

## CASE REPORT

# Revising a diagnosis of functional neurological disorder—a case report

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## Abstract

We report a case of a 62-year-old female diagnosed with functional neurological disorder (FND), where the diagnosis was eventually revised to progressive supranuclear palsy 3 years after symptom onset. FND is a commonly encountered condition and can be diagnosed with a considerable degree of confidence in most cases. FND is associated with significant functional impairment and may occur alongside other neurological disorders, and there is now a growing evidence base for symptom-specific FND treatments. Charting clinical progression of symptoms and serial neuroimaging were useful in refining the diagnosis in this case. Although the diagnosis was ultimately revised to a neurodegenerative disorder, a degree of functional overlay likely remained present. The case highlights the importance of recognizing and avoiding diagnostic overshadowing in those with FND.

## INTRODUCTION

Functional neurological disorders (FND) are defined by neurological symptoms not explained by identifiable neurological pathology and represent up to one-third of neurology outpatient clinic attendances [1]. There is growing emphasis on diagnosis involving demonstration of positive clinical signs (e.g. Hoover's sign), and a reduced emphasis on the demonstration of precipitating traumatic life-events (though adverse life events appear consistently overrepresented in FND patients compared to the general population) [1, 2]. FND diagnoses demonstrate high diagnostic stability, with a misdiagnosis rate of 4% according to one systematic review [3].

We report a case where an FND diagnosis was revised to that of a neurodegenerative disorder, 3 years after symptom onset.

## CASE REPORT

A 62-year-old female presented to neuropsychiatry services with a 3-year history of gradually progressive dysphonia, difficulty with keeping her eyes open and falls.

Her medical history consisted of chronic obstructive pulmonary disease, type 2 diabetes mellitus, ischaemic heart disease, hypertension, grade 3b chronic kidney disease (secondary to hypertensive disease) and anaemia. There was no personal or family history of medical or psychiatric disease, other than her mother having had a brain tumour in her 60s. She was married and unemployed. She has two siblings and 2 daughters; all of whom are well.

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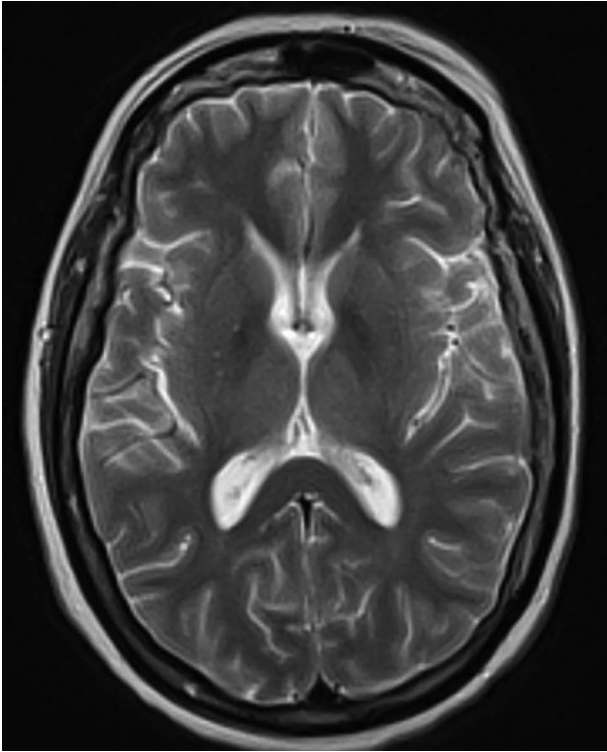


Figure 1: T2-weighted MRI scan showing normal appearances 1 year after symptom onset.

She was referred to otorhinolaryngology 1 year after the development of vocal symptoms. At the time, there was no associated odynophagia or dysphagia, but she had described all-over-body pain and difficulty with handwriting. She started experiencing difficulty keeping her eyes open voluntarily and found wearing sunglasses helped with this. Laryngoscopy revealed slowed movements of the hypopharynx and larynx. Speech and language therapy (SALT) assessment reported normal orofacial muscle function with effortful and delayed vocal production. Communication was often supplemented with hand gestures. She was referred to neurology for further opinion. Neurological examination reported as being normal apart from speech. Vocal output was variable, at times able to produce complete words audibly, at other times being unable to phonate or imitate sounds to command. She was able to cough and swallowing was preserved. Magnetic resonance imaging (MRI) at the time revealed no abnormalities (Fig. 1). A diagnosis of functional voice disorder was made, and she was referred to an inpatient rehabilitation programme for patients with FND.

Neuropsychiatric review (3 years after symptom onset) revealed that she had started falling and stopped cooking or going outdoors (though she denied affective symptoms). Montreal Cognitive Assessment revealed a score of 22/30. Neurological examination demonstrated aphonia, eyelid apraxia and blepharospasm, near-constant use of sunglasses indoors and frequent touching of the corner of her eyes (a sensory geste).

MRI showed normal midbrain and pontine volumes, with hypointense signal within the substantia nigra, red nuclei and globus pallidus on susceptibility-weighted imaging (SWI), suggestive of iron deposition (Fig. 2). Computed tomography showed no evidence of intracerebral calcification. The diagnosis was then revised from FND to an atypical akinetic rigid syndrome. Gait speed and efficiency had improved at the point of discharge

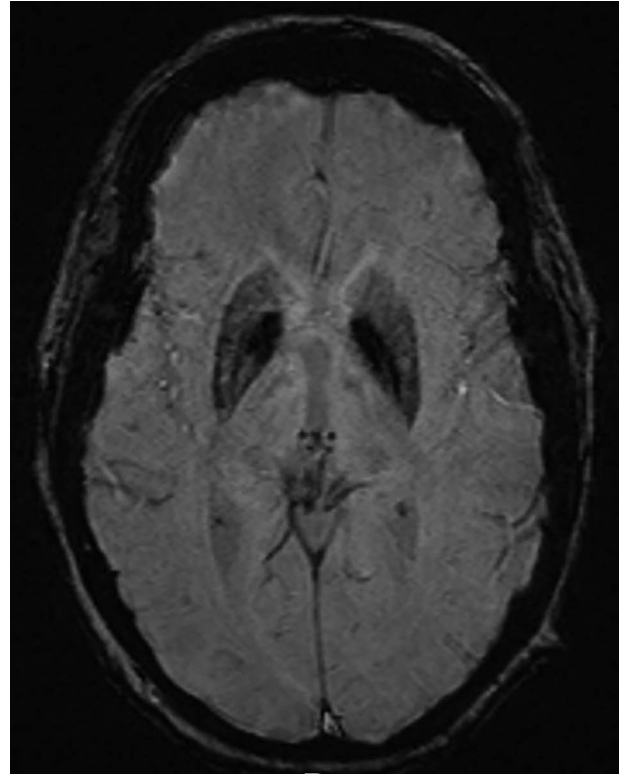


Figure 2: Susceptibility-weighted MRI scan showing hypointense signal within the bilateral globi pallidi, 3 years after symptom onset.

from the rehabilitation programme, which was felt to be a non-specific effect of physiotherapy.

Her care was then transferred to neurology. Clinical examination revealed aphonia and apraxia of eyelid opening, mild limitation of upgaze, hypometric vertical saccades and frontalis over-activity. Bilateral bradykinesia, right-sided rigidity and right foot dystonia also were noted. A summary of investigation findings is shown in Table 1, including genetic testing for atypical Parkinsonian syndromes associated with brain iron-deposition, and a DaTScan (Fig. 3). A clinical diagnosis of progressive supranuclear palsy was made, and she received ongoing botulinum toxin treatment and SALT input.

Her mobility and speech partially responded to levodopa treatment, and eyelid apraxia was partially responsive to botulinum toxin administered to the orbicularis oculi. Laryngeal botulinum toxin treatment was considered, but not used due to potential risk of aspiration. It was notable that SALT continued to identify features suggestive of an additional functional component to her phonation difficulties, where speech appeared to reliably worsen during times of testing and improved with distraction. Breath-holding during speech was particularly prominent, though she was noted to be able to demonstrate an ability for free breath-flow during non-speech tasks.

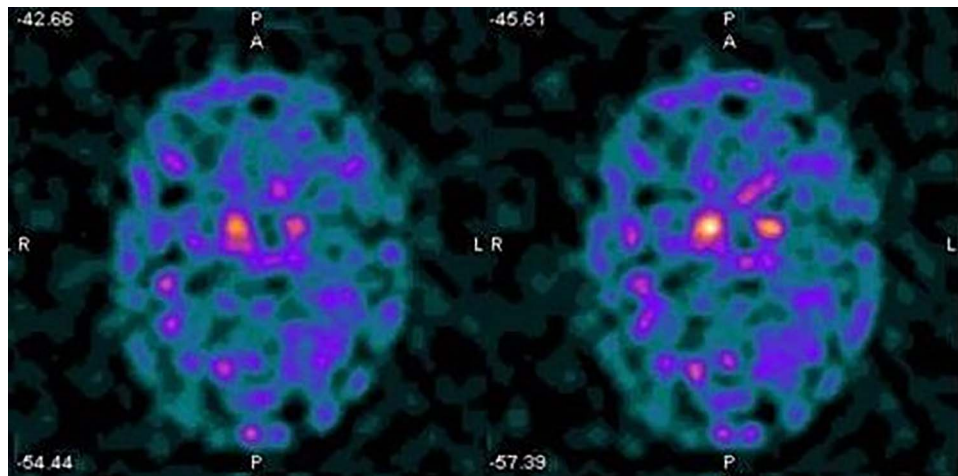
## DISCUSSION

PSP is a 4-repeat tauopathy, characterized clinically by gait-disturbance, Parkinsonian features, impaired ocular movement, neuropsychiatric changes, dysarthria and falls. Significant clinical heterogeneity amongst neuropathologically confirmed PSP cases has been increasingly recognized, including a phenotype characterized with non-fluent primary progressive aphasia and apraxia of speech [4].

**Table 1:** Summary of investigations: normal values are within brackets.

Investigation	Results
Full blood count	Haemoglobin 103 (115–155 g/L), haematocrit 0.329 (0.33–45 L/L), mean corpuscular haemoglobin 313 (320–360 g/L), mean corpuscular volume 103.1 (80–99 fL), white cell count and platelets within normal ranges
Renal function	eGFR 34 ml/min, creatinine 140 (49–92 µmol/L), urea 17.7 mmol/L, sodium and potassium within normal limits
Liver function tests	Alanine aminotransferase, aspartate aminotransferase, gamma glutamyl transferase and albumin within normal ranges
Iron studies	Ferritin 306 µg/L (13–150 µg/L), iron 12.8 (6.6–26 µmol/L), total iron-binding capacity 58 (41–77 µmol/L), iron-binding saturation 22% (15–50%)
Caeruloplasmin	0.22 g/L (normal range 0.16–0.45 g/L)
MRI brain	Hypointensity of the substantia nigra, red nuclei and globus pallidus on SWI sequence
CT head	No intracerebral calcification
DaTscan	Marked reduction in tracer binding bilaterally
Electromyography and electroencephalography	Subcortical negative myoclonus and polyminimyoclonus when attempting to flex upper limbs against force
Autonomic testing	Normal basal plasma catecholamines, no evidence of cardiovascular failure, and preserved responses to cold
Genetic testing	No pathogenic mutations identified within the following: <i>ATP7B</i> , <i>c19orf12</i> , <i>CP</i> , <i>FTL</i> , <i>PANK2</i> , <i>PLA2G6</i> , <i>SLC30A10</i> , <i>SLC39A14</i> , <i>WDR45</i>
Neuropsychometric testing	Slowed performances on tests of attention and processing speed, suggesting mild anterior and subcortical dysfunction

eGFR, estimated glomerular filtration rate; CT, computed tomography.



**Figure 3:** DaTscan results showing reduced [<sup>123</sup>I] FPCIT tracer uptake bilaterally, 3 years after symptom onset.

Basal ganglia iron deposition has been described in PSP, with hypointensities of the red nucleus and globi pallidi on susceptibility-weighted MRI showing some value in discriminating PSP from other Parkinson-plus syndromes [5]. Neurodegeneration with brain-iron accumulation, a range of inherited disorders characterized by abnormal brain iron deposition were considered as potential differential diagnoses—with special emphasis on aceruloplasminemia in light of the age-at-onset, raised serum ferritin, radiological evidence of red nucleus involvement and the presence of type-2 diabetes mellitus [6]. However, normal serum ceruloplasmin concentration and negative ceruloplasmin gene (*CP*) genetic testing ruled out aceruloplasminemia.

Functional voice disorders are typically characterized by exaggerated lip, tongue and respiratory movements during phonation (which may resemble apraxia of speech), a waxing-and-waning pattern of speech disturbance and demonstrable

inconsistencies (e.g. the voice may normalize during non-propositional speech or singing, laughing or coughing may be preserved, or normal vocal cord movement may be demonstrable on laryngoscopy) [7]. Treatment includes addressing psychosocial stressors and may involve cognitive-behavioural or family therapy-orientated approaches. The presence of an element of distractibility in this case may suggest functional ‘overlay’ (where functional symptoms present alongside a separate disorder). Whilst we cannot exclude confirmation bias from the SALT assessments, it is notable that multiple SALT therapists remarked on the presence of persisting functional-overlay, even after the diagnosis was revised to PSP. FND may be precipitated by the development of separate neurological disorders, or other psychosocial or physiological insults, though the mechanism underlying this association remains unclear [8].

‘Diagnostic overshadowing’ refers to the misattribution of physical symptoms or signs to psychiatric conditions, which

likely occurred in this case. For example, the indoor use of sunglasses (which has been associated with FND [9]) was misinterpreted as a sign of FND (in this case, sunglasses were used to prevent aggravation of blepharospasm) by a number of clinicians reviewing the patient following the initial diagnosis of FND. Though a preserved cough was noted in this case, we speculate that the acoustics may have been altered by the presence of upper airway mucus from COPD, raising the possibility of a false-positive sign (a ‘falsely-loud’ cough). The observation of hypokinetic movements on laryngoscopy is unlikely to be explained by FND and highlights the importance of a thorough review of historic investigations in cases where FND diagnoses have been considered.

Clinicians may encounter considerable psychological resistance from patients when attempting to revise a previous diagnosis to an FND diagnosis. Patients may similarly encounter psychological resistance from clinicians when attempting to argue their FND diagnosis should be revised to a structural neurological disorder. Interestingly, revising the diagnosis from FND to a neurodegenerative disorder was not met with resistance in this case, in spite of the arguably worse prognosis associated with PSP. Whilst neuropsychometric testing did not reveal gross cognitive impairment, it is possible a degree of alexithymia may have accounted for this (though this was not formally assessed) [10].

*Conflict of interest statement.* None declared.

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## ETHICAL APPROVAL

Ethical approval not required (available at request).

## CONSENT

Patient consent obtained in written form.

## GUARANTOR

Dr Alex J. Berry.

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