A Case of Two Brothers With Familial Frontotemporal Dementia Caused by a Progranulin Gene Mutation: A Case Report

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doi: 10.1192/bjo.2026.11897

Aims: Frontotemporal dementia (FTD) is the second most common cause of early-onset dementia accounting for approximately 10–20% of all dementia cases. The behavioural variant (bvFTD) is the most common presentation, comprising 50–57% of autopsy-confirmed FTD cases. bvFTD is highly heritable, and most implicated genes are MAPT, GRN (progranulin), and C9orf72.
Methods: We report a case of two brothers, the first brother, aged 62, was assessed in the memory service in 2022 following a five-year history of behavioural change including inappropriate behaviour, overeating, apathy, and memory impairment. His Addenbrooke's Cognitive Examination (ACEIII) score was 56/100. CT brain imaging showed generalised atrophy, more pronounced on the right. PET CT demonstrated hypometabolism particularly in the right frontotemporal region. Amyloid PET imaging showed no abnormal amyloid binding.

The second brother, aged 64, was assessed in 2024 with a two-year history of progressive cognitive decline and pronounced frontal lobesymptoms including apathy, irritability, lack of insight, impaired executive function, and poor financial management leading to debt. He required family support for most activities of daily living and scored 24/100 on the ACE. CT brain imaging showed pronounced frontal and medial temporal lobe atrophy. FDG-PET demonstrated reduced uptake in the frontal, temporal, and parietal lobes.

Both brothers underwent whole genome sequencing and were found to be heterozygous for a GRN mutation. Predictive genetic testing was recommended to their children, and two of four tested positive for the mutation.
Results: GRN mutations account for 35% of genetic FTD and around 10% of all FTD cases. GRN-FTD follows an autosomal dominant inheritance pattern. In our patients, there was no family history of FTD, although their father had possible undiagnosed dementia while their mother had Parkinson's disease and Alzheimer's disease. Notably, up to 13% of bvFTD cases carry a genetic variant despite no family history.

Genetic testing is a crucial diagnostic tool for defining the molecular pathology of the disease particularly in psychiatric settings where early bvFTD is often misdiagnosed as a primary psychiatric disorder. Furthermore, Identification of a GRN mutation is also essential for determining eligibility for clinical trials.

Predictive genetic testing for at-risk relatives enables them to make informed decisions regarding life and future care.
Conclusion: This case highlights the importance of whole genome sequencing and predictive genetic testing even in the absence of a convincing family history. This could improve both patient care and our overall understanding of the disease.

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Somatoform, Functional, and Secondary Psychiatric Disorders: Why the Distinction Matters

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doi: 10.1192/bjo.2026.11898

Aims: Distinguishing primary functional disorders from psychiatric illness arising secondary to chronic physical symptoms remains a significant clinical challenge, particularly when structural pathology is absent. Failure to make this distinction risks premature psychological attribution, diagnostic overshadowing, and invalidation of patient experience. Although ICD-11 offers updated frameworks for understanding disorders at the brain–body interface, their application to complex presentations requires careful clinical judgement to avoid misinterpretation of psychiatric risk.
Methods: Case Report
Results: We present a case that illustrates this diagnostic tension. A 48-year-old woman with high premorbid functioning and no prior psychiatric history developed a progressive multisystem physical illness following international travel. Symptoms included gastrointestinal dysmotility, bladder dysfunction, autonomic instability, and sleep disruption. Despite extensive investigation, no unifying structural or neurodegenerative diagnosis was identified.

As the physical illness persisted, the patient developed a severe depressive syndrome with suicidality. Notably, affective symptoms emerged only after the onset of physical decline and fluctuated in parallel with physiological distress, rather than following an autonomous psychiatric course.

This case highlights the importance of distinguishing primary functional disorders from psychiatric illness that is reactive to chronic physical dysfunction. Contemporary models conceptualise functional conditions as disorders of brain–body interaction, characterised by altered interoceptive processing and maladaptive predictive mechanisms. In such cases, these processes are central to symptom generation and represent appropriate targets for psychiatric intervention.

By contrast, secondary psychiatric illness arises in response to prolonged physical uncertainty, loss of bodily predictability, and erosion of trust in physiological functioning. In this context, the depressive syndrome does not account for the physical symptoms but develops as a consequence of them. Temporal sequencing is therefore a key diagnostic marker. Failure to recognise this distinction risks premature psychological attribution, erosion of the therapeutic alliance, and misinterpretation of suicide risk. In such cases, suicidality is often driven by existential distress related to persistent physical suffering and fear of irreversible decline, rather than affective pathology alone.
Conclusion: Not all distress associated with unexplained physical symptoms is somatoform. Psychiatry's role is not to resolve medical uncertainty through psychological explanation, but to locate distress accurately within the patient's causal narrative. Careful formulation, grounded in phenomenology and temporal sequencing, is essential for ethical practice and effective risk management - and in cases such as these can prove to be life saving

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