Frontotemporal dementia: remembering images from the past

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Abstract: Frontotemporal dementia (FTD) is the most common form of primary degenerative dementia after Alzheimer’s disease that affects people in middle age. The average delay in reaching an accurate diagnosis has been reported to be around 3 years. We report a case of FTD in a 35-year-old female who presented with complex symptoms and no clear physical signs. This case draws attention to the problems inherent in the traditional functional–organic divide that continues to characterize investigation and diagnosis in modern psychiatric practice, and highlights the importance of reevaluating the results of previous “normal” investigations in the light of the developing clinical picture.

Keywords: frontotemporal dementia, diagnosis, neuroimaging

Case summary

A 35-year-old female with a previous history of long-term high-dose benzodiazepine use presented in 2001 following an overdose of ibuprofen. She had concurrent symptoms of depression, persecutory ideas, and bizarre, chaotic behavior (eg, wandering the streets claiming she was being poisoned). There was no family psychiatric history. She was formally detained on a psychiatric inpatient ward. Physical examination was normal, except for an extensor left plantar reflex, as were her urea and electrolytes (U&Es), full blood count (FBC), thyroid function tests (TFTs), liver function tests (LFTs), and random blood glucose (RBG). Urine drug screen was negative except for benzodiazepines. CT and MRI brain scans and an EEG were reported as normal, and hence an organic etiology was excluded. A diagnosis of severe psychotic depression was made and she was treated with a variety of antidepressant, antipsychotic, and mood stabilizing agents for over twelve months, together with electroconvulsive therapy without significant response. No adverse side effects to medication were reported. Throughout her admission she displayed behavioral difficulties including poor self care, agitation, and she was intrusive and demanding.

Twelve months later, a second opinion was sought at which time the patient had intermittent paranoid ideas, mood congruent auditory hallucinations, and psychological pillow. A diagnosis of schizophrenia was made and clozapine was commenced, again with no significant impact. In July 2002, her family relocated and she was transferred to another psychiatric hospital. Her presentation was unchanged except for the emergence of hypochondriacal ideas and worsening behavioral difficulties such as disinhibition, coarsening of social skills, and deteriorating self care. Alternative pharmacological strategies were employed without success.

The patient was referred for a further opinion in November 2003 at which time her main difficulties were a mixture of depressive, psychotic, and anxious symptoms...
with marked behavioral disturbance. She was transferred to a regional affective disorders unit for a period of assessment. Physical examination revealed a left extensor plantar reflex, a pout, and palommental primitive reflexes but no other neurological signs. A battery of investigations was arranged, including U&Es, FBC (including screen for acanthocytes), TFTs, LFTs, RBG, C-reactive protein test, calcium, phosphate, copper, ferritin B 12 and folate, pituitary hormones, autoantibodies, chest x-ray, and ECG. All were within normal limits. An EEG recording revealed a slightly slow posterior rhythm suggestive of a mild non-specific cortical disturbance. CT scanning showed atrophic cerebral hemispheres especially in the right frontal region. The previous CT scans from 2001 were reviewed, and despite a normal report, there were significant atrophic changes which had progressed (Figures 1 and 2).

SPECT scanning revealed a diffuse abnormality with focal deficits in the temporoparietal regions. A lumbar puncture revealed normal cerebrospinal fluid, glucose, protein, angiotensin-converting enzyme, and cytology. On neuropsychological assessment she scored 68/100 on the extended mental state examination, having deficits in mental reversal, orientation, verbal fluency, and recall. She scored on the 8th percentile of the Graded Naming Test. A clinical diagnosis of frontotemporal dementia (FTD) was made, in accordance with the consensus diagnostic criteria (Neary et al 1999).

Discussion

Arnold Pick described clinical syndromes associated with frontal and temporal lobe degeneration over a century ago, but for many years these conditions were unrecognized as specific subtypes of dementia. In recent years, these conditions have been “rediscovered” (Gustafason 1987) and diagnostic criteria have been developed. FTD comprises a pathologically heterogeneous group of disorders characterized by behavioral change. Only a minority of patients exhibit Pick-type histological changes, which includes loss of large cortical nerve cells with widespread gliosis and swollen neurons or inclusions positive for both tau and ubiquitin. Hence, the term “frontotemporal dementia” is preferred, although “Pick’s disease” is the official classification for these forms of dementia in ICD-10 and DSM-IV.

FTD is the most common form of primary degenerative dementia after Alzheimer’s disease that affects people in middle age. It occurs most commonly between the ages of 45 and 65 years (Snowden et al 2002). There is an equal incidence in men and women (Gustafason 1987). From the onset of symptoms the delay in diagnosis has been reported to be on average 3 years, and death usually occurs within 6 years of the development of symptoms (Hodges et al 2003). When viewed with the wisdom of hindsight, the emerging clinical characteristics of FTD in this case are clear. However, the age of onset is unusual, and we highlight the
complexity of reaching a diagnosis in the absence of clear physical signs and when investigations are reported to be normal.

This case draws attention to the problems inherent in the traditional functional–organic divide that continues to characterize investigation and diagnosis in modern psychiatry. The presenting symptoms in this case caused diagnostic uncertainty, and a variety of “functional” diagnoses were made, even though the symptomology was atypical and did not fit neatly into any diagnostic category. Although clinicians may be reassured of the absence of an underlying organic etiology following normal neuroimaging and electrophysiological studies in psychiatric patients presenting with atypical features, this is clearly not always the case. Once the momentum behind a “functional” diagnosis has been established, consideration of alternative etiologies is often abandoned and reappraisal of the biological underpinnings of the disorder may be neglected. We advocate that physical investigations are repeated if patients continue to present a diagnostic challenge. The reevaluation of the results of previous “normal” investigations, in the light of the developing clinical picture, may further aid the diagnostic process.

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