Reversible parkinsonism due to a large intracranial tumour

Helena Rocha,[1,2] António Cerejo,[2,3] Maria Carolina Garrett,[2,4] João Massano[2,4]

[1]Department of Neurology, Centro Hospitalar de São João, Oporto, Portugal
[2]Department of Clinical Neuroscience and Mental Health, Faculty of Medicine University of Porto, Porto, Portugal
[3]Department of Neurosurgery, Centro Hospitalar de São João, Oporto, Portugal
[4]Movement Disorders and Functional Surgery Unit, and Department of Neurology, Centro Hospitalar de São João, Oporto, Portugal

Correspondence to
Professor Maria Carolina Garrett,
garrett.mc51@gmail.com

To cite: Rocha H, Cerejo A, Garrett MC, *et al*. *BMJ Case Reports* Published online: 24 December 2012 doi: 10.1136/bcr-2012-007823

SUMMARY

A 77-year-old woman presented with progressively worsening apathy, depression, urinary incontinence and slowness of movement for the past 1 year. Asymmetric akinetic-rigid parkinsonism and mild left-sided hyperreflexia were seen on examination. No ocular movement impairment, cerebellar or sensory signs were noticed. Routine laboratory testing was normal. Brain imaging revealed a large frontal tumour which was subsequently excised and pathologically confirmed as a meningioma. Marked clinical improvement was documented 3 months after surgery, and persistent clinical and imaging remission have been confirmed annually for the following 3 years. There have been some reports of parkinsonism associated with intracranial tumours. Although this is probably an uncommon situation, it is potentially treatable, and symptoms might even remit completely following successful management.
Parkinson's disease is a common cause of parkinsonism, but alternative aetiologies should be suspected whenever atypical findings are demonstrated by clinical history or examination.

BACKGROUND

Parkinson's disease (PD) is a very common cause of parkinsonism, but suspicion about possible alternative aetiologies should be raised whenever atypical clinical findings are uncovered,[1–3] especially because some disorders require specific therapeutic interventions and might be potentially reversible. First, accurate medical history taking is paramount in defining when and which symptoms emerged and their clinical course. Motor features, as well as non-motor features, if present, may be useful clues for correct diagnosis.[1 4] Drug-intake history, especially with regard to the drugs which are able to cause parkinsonism is also important.[5] Mental state and cognition, eye movements and pyramidal and cerebellar functions should be carefully explored. Carefully selected examinations might guide the clinician to the correct diagnosis,[1] therapy and prognosis. These aspects are important for both experts and non-experts in the field, due to the implications of the diagnosis of PD and other parkinsonian disorders.[6] Intracranial tumours are an uncommon, albeit treatable and potentially reversible, cause of parkinsonism.

CASE PRESENTATION

A 77-year-old woman presented in 2009 with progressively worsening apathy and slowness of movement for the previous year. Her daughters reported that she had always been perfectly autonomous, and a very active and cheerful person. The family had attributed these symptoms to the death of her husband and subsequent depressive mood. Continuous urinary incontinence, of which the patient was unaware, had also recently emerged. By this time, she would need some supervision and prompting with regard to her hygiene, needed occasional assistance with financial management and had been prevented from driving by her children, who had become apprehensive with this change. On examination, she was alert and cooperative. There was clear psychomotor slowing, and reduced verbal initiative (5 animals in 1 min) were also observed, although verbal fluency was apparently intact during conversation; Mini Mental State Examination was 28/30. Left-sided moderate rigidity, bradykinesia and reduced arm swing were noticed (video 1), as well as slight left-sided osteotendinous hyperreflexia. No other particular clinical findings could be seen; eye movements (pursuit and saccades) were full range, with normal speed, latency and accuracy. She admitted mild depressive symptoms, with normal appetite and sleep. Her medical and drug-intake history were unremarkable. Brain imaging disclosed a large right frontal intracranial neoplasm of apparent meningeal origin (figure 1). Surgery was offered on an elective basis and carried out 4 weeks later. Apart from mild postsurgical pain for a few days, there were no short or long-term complications. Thorough pathological examination confirmed a large meningothelial meningioma (WHO grade 1).

INVESTIGATIONS

Blood tests were within normal range, namely, complete blood count, serum ions, creatine, urea, fasting glucose, bilirubin, liver enzymes, thyroid-stimulating hormone and C reactive protein. This excluded treatable conditions which might cause slowness or fatigue (thus mimicking bradykinesia) such as anaemia, hypothyroidism or renal failure. Cranial CT disclosed a large right frontal intracranial tumour with surrounding oedema and causing displacement of the right striatum. Subsequently, brain MRI has been conducted for further detailing lesion characteristics (figure 1). Imaging findings favoured the diagnosis of meningioma.

DIFFERENTIAL DIAGNOSIS

Parkinson's disease; normal pressure hydrocephalus; vascular parkinsonism; intracranial tumour (especially if located in the frontal region).

TREATMENT

The tumour was removed surgically on an elective basis. No antiparkinsonian drugs have been tried.

Video 1 Preoperatively, there is left-sided bradykinesia, here observed in the upper limb. There is reduced left-arm swing during walking. Three months after tumour removal, the gait is normal, and arm swing symmetrical (consent was obtained from the patient for video capture and publication).

OUTCOME AND FOLLOW-UP

Marked clinical improvement, with regard to parkinsonism and apathy, has been seen a few days after the neurosurgical procedure. The patient has been assessed clinically at 3 months, 6 months, 1 year, 2 years and 3 years, after surgery. Persistent symptom remission, including apathy, urinary incontinence and parkinsonian signs, have been documented 3 months after surgery (video 1) and her clinical condition remains stable 3 years after surgery. Annual follow-up brain MRI has excluded neoplastic resurgence.

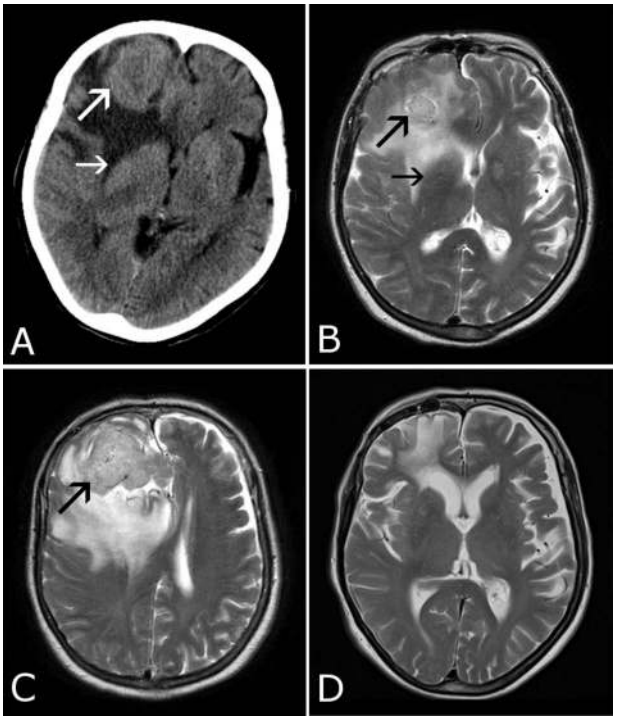

Figure 1 Large right frontal intracranial tumour (large arrows) with surrounding oedema, compressing and displacing the ipsilateral striatum (small arrows). (A) preoperative CT scan; (B) and (C) preoperative axial T2-weighted MRI (B) more caudal than (C); (D) axial T2-weighted MRI 3 months after surgery.

Of note, the patient again became completely independent, resumed successful driving and financial management. She is now able to deal again with all activities of daily living by herself. Mood has been normal since surgery.

DISCUSSION

Parkinsonism refers to the clinical syndrome characterised by four main features: bradykinesia, rest tremor, rigidity and postural and gait impairment.[1] These can be seen in various combinations, but bradykinesia is the core feature for the diagnosis. True bradykinesia refers to the progressive loss of speed or amplitude with repetitive movements, unlike simple slowness, which can be seen for instance in spasticity, painful conditions or depression.[1]

PD is the most common cause of neurodegenerative parkinsonism.[3] The prevalence of this disorder gradually increases after 50–60 years of age. Pathologically, it is defined by dopaminergic neuron loss in the substantia nigra and by the presence of intraneuronal Lewy bodies composed of α-synuclein.[7 8] The diagnosis is achieved essentially through accurate clinical exploration and reasoning, as there are no tests which can confirm the diagnosis in vivo, apart from genetic testing in a few cases.[1] PD usually has a slow onset and gradual progression. Motor symptoms present typically in an asymmetric fashion, with gait and balance being affected only a few years after clinical onset of the motor signs.[1 9] The clinical picture of PD is characteristic, and features suggesting the diagnosis of other parkinsonian disorders should be thoroughly sought, including: symmetrical symptoms, axial or lower limb involvement early in clinical course (including falls); quick progression of disability; cerebellar or pyramidal features; other associated unexpected movement disorders (eg, myoclonus and tics); abnormal eye movements (eg, supranuclear gaze palsy, hypommetric saccades); prominent cognitive or behavioural changes, particularly if early in disease course (including apraxia, alien limb or psychosis); disproportionate autonomic dysfunction; and poor benefit from an adequate levodopa therapeutic trial.[1]

Non-motor symptoms are increasingly recognised as a major cause of disability in PD. Some of them can manifest many years before motor symptoms and contribute prominently to declining quality of life. Their recognition is important because they can be useful clues for diagnosis, and also warrant specific management. Neuropsychiatric features such as apathy, anxiety and psychosis are common.[4 10 11] Depression is also frequently seen, and patients often become withdrawn from socialisation, with anhedonia and reduced motivation. Cognitive impairment is a very common occurrence, and might range from mild decline to full-blown dementia, the latter emerging typically a few years after the onset of motor symptoms.[12] Dysautonomia includes constipation, sexual dysfunction, urinary frequency and urgency, sometimes with incontinence, excessive sweating and orthostatic hypotension. Sleep disorders such as insomnia and rapid eye movement behaviour disorder can also have a significant impact on the overall quality of life and disability.[13 14] However, caution should be exercised when assessing non-motor symptoms, as these might be seen also in other disorders, although the clinical presentation and severity are usually dissimilar from what can be typically observed in PD.

The patient reported in the text presented signs suggestive of significant frontal lobe dysfunction, such as prominent apathy, reduced verbal initiative and psychomotor slowing, apparently disproportionate to the severity of the parkinsonian signs, thus atypical for PD. Moreover, urinary incontinence with no insight from the patient was also present, as well as slightly asymmetric

tendon reflexes, which also prompted concern about a dissimilar condition from PD. However, the marked asymmetry of parkinsonism and absence of prominent postural or gait impairment favoured the diagnosis of PD.

Parkinsonism, specially rigidity and bradykinesia have been reported in normal pressure hydrocephalus (NPH), but these are usually symmetric and response to levodopa tends to be poor, in striking contrast with PD.[15] Gait disturbances, frontal cognitive dysfunction and urinary incontinence compose the classical clinical triad of NPH, although it is not specific of the diagnosis.[16] The clinical characteristics appear in combination with non-obstructive enlargement of the cerebral ventricles in neuroimaging studies. In order to distinguish NPH from PD, gait should also be carefully assessed. Shuffling gait and retropulsion can be seen in both disorders, but in NPH, gait is more prone to have a wide-based pattern, whereas the PD gait occurs on a narrow base.[1 17] Gait in NPH has been described as 'magnetic' because the feet are moved in close relation ('glued') to the floor and there is a characteristic manner of turning, requiring several steps.[17 18] Also, freezing does not usually respond to external cues in patients with NPH. Non-motor symptoms in NPH are mainly significant frontal cognitive dysfunction and urinary incontinence occurring usually from the early stages of the disease. In the case reported here, the association of urinary incontinence and behavioural abnormalities suggesting frontal lobe dysfunction brought up the possible diagnosis of NPH, but gait disturbance was not present; on the other hand the parkinsonian features were quite asymmetric, which is also not consistent with NPH.

Vascular parkinsonism results from cerebrovascular disease and is responsible for 3–9% of all cases of parkinsonism.[3 19] Normally, it affects older patients with vascular risk factors. Bilateral lower limb bradykinesia associated with gait disturbances and postural instability seem to be the main motor findings. Rest tremor is absent or rarely seen. Additional signs such as pyramidal signs, pseudobulbar palsy, urinary incontinence and significant cognitive dysfunction can be observed.[20] The onset of symptoms may be acute or insidious, with faster clinical progression than PD. With regard to brain imaging, subcortical white-matter lesions, multiple lacunar infarcts or isolated infarcts of the basal ganglia are commonly found in patients with vascular parkinsonism. The integrity of the dopaminergic system confirmed by functional imaging studies helps to differentiate between vascular parkinsonism and true PD[21] and might explain why patients diagnosed with vascular parkinsonism tend to benefit less from dopaminergic therapy, although a significant proportion might have a reasonable response.[22] The case reported in this text presents quite differently from the parkinsonian picture usually seen in vascular parkinsonism, but the apparently disproportionate frontal cognitive impairment and urinary incontinence brought up this differential diagnosis.

There have been some previous reports of parkinsonism associated with intracranial tumours, namely low-grade astrocytomas, gliobastomas, meningiomas, oligodendrogliomas, lymphomas, epidermoid tumours and metastases.[23–27] Clinically, parkinsonian signs are rarely isolated, even at the onset of the disease, and pyramidal symptoms are often associated.[24] It has been reported that the response to dopaminergic treatment is clinically suboptimal in tumour-related parkinsonism, although significant symptomatic improvement and even remission has been achieved by successful surgical therapy.[25] The pathogenic mechanism is thought to involve compression or distortion by tumour infiltration of the basal ganglia and the nigrostriatal pathway.[26] Patients with purely compressive lesions, such as meningiomas, seem to have a better outcome than those with infiltrating tumours.[26] In the present case, the right striatum had clearly suffered anatomical displacement and compression due to the mass effect caused by the tumour and surrounding oedema, which resulted in contralateral bradykinesia and rigidity. In addition, the symptoms completely remitted following surgery with consequent striatal decompression and topographical normalisation, suggesting that this pathophysiological theory might be correct. In this case, successful management produced significant improvement with regard to symptoms, autonomy and quality of life. Symptom relapse has been reported in one case of recurrent meningioma,[23] thus clinical and imaging follow-up should be programmed, in accordance also with tumour histology and probability of recurrence.[28] We emphasise that intracranial tumours are a potentially treatable cause of parkinsonism, and reversibility of symptoms following adequate therapy is possible. Therefore, brain CT or MRI is recommended during diagnostic work-up, especially whenever atypical clinical features are observed.

Learning points

- Parkinsonism is a clinical syndrome characterised by four main features: bradykinesia, rest tremor, rigidity and postural and gait impairment.
- Parkinson's disease is a common cause of parkinsonism, with typical clinical features and progression.
- Some clinical characteristics should prompt suspicion for alternative diagnoses, such as absence of symptom asymmetry, early axial or prominent lower limb involvement; falls early in disease course; fast progression of disability; cerebellar or pyramidal features; other associated movement disorders; abnormal eye movements; prominent cognitive or behavioural symptoms, particularly if early in disease course; disproportionate autonomic dysfunction and poor benefit from an adequate levodopa therapy.
- Intracranial tumours are an uncommon cause of parkinsonism. Successful management might bring significant improvement and even complete remission of parkinsonian features and disability.
- Brain CT or MRI, according to availability and indication, should be routinely carried out in the diagnostic work-up of parkinsonism.

Competing interests None.

Patient consent Obtained.

REFERENCES

1 Massano J, Bhatia KP. Clinical approach to Parkinson's disease: features, diagnosis, and principles of management. *Cold Spring Harb Perspect Med* 2012;2:a008870.
2 Massano J. Parkinson's disease: a clinical update. *Acta Med Port* 2011;24 (Suppl 4):827–34.
3 Horvath J, Burkhard PR, Bouras C, *et al*. Etiologies of parkinsonism in a century-long autopsy-based cohort. *Brain Pathol* 2013;23:28–33.
4 Chaudhuri KR, Schapira AH. Non-motor symptoms of Parkinson's disease dopaminergic pathophysiology and treatment. *Lancet Neurol* 2009;8:464–74.
5 Alvarez MV, Evidente VG. Understanding drug-induced parkinsonism: separating pearls from oysters. *Neurology* 2008;70:e32–4.
6 Clarke CE. Parkinson's disease. *BMJ* 2007;335:441–5.
7 Taipa R, Pinho J, Melo-Pires M. Clinico-pathological correlations of the most common neurodegenerative dementias. *Front Neurol* 2012;3:68.
8 Dickson DW. Parkinson's disease and parkinsonism: neuropathology. *Cold Spring Harb Perspect Med* 2012;2:a009258.

9 Hawkes CH, Del Tredici K, Braak H. A timeline for Parkinson's disease. *Parkinsonism Relat Disord* 2010;16:79–84.
10 Lim SY, Fox SH, Lang AE. Overview of the extranigral aspects of Parkinson disease. *Arch Neurol* 2009;66:167–72.
11 Schapira AH, Tolosa E. Molecular and clinical prodrome of Parkinson disease: implications for treatment. *Nat Rev Neurol* 2010;6:309–17.
12 Meireles J, Massano J. Cognitive impairment and dementia in Parkinson's disease: clinical features, diagnosis, and management. *Front Neurol* 2012;3:88.
13 Weintraub D, Moberg PJ, Duda JE, *et al*. Effect of psychiatric and other nonmotor symptoms on disability in Parkinson's disease. *J Am Geriatr Soc* 2004;52:784–8.
14 Gallagher DA, Lees AJ, Schrag A. What are the most important nonmotor symptoms in patients with Parkinson's disease and are we missing them. *Mov Disord* 2010;25:2493–500.
15 Morishita T, Foote KD, Okun MS. INPH and Parkinson disease: differentiation by levodopa response. *Nat Rev Neurol* 2010;6:52–6.
16 Klassen BT, Ahlskog JE. Normal pressure hydrocephalus: how often does the diagnosis hold water? *Neurology* 2011;77:1119–25.
17 Rosseau G. Normal pressure hydrocephalus. *Dis Mon* 2011;57:615–24.
18 Tsakanikas D, Relkin N. Normal pressure hydrocephalus. *Semin Neurol* 2007;27:58–65.
19 Jellinger KA. Vascular parkinsonism. *Therapy* 2008;5:237–55.
20 Kalra S, Grosset DG, Benamer HT. Differentiating vascular parkinsonism from idiopathic Parkinson's disease: a systematic review. *Mov Disord* 2010;25:149–56.
21 Kägi G, Bhatia KP, Tolosa E. The role of DAT-SPECT in movement disorders. *J Neurol Neurosurg Psychiatry* 2010;81:5–12.
22 Antonini A, Vitale C, Barone P, *et al*. The relationship between cerebral vascular disease and parkinsonism: the VADO study. *Parkinsonism Relat Disord* 2012;18:775–80.
23 Bostantjopoulou S, Katsarou Z, Petridis A. Relapsing hemiparkinsonism due to recurrent meningioma. *Parkinsonism Relat Disord* 2007;13:372–4.
24 de Sèze J, Ceravolo R, Rossi C, *et al*. Hemiparkinsonism revealing an infiltrating low-grade oligodendroglial tumor. *Eur Neurol* 1998;40:234–6.
25 Frosini D, Defebvre L, Ruchoux MM, *et al*. Bilateral thalamic glioma presenting with parkinsonism. *Mov Disord* 2009;24:2168–9.
26 Ho BL, Lieu AS, Hsu CY. Hemiparkinsonism secondary to an infiltrative astrocytoma. *Neurologist* 2008;14:258–61.
27 Choi KH, Choi SM, Nam TS, *et al*. Astrocytoma in the third ventricle and hypothalamus presenting with parkinsonism. *J Korean Neurosurg Soc* 2012;51:144–6.
28 Riemenschneider MJ, Perry A, Reifenberger G. Histological classification and molecular genetics of meningiomas. *Lancet Neurol* 2006;5:1045–54.