Late-Onset Obsessive-Compulsive Disorder With Comorbid Narcolepsy After Perfect Blend of Thalamo-Striatal Stroke and Post-Streptococcal Infection

To the Editor: Concurrent or longitudinal overlaps of narcolepsy with obsessive-compulsive disorder have not been reported in medical literature as yet, despite having causal relations with many organic brain disorders. To our knowledge, we report the first unusual case of a 60-year-old hypertensive woman who presented with a classic "tetrad" of narcolepsy and obsessive-compulsive disorder immediately after a transient episode of reversible ischemic thalamo-striatal stroke, preceded by streptococcal infection.

Late-onset obsessive-compulsive disorder (OCD) appears to be quite rare, with most epidemiological studies reporting rates in the 1% range, with predominance of women that is significantly less pronounced than in other anxiety disorders.[1] The pattern of symptoms is similar to that seen in younger patients, with a few minor differences: elderly patients have fewer concerns about symmetry, need-to-know, and counting rituals, whereas handwashing and fear of having sinned are more common in elderly patients. Elderly individuals may be at higher risk for developing OCD because of their proneness to stroke-related neuropsychiatric disorders. Several reports suggested that late-onset OCD is frequently associated with organic brain diseases, including stroke, transient ischemic attack, and organophosphate poisoning[2–4] The common comorbidities associated with OCD include major depression, tic disorder, psychotic disorder, and impulse-control disorders; however, concurrent or longitudinal overlaps of narcolepsy within both functional and organic causes of OCD have not been reported in medical literature as yet, as shown from an extensive search on MEDLINE and PubMed.

Case Study

"Mrs. X," a 60-year-old, right-handed, graduate housewife, a known hypertensive patient controlled on enalapril 2.5 mg per day for 2 years, was referred to psychiatric services of our hospital on Day 3 of medical intensive care unit admission in October 2010 with the chief complaints of irresistible desire to sleep "in attacks" anytime during day hours, repetitive forward head droops and jaw sags, and persistent obsessive impulses of killing of her only grandson. She had an otherwise-negative medical and psychiatric history and was admitted with a first episode of transient right-sided hemiparesis and hemiballismic movements of the right half of her body, both of which lasted only for a few hours, due to left thalamo-striatal stroke. Her arterial blood gas analysis, liver function tests, and renal function tests were normal, but a recent MRI was noted to be significant for two small, lacunar infarcts in the left basal ganglia. Just a few weeks before admission, she had history of sore throat, fever, productive cough, and elevated antistreptolysin O (ASO) titres (610 IU/ml), which were treated with amoxicillin 500 mg tid for 7 days. She was provisionally diagnosed with organic narcolepsy and was given a morning dose of modafinil 200 mg/day before she was discharged from the hospital. Because her obsessive symptoms were only of 3 days' duration, we had not put her on anti-OCD drugs. For the next 2 weeks, her attacks of daytime sleepiness progressed and began occurring anytime: sitting and reading, watching television, traveling in a car for a short distance to attend social ceremonies or the hospital, and even while talking, and continued to increase initially in frequency, then in duration, but she had been reasonably alert between the attacks for an hour or so, and she described that she was fighting a constant battle against this unusual drowsiness. Her nighttime sleep was impaired. A few times, after awakening from sleep, she felt that she could neither speak nor move, but could open her eyes and was completely aware of her surroundings; she also experienced hypnogogic hallucinations now and then. The latter episodes never lasted more than a minute or so. Also, there were recurrent, persistent episodes of periodic loss of sudden muscular tone, especially of the head and neck region, as well as shoulder and hip-girdle region, which would be very transient, 2–3 times per day, varying in duration, and analogous to newer changes of her old personality, which has made family members more concerned about her. Her Epworth Sleepiness Score was 17, and polysomnography showed 3 to 4 minutes of mean sleep latency time (MSLT) and four-to-five episodes of rapid eye movement (REM) sleep during MSLT in three separate and serial evaluations.

Interestingly and simultaneously, from October 2010 onward, she had progressively worsening anxiety, provoking repetitive, intrusive, and absurd thoughts and impulse of taking her grandson to the terrace

and pushing him down from the second floor. She never liked these thoughts, rather resisted them with internal will and prayed and dreamt that this should never happen to her, and felt guilty that these were her own thoughts about her beloved and only grandson. She described recurrent obsessions of "needing to know" information about her grandson, with resultant checking rituals. This "need to know" was primarily related to the fear of losing control of her own thoughts and impulses. Nevertheless, she never acted on her thoughts and would rather ask her son and grandson to stay away from her. The storming emotions and anxiety would frequently precipitate previously described cataleptic attacks. She had no history of sleep apnea, excessive snoring, epilepsy, head injury, parkinsonism, hepatic or renal encephalopathy, tic disorder, psychosis, mood disorder, drug intoxication, other drug abuse, substance-induced disorder, or family history of psychiatric disorders. Modafinil 200 mg/day did not help in any of these features. She took traditional Ayurvedic treatment for about 2 months on firm insistence of her son and returned to us about 3 months later, in January 2010, disillusioned and frustrated. She recovered dramatically in her unintended sleep episodes and daily naps within 3 weeks with 20 mg of sustained-release formulation of methylphenidate divided in two doses. Cataplexy and obsessive thoughts and impulses almost returned to her premorbid state with 25 mg per day of sustained-release paroxetine by Week 4, and she has been symptom-free for about the last 7–8 months without relapse.

Discussion

This index case, to our knowledge, is the first case to be reported in the literature with comorbid narcolepsy and OCD in stroke or in any organic brain disorder. Our patient had perfect blend of temporal association in the onset and typical features of the narcolepsy tetrad, as well as OCD preceded by streptococcal infection, followed by reversible ischemic stroke. Onset of OCD and narcolepsy is usually in the second decade of the life, and their onset after age 50 is relatively rare and may be more likely to have an organic etiology. Of an OCD patient population of over 1,000 in their landmark study, Weiss and Jenike found only five cases in which symptoms of OCD first developed late in life. Four of these five patients had intracerebral lesions in the frontal lobes and caudate nuclei, findings consistent with current theories about the pathogenesis of "idiopathic" OCD.[4–6] The recency and location of these lacunar infarcts, coupled with the abrupt onset of this patient's symptoms, suggested a causal relationship to the patient's OCD. This explanation is consistent with current etiologic theories of OCD that support a disruption in serotonergic pathways involving the basal ganglia and orbital frontal cortex.[7] One of the elegant fMRI study conducted at the Institute of Psychiatry, London, reported a distinct pattern of neural activation between the washing, checking, and hoarding symptom-profile of OCD. Their results showed that patients demonstrated significantly greater activation than controls in bilateral ventromedial prefrontal regions and right caudate nucleus (washing); putamen/globus pallidum, thalamus, and dorsal cortical areas (checking); left precentral gyrus and right orbitofrontal cortex (hoarding); and left occipitotemporal regions (aversive symptoms, unrelated).[8] These results were further supported by correlation analyses within patients, which showed highly specific positive associations between subjective anxiety, questionnaire scores, and neural response in each experiment. The emergence of obsessive thoughts and impulse of "killing of grandson" and "needing to know" information may be the direct consequence of damage to complex and partially overlapping neural systems that serve to detect, appraise, and react to potential threats.

Excessive daytime sleepiness with involuntary daytime sleep episodes, disturbed nocturnal sleep, and cataplexy are the most common symptoms of narcolepsy. The multiple sleep latency tests[9] clearly helped us in confirming the diagnosis of narcolepsy. The "tetrad" of all four symptoms of narcolepsy occurs in less than 10% of cases which, as seen in the index case, may be explained by the preceding episode of streptococcal throat infection. Several convergent lines of evidence suggest that autoimmune processes may be responsible to a certain extent in narcolepsy, as supported by keen observational findings such as a mutation in the hypocretin receptor gene that has been associated with canine narcolepsy;[10] hypocretin knock-out mice that are genetically unable to produce this neuropeptide exhibit behavioral and electrophysiological features resembling human narcolepsy;[11] finally, CSF levels of hypocretin are reduced in most patients who have narcolepsy with cataplexy.[12] Also, secondary narcolepsy is reported by Marcus et al. in children suffering from brain tumors and also in head trauma and stroke.[13]Aran et al. had demonstrated elevated ASO titres in recent-onset narcoleptic patients, as was also seen in our index case.[14] There has been increasing interest in finding a possible bridge between streptococcal infections and the development of OCD and tic disorders in children,[15] but no such association is reported in the literature in elderly patients

except in our the index case. Also, our case is the first in the literature to bridge the importance of raised ASO titer in both OCD and narcolepsy. However, it is difficult to tease out whether streptococcal infection and the auto-antibody could have also been responsible for producing OCD with comorbid narcolepsy alone or in combination with basal ganglia infarct.

One of the major limitations of our case is that we could not measure CSF orexin level because of unavailability of the facility in our hospital's central clinical laboratory and refusal of the patient to get its level tested from outside. Nevertheless, nature and chance rarely converge to produce wonders or "atypicalities" so as to reveal these very complexities in the field of medicine, and this clinical case is an excellent example of how one can effectively amalgamate, validly analyze, integrate, and understand proposed neurobiological hypotheses in the field of neuroscience for such unrelated neuropsychiatric disorders.

Conflict of Interest: None Declared.

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