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Calcification of the Pineal Gland and Psychopathology in Obsessive-Compulsive Disorder in Children and Adolescents: A Clinical Case Study

Z. El Maataoui[1*], H. Belhadga[1], H. Kisra[1]

[1]Child and Adolescent Psychiatry Service, Ar-Razi Hospital, Salé

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***Corresponding author:** Z. El Maataoui
Child and Adolescent Psychiatry Service, Ar-Razi Hospital, Salé

Abstract **Case Report**

While it is generally believed that they result from the interaction of genetic and environmental factors, some cases of obsessive-compulsive disorder (OCD) can be attributed to specific neurological etiologies. Hence, the interest of this article, which discusses the case of a 13-year-old child, who has been experiencing sleep disturbances since early childhood and is seeking treatment for an obsessive syndrome with severe symptoms and a poor therapeutic response. An assessment revealed the presence of pineal gland calcification. Despite the patient being placed on a suitable treatment for obsessive-compulsive disorder, their symptoms only improved after the addition of melatonin, resulting in a significant enhancement in both their sleep and obsessive-compulsive symptoms on the Yale-Brown Scale**.** Thus, this article highlights the role of the pineal gland in melatonin secretion and also discusses the role of this hormone in the occurrence of mental disorders as well as its therapeutic attributes in psychiatry.

Keywords: Pineal Gland, obsessive-compulsive disorder, neurological etiologies, mental disorders.

INTRODUCTION

Obsessive-Compulsive Disorder (OCD) is a common, chronic, and often debilitating condition characterized by unwanted and distressing thoughts (obsessions) and repetitive behaviors that an individual feels compelled to engage in (compulsions) [1, 2]. Compulsions can manifest as either overt actions or mental rituals, typically aimed at alleviating the distress caused by obsessions. OCD affects 2-3% of the American population [3] and is associated with significant functional impairment [4, 5] and an increased risk of premature mortality [6]. The established first-line treatments for OCD include cognitive-behavioral therapy with exposure/response prevention (ERP) [7, 8] and serotonin reuptake inhibitors (SRIs) [8 - 9]. Approximately 25-40% of patients do not respond to either of these modalities [10, 11], and few achieve complete symptom resolution [12].

Although it is generally believed that they result from the interaction of genetic and environmental factors, some cases of OCD can be attributed to specific neurological etiologies [13]. Evidence of the role of the basal ganglia in the pathophysiology of OCD comes from case reports of 'nature's accidents' such as Sydenham's chorea [14], von Economo's encephalitis [15], and ischemic events [16, 17].

The Obsessive-Compulsive Disorder (OCD) working group within the Enhancing Neuro Imaging Genetics through Meta Analysis (ENIGMA) consortium led the efforts to identify structural brain anomalies in OCD. An analysis of 16 pediatric datasets and 30 adults revealed subcortical structural asymmetry in pediatric cases but not in adults with OCD [18]. In another ENIGMA study, no detectable structural brain differences were identified when comparing MRI scans from 2,304 OCD patients to 2,068 healthy controls [19].

Other studies have focused on the processes of central nervous system calcifications and their impact on the psychopathology of mental disorders. Hence, the interest of this work is to highlight the calcification of the pineal gland and its involvement in the development of OCD in children and adolescents

CLINICAL OBSERVATION

This is a 13-year-old child, born from a well-monitored pregnancy with a medically-assisted vaginal delivery. His psychomotor and emotional development was marked by sleep disturbances, including difficulties falling asleep and frequent awakenings.

The patient first visited our service two years ago, presenting with a symptomatology characterized by

intrusive thoughts related to cleanliness. He would wash his hands multiple times a day, take showers lasting several hours, perform movements in a specific order that he felt compelled to follow in response to internal urges, along with rituals of organization and frequent checks. These thoughts were associated with internal tension and anxious rumination related to the compulsive activities, which only slightly alleviated his anxiety. Given the severity of the symptoms and their impact on the child's and his family's functioning, an evaluation was conducted, including a brain MRI, which indicated pineal gland calcification.

The patient was initially placed on selective serotonin reuptake inhibitors (SSRIs). A few days later, he exhibited psychomotor agitation, logorrhea, disinhibition, racing thoughts, and insomnia, with a score indicative of a hypomanic syndrome on the Young Mania Rating Scale. This symptomatology subsided after discontinuing the treatment. The patient was then switched to another class of SSRIs, resulting in the reappearance of the hypomanic syndrome. Subsequently, the patient was prescribed Aripiprazole, which led to a slight improvement in obsessive and mood symptoms according to the Yale-Brown Obsessive Compulsive Scale and the Young Mania Rating Scale, respectively. However, the patient continued to experience sleep disturbances, for which he was started on 10mg of melatonin. One month later, the patient was seen for a follow-up consultation with a significant improvement in his sleep and obsessive symptoms.

DISCUSSION

Before the presentation of a complete obsessive-compulsive disorder (OCD) picture, the patient in our study had been experiencing sleep disturbances since early childhood. Although relatively understudied, sleep disorders have also been implicated in obsessive-compulsive disorder (OCD) [20]. OCD is characterized by obsessions, or intrusive and repetitive thoughts, and compulsions, which are behaviors adopted repetitively to alleviate distress associated with obsessions [21]. Indeed, a limited yet growing body of literature has revealed associations between insomnia and OCD symptoms [22], as well as disruptions in sleep continuity.

Melatonin and Sleep Disorders

In addition to subjective sleep disturbances, recent studies have also examined sleep continuity in OCD, but the results have not been entirely conclusive. Indeed, subjective sleep continuity is not related to OCD symptoms in cross-sectional samples [23] and does not predict OCD symptoms over three months [24]. Similarly, a recent study examining daily sleep and OCD symptoms in a sample of adults with and without OCD found no relationship between last night's subjective sleep continuity and OCD symptoms the following day [25]. In contrast, a study using actigraphy, an objective measure of sleep continuity, revealed decreased continuity and sleep efficiency, as well as increased sleep onset latency in adults with OCD compared to healthy controls [16]. These divergent results suggest an intriguing possibility that individuals with OCD may overestimate the duration of their sleep while presenting objective indicators of disrupted sleep continuity. In addition to discontinuous sleep, the patient in our study also experiences difficulties falling asleep. In this regard, there is a growing body of work implicating circadian rhythms in OCD (see Nota, Sharkey, and Coles [28] for a review). For example, a later sleep time was associated with increased OCD symptoms the following day in a recent daily monitoring study of adults with and without OCD, even when controlling for depression and previous OCD symptoms [25]. These findings could indicate the role of delayed circadian rhythms in the experience of OCD symptoms. Alternatively, sleep delay may lead to a reduction in total sleep time [26]. Together, these results further underscore the importance of evaluating both objective and subjective sleep synchronization and continuity in OCD."

Despite our patient being initially treated appropriately for his condition, a significant improvement in obsessive and compulsive symptoms only occurred after adding melatonin to address his sleep disturbances. In a similar vein, in a study involving adults with OCD who received repetitive transcranial magnetic stimulation, non-responders to the treatment reported increased sleep disturbances before treatment compared to treatment responders, and circadian rhythm disturbances predicted treatment response [26]. Other studies have shown that more general sleep disturbances were associated with the severity of OCD symptoms (Raines, Franklin, and Carroll, 2019; Sevilla-Cermeño et al., 2019) – however, existing literature suggests that examining sleep behavior aspects most closely associated with biological and behavioral circadian rhythms (e.g., bedtime) may be the most likely to be associated with the severity of OCD symptoms and treatment outcomes, especially in a sample of individuals with more severe OCD.

Thus, several studies have demonstrated the involvement of melatonin in sleep disorders, and it has recently garnered significant attention due to the observation that patients with neuropsychiatric disorders generally have abnormal melatonin secretion. Many neuropsychiatric disorders, including anxiety, depression, insomnia, narcolepsy, epilepsy, schizophrenia, Parkinson's disease (PD), and Alzheimer's disease (AD), exhibit disrupted circadian rhythms [27]. A recent review on melatonin usage indicated the involvement of the melatonin MT2 receptor in the pathophysiology of sleep disorders, anxiety, depression, Alzheimer's disease, and pain. It also reported that selective MT2 receptor agonists have hypnotic and anxiolytic properties, and selective MT2 receptor agonists are being investigated for the potential treatment of mental disorders with limited available

pharmacotherapies. The potential of melatonin to treat various neuropsychiatric diseases could be explained by its pleiotropic biological effects, some of which are mediated through MT receptor activation, while others are due to its strong antioxidant activities that protect nuclear and mitochondrial DNA from reactive oxygen species. AFMK and AMK are melatonin degradation products with excellent radical scavenging activity [28] [29].

Melatonin and Pineal Gland Calcification:

Melatonin is secreted by the pineal gland, a small neuroendocrine organ in the brain resembling a pine cone that regulates circadian rhythms and sleep through circadian melatonin secretion [29]. The pineal gland's functions in terms of altering melatonin secretion and modifying daytime or nighttime peaks have been assessed in patients with schizophrenia, bipolar disorder, and major depressive disorder [30,31]. In recent years, the examination of circadian rhythms and neuropteroid imbalance has been considered in the investigation of OCD [31]. Furthermore, it has been reported that there was a delay in slow-wave sleep and an increase in nocturnal secretion of adrenocorticotropic hormone (ACTH) and cortisol, a stress hormone linked to melatonin [32]. Catapano and Monteleone assessed 24-hour melatonin and cortisol secretion in OCD patients compared to healthy control subjects [33]. OCD patients may exhibit hypervigilance and difficulty falling asleep [33]. On the other hand, circadian rhythm biomarkers have been reported in OCD patients. OCD can manifest as hypervigilance and difficulty falling asleep. OCD patients may have hyperactivity of the hypothalamic-pituitary-adrenal axis, increased secretion of adrenocorticotropic hormone and cortisol, as well as reduced melatonin secretion."

The secretion of pineal melatonin may be disrupted by various dysfunctions that can affect this gland, both morphological and functional.

In this regard, the brain MRI conducted on our patient revealed calcification of this gland responsible for melatonin secretion. Pineal gland calcifications are formed around corpora arenacea, which are primarily composed of magnesium and calcium [34]. Due to the high vascularity of the gland, it is often described as resembling a renal glomerulus. Therefore, it is common to find calcium deposits in the pineal gland, which is why they appear on an MRI. This process is widespread among all species and its rate increases with aging [35]. Physiologists have proposed some mechanisms for pineal calcifications, but the exact cause remains unclear [36]. Although these calcifications have been considered entirely physiological anomalies, physiologists are now beginning to view them as pathological entities and metabolic abnormalities [37]. Advanced research into the biochemistry of this process could lead to new discoveries. With the advances in medical imaging, various types of intracranial calcifications have been discovered. Although many types of calcifications are observed in the brain, both in computed tomography and MRI, the pineal gland has one of the highest rates of calcification in the human body. In a study involving 12,000 healthy subjects, it was observed that 71.6% of them had pineal gland calcifications [37]. It is worth noting that patients who died from renal failure had some of the highest rates of pineal calcification.

CONCLUSION

Therefore, our analysis supports the hypothesis that the patient in our study is experiencing obsessive-compulsive disorder secondary to a disruption in melatonin secretion, which is attributed to calcification of the pineal gland. This warrants further evaluation for other calcifications and long-term monitoring.

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