a candidate for shunt placement due to the combination of an early onset of the disease, positive response to a large-volume lumbar puncture, presence of the DESH pattern, and a callosal angle of greater than 63 degrees. As the main benefit of shunt placement is long-term relief, the post-operative outcome for our patient remains to be seen.

Ruling out Neurodegenerative Diseases

NPH can be misdiagnosed as neurodegenerative conditions like AD due to similar symptoms, radiological findings, and prevalence in older patients. While NPH presents with the typical clinical triad of urinary incontinence, cognitive impairment, and gait disturbances, this triad is only found in <60% of patients [8]. Similar symptoms can be seen in neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease. The CSF tap test is usually done in suspected NPH patients to determine if the patient would benefit from a shunt. This is a useful tool because improvement after removal of CSF usually supports NPH; however, patients with neurodegenerative diseases have shown some transient clinical improvement as well [8]. Therefore, other factors should also be considered, including cortical signs, brain imaging, and CSF studies.

NPH usually does not present with cortical signs like apraxia, agnosia, and aphasia, and the absence of these signs makes AD less likely [27]. On neurological exams, including the MOCA test, our patient showed cognitive decline and memory impairment, but no signs of cortical impairment, which is consistent with NPH.

As discussed previously, brain MRI and CT are useful for ruling out neurodegenerative diseases. AD is characterized by brain atrophy with widening of sulci and decreased volume of gyri [28]. Our patient had a brain MRI and CT, neither of which showed signs of atrophy. Another useful imaging technique includes an FDG-PET scan, which uses 18-F-fluorodeoxyglucose to visualize metabolism. FDG-PET scan in iNPH patients shows hypometabolism in the caudate and putamen with preserved cortical metabolism [29]. While an FDG-PET scan can help rule out neurodegenerative diseases, this was not done in our patient due to the patient's young age, clear clinical signs of NPH, good response to a large-volume lumbar puncture, and insurance coverage.

While CSF studies were not done in our patient due to the same reasons mentioned above, they can be useful in ruling out AD. CSF biomarkers such as phosphorylated Tau (p-Tau), total Tau (t-Tau), and 42 amino acid forms of amyloid-β (Aβ42) can be abnormal in AD. High T-tau indicates neuronal damage, while high P-tau indicates the formation of neurofibrillary tangles in the brain [30]. Aβ42 is reduced in AD patients because of its aggregation into plaques and is therefore less available in the CSF [30]. Thus, in AD patients, there is elevated T-tau, elevated P-tau, and decreased Aβ42. However, studies have found that Aβ42 can be elevated in patients with iNPH; thus, using an Aβ42/Aβ40 ratio can better reflect amyloid pathology [31]. Aβ40 is the most abundant form of amyloid-β in the CSF, and its levels do not correlate with AD [30]. Therefore, AD patients have a lower Aβ42/Aβ40 ratio than patients without AD and can be used as a measure to distinguish whether a patient has AD or iNPH.

CONCLUSION

Here we present a unique case of a 56-year-old right-handed woman diagnosed with idiopathic Normal Pressure Hydrocephalus (iNPH) that rapidly improved following lumbar puncture with removal of 30 milliliters of CSF. iNPH is generally unexpected in patients as young as 56 years old; however, clinical suspicion was raised in the patient presented here due to her confusion, urinary incontinence, and magnetic gait. The diagnosis of iNPH was further strengthened by the ventriculomegaly, anterior sulci crowding, Callosal angle of 65.3 degrees, and Evan's index of 0.42 were observed via MRI and CT scans of the brain. We reviewed the significance of each of these radiological indices in the diagnosis of iNPH and the importance of DESH in these cases. It is also important to exclude other common neurodegenerative disorders. We also reviewed the importance of DESH, high-volume spinal tap, and lumbar drain in predicting the response to shunt surgery. Finally, this case demonstrates the necessity of including iNPH in the differential diagnosis when a patient presents with cognitive impairment, as there is a potential for treating an underlying reversible condition.

Authorship

Steven M. Ibrahim, Katherine Kim, Juwon Lim, and Anya Ramsamooj designed and drafted the manuscript

Jason Chang provided and managed the case, and provided analysis and interpretation of the data

Forshing Lui provided critical revisions and serves as the guarantor and corresponding author

Conflicts of Interest

All authors declare no conflicts of interests.

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IRB

This case report is IRB-exempt with all patient information de-identified.

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