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Case Study

Challenges in diagnosing Treatment-Resistant Schizophrenia (TRS) with Frontal Lobe Atrophy from MRI Imaging: Case Study

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Abstract

The diagnostic criteria for the behavioral variant of frontotemporal dementia were revised recently. Distinguishing both disorders apart as brain imaging studies in patients with schizophrenia also demonstrate changes in the frontal and temporal lobes which can help in the diagnostic process. This paper highlights the challenges in diagnosing Treatment-Resistant Schizophrenia (TRS) with a differential diagnosis of Fronto-Temporal Dementia (FTD) from magnetic resonance imaging (MRI) imaging. From the diagnosis of the case study, it can be summarized that frontotemporal atrophy is often associated with FTD but it may also occur in a patient suffering from schizophrenia. This provides a challenge for medical practitioners to distinguish between FTD and schizophrenia as disinhibition and executive dysfunction may prominent in schizophrenia with (Frontotemporal Atrophy) FTA.

Introduction

Schizophrenia is a common psychiatric disorder [1], characterized by positive and negative symptoms in which the latter is a result of progressive deterioration of frontal lobe function. These symptoms may overlap with frontal lobe syndromes such as Fronto-Temporal Dementia (FTD) where behavioral changes are more prominent than memory loss. This provides difficulty in distinguishing both disorders apart

as brain imaging studies in patients with schizophrenia also demonstrate changes in the frontal and temporal lobes. This paper highlights the challenges in diagnosing Treatment-Resistant Schizophrenia (TRS) with a differential diagnosis of FTD.

Case

Mr. H is a 44 years old Malay man noted to be socially withdrawn and displayed disorganized behavior since the age

of 18. His first admission was when he was 20 years old and for the next 15 years, there have been multiple admissions with no significant improvement despite the many changes in medications and several courses of Electroconvulsive Therapy (ECT). He was transferred to Hospital Tengku Ampuan Afzan (HTAA) in 2007 with a diagnosis of TRS and was already prescribed clozapine. Despite his compliance with medication, there were multiple admissions due to impulsive behavior in response to auditory hallucinations. Different types of medications and therapies were prescribed but the impulsivity persisted. In May 2017, he developed an episode of seizures while on clozapine. A Computerized Tomography (CT) scan of the brain demonstrated bilateral frontal lobe atrophy. There was no bleeding or infarct noted. A Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) test revealed features correlating with frontal and temporal lobe impairment with prominent frontal lobe function deficit. A Magnetic Resonance Imaging (MRI) of the brain (Figure 1) showed features of bilateral Fronto-Temporal Atrophy (FTA). He was discharged to family members with psychoeducation primarily focusing on the management of persistent impulsivity despite the optimal dose of clozapine.

Discussion

Schizophrenia is a common psychiatric disorder that begins in the late teens with a peak age of onset for the first psychotic episode in the early to mid-20s for males and late 20s for females [2]. Individuals with schizophrenia manifest a variety of clinical signs and symptoms, characterized by hallucination, delusion, disorganized speech, grossly disorganized or catatonic behavior, and negative symptoms (apathy, avolition, anhedonia, asociality) associated with impairment of occupational and social functioning, in the absence of

substance misuse and other medical condition that may give rise to the symptoms [2-6].

The negative symptoms account for a substantial amount of morbidity of schizophrenia [2] as a result of progressive deterioration of frontal lobe function [7,8]. However, the deterioration remains stable throughout the course of the illness as opposed to frontal lobe syndromes which are more progressive in nature [8]. Therefore, the negative symptoms of schizophrenia may seem to be overlapping with symptoms of frontal lobe disorders, particularly Frontotemporal Dementia (FTD) where behavioral changes are more prominent than memory loss [7,8].

In contrast, FTD is a progressive neurocognitive disorder that may present as a behavioral variant (behavioral disinhibition; apathy or inertia; loss of sympathy or empathy; preservative, stereotyped, or compulsive/ritualistic behavior; hyper-orality and dietary changes; prominent decline in social cognition and/or executive ability) and/or language variant (semantic; agrammatic/nonfluent; and logopenic), with relative sparing of learning and memory function and visuospatial function. The variants of FTD exhibit a distinct pattern of brain atrophy [2-6].

The progressive development of behavioral changes in FTD provides to be the most interesting area in relation to schizophrenia, particularly negative symptoms [8]. Furthermore, brain imaging studies of patients suffering from schizophrenia have identified the structural and functional changes in the frontal and temporal lobes, even in the first episode, and more extensive changes throughout the course of the illness [8,9]. It is noted that the overlapping symptoms of these two disorders indicate the dysfunction of similar brain

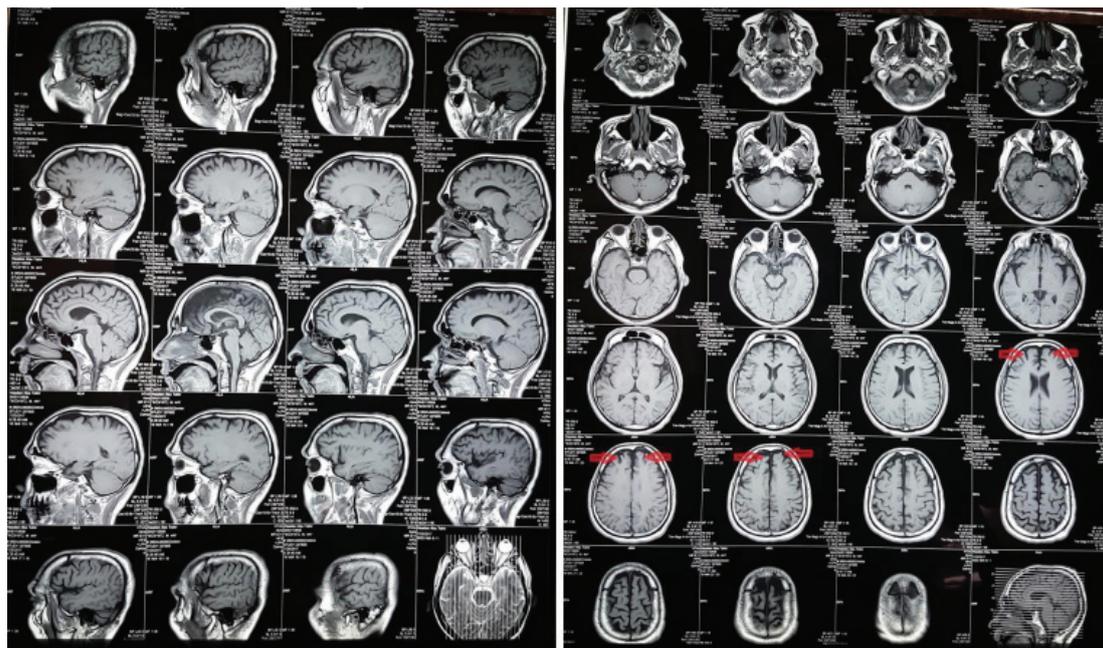


Figure 1: MRI Brain on 25th July 2017 reported features of bilateral frontotemporal atrophy. No focal brain lesion. Blooming artifacts are seen at bilateral basal ganglia suggestive of calcification.



systems and pathways. This exists in either structural changes like Frontotemporal Atrophy (FTA) or functional changes such as impaired functional connections and networks in the frontal and temporal regions [7,8]. Several studies at the molecular level have also demonstrated a potential connection between schizophrenia and FTD, such as TDP-43, tau phosphorylation and grains [8].

Despite the availability of several studies conducted to determine the relationship between schizophrenia and FTD, there is no definite evidence to support the link between these two conditions which leads to diagnostic confusion [8]. More than one-half of patients were misdiagnosed during the initial presentation and the possibility of misdiagnosis is likely due to unusual early age of onset, clinical symptoms (Especially Behavioral Variant) and pathological heterogeneity [8]. The difficulty faced is that schizophrenia is likely to be a phenotypic grouping disorder of heterogeneous (Multiple) etiologies with no consistent neuropathologic hallmarks [8]. The possibility of dementia particularly FTD in patients with schizophrenia is to be considered when there is evidence of prominent cognitive impairment [8]. However, the progressive nature of the cognitive decline in FTD generally reduces the diagnostic confusion and should there be a high suspicion of a neurocognitive disorder: a functional imaging study is warranted such as MRI.

MRI is not routinely done in a patient with schizophrenia, because the main method of diagnosing schizophrenia is based on clinical diagnostic criteria, psychiatric history, and mental examination of the patient [10]. Usually, imaging techniques are used to rule out the differential diagnosis of the organic brain that could cause psychosis. That is why it is important to do brain imaging for early detection of brain abnormalities before the patient was diagnosed with schizophrenia. Recently, MRI is recommended as an important tool in the follow-up process of patients with schizophrenia because few neuroimaging studies have identified substantial evidence of structural and functional brain abnormalities in schizophrenia. However, it is still under debate whether the abnormalities described in this condition can be used as diagnostic biomarkers [3,10].

Therefore, apart from clinical interview and observation which include mental status examination, neuropsychological tests, laboratory investigations and brain imaging (MRI as shown in Figure 1); neurophysiological investigations are also necessary to be carried out in order to achieve high accuracy in the diagnosis. Figure 1 shows the MRI Brain reported features of bilateral frontotemporal atrophy. From the image obtained, it was found that there is no focal brain lesion. Blooming artifacts are seen at bilateral basal ganglia suggestive of calcification. With all the information obtained throughout the management of this case, the impulsivity displayed by Mr.H in response to the auditory hallucination can be explained by the presence of bilateral frontotemporal atrophy as the course of schizophrenia rather than due to FTD [4].

The aims of the diagnosing of this case study using MRI for this patient are to understand more about the disorder e.g. impulsive behavior in response to psychosis, resistance to treatment and another positive finding in line with FTD, etc. The relationship between MRI findings and clinical symptoms becomes more meaningful for this patient, family and therapist as the clinician is able to psychoeducation the family about the relationship and what to expect which can reduce the cost of staying in the institution. It is also for learning purposes for peer practitioners in medicine because this case can be categorized as an unusual case. So it needs to be investigated thoroughly to rule out all possible differential diagnoses like FTD.

Summary

Frontotemporal atrophy is often associated with FTD but it may also occur in a patient suffering from schizophrenia. This provides a challenge for medical practitioners to distinguish between FTD and schizophrenia as disinhibition and executive dysfunction may prominent in schizophrenia with FTA.

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