

## GENE THERAPY

In PD, the selective degeneration of dopaminergic neurons from the SNc is coupled with the loss of dopamine synthesizing enzymes. The goal of gene therapy is to restore the ability of the brain to synthesize dopamine in the striatum. Packaging novel genes in to viral vectors and delivering them to brain is currently under active experimental evaluation. Adeno-associated Virus (AAV) has been most commonly used vector for such purposes. The potential genes are tyrosine hydroxylase (TH), L-amino acid decarboxylase (AADC), GTP cyclohydrolase (GCH1), glutamic acid decarboxylase (GAD), glial derived neurotrophic factor (GDNF) and neurturin.

## CONCLUSION

PD is a commonly encountered neurodegenerative disease with impaired voluntary movement and non-motor symptoms which results in severe impairment of quality of life. The cause of PD still remains unknown and treatment is symptomatic. Since the Levodopa revolutionised the care in 1960s there has been continuous advances in the medical and surgical fields to provide the clinicians a number of viable treatment options. Although this review is intended to highlight the newer and emerging advances in the treatment of PD, it is important to remember that new treatments are not necessarily better than the established conventional therapy and treatment options must be individualized.

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## Glioblastoma Multiforme Presenting as Parkinsonism.

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**Abstract :** This is a case report of parkinsonism secondary to intracranial tumor. Who presented with typical parkinsonian feature contralateral to the lesion. His imaging was suggestive of large glioma in right fronto-parietal region with mass effect. The mechanism for parkinsonism may be due to mass effect or direct infiltration into basal ganglia region. This case highlights that brain tumors can present with parkinsonian features and it also shows importance of imaging in patients presenting with parkinsonism to rule it out.

## INTRODUCTION

The cardinal symptoms of Parkinson's disease are akinesia, rigidity, resting tremor and impairment of the postural reflex<sup>1</sup>. As widely understood, parkinsonism is divided into idiopathic parkinsonism including Parkinson's disease and symptomatic parkinsonism with causative diseases. Symptomatic parkinsonism may have various causes, and one of the important cause is intracranial space occupying lesion (ICSOL). There are case reports mentioning the parkinsonism as the presenting feature or additional feature to

other focal neurological symptoms and signs. Here we are reporting an additional case of ICSOL (glioblastoma multiforme) presenting as parkinsonism.

## CASE REPORT

A 56-year-old male, non-diabetic, non-hypertensive, right handed, educated up to 12<sup>th</sup> standard, driver by occupation presented with one episode of generalized tonic and clonic seizure with tongue bite and urinary incontinence one month back at the time of presentation and tremulousness of left sided limbs and drooling from left angle of mouth of seven days duration. He had tremors in left hand which were present at rest but disappeared during activity. The tremor used to get aggravated during walking. There was no aggravation of tremor

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on approaching the target. He also noted tightness of left half of body with weakness on attempting to lift some heavy objects. There was no dragging of foot or difficulty in arising from squatting position. He also noticed slowness in his activity especially while using left hand. He experienced difficulty in buttoning and unbuttoning with left hand. For the last one week, he also complained of drooling of saliva and water as well as food material from the left angle of mouth while eating. There was no difficulty in closing left eye or facial numbness. There was no prior history of headache, vomiting, diplopia, dysphagia or forgetfulness. General physical and systemic examination was unremarkable. Neurologically he was conscious, cooperative and well oriented to time, place and person. All cranial nerves including optic fundii were normal except left supranuclear

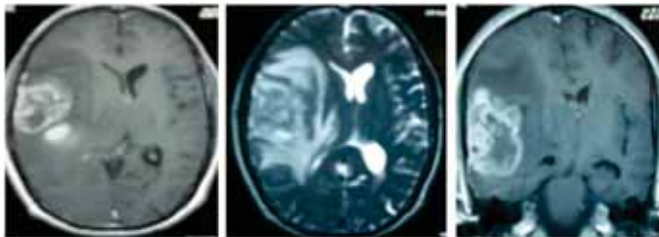


Figure 1,2,3: respectively T1 axial, T2 axial T1 contrast coronal showing heterogeneously enhancing mass lesion in right frontoparietal region with mass effect s/o glioglastoma.



Figure 4: Showing typical hypomimia.

facial nerve palsy. Motor system examination revealed coarse, high amplitude resting tremor in left hand and foot, bradykinesia on left finger and foot tapping, cogwheel rigidity at left upper and lower extremities with minimal weakness of left handgrip 4+/5(MRC grade). Motor power was 5/5 in rest of the muscle groups. Deep tendon reflexes were bilaterally symmetrical and normal (2+). Planter reflex was flexor on both sides. Sensory system examination was normal. There were no cerebellar signs. Gait was slow with reduced left arm swing and prominent left forearm and hand tremors. Routine hematological and biochemical investigations were within normal limits. Chest skiagram revealed no radiological abnormality. Electrocardiogram showed normal sinus rhythm. Magnetic resonance imaging (T1, T2, Flair, contrast) of brain revealed large heterogeneously enhancing mass lesion in right fronto-parietal region midline shift to left. Magnetic resonance spectroscopy suggested malignant pathology (Fig 1 to 4).

## DISCUSSION

Structural lesions of the basal ganglia are well recognized which leads to various extrapyramidal symptoms<sup>2</sup>. Most of these cases have

been due to hemorrhages, infarction or tumors. Tumors may produce parkinsonism either by pressure on the basal ganglia<sup>3,4</sup> or more rarely by direct infiltration<sup>5,6</sup>. Kondo and colleagues<sup>7</sup> in their review paper entitled as 'brain tumor and parkinsonism' proposed 6 reasonable mechanisms: 1. Direct oppression to the basal ganglia of the tumor itself; 2. Distortion and stress to the midbrain; 3. neuronal loss in the substantia nigra by the tumor invasion; 4. involvement of the basal ganglia by the deep-seated tumor; 5. damage of the fiber connection between the basal ganglia and supplementary motor area; 6. old age. Extra-axial masses impinging on the basal ganglia appeared to be more common than infiltrating lesions<sup>5</sup>. Several authors have shown the reversibility of clinical findings after resection of the tumour which caused compression and displacement of the basal ganglia structures rather than infiltration or destruction<sup>5</sup>.

In our case parkinsonism manifested along with preceding history of generalized tonic and clonic seizure. In the review paper by Kondo<sup>7</sup>, 44% of the patients with brain tumor presenting parkinsonism began at only parkinsonism and the half began at parkinsonism with or without other symptoms. The presenting manifestation depends upon the size, nature and location of the lesion. In our case considerable size of lesion with surrounding edema and midline shift might be the reason for the other neurological manifestation in addition to parkinsonism. Yasuhara<sup>8</sup> in their review found 16 recent case reports of parkinsonism related to brain tumor and the pathology were- 8 gliomas (including 2 gliomatosis cerebri), 2 meningiomas, 2 malignant lymphomas, 2 angiomas, 1 craniopharyngioma, 1 primitive neuroectodermal tumor (PNET). In our case imaging was suggestive of glioblastoma multiforme, but histopathological confirmation was not done. In our case parkinsonism was contralateral to the lesion as reported by other authors<sup>5,6</sup> but importantly ipsilateral parkinsonism has also been reported. Oliver<sup>9</sup> and Kulali et al<sup>10</sup> reported two patients who presented with an ipsilateral resting tremor and rigidity due to a parieto-occipital and a thalamic glioma respectively. The explanation for ipsilateral sign given was the parkinsonism in these cases were not due to direct pressure on or invasion of the basal ganglia but were due to midbrain compression from upward or downward herniations displacing the midbrain against the tentorial edge.

## CONCLUSION

Our case report suggest that intracranial tumor can present with parkinsonism as in earlier case reports and it also showed the importance of imaging in patients presenting with parkinsonism as when symptoms of parkinsonism occur in a patient with intracranial tumour, it is not uncommon to make an incorrect diagnosis of Parkinson's disease.

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