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Parkinsonism associated with acute changes in ventricular size secondary to ventriculoperitoneal shunt malfunction

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Abstract

Background: Parkinsonism secondary to shunt malfunction and alterations in ventricular size is a rarely described phenomenon. We report a patient who developed pre-synaptic progressive parkinsonism as a complication associated with ventriculoperitoneal shunt placement and adjustment for symptomatic hydrocephalus caused by late-onset idiopathic, potentially, congenital aqueductal stenosis. Clinical findings of parkinsonism were deemed primary/pre-synaptic after dopamine transporter (DaTSCAN) imaging showed decreased putaminal binding. The patient responded to medical treatment with dopaminergic therapy. Here, we discuss possible mechanisms behind this complication, as well as the use of DaTSCAN in supporting her diagnosis.

Keywords

ventriculoperitoneal shunt; aqueductal stenosis; parkinsonism

Abbreviations

AQS: Aqueductal stenosis; ICP: Intracranial pressure; VPS: Ventriculoperitoneal shunt; NCHCT: Non-contrast head CT; MDS-UPDRS: Movement disorder society unified parkinson's disease rating scale; EEG: Electroencephalogram

Introduction

Parkinsonism is a clinical syndrome manifesting as a combination of decrementing bradykinesia, axial or limb cogwheeling rigidity, and the presence of a resting tremor [1-4]. Parkinsonism may be primarily due to progressive loss of dopamine-secreting neurons within the substantia nigra, associated with other neurodegenerative disorders or secondarily as a consequence of medication, ischemia, or trauma [3,5]. The development of parkinsonism secondary to neuroanatomical changes such as chronic subdural hematomas and brain tumors has been previously described [6-12]. Less frequently reported, however, are cases of parkinsonism associated with acute changes in ventricular size due to hydrocephalus, slit ventricles, or a combination of both [13-23]. We report a case of rapid-onset parkinsonism in a patient with aqueductal stenosis (AQS) secondary to dynamic changes in intracranial pressure (ICP) associated with recurrent ventriculoperitoneal shunt (VPS) failure

Case Presentation

A 47-year-old woman with a long-standinghistory of headaches presented with obtundation occurring after an acute gastrointestinal condition while traveling. Initial non-contrast head CT scan (NCHCT) revealed dilation of the lateral and third ventricles with a normal sized fourth ventricle, concerning for acute hydrocephalus secondary to AQS (confirmed with MRI, Figure 1a,b,c). She reported resolution of previous chronic headaches after VPS placement. Subsequently, over the course of a year, she experienced several episodes of progressively worsening altered visual acuity, dizziness, headaches, lethargy, nausea, and confusion. Repeated NCHCT during each episode showed ventricular dilation or slit ventricles, leading to VPS adjustments (Figure 1 d) and a gradual return to baseline.

Approximately 1.5 years after shunt placement, she once again presented with symptoms of shunt failure and, ultimately, underwent VPS replacement. Following revision, she experienced a three week period with visual impairment, progressive hypophonic dysarthria evolving to mutism, sialorrhea, and generalized bradykinesia.

Serial neurological examinations resulted in variable levels of hypersomnolence, abulia, akinesia, and mutism [24] improving to increased levels of alertness in which she could follow one-step commands, masked facies, hypophonic speech, and bradykinesia (both decrementing and non-decrementing). There was no notable motoric weakness or sensory anesthesia. She, intermittently, demonstrated a moderate frequency low amplitude asymmetric resting tremor. Cranial nerve examination revealed a supranuclear gaze ophthalmoparesis (vertical > horizontal, consistent with Parinaud Syndrome), bilateral lid retraction without papilledema. Additionally, she variably demonstrated generalized hyperreflexia, extensor plantar response, and frontal release signs. Scoring via Movement Disorder Society Unified Parkinson's disease rating scale (MDS-UPDRS Part 3) [25] revealed severe parkinsonism, (85/132) on part 3 (motor examination). Continuous electroencephalogram (EEG) was without epileptiform abnormalities and distortion of sleep-wake architecture without normal sleep periods.

Clinical improvements were sustained one and three months after discharge with convalescence to premorbid baseline. She was ambulatory without assistance and spontaneously conversant with recovered prosody. Examination still reveals minor restriction with upward vertical gaze, slight asymmetric Grade I/IV rigidity and diminished right-sided arm swing. MDS-UPDRS part 3, 7 hours since last levodopa dosing, was greatly improved (3/132).

Discussion

Multiple cases of parkinsonism secondary to hydrocephalus complicated by shunt failure have been reported [13-17, 19, 21-23, 27, 28]. Similar to our patient, parkinsonian features only manifested after VPS placement for symptomatic hydrocephalus. Prior to and during her hospitalization, serial NCHCT revealed acute changes in her ventricle size ranging from dilated ventricles to slit-like ventricles (Figure 1 d). Alterations in ICP stemming from VPS complications may lead to ventriculomegaly or slit-ventricle syndrome [29-31]. In slit-ventricle syndrome, CSF over-drainage results in a progressive decline of lateral ventricular size, proximal shunt obstruction, and ultimately an increase in CSF accumulation and ICP. Upon subsequent intervention to dilate the ventricle, the shunt can again function

properly. Repeated shunt adjustments may lead to over correction in either direction causing fluctuations in ventricular size and ICP and, arguably, alternating compressive and tensile stress on the surrounding parenchymal tissue either adjacent to lateral ventricles or across ventricular aqueducts.

The neuro-pathophysiologic mechanism(s) of secondary parkinsonism associated with changes in ventricular size have yet to be determined. Chronic compressive, tensile, and shearing forces at the striatopallidal level (basal ganglia structures such as the caudate, putamen, and globus pallidus are located at the caudolateral aspect of the lateral ventricles) and mesencephalic level (third ventricle) have been implicated. Recurrent compression and stretching of striatal tissue in response to ventricular dilation and shrinking may disrupt dopaminergic pathways, leading to symptoms of parkinsonism [27]. In these cases, the DaTSCAN is useful to visualize striatal dopaminergic transport by assessment of binding to presynaptic dopamine receptors. A loss of receptors is seen in degenerative parkinsonian disorders and is reflected in decreased tracer uptake. This is in contrast to drug-induced or vascular parkinsonism, which largely involves postsynaptic dopamine receptor blockade with intact presynaptic dopamine receptors, and therefore normal DaTSCAN tracer uptake [26,32,33] Anomalous DaTSCAN in pesons with presumed drug-induced or vascular parkinsonism are suggested to be due to an unmasking of latent disase.

A 9-year study published on the use of DaTSCAN for diagnosis of degenerative parkinsonism showed a specificity of 98.6%, sensitivity of 99.4%, positive predictive value of 98.7%, negative predictive value of 99.4%, and overall accuracy of 99.1% [26]. In our patient, DaTSCAN showed relatively decreased presynaptic dopamine transporter activity in the right putamen (Figure 2), similar to that seen in Parkinson's disease, where death of substantia nigra neurons decreases stimulation of putaminal presynaptic dopamine receptors. Succinctly, decreased dopaminergic innervation of the putamen disinhibits globus pallidus interna suppression of thalamic activity, contributing to hypokinesia and the development of an akinetic-abulic-mute catatonia-like state, particularly if preferentially involving limbic and associative regions of the striatum or thalamus [34-36].

Although a comprehensive characterization of cortico-subcortical network impairment in our patient is not possible, presynaptic dopaminergic dysfunction is apparent due to: DaTSCAN findings (substantia nigra), partial Parinaud Syndrome (dorsal midbrain), hyperreflexia (corticospinal pyramidal tract), and alterations in arousal and sleep-wake cycle (reticular activating system). Chronic pathway obstruction has also been associated with glutamatergic hyperactivity due to decreased inhibition via dopamine and frontostriatal GABA projections [37]. Ultimately, net glutamatergic inhibition either via positive GABAergic modulation (benzodiazepines), NMDA-receptor antagonism (amantadine) or indirectly via dopamine modulation (levodopa or dopamine agonists) may be most helpful [38-40]. Though large-scale clinical trials are lacking, this is supportive by functional imaging, historical data and anecdotally, as with our patient. As found in previous cases, stabilization of underlying etiology, ventricular size in our case, resulted in a reversible effect and cessation of medical therapy [19,27,28] Multiple studies have now endorsed the use of third ventriculostomy in the place of a shunt for treatment of hydrocephalus to prevent or even reverse parkinsonism by allowing for more ventricular stability [18,20,41].

Another cause of parkinsonismin our case may be due to decreased blood flow to the midbrain

and striatal structures in the setting of compression from ventricular expansion [22]. Our patient did have a ^{18}F Fluorodeoxyglucose Positron Emission Tomography scan, which did not show any clear focal deficits (images not shown). However, she had corpus callosum T2-weighted signal abnormalities on MRI (not shown), which has been described in previous reports of shunt-induced parkinsonism and may be indicative of focal vascular insufficiency [41-43]. If our patient did have some minor vascular compromise, dopaminergic treatment might have exerted a secondary vasodilatory therapeutic effect, allowing for increased intracranial blood flow [44,45]. Additionally, the chronic compression of striatal tissue from hydrocephalus before shunting may have caused subclinical (well-compensated in this relatively young patient) tissue damage, which may have been exacerbated by shunting and alternating size of the ventricles in the setting of shunt failure and multiple shunt adjustments/revisions. Over time, brain tissue becomes less compliant and more vulnerable to damage [41]. This may explain why the patient's symptoms progressively worsened with each adjustment, and why she was unable to recover after her last shunt adjustment.

Figures

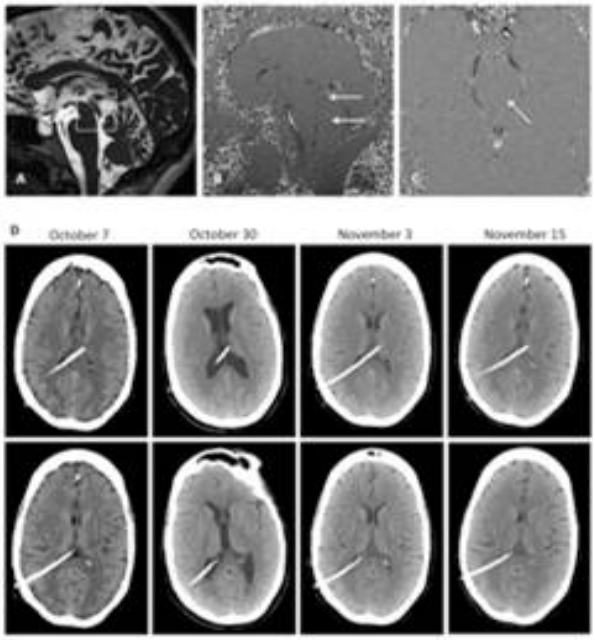

Figure 1: MRI CISS/CINE to support head CT findings of AQS. Sagittal CISS image shows focal obstruction of the cerebral aqueduct (box, A). Sagittal and axial CINE images show absent flow in the cerebral aqueduct (arrows B, C).Serial axial head CT scans showing significant changes in ventricular diameter over the course of 5 weeks (D). The patient received the last adjustment to her shunt valve after the CT scan on October 30. Treatment with dopaminergic therapy was initiated during the time that the last CT scan was completed.

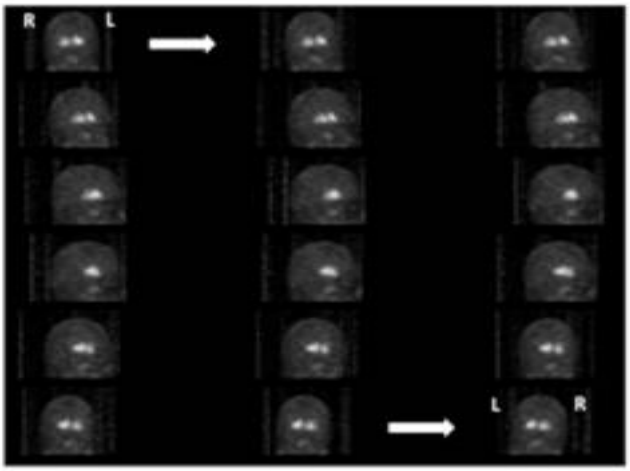

Figure 2: (^{123}I)Ioflupane or DaTSCAN 360 rotational images showing binding of radiotracer to presynaptic DaT receptors in the striatal region. The binding ratios were calculated suing GE DaTQUANT software (GE Healthcare, Little Chalfont, United Kingdom) and were as follows: right caudate 2.5, left caudate 2.72, right putamen 2.14, and left putamen 2.53. The decreased radiotracer binding activity in the right putamen relative to the left is supportive of a parkinsonian syndrome, although the calculated binding ratios are within normal limits.

Conclusion

The definitive diagnosis of an etiology of secondary parkinsonism is fraught with vagaries of available history and muddied phenotypically-similar clinical examinations with confounded volition, mood, and attention. In this setting of diagnostic dilemmas, psychogenic or functional disorders may often be implicated. Nonetheless, diligent review and pursuit of more objective findings often reveals subtle cortico-subcortical dysfunction rooted in fundamentals of neuroanatomy, physiology, and physics. This case nicely illustrates how VPS management can directly and indirectly modulate both regional and global neurological function.

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