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A Mania that is not Mania: A Case of Frontotemporal Dementia with Early Onset

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Abstract: *The clinical picture of the behavioural variant of frontotemporal dementia can be very similar to a manic episode. Paying a careful attention to memory and attention problems and assessing the cognitive status of a patient with mania-like symptoms and no previous psychiatric history should be a standard procedure in order to distinguish mania from behavioural variant of frontotemporal dementia. Sometimes, imaging techniques are revealing important aspects that are essential for a correct diagnosis and treatment plan. Here, we present a case of frontotemporal dementia with early onset that had a manic like clinical presentation. Also, we shortly discuss the available pharmacological approaches and outline the importance of thorough differential diagnosis.*

Keywords: *frontotemporal dementia; mania; bipolar disorder; behaviour disorder; frontal lobe.*

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1. Introduction

Mania is an emotional state where an elevated, expansive, or unusually irritable mood exists. People can also experience other symptoms, including: high level of energy and activity, but in an unproductive way, sometimes with unwanted consequences; decreased need for sleep, the person usually awakens several hours earlier than usual, feeling full of energy; grandiosity, an exaggerated sense of importance which may be in power, knowledge or identity; rapid or pressured speech; rapid thinking; tendency to be easily distracted, "clang" associations; increase in risky behaviours, like overspending money; false beliefs (delusions) or false perceptions (hallucinations). The symptoms can last for a week or more and can be a medical emergency. The median age of onset of mania is around age 25. Men and women are equally likely to be affected, but men typically have an earlier age of onset than women (Dailey & Mania, 2020).

Alzheimer's dementia is the most common type of dementia. Frontotemporal dementia (FTD) is an uncommon type of dementia but it is the second most common type in people under 65 years old. Dementia is caused by gradual changes and damage in the brain. FTD is caused by progressive nerve cell loss in the brain's frontal lobes or temporal lobes due to hyperphosphorylated tau proteins that affect axonal transport and microtubule formation. All these histopathological changes determine neuronal apoptosis. Symptoms of FTD, alongside memory and language problems, problems with mental abilities, can include dramatic personality and behaviour changes like: acting inappropriately or impulsively, losing inhibitions (making rude comments about someone appereance, stealing, making sexual gestures in public), overeacting, neglecting personal hygiene, increased interest in sex. These signs are often the first noticeable, therefore diagnosing this type of dementia can be a challenge.

The aim of this paper is to present a case of behavioural variant of frontotemporal dementia (bvFTD) that has a similar clinical presentation to a manic episode. Also, our purpose is to raise awareness of the importance of differential diagnosis at the initial evaluation of a first manic episode, including cognitive and neuroimaging testing. Moreover, we provide a short overview of the current available treatments for bvFTD.

2. Case presentation

A 48-year-old female, Mrs. A, was brought to the psychiatric emergency unit by her son for the following complaints: childish behaviour,

various and repeated verbal and physical conflicts with different people (especially when the patient is contradicted), dromomania, excessive spending (the son complains that his mother spent the entire last salary on second-hand clothes or odds and ends), inappropriate and disinhibited behaviour (the patient is very friendly with strangers). These behaviours were reported by her son to be uncharacteristic for the patient's personality baseline. At the moment of admission, the patient was under treatment with valproic acid 1000mg/day and quetiapine 400mg/day for the last month, being diagnosed with a manic episode in an outpatient setting. Under this treatment, the patient's mental state did not improve, on the contrary, the collateral information provided by her son suggested that the mental state deteriorated in the last month.

The patient worked as a high school teacher, was divorced and living alone and had two sons. The patient had no previous history of psychiatric disorders and did not report having somatic diseases. Also, the patient had no family history of psychiatric disorders. She smoked approximately 15 cigarettes/day and denied using recreational drugs or drinking excessive alcohol.

2.1. Mental state examination

The patient appeared well dressed and well-groomed with a moderate psychomotor agitation state. She was fully oriented in time and space at the moment of admission. The patient initiated and maintained good eye-contact, had hypermobile mimics and extensive gestures. The patient denied experiencing hallucinations. She reported having concentrations problems and a moderate level of distractibility was observed.

At the moment of admission the patient appeared to have good memory function and she did not report any memory complaints. During hospitalization, the patient had numerous episodes of disorientation in time and space and retrograde and anterograde memory deficits. The patient had a fluent, coherent, rapid, and pressured speech. Her thought process was coherent but circumstantial, with flight of ideas and episodic loosening of associations. Overall, Mrs. A thought process was dominated by stereotypy. Mrs. A. denied any delusional ideation or suicidal or homicidal thoughts. She has numerous mnestic confabulations and high self-esteem.

The patient reported "happy" mood with episodes of irritability and her affect was expansive. Her behavior was inappropriate at admission being characterized by excessive familiarity (the patient breached personal limits with the medical stuff several times). She maintained this behavior during

hospitalization but also the patient had numerous moments of disorganized behavior (she pulled out her iv perfusion, wanted to leave the room without any reason during the computer tomography examination). The patient reported high physical energy.

Mrs. A.'s sleep was normal with approximately 8 hours of uninterrupted sleep per night. Her food appetite was within normal limits.

The patient's insight into illness was absent.

Mrs. A. scored 19/30 points in the Mini-Mental State Examination, with zero points in attention, calculation and remote memory domains.

2.2. Course during admission

Mrs. A. vital signs were within normal limits and the complete physical examination was unremarkable. A complete blood count, liver and renal tests, tests of thyroid-stimulating hormone, free thyroxine, vitamin B12 were performed. The blood tests were in normal range. Moreover, the patient was screened for HIV infection and B and C hepatitis viruses infection, all with negative results. The ECG showed no specific changes.

An emergency computed tomography (CT) brain scan was performed and revealed significant global cerebral atrophy. A Magnetic Resonance Imaging (MRI) brain scan revealed significant bilateral temporal and frontal cortical atrophy, the temporal lobes being more affected than the frontal lobes.

Based on MRI brain scan result and the psychiatric symptoms, the diagnose of frontotemporal dementia – behavioural variant was formulated.

Mrs. A was initially treated with a combination of valproic acid, clonazepam and medium to high dose olanzapine (15mg/day) without any substantial improvements. This led to a change of antipsychotic, from olanzapine to risperidone. Also, memantine was added to the treatment plan. Low dose risperidone (3mg/day) and memantine combination led to significant symptom control, managing the disorganized or inappropriate behaviour, the physical aggressive outbursts and other mania-like symptoms. During hospitalization, the social and personal functioning of the patient was improved over roll.

The patient was discharged home with recommendation for close monitoring from her caregivers and family, given that she relied on others for planning and carrying out activities of daily living.

3. Discussion

This case detailed about the importance of excluding an organic cause for any acute psychiatric presentation with no psychiatric history. These patients require a neurological examination, neuroimaging and other selected tests.

Behavioural symptoms in FTD are characterized by disinhibition that produces impulsive actions and a socially embarrassing behaviour, changes in eating behaviour, hoarding, repetitive or stereotypic behaviour, blunting of affect, mental rigidity, loss of empathy, apathy (Piguet & Hodges, 2013). Mrs. A symptoms of elevated mood, irritability, racing thoughts, pressure to keep talking, inappropriate and disinhibited behaviour, dromomania, excessive involvement in pleasurable activities that have a high potential for painful consequences (unrestrained spending money) all suggested mania. Clues that the patient had a neurodegenerative disease included the lack of a psychiatric history, a progressive nature of her symptoms despite appropriate anti-manic treatment and the changes on MRI (bilateral temporal and frontal cortical atrophy). Cognitive test helped the diagnostic process, even if the presence of cognitive deficits would not necessarily excluded a diagnosis of mania. A degree of cognitive deficit is a part of a manic episode, like difficulties with executive function, with linguistic working memory, problems with retention of what's been read or listened to. For example, accelerated thought is a common experience in mania, the consequence can manifest as impaired focus and faulty memory. Also, an unusually volume of thoughts can flood a person's awareness, making difficult to prioritize effective responses. Sometimes, mania comes with the experience of being too focused. Experiencing hyperprosexia can also result in a failure to attend things that really need attention.

In terms of treatment, there are currently no evidence based pharmacological interventions that can change the course of frontotemporal dementia. At this moment, used pharmacological treatments are prescribed off-label and with the scope to manage some symptoms, especially the behavioural ones (Tsai &Boxer, 2014).

Cholinesterase inhibitors and N-methyl-D-aspartic acid (NMDA) receptor antagonists are indicated for the treatment of Alzheimer's disease. A recent paper reviewing the pharmacological treatment of cognitive symptoms in frontotemporal dementia outlined that neither cholinesterase inhibitors (donepezil, rivastigmine, and galantamine) nor NMDA receptor antagonist had an impact on the cognitive decline (Tsai &Boxer, 2014).

Moreover, Tsai and Boxer (2014) concluded that cholinesterase inhibitors could worsen the behavioural symptoms.

Memantine was first thought that could have a role in preventing neuronal cell loss induced by glutamate excitotoxicity and apoptosis. Regarding the benefit of memantine use in FTD, conflicting data is reported in the literature. Some studies assessing the potential positive effect of memantine failed to provide strong evidence in this direction (Tsai & Boxer, 2014). On the other hand, there is some evidence supporting the beneficial effect of memantine in patients with FTD (Kishi et al., 2015). Further research is needed in order to be able to draw conclusive statements regarding the use of memantine in bvFTD.

Several studies indicate selective serotonin reuptake inhibitors to be effective in alleviating the behavioural symptoms present in patients with behavioural variant of frontotemporal dementia (Young et al., 2017). Of all selective serotonin reuptake inhibitors, sertraline, paroxetine, citalopram, and fluoxetine have been studied and might mitigate some of the behavioural symptoms of bvFTD (Young et al., 2017; Tsai & Boxer, 2014). We were cautious in using selective serotonin reuptake inhibitors due to the concern that these drugs could worsen the expansive mood and high energy experienced by our patient.

For managing the behavioural symptoms of bvFTD several antipsychotics have been studied. Quetiapine, olanzapine, risperidone and aripiprazole seem to have a potential role in mitigating behavioural symptoms (Curtis & Resch, 2000; Fellgiebel et al., 2007; Reeves & Perry, 2013; Moretti et al., 2003). In our case, neither olanzapine nor quetiapine improve the behavioural symptoms. Low-dose risperidone (3mg/day) managed successfully the patient's clinical symptoms.

Psychological therapy, including occupational, speech, and language therapy, can be recommended for patients with bvFTD even though controlled evidence is lacking in this area (Warren et al., 2013).

The behavioural variant of frontotemporal dementia can present with marked changes in a patient's personality and behaviour, that may be misdiagnosed. FTD must be distinguished from a non-degenerative illness and from other neurodegenerative diseases. It is very important to rule out medical causes in the case of a new-onset mania. Our case highlights that FTD can present in an acute manner that mimics a manic episode and the importance of a correct diagnosis.

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