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Original Article

Idiopathic Normal Pressure Hydrocephalus: Case Series

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BACKGROUND: Idiopathic normal pressure hydrocephalus (iNPH) was first described by Dr Hakim and Dr. Adam in 1964 in a case series describing a triad of symptoms of difficult walking, dementia and urine incontinence. Diagnosis of iNPH is difficult and should be differentiated from other neurodegenerative diseases.

OBJECTIVE: The aim of this study is to increase awareness of iNPH and its diagnostic criteria that ensure good response to CSF diversion surgery.

PATIENTS AND METHODS: A retrospective, hospital based descriptive study to evaluate a one year outcome of patients who were diagnosed with iNPH according to certain clinical and radiological criteria and then treated with ventriculoperitoneal shunt in the period between 2018 to 2023. Demographic data were listed, clinical evaluation, radiological specifications, diagnostic measures and algorithm of management were described and clinical follow up was documented.

RESULTS: Among 69 patients evaluated for possibility of iNPH, 17 patients had their diagnosis confirmed. Age mean was 68.5years and included 15 males (88.2%) and 2 females (11.8%). Co-morbidities were multiple including lacunar infarcts, diabetes, hypertension, ischemic heart disease, Parkinsonism and Alzheimer's disease. First presentation of all patients was difficult walking with a mean duration of 15.8 months. Good response to CSF tapping test after fulfilling the determined radiological criteria. Different degrees of clinical improvement were reported after ventriculoperitoneal shunt insertion.

CONCLUSION: Our diagnostic criteria help distinguishing those with iNPH. These criteria could be considered as predictors for good outcome after shunt insertion. Symptoms duration is a cornerstone in determining the degree of improvement. Co- morbidities may affect degree of improvement. Difficult walking is the first symptom to improve and adjustable valves were better to be used.

KEYWORDS: CSF diversion, Dementia, Idiopathic Normal pressure hydrocephalus, Urinary incontinence.

INTRODUCTION

Idiopathic normal pressure hydrocephalus (iNPH) was first described by Dr Hakim and Dr. Adam in 1964 in a case series describing a triad of symptoms of difficult walking, dementia and urine incontinence with enlarged ventricles despite CSF pressure within normal ranges.[1,2] Diagnosis of iNPH is difficult and should be differentiated from other neurodegenerative diseases especially parkinsonism and different types of dementia. Insertion of CSF diversion system is the treatment of choice in diagnosed patients with iNPH. Determination of diagnostic criteria that guarantee response to CSF diversion is matter of debate.

OBJECTIVE

The purpose of this research is to raise awareness of iNPH as a potential cause of walking difficulties and cognitive function regression. Additionally, to illustrate its diagnostic standards that support precise diagnosis and guarantee recovery following CSF diversion surgery.

PATIENTS AND METHODS

We conducted a retrospective, hospital based descriptive study to evaluate the one year outcome of patients who were diagnosed with idiopathic normal pressure hydrocephalus (iNPH) according to certain clinical and radiological criteria then treated with ventriculoperitoneal shunt in the period between 2018 to 2023. Patients' approval to be included in this study and consents were obtained and the institutional review board IRB approval number is 04-2024-300436.

Patients' demographic data were listed, clinical evaluation, duration of symptoms, radiological specifications, diagnostic measures and algorithm of management were described. Patients' clinical follow up was enrolled.

The included patients had escalating clinical symptoms over an extended period of time, including difficulty walking and a decline in cognitive function in addition to urinary incontinence. A ventriculomegaly with an Evans index (EI) greater than 0.3 was seen in their brain imaging (EI is defined as the ratio of the maximum width of the frontal horns of the lateral ventricles and the maximal internal diameter of the skull at the same level employed in axial CT or MRI images, normally it equals 0.2 to 0.25 and over 0.3 it refers to ventriculomegaly)[1] and presence of disproportionate subarachnoid space dilatation in form of wide and dilated basal space and cisterns especially Sylvian fissure and tight and narrow space over cerebral convexities, loss of the obtusity of corpus callosal angle (at the level of posterior commissure) and MRI

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CSF flowmetry that revealed measures consistent with hyperdynamic CSF circulation.

Following a clinical assessment and radiological confirmation, patients underwent a lumbar puncture (LP) and a CSF tapping test, which involved withdrawing a significant volume of CSF (around 40 ml). Following this, patients were monitored for both objective and subjective improvements in their clinical state.[2] Using the Japanese scale's grades for idiopathic normal pressure hydrocephalus (JSINPH), we conducted objective follow-up.[3] Subjective follow-up that is described based on family reports and the degree of agreement between the subjective and objective assessments was assessed.

Patients were submitted for CSF diversion shunt insertion if they satisfied the previously stated clinical and radiological criteria and showed a positive response to the LP tapping test. Shunt protocol was insertion of ventriculoperitoneal system, burr hole placed at parietal point either right or left. In cases of asymmetrical ventricular dilatation burr hole was placed on the side of more ventricular dilatation. In the first 2 patients of the series, low pressure valve (PS medical, Medtronic system) was used but in the rest of patients, medium pressure valve (PS medical, Medtronic system) was used.

The Japanese Normal Pressure Hydrocephalus Grading Scale (JNPHGS) was used to objectively examine the patients' outcomes in addition to subjective analysis based on reporting data from the patients and family. This was obtained through early postoperative evaluation (First 48 hours postoperatively) and visits in the outpatient clinic at 3 months, 6 months and one year postoperatively. Age, sex, co-morbidities and duration of symptoms were taken as potential outcome predictors.

RESULTS

Demographic data

During the course of the study, 17 of the 69 patients who were assessed for the possibility of iNPH were found to have idiopathic normal pressure hydrocephalus. Age ranged between 55 – 82 years old (Mean=68.5 and median= 71) **(Table 1).** Males were 15 patients (88.2%) and females were 2 (11.8%). All patients were diagnosed previously with multiple lacunar infarcts. 9 were diabetic, 12 were hypertensive and 9 had ischemic heart disease. 7 patients had previous diagnosis as a Parkinsonian patient on antiparkinsonian treatment (41.2%), 8 patients had diagnosis of Alzheimer's disease (47.1%), 17 patients with multiple lacunar infarctions (100%), 9 patients (52.9%) with diabetes and 9 patients with ischemic heart disease (52.9%).

Symptoms and clinical presentation

All patients initially presented with difficulty in walking, that progressed over time with duration of symptoms ranging between 9 to 26 months (Mean: 15.8 months). Patients' clinical presentation was graded according to Japanese grading scale. As regards difficult walking 9 patients were completely dependent (Grade IV), 5 needed walking frames to walk (Grade III) and 3 needed a cane to walk (Grade II). As regards dementia, different degrees of dementia and decline of cognitive function was reported with duration of symptoms ranged between 17 to 31 months (Mean: 22.9) as 4 patients were totally dependent (Grade IV), 9 patients were partially dependent at home (Grade III), 2 patients were socially dependent but independent at home (Grade II) and 2 has no dementia but apathetic (Grade I). Loss of urine control was reported in 11 patients (64.7%), with duration of symptoms ranging between 7 to 18 months (Mean: 11.9 months) according to Japanese scale, 2 patients had frequent urine incontinence (Grade IV), 6 patients had urine incontinence during the day (Grade III) and 3 patients their urine incontinence is at night only (Grade II). We had 6 patients who did not report any urine problems **(Table 2).**

Imaging

MRI brain revealed ventriculomegaly in all patients that was estimated via Evan's index (EI) more than 0.3 (Mean= 0.47). The ventriculomegaly was associated with wide basal subarachnoid space (wide Sylvian fissure), tight and narrow subarachnoid space over the convexities in all patients. Acute angle of corpus callosum was seen in 12 patients and 5 patients showed almost right angle **(Fig.1).** MRI flowmetry of these patients revealed hyperdynamic CSF circulation at aqueduct of Sylvius that indicates impaired CSF circulation. Patients that did not meet the previous radiological criteria were excluded from the diagnosis of iNPH.

All patients with previously mentioned radiological criteria revealed degree of clinical improvement (especially the gait) secondary to lumbar puncture and CSF tapping test but symptoms recured again after a period of time. Periods of improvement differed between patients. Improved lower limb tightness and ability of walk was reported in all included patients. Patients were evaluated subjectively based on their reports and objectively based on Japanese grading scale system. There was correspondence between objective and subjective evaluation.

Surgical treatment and follow up

After ventriculoperitoneal shunt, patients were evaluated in the early postoperative period (within the first 48 hours postoperatively), 3 months, 6 months and 1 year postoperatively. Rapid improvement of gait and lower limb tightness was reported subjectively in all patients **(Table 3)**. All patients showed degree of improvement within less than 6 months. Dementia and urine incontinence did not show rapid improvements as gait but showed improvements along the follow up period **(Tables 4,5).** Degree of improvement differed between patients, those with shorter duration of symptoms revealed rapid improvements. Those with longstanding symptoms and delayed diagnosis showed slow improvements and to a degree less than those had earlier diagnosis. During

follow up, 3 patients showed clinical deterioration after period of improvement because of shunt complications.

By the time the study was over, patients with iNPH who were diagnosed and had shunts early improved more quickly and to greater degrees than those who were diagnosed later, who only had partial or no improvement at all **(Table 6)**. All patients with difficult walking showed improvement (100%), whether it was partial or complete. It differs in the degree of improvement according to severity and duration of symptoms. As regards dementia, we had three patients did not improve (17.6%) till the end of follow up. Two patients of them diagnosed with iNPH and sent for shunt after 30 months of dementia onset (Presented with dementia grade III) and 37 months (Presented with dementia grade II) of their dementia presentation. The third one had multiple lacunar infarctions and grade IV dementia at time of diagnosis despite the diagnosis with iNPH was 13 months after onset of the symptom, this patient also did not improve urine control despite he improved walking ability to GII.

Complications

As regards shunt complications, two patients developed bilateral chronic subdural hematoma that was discovered as patients showed clinical deterioration after improving during follow up. Low pressure shunt system was applied in both patients and we managed both of them through evacuation of the hematoma and shunt upgrading to medium pressure **(Fig. 2).** Both patients were in the beginning of our series as we were using low pressure shunts then we changed the routine to be medium pressure shunt. We had one case that showed clinical deterioration during follow up because of shunt obstruction and experienced clinical improvement after shunt revision.

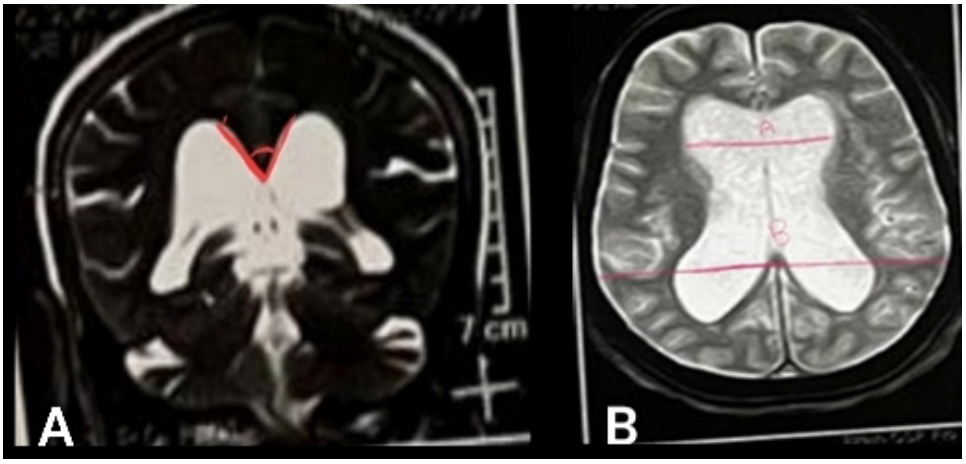

Fig 1 (A): MRI T2 weighted coronal cut of female 79 years old revealing acute callosal angle (Angle measured on coronal image at the level of posterior commissure perpendicular to the anterior commissure posterior commissure plane) and tightness of subarachnoid space at high convexities. (B): Axial MRI A represents the Evan's index (The ratio widest width of frontal horns and B represents the widest biparietal diameter).

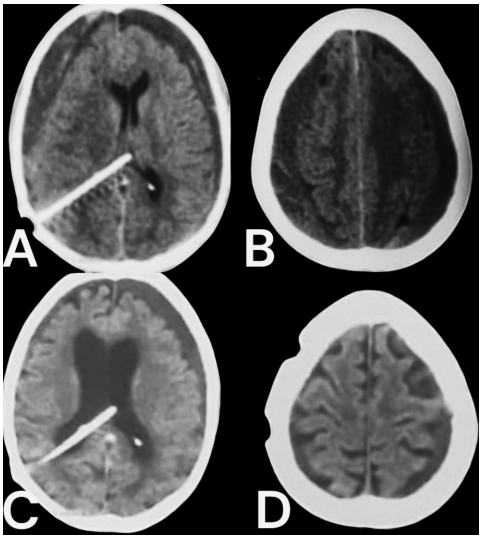

Fig 2: Female patient, 75 years old and diagnosed as iNPH. She was operated for ventriculoperitoneal shunt using low pressure valve. After about two months of improvement, she experienced gradual deterioration of motor power, urine control and consciousness. Following hematoma evacuation and shunt pressure upgrading to medium pressure she recovered again. (A and B) axial CT brain cuts revealed bilateral chronic subdural hematoma with drained ventricles (C and D) CT brain axial cuts after hematoma evacuation and shunt valve pressure upgraded for medium pressure shunt.

Table 1: Age distribution of included patients

Age group	Number of patients
50 - 59	1 (5.9%)
60 - 69	5 (29.4%)
70 - 79	9 (52.9%)
80 and more	2 (11.8%)

Table 2: Summary of patients' clinical presentation and grading according to normal pressure hydrocephalus Japanese grading scale

	Difficult walking	Dementia	Urine incontinence
Grade 0	-	-	6 (35.3%)
Grade I	-	2 (11.8%)	-
Grade II	3 (17.7%)	2 (11.8%)	3 (17.7%)
Grade III	5 (29.4%)	9 (52.9%)	6 (35.3%)
Garde IV	9 (52.9%)	4 (23.5%)	2 (11.8%)

Table 3: Summary of difficult walking symptom outcome over the periods of follow up

Difficult walking	Early postop	3 months follow up	6 months follow up	One year follow up
Grade 0	-	2 (11.8%)	4 (23.5%)	5 (29.4%)
Grade I	2 (11.8%)	2 (11.8%)	8 (47.1%)	9 (52.9%)
Grade II	4 (23.5%)	5 (29.4%)	5 (29.4%)	3 (17.7%)
Grade III	5 (29.4%)	6 (35.3%)	-	-
Grade IV	6 (35.3%)	2 (11.8%)	-	-

Table 4: Summary of dementia symptom outcome over the periods of follow up

Dementia	Early postop.	3 months follow up	6 months follow up	One year follow up
Grade 0	-	2 (11.7%)	2 (11.7%)	4 (23.5%)
Grade I	2 (11.8%)	2 (11.7%)	7 (41.2%)	5 (29.4%)
Grade II	2 (11.8%)	5 (29.4%)	5 (29.4%)	6 (35.3%)
Grade III	9 (52.9%)	7 (41.2%)	2 (11.7%)	1 (5.9%)
Grade IV	4 (23.5%)	1 (5.9%)	1 (5.9%)	1 (5.9%)

Table 5: **Summary of urine incontinence symptom outcome over the periods of follow up**

Urine incontinence	Early postop.	3 months follow up	6 months follow up	One year follow up
Grade 0	6 (35.3%)	6 (35.3%)	8 (47.1%)	9 (52.9%)
Grade I	-	-	7 (41.2%)	8 (47.1%)
Grade II	3 (17.7%)	5 (29.4%)	2 (11.8%)	-
Grade III	6 (35.3%)	6 (35.3%)	-	-
Grade IV	2 (11.8%)	-	-	-

Table 6: Summary for patients' outcome distributed in relation to duration of symptoms

	Duration of symptoms	Number of patients	No improvement	Improved
Difficult walking	Less than 16 months	10 patients	-	10 (100%)
	16 months and more	7 patients	-	7 (100%)
Dementia	Less than 23 months	9 patients	1 (11.1%)	8 (88.9%)
	23 months and more	8 patients	2 (25%)	6 (75%)
Urine incontinence	Less than 12 months	5 patients	-	5 (100%)
	12 months and more	6 patients	1 (16.7%)	5 (83.3%)

DISCUSSION

NPH was first reported by Drs. Hakim and Adams in 1965. They described a case series of the triadic syndrome presentations of difficult walking, cognitive decline and urine incontinence along with ventricular enlargement (Ventriculomegaly detected on pneumoencephalogram at that time) despite cerebrospinal fluid (CSF) pressure being within the normal ranges.[4,5] Despite the early identification of the disease, we believe that diagnosis of iNPH is still underestimated and there are many cases that are managed as other neurodegenerative disorders or overestimated that led to failure of CSF diversion as a management tool.[5] This could be explained as diagnosis of iNPH is still debatable and lack of consensus about its diagnostic criteria.

iNPH is considered the disease of elderly and the prevalence of iNPH has been estimated to be 10 per 100 000 to 22 per 100 000 overall, with 1.30% in those aged ≥65 years and 5.9% in those aged ≥80 years.[7,8] In our study, we had all patients above sixty except one. The majority of patients in our study were males (88.2%), and the literature shows no sex predilection in NPH. As regards co-morbidities, our findings are in line with many reports that showed co-existence between specific comorbidities and NPH especially multiple strokes, Parkinsonism and Alzheimer disease, its identification is important to design the management plan and considered as a major prognostic factor in iNPH management.[9]

The exact pathogenesis of iNPH remains unclear.[10] Normally, CSF flow could be explained according to two components, bulk flow component and pulsatile flow component. Bulk flow component is controlled by continuous production of CSF and forces CSF to move from lateral ventricles to third ventricle through foramen of Monro then to the fourth ventricle through aqueduct of Sylvius, then through foramena of Luschka and Magendie to the subarachnoid space where CSF is absorbed by arachnoid granulations and taken by superior sagittal sinus.[11] Glymphatic system facilitates bulk flow of CSF into the brain parenchyma along para-arterial space, interstitial space and along para-venous space (perivascular spaces or Virckow Robin spaces). This pathway is mediated by Aquaporin-4 (AQP4) channels at astrocytic perivascular endfeet,[12] and this considerable amount could be drained via cervical lymphatic system.[13] Several studies revealed abnormalities in CSF outflow in patients of iNPH.[14-16] Outflow resistance is compensated with trans ependymal CSF permeation in the periventricular white matter.[17] With aging, resistance to outflow increases as a result of increased rigidity of intracranial compartments (decreased subarachnoid space and veins compliance) which causes lack of CSF absorption and CSF accumulation in the ventricles.[18,19] Changes of CSF dynamics affect neural tissue metabolism and normal cellular homeostasis and lead to accumulation of vasoactive metabolites.[20,21]

While CSF pulsatile flow component follows blood vessels pulsatility (controlled by cardiac circulation), it is obvious at the aqueduct of Sylvius where CSF goes forward with systole and backward with diastole (CSF oscillation).[21] Aging process and neurodegeneration lead to rigid CSF compartments at the subarachnoid space and over cerebral convexities, in addition to the decrease in pulsatility of blood vessels due to the atherosclerotic process, all of the previous increase CSF hyperdynamic in the aqueduct reverse CSF flow direction and turn it back to the ventricles.[13,22-24] Abnormal CSF dynamics leads to ventriculomegaly that could initiate a vicious cycle of neurological damages and presentation of iNPH. Detection of CSF hyperdynamic flow through the aqueduct of Sylvius is an indicator of iNPH. This could be detected with MRI and considered as aqueduct stroke volume (ASV) which is evaluated with phase contrast PC-MRI.[25]

According to different guidelines, diagnosis of iNPH relies on a combination of clinical triad (gait dysfunction, dementia and loss of urine control) and radiological criteria. As regards gait dysfunction, it is the main clinical presentation in all cases of iNPH. It involves difficulty in integrating sensory information about the body's position in its environment in the absence of primary sensorimotor deficits, cerebellar dysfunction, or involuntary movements. Gait dysfunction could be in form of hesitation or difficult to initiate the gait, shuffling and wide based gait, reduced foot clearance and difficulty with turning with 60-80% probability of falling.[26] As regards to the dementia, 78-90% had different degrees of cognitive impairment in addition to executive dysfunction, psychomotor slowing and apathy.[27] As regards to the urine incontinence, it affects 76–83% of patients with iNPH which are characterized by urgency, involuntary urination and difficulty.[28] In cases of urine incontinence, other urological causes should be evaluated. In our study, we found 100% of patients presented with gait dysfunction, 100% with dementia and 64.7% with urine incontinence. All patients with gait dysfunction shared the inability to initiate movements and shuffling gait. Dementia presentation in our patients was in the form of different degrees of psychomotor slowing and apathy while urine incontinence was in the form of uncontrolled urination.

Distortion of the central portion of the corona radiata by the distended ventricles initiates patients' symptoms. This may also lead to interstitial edema of the white matter and impaired blood flow, as suggested in nuclear imaging studies. White matter in the periventricular region includes sacral motor fibers that innervate both legs and bladder, so gait dysfunction and loss of urine control were explained. Compression on pedunculopontine nucleus could explain gait dysfunction, particularly the freezing of gait that has been considered part of clinical presentation of iNPH in many patients. Due to continuous ventricular enlargement, the cortex is pushed against the inner table of the skull causing radial shearing forces that result in dementia.[29]

For radiological diagnostic criteria, it is improper to

depend only on dilated ventricles and Evan's ratio for diagnosis of iNPH as 20% of the population over 70 years have dilated ventricles (Evan's ratio more than 0.3). Also dilated ventricles could be common radiological finding in both iNPH and neurodegenerative diseases.[30] So in addition to Evan's ratio that should be more than 0.3, there are other findings as disproportionately enlarged subarachnoid-space "DESH" in which there is narrow high convexity sulci, dilated sylvian fissure, focally dilated sulci. Other radiological findings that refer to iNPH is more acute callosal angle (Normally it is right to obtuse angle) which refers dysfunction of glymphatic system. Voxel based morphometry (CSF flowmetry) helps the diagnosis, if added to the previous finding.[31] For diagnosis of NPH, these radiological criteria should be associated with the clinical criteria. In many cases these radiological findings could be seen without the clinical triad of NPH. In this occasion the condition is termed asymptomatic ventriculomegaly with features of idiopathic normal pressure hydrocephalus on MRI (AVIM), by some authors it is considered preclinical condition.[32]

Debate is ongoing about cases that have clinical presentation similar to iNPH but fail to meet the specific radiological criteria as EI <0.3, or do not exhibit high-convexity tightening. Some authors refer to these cases as non-DESH NPH. These presentations are difficult to distinguish from mere brain atrophy, and no systematic data up till now to consider this as a subtype of NPH. Therefore, we did not consider "non-DESH" patients in this series till a formal definition of this subtype is applied and included in the guidelines.

According to guidelines CSF drainage tests are clinical tests that used to confirm diagnosis of iNPH for those cases met the previous clinical and radiological specifications of iNPH.[33] The commonly applied tests are; tap test, external drainage test and infusion test. In our study, we did not perform the other two tests as they are not superior over tap test and need hospitalization, high incidence of complications and a lot of specialized requirements. Tap test is an important diagnostic tool to confirm the diagnosis of iNPH, confirm normal pressure of CSF and detect those who will benefit from CSF shunting. In cases of iNPH usually gait improvement is the most common symptom to respond achieved within 4 hours after withdrawing a large amount of CSF.[34] In our practice, we used to withdraw 30 cc of CSF and the test showed 100% positive predictive value. According to the literature, the positive predictive value (PPV) of tapping test is approximately 73-100%, negative predictive value is 16-42% (NPV).[35]

In our study, we diagnosed iNPH using the previously stated radiological criteria. The CSF tapping test was then used to confirm the diagnosis and evaluate the benefit of shunt insertion. Our results consider this algorithm as very helpful to diagnose patients with iNPH and detect patients that will benefit from shunt insertion. After one year follow up, we found that our patients benefited and showed different degrees of clinical improvement, either complete or partial and we did not face any treatment failure. Many authors suggested that patients with typical clinical and imaging findings who did not respond or partially responded to shunting must have had the intervention too late,[36] while others proposed that there is coexistence for neurodegenerative disease.[37] The two previous facts, duration of symptoms and interlacing between neurodegenerative disease and iNPH, may explain the different degrees of improvement that we had in our study despite fulfilling clinical, radiological criteria and positive response to CSF tapping test.

We did not conduct any long-term follow up for patients in our series, however long-term follow up in many studies revealed changes in the degree of clinical response to shunting compared to the baseline symptoms over time.[38] Gait disturbance showed the longest lasting response while dementia and urinary incontinence tend to be worse earlier.[39] Overall, it has been determined that while all symptoms initially improved, there would likely be a propensity for them to worsen at a later follow-up.

In the literature, there is no fixed recommendation about the type of valve used or its pressure. Adjustable valves offer the advantage of being able to adjust the pressure till improving the symptoms or raise the pressure in cases of low-pressure symptoms and complications as developing subdural hematomas.[34] In our study, we used fixed pressure valves. We faced two cases of subdural hematoma formation because of low pressure valves in the beginning of the series so shunt revision and valve upgrading was performed.

CONCLUSION

Our diagnostic criteria help distinguishing those with iNPH. These diagnostic criteria could be considered as predictors for good outcome after shunt insertion. The duration of symptoms is a cornerstone in determining the degree of response to CSF diversion and improvement. Association of co-morbidities (especially neurodegenerative diseases) may affect the degree of improvement. Difficult walking is the first symptom to improve. Adjustable valves are better to achieve suitable pressure that relieve patients' symptoms and avoid low pressure complications. More studies are needed to distinguish those patients with NPH that do not follow these diagnostic criteria.

List of Abbreviations

ASV: Aqueduct stroke volume.
AVIM: Asymptomatic ventriculomegaly with features of idiopathic normal pressure hydrocephalus on MRI.
CSF: Cerebrospinal fluid.
DESH: Disproportionately enlarged subarachnoid space.
EI: Evans index.
JSINPH: Japanese normal pressure hydrocephalus grading scale.
LP: Lumbar puncture.
NPH: Idiopathic normal pressure hydrocephalus.

NPV: Negative predictive value.
PC-MRI: Phase contrast MRI.
PPV: Positive predictive value.

Disclosure

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