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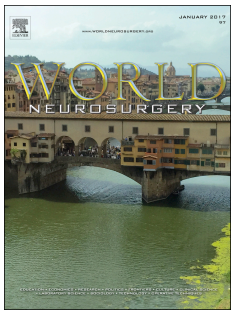

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ABSTRACT:

Idiopathic normal pressure hydrocephalus (iNPH) is a disorder of aging that is characterized by enlarged cerebral ventricles, gait apraxia, dementia, and urinary incontinence. iNPH is frequently misdiagnosed, in part because the symptoms resemble other neurological disorders, and because other associated symptoms have not been fully characterized. Importantly, iNPH has not previously been associated with stuttering, and shunting has not been shown to alleviate the symptom of stuttering.

Here, the authors report two cases of patients with iNPH presenting with stuttering that resolved after ventriculoperitoneal (VP) shunt placement. Each patient presented with gait difficulty, incontinence, cognitive impairment and stuttering. Lasting improvements of the symptoms (including stuttering) were seen in both patients after CSF drainage procedures that included lumbar puncture, extended lumbar CSF drainage, placement of a VP shunt, and VP shunt revision.

These findings suggest that iNPH can present with stuttering or dysarthria. The significant improvement in stuttering and dysarthria, along with the improvements in gait difficulty, incontinence, and cognitive impairment that occurred after CSF drainage, suggests that the motor apraxia observed in NPH can affect speech production. Practitioners should be aware that iNPH can present with stuttering, and that CSF drainage can improve stuttering in select circumstances.

KEYWORDS: normal pressure hydrocephalus, stuttering, ventriculoperitoneal shunt, neurological disorders of aging

INTRODUCTION

Normal pressure hydrocephalus (NPH) is a neurological disorder of aging that is characterized by enlarged ventricles, gait difficulty, incontinence, cognitive impairment, and normal (or only slightly elevated) intracranial pressure. Patients with NPH are diagnosed as having primary (idiopathic) or secondary NPH, based on the etiology of the disease. Secondary NPH can affect individuals of any age. Common causes are subarachnoid hemorrhage, head trauma and meningitis, all of which may lead to increased brain inflammation and fibrosis of CSF resorption pathways[1]. Idiopathic NPH (iNPH) is most commonly seen in adults over the age of 60. The pathophysiology of iNPH is poorly understood. Proposed mechanisms suggest decreased cerebral blood flow, poor cerebral vascular autoregulation, and impaired CSF production, absorption,

and turnover rate[2,3]. The treatment for NPH, regardless of etiology, is the placement of a ventriculoperitoneal (VP) shunt[4].

iNPH remains a difficult disease to diagnosis, given its late age of onset and the notable overlap of its presenting symptoms with other diseases of aging, including Lewy body dementia, Parkinson's Disease, progressive supranuclear palsy, and Alzheimer's Disease[2]. To date, however, there are no reports that describe stuttering or dysarthria as presenting symptoms in iNPH. This case report describes two patients who presented with iNPH symptoms with stuttering, and who displayed sustained symptomatic improvement after VP shunt placement.

CASE REPORTS

CASE 1

Clinical Presentation and Diagnostic Work-up

A 72-year-old female with no significant past medical history presented with a complaint of intermittent headaches, progressive gait difficulty, urinary incontinence, memory loss and stuttering. She had transiently experienced similar symptoms approximately 12 years earlier. Imaging at that time showed evidence of an 8mm lesion in the region of the foramen of Munro consistent with a colloid cyst, but no surgery was performed. Her symptoms improved and she did well for many years. She presented 12 years later after a fall and was again noted to have stuttering, intermittent headaches and gait difficulty that was characterized by imbalance, short stride length and intermittent freezing. Cranial imaging showed mild to moderate hydrocephalus (Figure 1A). The previously

observed 8mm colloid cyst was unchanged in size from 12 years prior. A craniotomy for resection of the colloid cyst was performed without complications. Postoperatively, her stuttering resolved with significant improvement of her gait and incontinence. After several weeks, however, her symptoms of stuttering, incontinence and gait difficulty returned. She underwent a lumbar puncture that demonstrated a normal opening pressure. After the lumbar puncture, her stuttering and other symptoms resolved, but these symptoms recurred after several days. The patient was subsequently admitted to the hospital for a lumbar drain trial. After several days of lumbar CSF drainage, the stuttering and gait difficulty markedly improved. She was discharged to home, but over the next few weeks, her symptoms gradually returned. Based on these observations, a diagnosis of iNPH was made, and she underwent placement of a ventriculoperitoneal (VP) shunt (Figure 1B). Her symptoms, including the stuttering, resolved after the procedure.

Postoperative Course

Seven months later, the patient's stuttering, gait difficulty and incontinence returned. A radionuclide shunt patency study showed evidence of shunt obstruction, and her VP shunt was revised with a subsequent improvement in her symptoms. Six years later, she presented again with stuttering, gait difficulty, cognitive impairment and urinary incontinence. A radionuclide shunt patency study again showed evidence of shunt obstruction. She underwent replacement of the VP shunt, and her stuttering and other symptoms again improved. Subsequent clinic visits over the next three years indicated continued improvement in her symptoms.

CASE 2

Clinical Examination and Diagnostic Work-up

The patient is a 68-year-old left-handed man with a history of speech difficulty since childhood who presented with progressive gait difficulty, urge incontinence, cognitive impairment, dysarthria and stuttering over a five-year period. He had suffered from incontinence and frequent falls for several years prior to presentation, and was ambulating using a walker and a gait belt. His cognitive impairments began a few years later after a car accident. Formal neuropsychiatric testing revealed moderate impairments in executive functioning and memory. Cranial imaging revealed ventricular enlargement, no evidence of obstruction to CSF flow on cineflow sequences, and moderate small vessel ischemic changes (Figure 2A). He was evaluated by a neurologist who felt that his shuffling and festinating gait were indicative of Parkinson's Disease. L-DOPA therapy resulted in a modest improvement in his gait. He also underwent a lumbar puncture on two occasions and transiently improved after each procedure. He underwent a four-day trial of lumbar CSF drainage, and the physical therapists documented progressive improvement in his gait each day, such that he was able to ambulate without assistance. Thus, a diagnosis of iNPH was made. The patient underwent placement of a VP shunt (Figure 2B).

Postoperative Course

As predicted by the lumbar drain trial, shunt placement resulted in a marked improvement in his gait, incontinence, memory function, dysarthria and stuttering. He

returned to clinic several months later with a complaint of a slight decline from the level of improvement that he experienced after the initial CSF drainage. The programmable shunt valve was adjusted to increase the drainage of CSF, and he experienced a further improvement in his symptoms that lasted over 5 years (the most recent follow up).

DISCUSSION

Speech disfluency is commonly seen in Parkinson's Disease, progressive supranuclear palsy and multiple systems atrophy[5]. Neither of the patients described here displayed the autonomic dysfunction or gaze deficits commonly seen in multiple systems atrophy or progressive supranuclear palsy, respectively. However, stuttering has not classically been considered part of the symptomatology of iNPH. Indeed, some practitioners have used the presence of speech disorders as a reason to eliminate iNPH from the list of possible diagnoses in adult patients who also present with gait and cognitive dysfunction. The robust and reproducible improvement observed in these two patients after CSF drainage challenges this assumption and suggests that stuttering can be a part of the constellation of symptoms observed in NPH.

The classic symptoms of iNPH are gait difficulty, incontinence and cognitive dysfunction. Because weakness, sensory loss and vertigo are generally not present, the gait dysfunction observed in iNPH may best be described as a gait apraxia. The incontinence observed in iNPH is due primarily to detrusor overactivity[6] and may also represent a form of apraxia. Apraxia is generally the result of sensorimotor incoordination, as is often seen in patients with posterior parietal or deep white matter lesions. Some investigators have suggested that the motor symptoms of iNPH arise

from dysfunction of supplementary motor areas of the frontal lobe and periventricular white matter tracts, particularly those subserving frontal lobe connections[7].

Childhood onset fluency disorder can begin in children who are just learning to speak, and can sometimes persist into adulthood (e.g. persistent developmental stuttering). MRI studies on adults with persistent developmental stuttering (PDS) have found that these patients have significantly more gyral variants[8]. Other neuroimaging studies demonstrate that PDS may be associated both with an abnormality in the white matter of left-hemispheric speech areas and a right hemispheric hyperactivity. The latter may compensate for the deficient structural connectivity in the left hemisphere[9]. A recent study of non-verbal sensorimotor timing in patients who stutter suggests that children and adolescents who stutter display abnormalities in predictive timing during auditory-motor coupling. The results suggest that stuttering can be an expression of a broader underlying deficit in sensorimotor coupling[10]. The patient in Case 2 experienced speech difficulty as a child, but this worsened in parallel with the adult onset of gait, urinary and cognitive dysfunction. All of the symptoms improved after CSF drainage. The findings suggest that this patient had baseline deficits in sensorimotor coupling that were made worse by the onset of NPH later in life, and they raise the intriguing possibility that the childhood sensorimotor deficits were a precursor to the development of iNPH.

Stuttering can also be acquired during adulthood, as occurred in the first patient. Although adult onset stuttering can result from well-defined etiologies such as stroke, in many cases the cause is unknown. Stuttering has not previously been reported as a symptom of iNPH. However, a single case report of a child with agenesis of the corpus

callosum, hydrocephalus and stuttering has been published[11]. Interestingly, the child's stuttering resolved reversibly with steroids, leading the author to hypothesize that the presumed alterations of white matter tracts associated with corpus callosum agenesis and hydrocephalus affected speech rhythms and stuttering.

A recent study of people who stutter examined possible neural mechanisms that may contribute to this phenomenon. The investigators determined that the timing of neural activity in different brain regions may be abnormal in such patients. The findings also suggested that the primary speech and language areas are not responsible for the deficits, but rather lesions involving other structures (such as the basal ganglia) may modulate the primary speech and language regions and contribute to the stuttering[9].

CONCLUSION

In summary, we describe two novel cases where stuttering presented as a symptom of iNPH along with the classic triad of symptoms associated with iNPH, i.e. urinary incontinence, gait impairment and dementia. Given the time-locked and reproducible improvement in both stuttering and the classic iNPH symptom triad after CSF drainage, it seems clear that stuttering was an expression of the disease process in these patients. The recognition of stuttering as a rare presenting symptom of iNPH may lead to a more accurate diagnosis of iNPH. Moreover, the lasting improvement in stuttering that occurred after CSF drainage raises the possibility that CSF drainage may benefit a subgroup of patients who suffer from stuttering.

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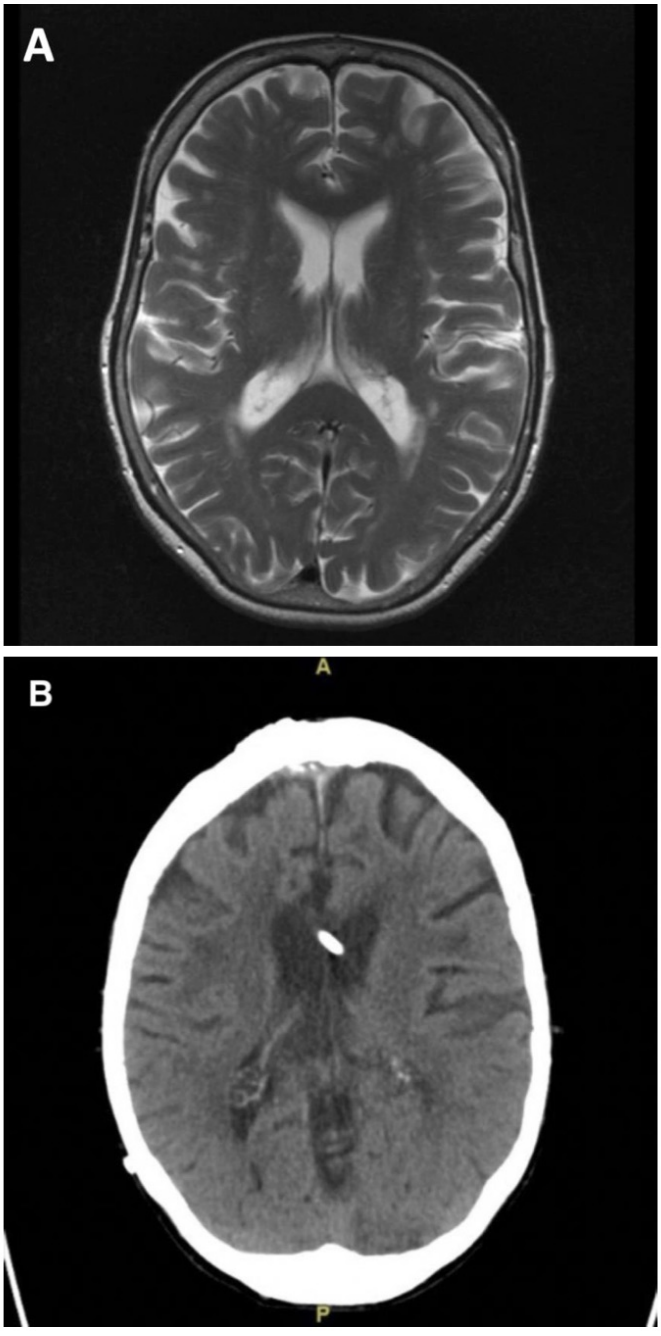
Figure legends:

FIG. 1: A) *Pre-operative axial T2-weighted MRI scan of the head for Patient 1.* ***B)*** *Post-operative axial non-contrast computed tomography (CT) scan of the head. A right frontal shunt catheter is visible.*

FIG. 2: A) *Pre-operative axial T2-weighted MRI scan of the head for Patient 2. There is moderate enlargement of the lateral ventricles.* ***B)*** *Post-operative axial non-contrast computed tomography (CT) scan of the head. The shunt reservoir is visible in the right parieto-occipital area.*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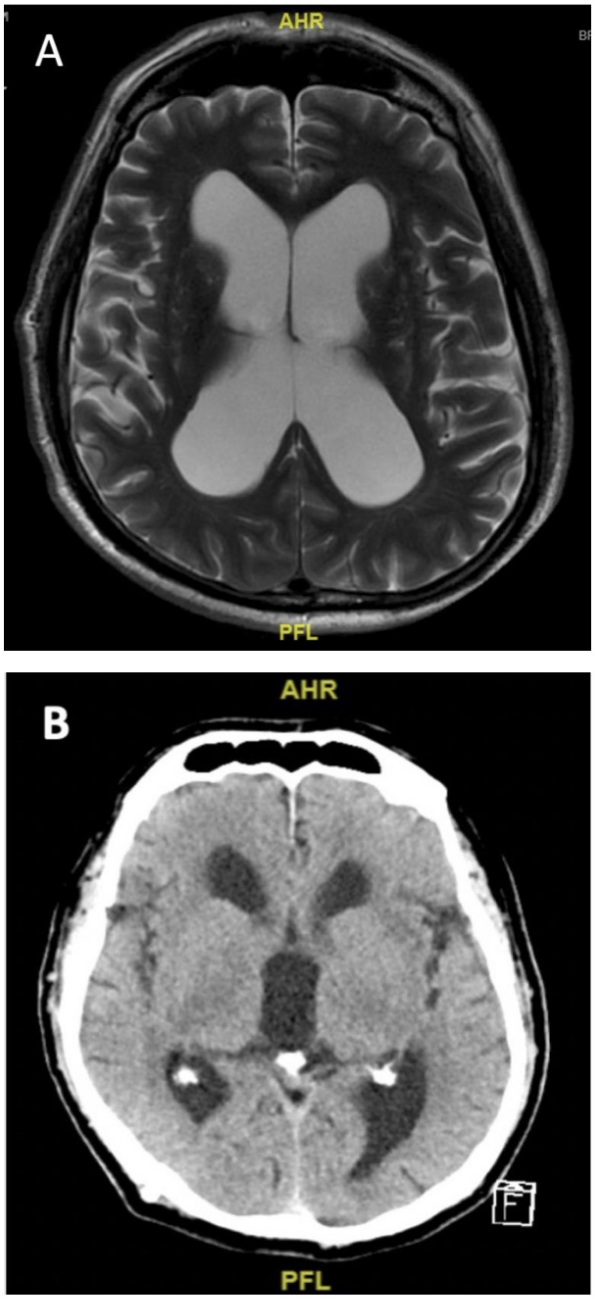
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ABBREVIATIONS: NPH = normal pressure hydrocephalus, iNPH = idiopathic normal pressure hydrocephalus, VP = ventriculoperitoneal, PDS = persistent developmental stuttering