



CASE REPORT

Primary Progressive Freezing: does it stand on its own?

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Abstract

Background: Freezing of gait is a gait disorder frequently attributed to Parkinsonism. When it occurs in isolation the term Primary Progressive Freezing can be applied. It is a rare finding and recently its validity was questioned.

Case report: An 85-year-old man, without known vascular risk factors, came to our attention after falling several times. He complained of difficulty initiating gait and turning. Neurological examination in the initial consult unveiled freezing, particularly when initiating gait, without other overt signs of Parkinsonism. Levodopa+carbidopa+entacapone had already been introduced by another physician, and later rasagiline was added, but the latter was suspended due to absence of response. Imaging studies showed ischemic lesions in the posterior aspect of the left corona radiata and diffuse supratentorial and infratentorial atrophic lesions.

Conclusion: Primary progressive freezing is a movement disorder that can be considered in the differential diagnosis of the Parkinson-Plus syndromes currently in need of better characterization. In this patient, after excluding other causes, it appears to be an adequate explanation for this unusual presentation.

Keywords: Freezing, Gait disorder, Parkinson-plus syndromes.

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Introduction

Primary progressive freezing (PPF) is a gait disorder characterized by freezing of gait (FOG) [1, 2]. It is found during gait initiation, turning and overcoming obstacles [3, 4], resulting in falls [1].

The pathophysiology of freezing is not yet fully understood. Disturbances in frontal cortical regions, the basal ganglia, and the midbrain locomotor region have been implicated [5]. The nigrostriatal dopaminergic system is thought not to be involved, and the affected patients do not respond to dopaminergic medications [1].

Primary progressive freezing was first described in 1993 [6] and various names were used to describe it [1, 7]. Furthermore, distinct criteria were used (some studies consider parkinsonian features as part of the clinical syndrome [1, 2] while others consider only isolated freezing of gait [7]). This entity was considered part of the Parkinson-plus syndromes [1, 2] but recent papers [2, 3, 8] suggested that it is caused by other neurodegenerative diseases, such as progressive supranuclear palsy, corticobasal degeneration, dementia with Lewy bodies, pallidonigroluysian degeneration [7], primary lateral sclerosis [9].

Case report

An 85-year-old Caucasian man was referred to our hospital in January 2014. He had a history of chronic hepatic

disease of unknown etiology, benign prostatic hyperplasia and there were no known vascular risk factors.

At our first examination, he presented with a series of falls and complained of difficulty initiating gait, particularly with the left leg, and turning. He walked with unilateral support. At this stage Carbidopa/Levodopa + Entacapone 25/100 bid had already been instituted. Neurological examination in the initial consult unveiled freezing, particularly when initiating gait, but maintained during all the gait cycle, without other overt signs of Parkinsonism. A CT scan was available from 2013, prior to the first symptoms, that disclosed old bilateral vascular lacunae involving the corpus striatum and internal capsule.

In May 2015, Carbidopa/Levodopa + Entacapone was augmented to 600mg and rasagiline was introduced. Datscan showed bilateral degeneration of the dopaminergic nigro-striatal pathways, although more pronounced on the left putamen (Figure 1).

Meanwhile there was no evidence of response to medication and in September 2015 it was suspended. Brain MRI in October 2015 unveiled T2 hyperintensities on the left side of the Splenium of the corpus callosum, with T1 hypointensity; enlargement of perivascular spaces in both lenticulostriate capsular regions; ischemic lesions in the posterior aspect of the left corona radiata and diffuse supratentorial and infratentorial atrophic lesions (Figure 2).

In the last re-evaluation in February 2016, the patient did not mention progression of the freezing of gait. There

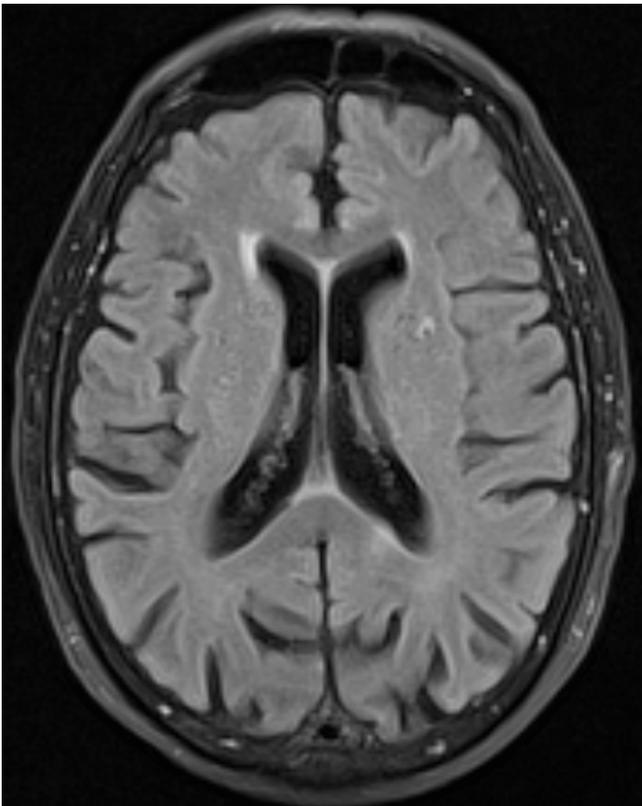


Figure 1. Brain MRI.

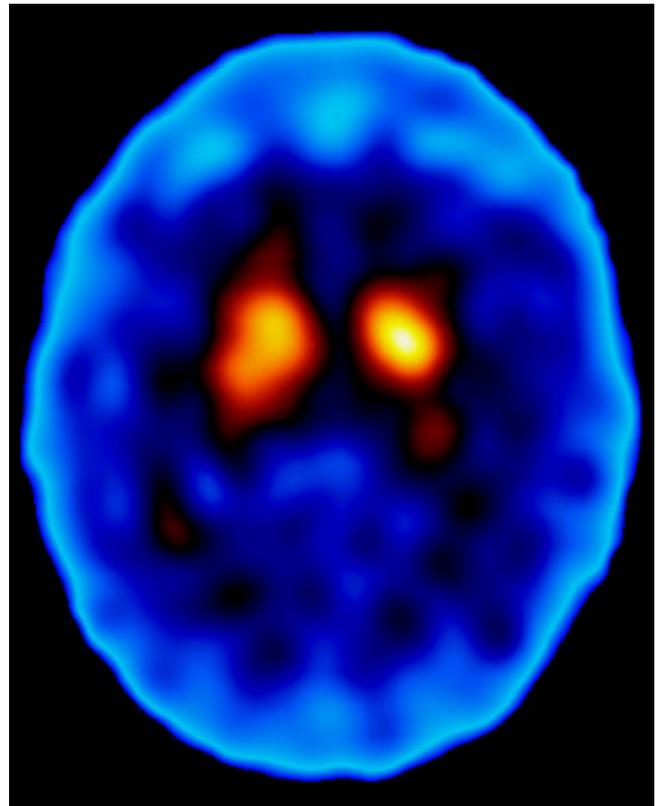


Figure 2. Datscan.

were no signs of cognitive impairment, knowing that he was a retired accountant (scored 30 in the MMSE), cranial nerve observation was unremarkable and there was paratonia in the left elbow mobilization, without further signs of rigidity in the other limbs. He showed no tremor or bradykinesia. Postural reflexes were impaired (UPDRS III – 2) and he presented with a narrow stance, freezing with gait initiation and doing turns, that improved in the presence of obstacles.

Discussion

Despite recent suggestions, the authors find that PPF is a distinct entity. We presented a case of a patient with a 2-year history of freezing resulting in falls, without other major signs of Parkinsonism. He did not respond to treatment with levodopa.

Considering that freezing is a common feature among gait disorders [7], particularly in patients with Parkinsonism [10], other diagnoses must be excluded. In Parkinson's disease (PD) freezing of gait increases with disease duration, affecting 60% of patients after 10 years of disease and 80% after 20 years [11]. Nevertheless, the early appearance of freezing in this patient, the paucity of other parkinsonian features and lack of response to levodopa virtually exclude this diagnosis.

Several studies suggest that PPF is part of the spectrum disease of progressive supranuclear palsy (PSP)[1, 2, 7, 8, 12], particularly the Pure-akinesia subtype [1, 12]. In these patients, although freezing of gait may be the presenting feature, they latter show micrographia, abnormalities of speech, axial rigidity, vertical supranuclear gaze palsy and postural instability [13]. The very early onset of freezing in our patient points to PPF rather than pure akinesia [1, 2, 7].

Diagnostic criteria for PPF were suggested [7]: 1) early freezing gait (onset within 3 years of the onset of the disorder); 2) gait freezing as the primary feature; 3) absence of clinical findings consistent with PD or Parkinson Plus syndrome; 4) absence of findings on clinical evaluation/imaging/laboratory data suggesting other diagnoses; 5) lack of dyskinesia or motor fluctuations with levodopa. All these criteria are fulfilled by our patient.

Concerning Vascular Parkinsonism, it presents with a lower-body parkinsonism consisting of gait impairment (among other features with freezing [14]), pyramidal signs, cognitive impairment in a patient with multiple vascular risk factors [15]. Lacunae and white matter lesions found in MRI studies are not specific and are common features in elderly individuals [15]. Two different sets of criteria were proposed for the diagnosis of Vascular Parkinsonism [16, 17]. At this stage, our patient does not fulfil either of these criteria. It is of note that this diagnosis has been questioned [18, 19] and another entity was suggested—Vascular pseudoparkinsonism, a higher-level gait disorder (HLGD). One of the five subtypes initially proposed of HLGD was isolated gait ignition failure (IGIF), one of the names used as

synonyms of PPF. These patients present with a marked difficulty with initiating gait in the absence of impairment of equilibrium, cognition, limb praxis or parkinsonism [20]. In spite of our patient, those with IGIF show normal rhythm and step size once gait is continued [20].

In summary, considering our patient's presentation, the lack of accompanying parkinsonian features and vascular risk factors other than age, PPF is still a plausible diagnosis. Its pathophysiology is still unknown and it could be included in the anterior HLGD [21], as a distinct entity since its features are distinct from the previous descriptions of IGIF.

Abbreviations

FOG: Freezing of gait; HLGD: Higher-level gait disorder; IGIF: Isolated gait ignition failure; PD: Parkinson's disease; PPF: Primary progressive freezing; PSP: progressive supranuclear palsy.

Competing interests

The author declares no conflict of interest.

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