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Please be Aware: Some Parkinson Plus Syndromes are Treatable

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Abstract

Background: Progressive supranuclear palsies (PSP) are usually considered untreatable with either medications or surgery.

Objective: Six patients who were being treated as PSP for some time are presented. Detailed clinical and radiological assessments were suggestive of normal pressure hydrocephalus (NPH).

Results: All of them underwent trial drainage lumbar puncture (LP) and showed very good improvement. All of them were then taken up for theco-peritoneal shunt. Four patients are doing well at follow up (upto 4 years). The Parkinson medications have been completely stopped. The other two are showing much better response to medications.

Conclusion: It may be a good idea to assess in detail both radiologically as well as clinically all patients with suspected PSP. An extensor planter is often a clue. If suspicious of NPH, a trial drainage LP (and shunt) may be worthwhile. Some patients not initially responding to drugs may do so after the shunt.

Keywords: *Parkinson Plus Syndromes; Normal Pressure Hydrocephalus; Surgery; Lumbar Puncture; Theco-Peritoneal*

Introduction

Progressive supranuclear palsy is a neurodegenerative disorder presenting with features like bradykinesia, rigidity, frequent falls, eye movement disorders, tremor, gait difficulties and urinary incontinence. Normal pressure hydrocephalus (NPH) presents with cognitive decline, gait difficulties and urinary incontinence and is treatable [1]. Krauss and others [2] reported a high incidence of movement disorders in NPH. In this study, few patients who were being treated as PSP syndromes were investigated in detail and found to be having NPH.

Materials and Methods

Our unit has an active DBS programme for Parkinson's disease and gets a good number of referrals for the same. It is out of this series of patients that the six cases were picked up. Five patients were men.

Patient A (68, Male) a retired government officer started noticing that his handwriting was becoming different. He was diagnosed as having Parkinson's disease and put on medications. For about two years he felt better but started deteriorating. His voice had become slow, with tremor of the right hand and he complained of occasional diplopia. He was diagnosed as having PSP. Unfortunately, no detailed radiological investigation was done. When patient was referred to us, a detailed clinical assessment showed rigidity of all the limbs with minimal pill rolling tremor and extensor plantar. He also had significant memory disturbances and was on a Foley's catheter for inconti-

nence. He underwent brain MRI which was suspicious of NPH. He was taken up for trial lumbar puncture (LP) drainage. Post procedure patient had very good improvement of his deficits. He underwent a theco-peritoneal (TP) shunt and is doing very well for the last four years.

Patient B (56 Male) was a ticket cashier in the Indian Railways. He first noticed some memory disturbances about three years back which was ascribed to aging. He then noticed that he was unable to turn in bed which affected his sleep. He started having difficulty in walking and slowed down. He also started falling backwards repeatedly and slowly developed dysphonia and nasal regurgitation. As the previous case he was put on treatment for many years without investigation. He also confirmed several episodes of incontinence during this period. During our assessments he was having memory disturbances with rigidity and bradykinesia. He underwent theco-peritoneal shunt as before and all his symptoms disappeared. He is doing well for more than five years now.

Patient C was a 53-year-old active banker who developed unilateral resting tremor of many years. He had a road traffic accident two years ago and from about the same time, he noticed difficulty in walking and had a few episodes of falling down backwards. His wife informed that his walking pattern has changed; now it has become much slower and with short shuffling steps. She also informed that he had wetted his bedclothes during sleep a few times. Clinical assessment showed memory affection with pill rolling tremor of both hands and bradykinesia and extensor plantar. He also underwent shunt and became normal. In fact, he went back to work in the bank for about three years and retired recently.

Patient D was a 62 year old woman. Her family members noticed that she is becoming slow and more forgetful. She also had multiple episodes of incontinence. She was also diagnosed as PSP and put on medications, but she had gradual deterioration. She had a tremor on the left hand initially, but it subsided with treatment. She was on dopamine but had no effect. She also underwent shunt and improved significantly. She is on follow up for 14 months now.

Patient E was a 68-year-old gentleman who was having tremor and incontinence along with other features of PSP. He was also having frequent falls, his speech was dysarthric and he had gaze paresis and extensor plantar. He had no effect with high dose anti Parkinson medications. He had trial CSF drainage after which he improved tremendously and ten shunt was done. His anti-Parkinson medications were stopped. However, he started developing tremor and rigidity of both hands and the drugs were restarted. This time he had very good results with the medicines and was very much better. He is on follow up for one year now.

Patient F (54, M) also had a similar history of being diagnosed as PSP. He also had no response to dopa drugs. He also underwent trial and then shunt was done. In the postoperative period he also had good response to dopamine drugs and became independent.

Results

All the six patients were diagnosed as progressive supranuclear palsy elsewhere and were being treated. However, none of them showed any benefit with medical management. Radiology was either not done or not critically evaluated in all these cases. Interestingly all patients had bilateral extensor plantar reflex. CT scans and MRI were done which showed features suggestive of NPH. All the patients underwent lumbar puncture drainage (30 - 60 ml) after which they had good improvement in the neurological status. All the patients underwent theco-peritoneal shunt. Two patients had almost immediate improvement in the tremor, rigidity and gait, one patient improved over one week and fourth over one month. The anti-Parkinson medications were stopped in all these four patients. The last two patients had only some improvement in the symptomatology but became much more responsive to anti-Parkinson medications.

Discussion

Progressive supranuclear palsy (PSP) is a progressive neurodegenerative disorder and has no definite treatment at the present time. It presents with features like tremor, rigidity etc. and so it is considered as a Parkinson plus disorder. It also presents with incontinence,

gait abnormality and cognitive decline and other features. Normal pressure hydrocephalus (NPH) on the other hand is a treatable disorder and presents with cognitive decline, gait abnormality and incontinence [1].

In 1987, Miodrag [3] presented a report of a 71-year-old lady presenting with progressive difficulty in walking, tremor of hands, frequent backward falls and incontinence. Clinical examination showed extensor plantar and cog wheel rigidity. CT scan showed dilated ventricles. She underwent ventriculo-peritoneal shunt and by eight weeks became normal. Krauss and coworkers [2] studied prospectively 118 adult patients with hydrocephalus. Among these 88 patients (75%) had additional movement disorders. Also 86% of patients with idiopathic normal pressure hydrocephalus had these movement disorders. Parkinsonism was found to be secondary to NPH in five patients and was found improved after shunting. They suggested that bradykinesia and other akinetic symptoms in NPH improved very much with shunting. A report by Masucci and Kurtzke [4] described that tremor may be the presenting complaint in PSP. They maintained that 12 - 16% of patients with PSP may have tremor. They concluded that tremor may be the presenting complaint and a prominent finding in PSP and the presence or absence of tremor is of no value in the differential diagnosis of PSP from Parkinson's disease. A similar observation was also published by Fujioka., *et al* [5]. They opined that tremor is an inconspicuous feature of PSP and 42% (146/344) of the PSP patients in their study presented some form of tremor.

Akiguchi and group [6] studied 17 patients with confirmed idiopathic NPH who underwent shunt surgery. Among these, 71% of patients had features of Parkinsonism. After surgery most features including gait abnormalities and bradykinesia as well as the radiological picture improved significantly. They concluded that idiopathic NPH could appear as a shunt-responsive type of Parkinsonism and reversible white matter lesions among the geriatric population.

Morishita, Foota and Okun [7] lamented how challenging it could be for the clinician to differentiate between Parkinson disease (PD) and idiopathic normal pressure hydrocephalus (INPH). They felt that patients with undiagnosed PD but with incidental ventriculomegaly run the risk of being subjected to unnecessary shunt surgery. The authors noted that a good family history including both motor and non-motor symptoms could be helpful. The authors also suggested a dopamine challenge test could be useful when in confusion.

Curran and Lang [8] presented nine cases of obstructive hydrocephalus associated with marked Parkinsonism. Three patients responded to levodopa well. Three cases responded to shunting well but later developed progressive Parkinsonism. Among these, one had clinical PSP, one had atypical features suggestive of PSP and one had PSP at autopsy. It was suggested by the authors that the pathophysiology of hydrocephalic Parkinsonism involves variable sites of dysfunction along the nigrostriatal pathway and/or the cortico-striato-pallido-thalamo-cortical circuit. At certain locations these pathways lie in close proximity to the ventricular system and may be subjected to mass effects and ischemic changes secondary to ventriculomegaly.

Weng, Yen and Lu [9] described SPECT studies in two patients with Parkinsonism syndromes with hydrocephalus. MRI showed communicating hydrocephalus. Patients did not improve with levodopa but improved after shunt placement. 99mTc-TRODAT-1 SPECT imaging revealed no significant reduction of 99mTc-TRODAT-1 uptake in both the caudate and putamen. The authors opined that 99mTc-TRODAT-1 SPECT imaging might be useful in differential diagnosis of Parkinsonism syndromes secondary to hydrocephalus. There was another case report of a patient [10] with hydrocephalus who developed levodopa responsive Parkinsonism from shunt malfunction which improved after revision.

Mandir and co-workers [11] speculated that NPH patients also have other signs of motor dysfunction. They performed an upper limb motor task battery where highly sensitive and objective measures of akinesia/bradykinesia, tone, and tremor were conducted. NPH subjects performed this test battery before and more than 36 h after continuous CSF drainage via a spinal catheter over 72 h and, in those subjects undergoing permanent ventriculo-peritoneal shunt placement, at least 12 weeks later. Twenty post shunt NPH subjects and 14 controls were included in the study The study Parkinson disease and Parkinson Plus Syndromes can be presented similar to idiopathic

Normal Pressure Hydrocephalus (INHP). Some minor differences can distinguish between them. For this reason, to safely diagnose Parkinson Syndrome, it is important to do a neuroimaging study. However, in Parkinson profile patients, a levodopa trial might can to be a useful diagnostic tool to differentiate between PD and INPH. It was concluded that clinical motor signs of NPH subjects extend beyond gait deficits and include extrapyramidal manifestations of bradykinesia/ akinesia, rigidity, and propensity to perform more poorly when external cues to move are absent. Objective improvement of some but not all of these features was seen following temporary or permanent CSF diversion.

Lobo Antunes, Fahn and Cote [12] presented three patients with both normal pressure hydrocephalus and Parkinson's disease. All patients had good response to shunting inspite of the Parkinson's disease. The authors opined that recognition of the existence of both disorders in the same patients is important since appropriate treatment of each of them led to marked improvement of their symptoms. We also had two such patients who started responding well to levodopa after the shunt.

There is another randomized prospective recent study from Broggi., *et al* [13]. They compared adjustable ventriculoperitoneal (VP) shunt insertion plus dopamine oral therapy (group A) versus VP shunt alone (group B) in patients affected by NPH associated with Parkinsonism. There were fifteen patients in each group. At follow up of 12 months they found that in patients with NPH and Parkinsonism, VP shunt plus dopamine oral therapy was highly beneficial.

There have been some studies on radiologically identifying NPH from other neurodegenerative disorders. These studies have described ways of differentiating NPH and Parkinsonism. The most recent study was by Miskin., *et al* [14]. They studied 36 shunt-responsive patients with normal-pressure hydrocephalus with age and sex-matched patients with Alzheimer disease (n = 34) and healthy control volunteers (n = 36). They found that callosal angle/Evans index measurements were upto 93.4% accurate in differentiating NPH from other conditions whereas volumetric predictors were 94.3% accurate. So, they concluded that the traditional callosal angle/Evans index method should be used as a screening tool in patients showing diagnostic dilemma between NPH and no NPH ventricular dilatation. Szczepek and coworkers [15] evaluated the volumetric changes CT scans in differential diagnosis of brain atrophy and normal pressure hydrocephalus using VisNow proprietary software. They found that the mean volumes of CSF in patients with NPH differed significantly from those with brain atrophy due to other causes. So, they have suggested using volumetric assessments with VisNow software in the evaluation of NPH and brain atrophy.

Another interesting study was published by Starr, Hagen and Espay [16]. They presented four patients with NPH like presentations. Of these three had autopsy proven PSP. All patients had gait impairment and oculomotor paresis with disproportionate ventriculomegaly. Shunt was not done in any of these three. The conclusions from this study were that hydrocephalus in the setting of postural impairment and/or oculomotor abnormalities most probably represent PSP. An initial promising response to VP shunt placement does not exclude the possibility of an underlying neurodegenerative disease. Recognition of the hydrocephalic presentation of PSP can avoid unnecessary and potentially harmful shunting.

In our study all patients had been diagnosed as PSP elsewhere clinically. Our assessments showed some evidence of pyramidal involvement in all patients. Radiology also showed out of proportion ventriculomegaly. We used the callosal angle/Evans index measurements in suspicious cases and then drainage LP followed by theco-peritoneal shunt. Four out of six patients have done very well during the last 4 - 5 years of follow up.

Conclusion

Please be aware that NPH may present with or coexist with Parkinsonism features causing problems in treatment. A good number of patients improve after shunt surgery and some become more responsive to medications. A detailed neurological assessment followed by appropriate radiology will help in short listing patients who may benefit from shunt procedures.

Disclosure

Informed consent has been obtained from the individual patients before writing this article. There is no conflict of interest and no funding received for this article.

Bibliography

1. Adams RD., *et al*. "Symptomatic occult hydrocephalus with "normal" cerebrospinal fluid pressure: A treatable syndrome". *New England Journal of Medicine* 273 (1965): 117-126.
2. Krauss JK., *et al*. "Movement disorders in adult hydrocephalus". *Movement Disorders* 12 (1997): 53-60.
3. Miodrag A., *et al*. "Normal pressure hydrocephalus presenting as Parkinson's syndrome". *Postgraduate Medical Journal* 63 (1987): 113-115.
4. Masucci EF and Kurtzke JF. "Tremor in progressive supranuclear palsy". *Acta Neurologica Scandinavica* 80.4 (1989): 296-300.
5. Fujioka S., *et al*. "Tremor in progressive supranuclear palsy". *Parkinsonism and Related Disorders* 27 (2016): 93-97.
6. Akiguchi I., *et al*. "Shunt-responsive parkinsonism and reversible white matter lesions in patients with idiopathic NPH". *Journal of Neurology* 255 (2008): 1392-1399.
7. Morishita T., *et al*. "INPH and Parkinson disease: differentiation by levodopa response". *Nature Reviews Neurology* 6 (2010): 52-56.
8. Curran T and Lang AE. "Parkinsonian syndromes associated with hydrocephalus: case reports, a review of the literature, and pathophysiological hypotheses". *Movement Disorders* 9 (1994): 508-520.
9. Weng YH., *et al*. "Parkinsonian Syndromes Associated with Hydrocephalus". *Annals of Nuclear Medicine and Science* 15 (2002): 97-102.
10. Racette BA., *et al*. "Pathophysiology of parkinsonism due to hydrocephalus". *Journal of Neurology, Neurosurgery, and Psychiatry* 75 (2004): 1617-1619.
11. Mandir AS., *et al*. "Extrapyramidal signs in normal pressure hydrocephalus: an objective assessment". *Cerebrospinal Fluid Research* 4 (2007): 7.
12. Lobo Antunes J., *et al*. "Normal pressure hydrocephalus and Parkinson's disease". *Journal of Neural Transmission. Supplementa* 19 (1983): 225-231.
13. Broggi M., *et al*. "Normal Pressure Hydrocephalus and Parkinsonism: Preliminary Data on Neurosurgical and Neurological Treatment". *World Neurosurgery* 90 (2016): 348-356.
14. Miskin N., *et al*. "Diagnosis of Normal-Pressure Hydrocephalus: Use of Traditional Measures in the Era of Volumetric MR Imaging". *Radiology* 10 (2017): 161216.
15. Szczepek E., *et al*. "Evaluation of volumetric changes in differential diagnosis of brain atrophy and active hydrocephalus". *Advances in Experimental Medicine and Biology* 840 (2015): 59-67.
16. Starr BW., *et al*. "Hydrocephalic Parkinsonism: lessons from Normal pressure Hydrocephalus mimics". *Journal of Clinical Movement Disorders* 1 (2014): 2-6.

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