

Large left posterior fossa meningioma presenting with quadriplegia in a woman with history of carbidopa-levodopa resistant parkinsonism

Antonio Jose Reyes,¹ Kanterpersad Ramcharan,² Maria Alvarez,³ Wesley Greaves,⁴ Fidel Rampersad⁵

¹Neurology Unit, San Fernando Teaching Hospital; ²Department of Medicine and ⁵Radiology Unit, Surgi-Med Clinic; ³Department of Neurosurgery, San Fernando Teaching Hospital; ⁴Department of Pathology and Laboratory, San Fernando Teaching Hospital, Trinidad and Tobago, West Indies

Abstract

A 56-year-old Afro-Trinidadian woman with a history of a carbidopa-levodopa resistance Parkinsonian-like syndrome for 2 years, presented with acute onset spastic quadriplegia and decreased responsiveness. Diagnosis involved clinical and MR-imaging correlation consistent with a large left posterior fossa meningioma. Surgical removal of the tumor led to complete reversibility of the neurological manifestations associated with cerebellar tonsillar herniation beyond the foramen magnum and mass effect on the brainstem, cerebellum and midbrain regions. Pathological findings were typical of a meningioma. This case demonstrates the association of a large left posterior fossa meningioma and carbidopa-levodopa resistant parkinsonism in an Afro-Trinidadian woman who presented with acute onset acute quadriplegia and decreased responsiveness. This case reminds clinicians that patients with dopa unresponsiveness and/or acute neurological deficit or deterioration should be worked up for other possible causes and adds to the literature on the association of parkinsonism and intracranial space occupying lesions.

Introduction

Brain tumors including meningioma are seen in patients with Parkinsonism and Parkinson's disease (PD).¹ Certain identified genetic abnormalities associated with meningioma and other brain

tumors suggest potential genetic linkage with PD as well.^{2,3} We document a case of concurrent Parkinsonism and meningioma that manifested in a woman with acute quadriplegia and decreased responsiveness where surgery was successful despite the presence of cerebellar tonsillar herniation.

Case Report

A 56-year-old Afro-Trinidadian woman was brought to the accident and emergency department of hospital with acute onset of paralysis which began in both lower limbs and spread to involve the both upper limbs in a period of 3 days and was associated with decreased responsiveness for 1 day. She was attending the neurology outpatient clinic at another hospital where based on her two-year history of uncomplicated stage II (Hoehn and Yahr) Parkinson's disease (PD) characterized by bradykinesia, rigidity, bilateral upper tremor more prominent in the right side, and cogwheel rigidity at the wrists, she was eventually diagnosed as having a Parkinson-plus syndrome with poor response to carbidopa-levodopa (25-100 mg) orally three times daily and trihexyphenidyl HCL 2 mg orally three times daily.

There was also a history of paroxysmal vertigo, tinnitus, mild subjective hearing loss, and worsening gait disturbances for 6 months. Brain imaging or other investigations to clarify this vestibulocerebellar syndrome had not been done previously. She had no children, personal history of other medical disease or surgical procedures, or exposure to chemicals, ionizing radiation, recreational drugs, alcohol or smoking. There was no family history of neoplasm or neurological diseases.

On initial examination she was afebrile (37.3°C), anicteric, tachycardic (110 beats per minute) and normotensive (140/70 mm Hg). Her oxygen saturation was well maintained on room air (100%) and she was not tachypneic (20 breath per minute). Patient's body mass index (BMI) was 32 units per kg/m². Examination revealed a Glasgow Coma Scale of 10/15 with disorientation to time and place but not to person. Parkinson's facies, right VI nerve palsy and global weakness were observed. Power score in all limbs was 0/5 according to the Medical Research Council scale which compromised the undertaking of diadochokinesis and finger-nose-finger tests. *Hyperreflexia* was present in all limbs. Babinski's sign was

Correspondence: Antonio Jose Reyes, Neurology Unit, San Fernando Teaching Hospital, Independence Avenue, San Fernando, Trinidad, West Indies. Tel.: +18687221270. E-mail: reyesax@yahoo.com

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Contributions: The idea for reporting this case was that of AJR and KR. AJR drafted the first draft of the manuscript. Further intellectual content and editing was done by AJR, KR, MA, WG and FR. FR also provided advice on selection and interpretation of the radiological images. MA performed the tumour surgical removal. WG prepare the histopathology aspect of the case. All authors saw, edited and approved the final contents. KR assumes responsibility for the integrity of the contents.

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negative bilaterally with horizontal gaze nystagmus positive to the left. Neck rigidity was found with Kernig and Brudzinski signs negative bilaterally. Other cranial nerves and sensory system were intact. The rest of the physical examination was normal.

Extensive investigations for infectious, autoimmune, and metastatic diseases were negative. Cerebral Magnetic Resonance Imaging (MRI) showed a solid, well circumscribed T2 isointense, left posterior cranial fossa extra-axial mass, measuring 3.7×3.5×4.0 cm, arising from the left cerebellopontine angle, causing cerebellar tonsillar herniation of 6 mm beyond the foramen magnum, best seen in a midline sagittal T1 weighted view (Figure 1A). This compresses the

left cerebellar hemisphere and brainstem, best seen in T2 weighted coronal and T2 weighted axial views (Figure 1B,C), and midbrain distortion seen in T1 weighted and fluid-attenuation inversion recovery weighted axial views (Figure 1D,E). The mass was homogeneous in appearance, likely benign and enhanced homogeneously upon administration of intravenous Gadolinium. Magnetic Resonance Angiography scan (cerebral MRA scan) was normal. PET CT scan was unavailable.

The tumor was surgically removed, histology and immunohistochemistry were consistent with a meningioma (Figure 2).

There was a slow progressive good postoperative recovery within 14 days of ICU/High Dependency Unit care. Mechanical ventilatory support was given for 10 days. She received 7 days intravenous (IV) Vancomycin 1 g three times daily for a Hospital-Acquired Pneumonia with a positive methicillin resistant coagulase negative staphylococcus growth from tracheostomy secretion sampled. Hospital-Acquired Pneumonia was satisfactory resolved. After that she was gradually alert and oriented. She was discharged 21 days after admission on carbidopa-levodopa (50-200 mg) orally three times daily for outpatient clinic follow up. Figure 3A, a T2 weighted MRI axial view showed post-surgical tumor cavity with edema and an extra axial fluid collection posterior to the cerebellum. The patient's hand writing at admission was illegible (Figure 4A) but it improved 6 weeks after surgical intervention (Figure 4B). Figure 3B, a T1 weighted MRI axial view of the brain showed post-surgical tumor cavity 3 months later, with resolution of the extra-axial collection. Although, parkinsonism persists despite tumor removal and postsurgical treatment, the patient improved, walking without support 3 years later. She remains oriented to time, person, and place with a Glasgow Coma Scale of 15/15. Currently, 8 years later, she is at stage II (Hoen and Yahr), with persistent tremor but no vertigo, tinnitus, hearing loss, VI nerve palsy, nystagmus or significant gait disturbances. However, most differential diagnosis was ruled out (Table 1) with no evidence of autonomic neuropathy or features of progressive supranuclear palsy, multisystem atrophy or corticobasal degeneration.

Discussion

Parkinson's disease (PD) is a progressive and chronic non-communicable degenerative disorder of the central nervous system clinically characterized by four main types of movement disorders: a) Tremor: Trembling in the hands, arms, legs, jaw and/or head; b) Rigidity: Stiffness of the limbs and trunk; c) Bradykinesia: Slowness of movement; and d) Postural instability: impaired balance. These symptoms usually begin gradually and worsen with time. As they become more pronounced, patients may have difficulty walking, talking, or completing other simple tasks.¹⁻⁵ There are a variety of different causes of parkinsonism including PD, secondary parkinsonism, and the parkinsonism plus syndromes. Secondary parkinsonism is caused by structural, toxic, metabolic, or infectious mechanisms. Among structural causes, intracranial neoplasms are a rare cause of secondary parkinsonism.^{1,2,6}

In recent years, increasing amount of epidemiological evidence points to a positive association between PD and cancers through several common genetic mutations in SNCA, PARK2, PARK8, ATM, p53, PTEN, and MC1R resulting in cellular changes such as mitochondrial dysfunction, aberrant protein aggregation, and cell cycle dysregulation. Genes multiple mutations associated to PD and neoplasm implies environmental and occupational factors involved. Although some cases of PD are hereditary and can be traced to specific genetic mutations, most cases are sporadic. PD and parkinsonism likely result from a combination of genetic susceptibility and exposure to one or more environmental factors that trigger the diseases. PD and neoplasm genetic-environmental links are poorly understood globally and cost-efficient therapeutic approaches for these cases remain unexplored.^{1,2,4,5,7}

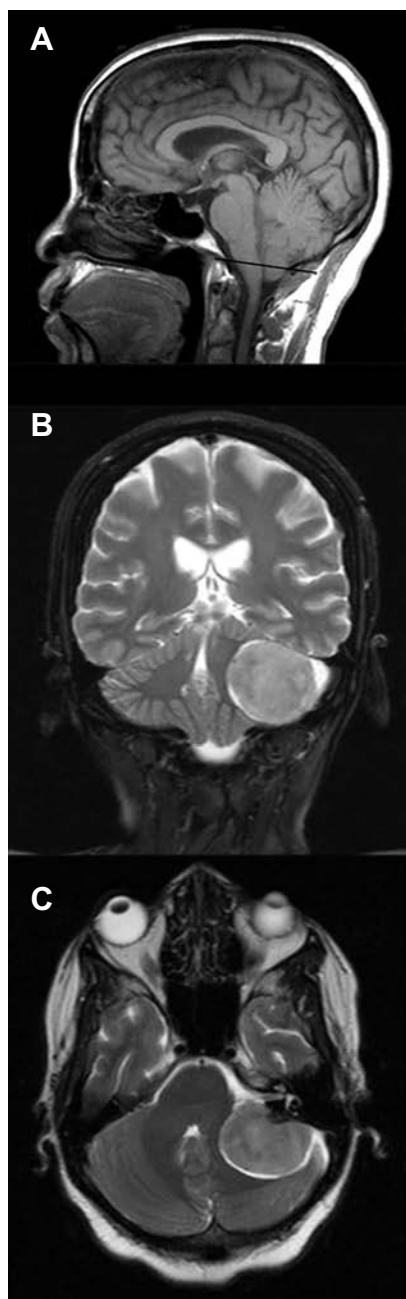
Epidemiological data support the increased risk of melanoma or breast cancer in patients with PD.^{1,6} On the other hand, the methylazoxymethanol metabolite formaldehyde is linked to the risk for PD, prostate cancer, and skin cancer, including melanoma.^{6,8-11} Depending on location, histology and extension of infiltration, any brain tumor has the potential to cause Parkinsonism. In brain neoplasm the cells reproduce out of control and fail to die but in PD the neurons that release the neurotransmitter dopamine in the substantia nigra region of the brain die. The main risks factors for brain tumors and/or

Parkinsonism are shown in Table 1.¹⁻¹¹ Reasons for these associations remain unknown.

Some cases of Parkinsonism may be associated with arterial compression of the cerebral peduncle by the posterior cerebral artery which may be seen on MRI studies. Improvement and prolonged relief of PD and/or parkinsonism in those patients may be possible in certain circumstances by the use of microvascular decompression of the brainstem.¹²

Meningioma is the second most common intracranial tumor and has been shown to demonstrate heterogeneous clinical features according to tumor size and location. Most meningiomas are slowly growing and result in benign clinical outcomes, but only 20% exhibit clinically aggressive features.

Although it is rare for intracranial space-occupying lesions to present with a Parkinsonism, a few cases of parkinsonism due to meningioma have been reported.¹⁻¹¹ Parkinsonism has been associated with space occupying lesions in the frontal lobe, temporal lobe, parietal lobe, septum pellucidum, brainstem, parasagittal region, suprasellar and sphenoidal wing regions. Kajijima *et al.*, reviewed 58 cases of Parkinsonism associated with intracranial space occupying lesions, out of which 8 were infiltrating gliomas involving thalamus, basal ganglia or mid-brain.¹³ Four supratentorial tumor sites are described in literature as being located in the frontal lobe, temporal lobe, parietal lobe and thalamus.^{14,15} An extensive review showed that almost all reported extrinsic occupying space lesions of the brain have been meningiomas in these patients. Gliomas and metastatic tumors in the frontal lobes have also been associated with Parkinsonian tremor. Subdural hematomas have also been reported producing Parkinsonism.¹⁶ Midline extrinsic lesions of the brain producing movement disorders are even more rare. Among them are anterior third ventricular meningioma, pituitary adenoma and cranio-pharyngioma.¹⁶ Rarely parkinsonism may be seen due to posterior fossa lesions.¹⁶⁻²⁰ Nearly all symptoms are possibly produced by compression of basal ganglia.¹²⁻²⁰ Quadriplegia and possibly Parkinsonism in our patient could have occurred secondary to peritumoral edema, compression due to mass effect, raised intracranial pressure, transient tumoral attack, blood flow changes induced by the mass effect, or a combination of some of these factors. The most likely cause of the quadriplegia in our patient was due to cerebellar tonsillar herniation into the



upper cervical canal from increased intracranial pressure, edema and/or mass effect. The cerebellar tonsil involved moved downward through the foramen magnum possibly causing compression of the ventral region of the lower brainstem and upper cervical spinal cord as they pass through the foramen magnum (Figure 1). This is a life-threatening condition as it causes increased pressure on the medulla oblongata which contains respiratory and cardiac control centers. Cases of limb weakness due to meningioma in the vicinity of the foramen magnum, or located in the clivus-anterior to the medulla, or in the left frontoparietal

region of the brain, have been reported.²⁰ We believe that a combination of cerebellar tonsillar herniation, and compression of brainstem and midbrain caused most of the acute and subacute symptoms and signs in our patient. Complete rapid reversibility of those clinical manifestation after removal of the tumor without recurrence of limb weakness or decreased responsiveness 8 years after surgery are also in keeping with that hypothesis. Furthermore, the Parkinsonism has not progressed.

Efficient treatment involved several disciplines spanning the medicine-surgery spectrum and both secondary and tertiary

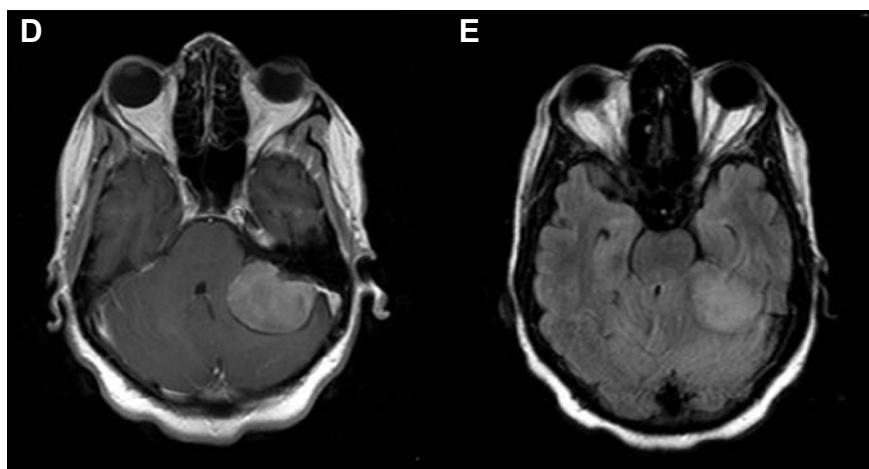


Figure 1. A) Middle Sagittal T1 weighted MRI image showing cerebellar tonsillar herniation of 6 mm, determined by extension beyond a reference line from the bastion to opisthion. B) T2 weighted MRI coronal view of the brain demonstrating a solid T2 isointense left cerebellopontine angle mass, measuring 3.7×3.5× 4.0 cm, with mild compression of the brainstem. C) T2 weighted MRI axial view showing the posterior fossa tumor in the left cerebellopontine angle compressing cerebellum. D) T1 weighted MRI axial post intravenous Gadolinium administration demonstrating homogeneous enhancement of the left cerebellopontine angle mass, which is a typical feature of a meningioma. There is no extension to the left internal auditory meatus to suggest an acoustic neuroma. E) Fluid-attenuated inversion recovery MRI axial view of the brain showing left posterior fossa tumor with mild distorted midbrain.

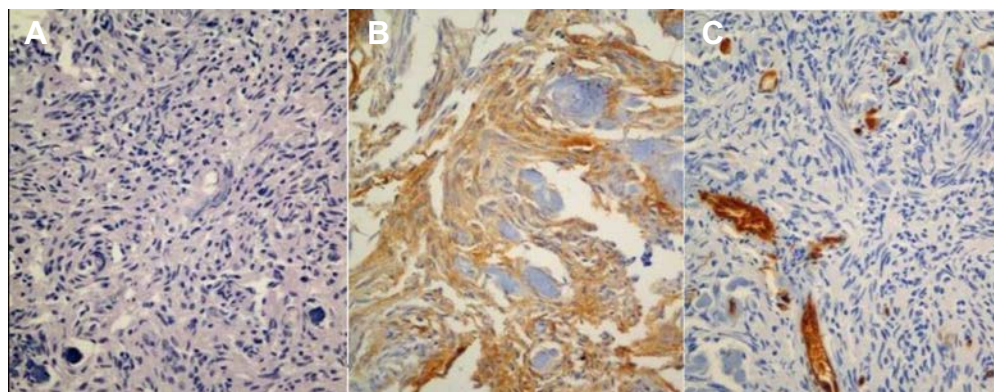


Figure 2. A) Photomicrography (Magnification 100x) of the posterior fossa tumor with routine H&E staining showing a spindle cell tumor with a somewhat whorled growth pattern typical of meningotheial meningioma. B) The tumor cells were positive for Epithelial Membrane Antigen expression by immunohistochemistry. C) Tumor cells were negative for CD34 and S-100, thus ruling out solitary fibrous tumor and schwannoma respectively.

care. Potential surgical reversibility of the neurological manifestations associated to the brain tumor, poses an imperative for early diagnosis and management. PD is the most common form of Parkinsonism, the name for a group of disorders with similar features and symptoms. No more than one in 1,000 diagnoses of PD are in reality parkinsonism due to an unrecognized neoplasm, especially prostate cancer, melanoma and brain tumors.^{1,2,4,5,6,18-20} Neuronal loss in the substantia nigra, compression to the basal ganglia, distortion to the midbrain and basal ganglia, brain network disturbances between the basal ganglia and supplementary motor area, and old age have been implicated.¹ Our patient clinical presentation with acute onset quadriplegia, decreased responsiveness, and a previous short history of PD stage II (Hoehn and Yahr) with bilateral parkinsonism affecting more the right side of the body with poor response to carbidopa-levodopa and rapid neurological deterioration, should have suggested the presence of a space occupying lesion of the brain. Global hyperreflexia with horizontal gaze nystagmus to the left and right VI nerve palsy should have also prompted a brain scan imaging study. Although patient clinical deterioration could have been wrongly attributed to progressive

PD, the previous history of paroxysmal vertigo, tinnitus, mild subjective hearing loss, and worsening gait disturbances for 6 months, were in keeping with a cerebello-

pontine angle mass or schwannoma. Under this circumstance, the brain scan imaging study could have been done 6 months previously to the acute onset quadriplegia and

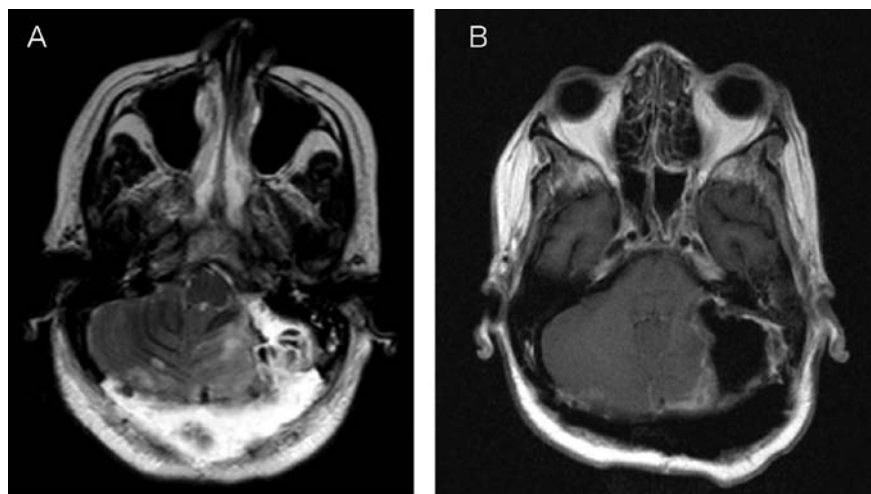


Figure 3. A) T2 weighted MRI axial view of the brain showing post-surgical tumor cavity, with edema and an extra axial fluid collection posterior to the cerebellum. B) T1 weighted MRI axial view, post intravenous Gadolinium, showing post-surgical tumor cavity, without edema. Post-surgical enhancement is seen in the tumor bed. No residual or extra axial fluid collection was seen.

Table 1. Main risks factors for brain tumors and/or parkinsonism.

Risk Factor	Tumors	Common Causes
Exposure to ionizing radiation	Meningiomas, sarcomas, and malignant gliomas	DNA mutations: Substitutions and frameshift mutations at any level
Von Recklinghausen disease	Schwannomas, gliomas, meningiomas, neurofibromas	Changes in the NF1 gene
Neurofibromatosis type 2	Bilateral or unilateral vestibular schwannomas, meningiomas	Changes in the NF2 gene
Von Hippel-Lindau disease	Hemangioblastomas of the Central Nervous System (CNS), eye, ear, kidney, adrenal gland, and pancreas	Changes in the <i>VHL</i> gene
Li-Fraumeni syndrome	Gliomas, breast cancer, sarcomas, leukemia, adrenal gland cancer, among other types of cancer	Changes in the <i>TP53</i> gene
Tuberous sclerosis	Astrocytoma, benign tumors of the brain, skin, heart, , kidneys and other organs	Changes in either the <i>TSC1</i> or the <i>TSC2</i> gene
Gorlin syndrome, Turcot syndrome and Cowden syndrome	CNS Tumors	Changes in genes: <i>PTCH</i> , <i>APC</i> , <i>MLH1</i> , <i>PMS2</i> , <i>PTEN</i> , <i>SDHB</i> , <i>SDHD</i> , and <i>KLLN</i>
Impaired immune system	Lymphomas of the brain	Acquired immunodeficiency syndrome (AIDS)
Drugs	No tumors but parkinsonism	Phenothiazine, chlorpromazine, prochlorperazine, perphenazine, fluphenazine, promethazine, butyrophenones, haloperidol, diphenylbutylpiperidine, pimozide, benzamide substitute, sulpiride, risperidone, olanzapine, ziprasidone, aripiprazole, reserpina, tetrabenazine, metoclopramide, levosulpiride, clebopride, flunarizine, cinnarizine, lithium, clozapine, quetiapine, valproic acid, phenitoina, domperidone, itopride, fluoxetine, sertraline, paroxetine and citalopram
Suspected but unproven risk factors	CNS tumors	Organic solvents and other hydrocarbons, zinc, paraquat, rotenone, maneb, manganese, MPTP (1-methyl 4-phenyl 1,2,3,6-tetrahydropyridine), toluene, N-hexane, carbon disulfide, carbon monoxide, mercury, cyanide, copper, lead, trichloroethylene, household paint, varnishes and garden sprays, cell phones, vinyl chloride and aspartame

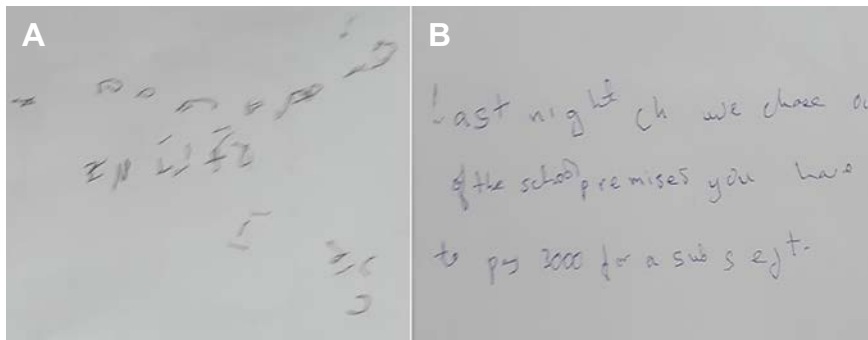


Figure 4. Patient hand writing illegible before (A) and six weeks after surgery (B) showing improvement.

decreased responsiveness when the tumor was smaller but detectable. MRI scan images showing a large left cerebellopontine angle tumor with brainstem and midbrain distortion, compression of the cerebellum with cerebellar tonsillar herniation were in keeping with the clinical manifestations in our patient. T1 weighted axial post IV Gadolinium administration demonstrated homogeneous enhancement of the left cerebello-pontine angle mass, which is a typical feature of a meningioma. There was no extension to the left internal auditory meatus to suggest an acoustic neuroma (Figure 1D). Previously responsive or unresponsive PD patients with unexpected deterioration despite conventional treatment should prompt reevaluation for new underlying disease preventing late diagnosis.

Conclusions

In conclusion, we report a rare case of a large left posterior fossa meningioma in an Afro-Trinidadian woman with carbidopa-levodopa resistant parkinsonism who presented with acute onset quadriplegia and decreased responsiveness. We highlight the surgical removal of the tumor that led to complete permanent reversibility of the neurological manifestations associated to the cerebellar tonsillar herniation into the foramen magnum, mass effect on the brainstem, midbrain region and cerebellum previously correlated by clinical findings and MRI studies. This case reminds clinicians that Parkinsonian-like patients with dopa unresponsiveness and/or acute neurological deficit or deterioration should be worked up for other possible causes.

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