

Schizophrenia or Frontotemporal Dementia in a Young Chinese Female: A purview of possible diagnoses



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SUMMARY

Frontotemporal dementia (FTD) is now increasingly being recognized as one of the causes of young onset dementia (YOD). The presentation of FTD can be subtle with a broad range of symptoms. This frequently causes misdiagnosis and a delay in initiating the correct treatment. While subtle personality changes, disinhibition and problems in executive functioning are frequently encountered in FTD, frank psychotic symptoms resembling schizophrenia are unusual. This is a case of a 38 yearold Chinese female that highlights how obsessive compulsive symptoms which progressed to florid psychosis and disorganized speech and behavior can be a presenting picture in FTD. For seven years, this patient was treated as a case of schizophrenia and was thought to have poor response to electroconvulsive therapy (ECT) as well as antipsychotic medication. Her blood work and electroencephalogram (EEG) were normal. Magnetic resonance imaging (MRI) showed progressive cerebral atrophy. This case report suggests that psychosis should be investigated in detail especially when the clinical presentation is not typical of a functional disorder and more so when the patient is not responsive to conventional treatment. This report also highlights the importance of eliciting symptoms suggestive of an “organic” etiology, such as incontinence and disorientation. In addition, the usefulness of repeated imaging to show the rapidly progressive course of FTD has been illustrated. Other possible differential diagnoses of this patient are also discussed.

Key Words: Schizophrenia, Fronto temporal dementia, psychosis.

INTRODUCTION

Frontotemporal dementia (FTD) is being increasingly recognized as one of the causes of young onset dementia (YOD) and accounts for 13% of all cases of YOD with a prevalence of approximately 9.3 per 100000 (Sampson et al. 2004). While it is less prevalent than Alzheimer’s disease, it is the main cause of dementia in patients between 30 to 60 years of age. FTD has a male preponderance, and the typical age of onset is between 45–60 years (Ratnavalli et al. 2002) and 50% of patients have a family history of the disease (Schott et al. 2002). The presentation can be subtle and indeed a broad range of symptoms are possible, frequently causing a delay in diagnosis. While subtle personality changes, disinhibition and problems in executive

functioning are frequently encountered in FTD, frank psychotic symptoms resembling schizophrenia are unusual. The case discussed in this paper highlights how florid psychosis can be a presenting picture in FTD.

CASE REPORT

A 38 year old Chinese female patient was brought by her family to a tertiary medical centre seeking a treatment for her illness that did not seem to respond to treatment from various other doctors. She had no family history of mental illness or early onset dementia and she had no significant medical illness or cardiovascular risk factors.

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She had been apparently well until the age of 30, when she began to exhibit insidious but obvious behavioral changes. She became withdrawn, argumentative and increasingly stubborn. She also began to have obsessive-compulsive disorder (OCD) like symptoms where she repeatedly cleaned and washed herself and kitchen utensils. She also insisted that family members adhere to certain cleaning rituals before entering the house. No psychotic symptoms were present and her cognitive functions remained intact. An initial diagnosis of OCD was made and she was started on selective serotonin reuptake inhibitors. She did not show any improvement and began having difficulties at work. She was unable to keep a job for more than 6 months and had to change jobs 3 times over the past 3 years. She was eventually dismissed from work because of poor performance.

Three years after the onset of her initial OCD symptoms, she began to display disorganized behavior with disorganized speech. There were also catatonic symptoms where she would keep still without moving for periods of time. A consultation with a psychiatrist led to the diagnosis of schizophrenia. However, she responded poorly to treatment with antipsychotics and experienced severe extra-pyramidal side-effects. She was later treated with electroconvulsive therapy (ECT) (2 courses in 2006) and had only a partial response. She was subsequently classified as treatment resistant schizophrenia as she failed to respond to adequate doses of quetiapine, olanzapine and risperidone and had a poor response to ECT. Treatment with clozapine also produced disparaging results and she developed seizures. Clozapine was eventually discontinued in 2009. Having developed seizures 6 times within a year, an electroencephalogram (EEG) was done and normal results were seen. However, magnetic resonance imaging (MRI) showed generalized cerebral atrophy. All laboratory investigations ruled out other causes for her clinical presentation.

7 years into her illness and after receiving numerous unsuccessful medical interventions, her overall condition continued to deteriorate. She began to have more frequent abnormal posturing, at times she was mute and at other times she made incomprehensible sounds. She was not able to feed herself and also began to lose bowel and bladder control. A computerized tomography (CT) scan concluded that she was actually suffering from frontotemporal dementia. Her family then decided to seek a second opinion at a tertiary center.

Physical examination of the patient did not reveal any significant neurological deficits other than a positive palmo-mental and grasp reflex bilaterally. Waxy flexibility was also noted on and off, as was abnormal posturing. As for her mental state there was poor eye contact and she appeared withdrawn. She spoke infrequently. At times she spoke in a childlike manner, however she was frequently electively mute. She had persecutory delusions and heard whispering sounds but was not able to elaborate further. Since she was unable to cooperate

adequately for the exam, it was difficult to assess the rest of her mental state. During her stay in the ward, she attempted to escape because she did not feel safe in the ward. She continued to wet and soil her bed frequently. She did not appear disorientated, though in reality, she was confused for most of her stay in the ward and at times did not even recognize her father.

Extensive blood work showed no positive results. Her full blood count, renal function and liver function tests were normal. Her hemoglobin was 12.1 g/dl, white blood count 6,600/uL and her platelet count was 301,000/uL. In addition, serum thyroid, folate, and B12 levels, as well as serum ceruloplasmin levels were also within the normal range. A lumbar puncture revealed a clear CSF at normal pressure with normal glucose and protein levels. No organisms were cultured.

The EEG showed a normal pattern. However the repeat MRI showed bilateral atrophy of the frontal, temporal and parietal lobes with ventricular dilatation particularly of the lateral ventricles. The atrophy was more extensive than that seen on the MRI done one year earlier. There was no evidence of any space-occupying lesions or infarcts. A brain biopsy was suggested to the family for a definitive diagnosis but they were not receptive to this suggestion.

The patient was eventually discharged home on amisulpride 500mg daily in divided doses. She was unable to come for her follow-up appointment and her father reported that her condition had deteriorated at home. The dose of amisulpride was then adjusted to 800 mg daily.

DISCUSSION

This patient was given the diagnosis of frontotemporal dementia due to her rapidly deteriorating clinical state and radiological findings. The patient exhibited a disorder with insidious onset and rapid progression and early decline of personal and interpersonal social conduct. She also had a change in personality, problems with speech, incontinence, primitive reflexes as well as a normal EEG in the presence of clinically evident dementia. Many of the features of the patient fit with the accepted criteria for the diagnosis of FTD. (Rosen HJ et al. 2002, Neary D et al. 1998)

A delay of 8 years from the onset of symptoms to establishing a diagnosis is certainly a long time. However, the presentation of her symptoms was unusual and inevitably led to an initial diagnosis of schizophrenia. Indeed, during the period of observation in the ward, she could have easily been identified as having catatonic schizophrenia. Obsessive compulsive symptoms are well known to occur during the prodrome in schizophrenia hence giving support to the diagnosis of schizophrenia in the initial phase of her illness (Rosen 1957). More recent evidence has shown that obsessive-compulsive symp-

toms presenting in the prodromal phase of schizophrenia is more often encountered in those whose illness begins in adolescence and has a prevalence of 2% (Rabe-Jablonska 2001). The patient's response to various treatment strategies was dismal and her condition steadily deteriorated suggesting that schizophrenia may not have been the appropriate diagnosis. Although certain primitive reflexes such as the palmo mental reflex and grasp reflexes were present and point to cerebral pathology, their usefulness is limited as they are also found in a quarter of the healthy population, schizophrenics, siblings of schizophrenics and are also seen in other conditions associated with cortical dysfunction (Hyde et al. 2007, Owen and Mulley 2002).

Another diagnosis to consider in this case is new variant

Creutzfeldt-Jakob disease (nvCJD). In comparison to classical CJD which presents with myoclonus, dementia and a rapidly fatal course, the nvCJD frequently presents with psychiatric disturbances and limb dysesthesia as early features and tends to afflict a younger group of patients in addition to having a more indolent course (Sampson et al. 2004). Although rare in Malaysia, it should be a differential diagnosis and a brain biopsy would have helped in making a diagnosis.

It is well documented that structural brain abnormalities are present in patients with schizophrenia and are thought to play a significant role in the pathology of the illness (Rapoport et al. 1997, Rapoport et al. 1999, Reig et al. 2010, Rosenbaum et al. 1994). The most consistent findings are enlargement of the lateral ventricles and the third ventricles (Raz S and Raz N 1990). The frontal lobes, thalamus and limbic structures such as hippocampus and amygdala are also frequently found to be structurally abnormal. The overall effects appear to be a reduction in brain volume and in cortical gray and white matter. While structural abnormalities are present before the onset of disease symptoms, neuroimaging studies have

shown that the changes progress over time with deterioration in brain structure (DeLisi et al 1990). Schizophrenia is an unlikely diagnosis in the case of this patient, as it does not explain the rapid and progressive change in the brain structures as seen in radiographic images within the relatively short duration of time.

There is little past research and literature on the relationship between schizophrenia-like symptoms and FTD. This is because research on schizophrenia generally excludes patients with 'organic' problems. In addition, most clinical diagnostic criteria for FTD available does not emphasize the presence of psychotic symptoms (McKhann GM et al. 2001). In one clinico-pathological case series, 5 out of 17 patients with YOD presented with psychotic symptoms (schizophrenia/schizoaffective disorder or bipolar disorder) for up to 5 years prior to the diagnosis of dementia (Velakoulis et al. 2009). All of these patients had an onset of symptoms at a younger age (mean-35.6) and all had been admitted to a psychiatric hospital where they were diagnosed and treated by psychiatrists (Velakoulis et al. 2009).

In the case of this patient, the delay in detection and treatment of her condition was due to a lack of awareness about FTD and the ambiguous presentation of FTD in the younger age group. She had been subjected to conventional treatment for schizophrenia with antipsychotics and even ECT for her catatonic presentation. Finally amisulpride was initiated to control behaviour and psychosis and was chosen to avoid the extrapyramidal side effects she had experienced with other antipsychotics. Acetylcholine esterase inhibitors were not recommended as they are generally not thought to be useful in FTD.

This case report suggests that psychosis must be investigated in detail, especially when the clinical presentation is not typical and the patient is not responsive to conventional treatment (Jambunathan and Aili 2001).

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