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Frontotemporal Dementia

Introduction

Frontotemporal dementia (FTD) is a neurodegenerative disorder of insidious onset, and the term encompasses several entities. It is mostly sporadic. Epidemiologically, its prevalence as a dementia is third behind Alzheimer's disease and dementia with Lewy bodies (Bang et al., 2018). The incidence of FTD is around 1.61-4.1 cases per 100,000 people annually (Coyle-Gilchrist et al., 2016), and the most common age of onset is in the sixth decade (Kelley and El-Khouri, 2016). This case report highlights the fact that the presentation of frontotemporal dementia can be subtle, and can present a diagnostic difficulty when differentiating it from vascular dementia and other cognitive disorders.

Case Presentation

Mr AF is a 72-year-old gentleman, former businessman who lives with his wife. He first presented to the Neurology Cognitive clinic on 04/04/2019 in view of a history of forgetfulness of unclear onset; one of the main complaints that most bothered the patient was that he could not remember where he had parked his car. Appropriate workup was done, and the clinical impression was that of mild cognitive impairment with insidious onset.

There were subtle changes in his behaviour, but no motor symptoms and no gait disturbance. His sleeping habits had not changed recently (he sleeps at 2am and wakes up at 7am), no weight loss was reported and there were no problems with continence. His wife stated that his initiative-taking was unchanged. There was no history of hallucinations, insight was retained and he was independent in daily life.

His functional status was assessed: he was managing all activities of daily living. He was still driving, but required someone to guide him regarding road directions. His wife stated that he did not drive dangerously and his difficulty in directions had always been present. The patient was still involved in some family business once a week.

The patient is the patient is healthy enough to perform activities of daily living but has a number of cardiovascular risk factors. He is a known case of hypercholesterolaemia

and diabetes mellitus, and has been hospitalised with compressive chest pain suggestive of angina pectoris. The patient experiences exertional dyspnoea on walking up hills, and also reported GI symptoms such as dyspepsia and occasional abdominal pain

As shown in figure 1, the patient was admitted with abdominal pain and had a colonoscopy on 09/09/2010. This showed diverticulosis, mainly in the sigmoid colon.

The patient had other comorbidities: on 31/08/2017, an MRI of the lumbar/sacral spine was performed in view of clinical findings suggestive of S1 radiculopathy: degenerative disc change was seen throughout the thoracolumbar spine, most prominent at the L4/5 and L5/S1 levels, contributing to severe vertebral canal stenosis at the L4/5 level. The patient also required a shoulder operation for severe stiffness and reduced joint mobility, which was performed on 29/11/2016.

Table 1 summarises the patient's drug history and allergies.

When assessing a neurocognitive disorder, it is important to ask for any family history of similar problems. The patient doesn't have any first-degree relatives who suffer from dementia. The patient has some family members who also suffer from hypertension, diabetes and hypercholesterolaemia The patient is a former businessman who still does

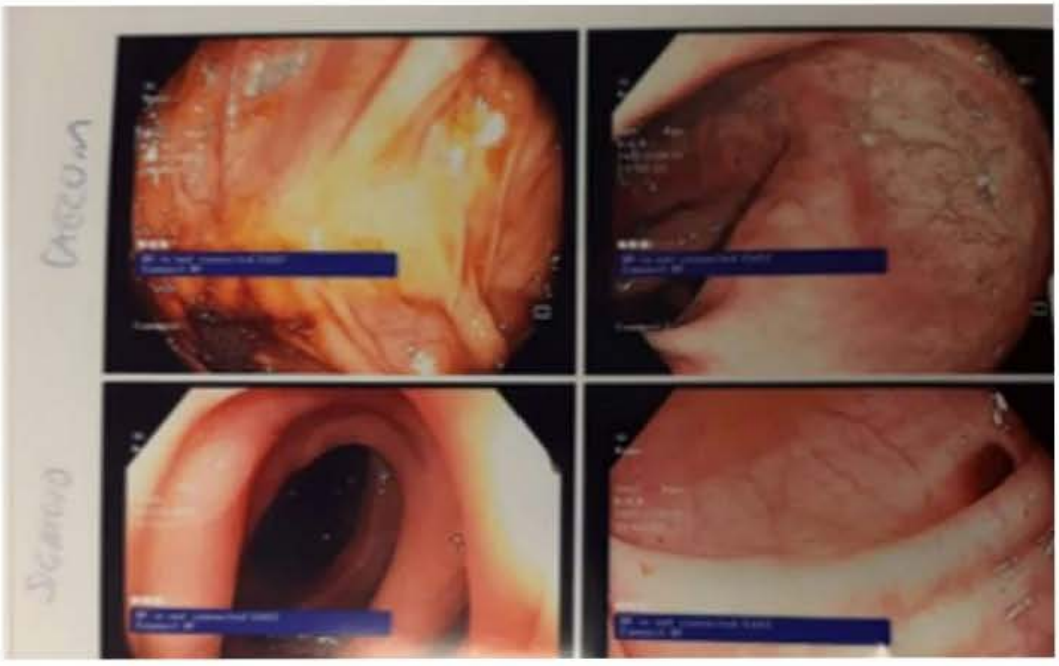

Figure 1:
Family Pedigree (Tazen et al., 2013). The proband – female with SCA2 with an unaffected mother and a deceased unaffected father, having CAG repeat expansions in ATXN2 . The paternal deceased uncle had ALS with the same trinucleotide repeat expansion as the proband but with different lengths.

Medication	Dose	Reason for taking Medication
Aspirin	75mg PO once daily	Ischaemic heart disease
Clopidogrel	75mg PO once daily	Ischaemic heart disease
Simvastatin	40mg PO nocte	Hypercholesterolaemia
Tamsulosin	1 tab daily	Benign prostatic hyperplasia

Table 1: Mr A.F.'s current medications. No known drug allergies

some family business affairs. He was a smoker from age 16 to 56, and only consumes alcohol socially.

On examination, respiratory rate was normal, SpO2 98% on room air, temperature 36.8oC, blood pressure 157/84mmHg, pulse 73 bpm. Neurocognitive testing showed that Mr A.F. was euthymic, with no difficulties with language comprehension or expression. The examination findings are summarised in table 2.

When formulating a differential diagnosis for such a case, one had to keep in mind that the clinical presentation of FTD is initially quite vague, so a number of neurological and psychiatric pathologies were considered:

1.Alzheimer disease (commonest cause of cognitive impairment)
2.Vascular dementia (multiple risk factors)
3.Schizophrenic personality disorder (psychiatric manifestations)
4.Dementia with Lewy bodies (unlikely)
5.Normal pressure hydrocephalus (cognitive impairment but no gait or urinary issues)
6.Benign/malignant brain tumour (change in personality)

Differentiating FTD from the other common cause of cognitive decline (Alzheimer's disease) and ruling out vascular causes is challenging because of overlapping symptoms and clinical features. FTD was the initial diagnosis in this patient, presenting mainly with behavioural changes and change in

Visuospatial Assessment	Normal except difficulties copying a cube (three-dimensionality not correct)
Attention: Serial 7s	4/5
Registration	Full marks
MMSE	Difficulties with recall
Clock Test	4/5, both hands drawn equally
Naming	Could not name 'penguin' and 'anchor'
Verbal Fluency	10 words starting with P in one minute
Three-stage command	Good
Sentence-writing	Good, except no question mark at the end
Antegrade memory	7/7
Episodic memory	Good
Attention	Serial subtraction 4/5

Table 2: Examination findings

affect. This was shown by his lack of spontaneous speech, coming through as apathetic, despite his preserved language ability. Although he had mild naming difficulties, Mr AF did well in verbal fluency tests, comprehension and writing. It would be interesting to check performance on tasks of facial expression recognition, as these patients typically do poorly.

Vascular dementia is typically characterised by a stepwise decline, particularly in executive functions. In contrast, Alzheimer's disease and FTD show a progressive course, mainly in episodic memory. Imaging techniques are useful in order to identify affected brain regions. Atrophy or hypometabolism of the right frontal or right temporal lobe is the hallmark neuroimaging finding in patients with bvFTD. When both frontal lobes are involved, language symptoms are typically also present.

A strictly vascular dementia in this case was less likely but could not be excluded. Mixed dementia is a dementia where both vascular lesions and other pathology co-exist to produce cognitive impairment. Demented patients have a greater incidence of stroke and stroke patients have a greater incidence of dementia (Leys et al, 2005).

Diagnostic investigations:

Investigation: blood investigations: complete blood count, renal profile, lipid profile
Justification: this patient has a history of prior admission with neutropenia, and he has multiple comorbidities which may result in anaemia of chronic disease. Renal profile helps to assess kidney perfusion in this patient with heart disease and other risk factors for chronic kidney disease. The lipid profile is important since the patient has hypercholesterolaemia
Result & conclusion: leukopenia (followed up by haematologist), normal U&E and creatinine, elevated LDL and total cholesterol

Investigation: nuclear medicine positron emission tomography (NM-PET/CT) brain
Justification: identify areas of the brain that are affected by the pathology, and help differentiate from conditions such as Alzheimer's disease.
Result & conclusion: decreased uptake in the left parieto-temporal cortex and the left posterior cingulate cortex. FDG-PET imaging showed non-specific changes, which helped the diagnosis veer away from Alzheimer's pathology.

Investigation: electroencephalogram (EEG)
Justification: forgetfulness, look for encephalopathic changes/ focal abnormalities
Result & conclusion: figure 2: the patient's EEG is abnormal and showed generalised non-specific slowing, symmetrical, so this was non-specific and did not help in the differential diagnosis. The generalised slow wave activity is consistent with a non-specific encephalopathy. There are no focal or epileptiform features. The background consists mainly of alpha rhythm at 8-9c/sec of medium amplitude (20-30μV) intermixed with theta activity at 6c/second over both hemispheres in the background.

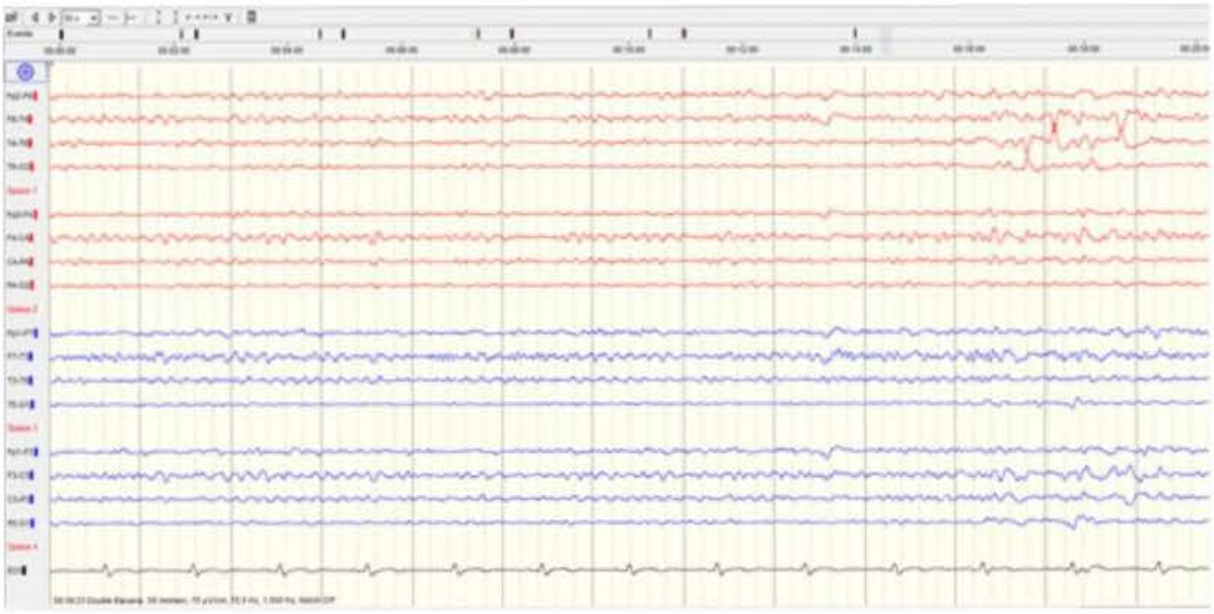

Figure 2: Mr AF's EEG showed generalised slow wave activity.

Investigation: magnetic resonance imaging (MRI)
Justification: patient has progressive neurological symptoms, and MRI is a useful modality for showing structural changes in the brain
Result & conclusion: refer to figure 3: MRI shows multiple peri-ventricular hyperintense foci in keeping with small-vessel ischaemic changes: this is consistent with the patient's cardiovascular risk factors.

Management:

Table 3 outlines the pharmacological management for this patient: Mr AF's regular medications were continued in view of his cardiovascular risk factors and prostate problems. Donepezil was prescribed: it is a cholinesterase inhibitor which can improve mental function.

Mr AF was referred for neuropsychology

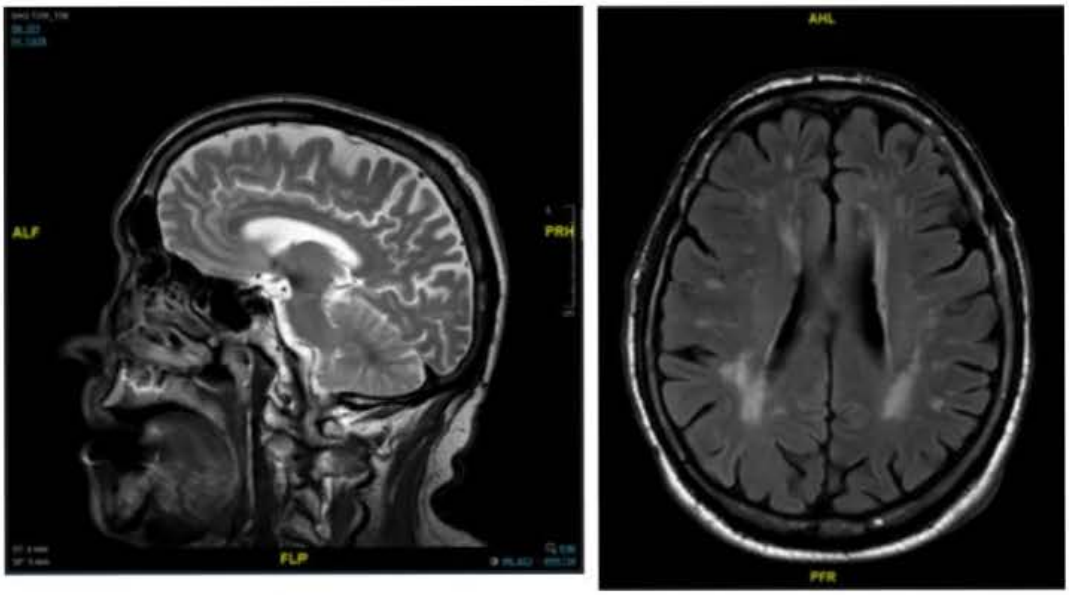

Figure 3: MRI: the axial view shows hyperintense periventricular foci. The sagittal view shows how the FTD pathological process mainly affects the frontotemporal regions.

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Simvastatin	40mg PO nocte	Hypercholesterolaemia
Tamsulosin	1 tab daily	Benign prostatic hyperplasia
Donepezil	5mg PO once daily	Mild cognitive impairment
Folate supplements	400µg PO once daily	Mild cognitive impairment

Table 3: Pharmacological Therapy

assessment, which confirmed mild cognitive impairment. According to his wife, Mr A.F.'s condition remained stable, however neuropsychology assessment noted decline in some functions, mostly relating to attention/recall. The patient reported that he was still capable of performing his activities of daily living independently, and his wife stated that he parks his car 'meticulously'. Notably, the patient experienced difficulty explaining himself.

Discussion: Frontotemporal Dementia

General signs and symptoms of FTD include progressive deficits in behaviour, executive function (including motor) and language. The features of the three major categories of FTD are summarised in Figure 4, and are: behavioural-variant FTD, non-fluent variant primary progressive aphasia, semantic-variant primary progressive aphasia. The likeliest subtype in this patient is behavioural-variant FTD, since it is characterised by changes in behaviour, personality and emotion control. Executive control is only lost once the dorsal lateral prefrontal cortex is affected (Seeley et al., 2007).

Inflammatory mediators such as tumour necrosis factor are involved in the pathophysiology (Bott et al., 2016).

In diagnosis, one must consider that FTD can present with symptoms that overlap with psychiatric disorders such as late-onset schizophrenia, bipolar disorder; or obsessive-compulsive disorder. Current available treatments do not cure or prevent the underlying neurodegenerative process, and mainly improve symptoms (Bott et al. 2016). Behavioural deficits can be moderately improved with the use of selective serotonin reuptake inhibitors and trazodone.

Conclusion

This case report describes the presentation, classification and treatment of frontotemporal dementia, while outlining the importance of holistic management in this patient with multiple comorbidities. This report outlines the diagnostic investigations which are necessary to distinguish frontotemporal dementia from other neurological or vascular conditions which may present in a similar manner.

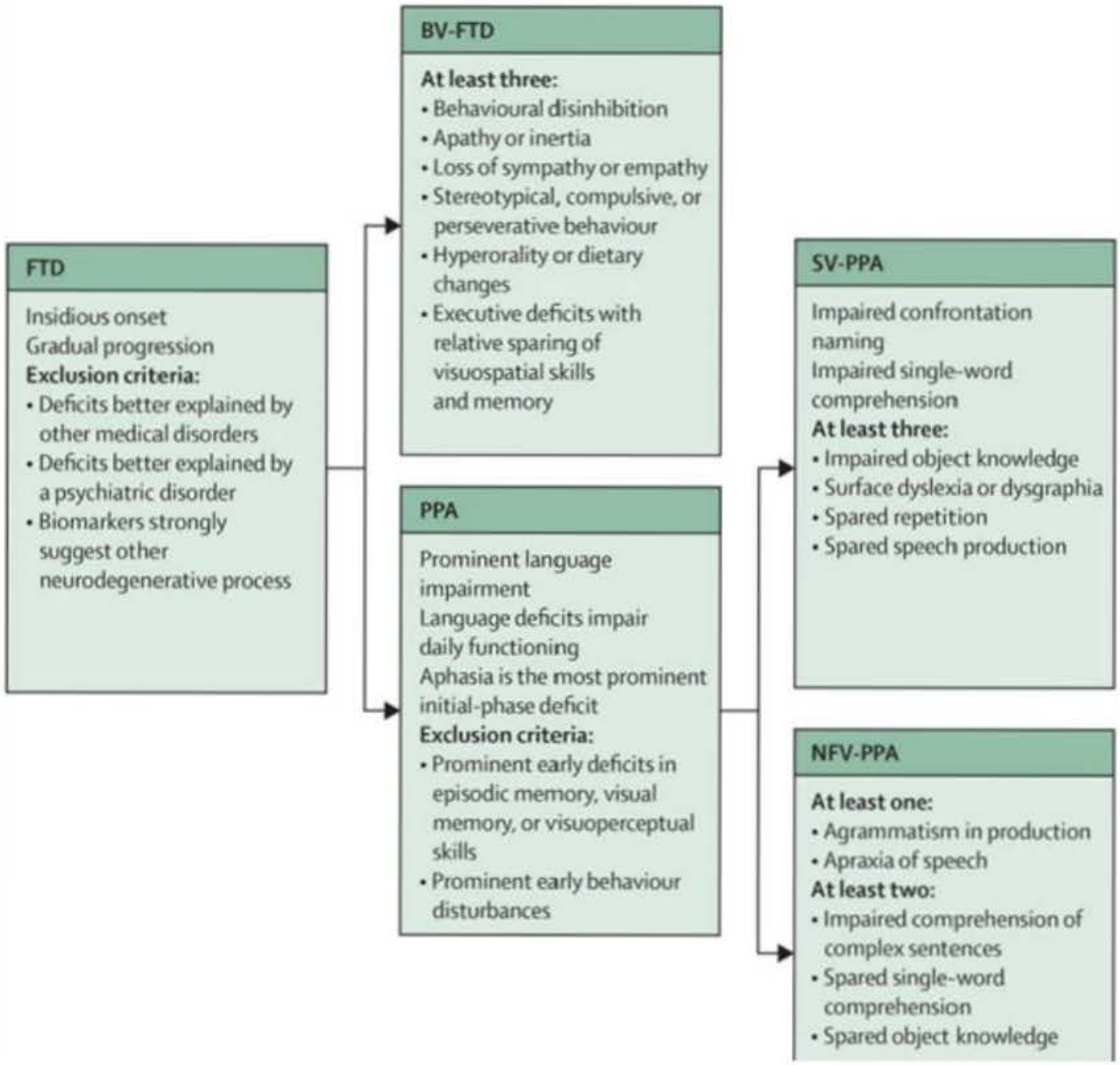

Figure 4 FTD is a clinical term which encompasses three different entities with a differing presentation.
(Source: Bang et al., 2018).

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