Development of Obsessive-Compulsive Disorder Following a Pineal Germinoma: A Case Report

To the Editor: Research on obsessive-compulsive neurobiology has focused on the orbitofrontal cortex and the basal ganglia, and less attention has been given to the functioning of the pineal body. A recent article by Vijay A. Mittal, Ph.D., and colleagues in the September 2010 issue of the Journal described a pediatric case in which a pineal region tumor was associated with simultaneous onset of obsessive-compulsive and psychotic symptoms (1). We report on the case of an adolescent with obsessive-compulsive and anxiety symptoms that emerged immediately subsequent to oncological treatment for a pineal germinoma.

“Jonathan” is a 16-year-old young man who presented with severe obsessive-compulsive symptoms, including contamination fears, cleaning rituals, scrupulosity, and checking compulsions, as well as significant generalized anxiety and depressive symptoms. Approximately 3.5 years before presenting to our clinic, Jonathan was diagnosed with a pineal germinoma. Before this diagnosis, he reported no obsessive-compulsive or anxiety symptoms of note and no relevant developmental issues. Jonathan completed radiation therapy and chemotherapy per protocol ACNS0232. Treatment of the germinoma was successful; a multiplanar multisequential brain MRI with and without contrast 2 years after treatment showed a stable postoperative appearance without evidence of tumor recurrence, and no other substantial changes in brain structure were observed. Immediately after completing the germinoma treatment protocol, Jonathan exhibited a dramatic onset of obsessive-compulsive symptoms in the absence of any immune triggers. At the time he presented to our clinic, he was taking fluoxetine (40 mg/day), duloxetine (90 mg/day), and risperidone (1 mg/day), which were collectively associated with partial response.

The timing of symptom onset suggests a possible association of obsessive-compulsive symptoms with pineal body functioning and its associated neurotransmitter, melatonin. In their case report, Mittal et al. (1) considered the obsessive-compulsive symptoms that developed after a pineal tumor to be possibly related to a basal ganglia stroke that occurred concurrently with the tumor. That did not occur in our case. While pineal functioning has received relatively little attention in obsessive-compulsive disorder (OCD), several lines of converging evidence may suggest relevance. First, case reports have focused on pineal lesion effects in anorexia nervosa (2), which has high comorbidity and some etiological concordance with OCD. Second, melatonin may alter serotonin metabolism (3), and melatonin disturbance has been reported in OCD (4). This case contributes to a small but growing evidence base for pineal gland functioning in the pathogenesis of OCD and related disorders and indicates future work to assess the relationship between melatonin and other biological mediators in OCD (e.g., serotonin).

References

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Response to De Nadai Letter

To the Editor: We appreciate the opportunity to respond and comment on this fascinating case, in which the presentation of obsessive-compulsive symptoms immediately followed the incidence and treatment of a pineal gland germinoma in an adolescent young man. In our case, the patient began to exhibit psychotic symptoms (e.g., olfactory and auditory hallucinations, belief in mind reading) and obsessive-compulsive symptoms (e.g., making idiosyncratic hand gestures, exhibiting a preoccupation with checking the time, and insisting that the bed covers be folded a certain way) during the development of a pineal tumor, but the precise etiology was obfuscated by a variety of factors, including a basal ganglia stroke. While the psychotic symptoms remitted after successful treatment of the tumor with chemotherapy, the obsessive-compulsive symptoms persisted. This is consistent with the case report of “Jonathan,” reported by Mr. De Nadai and colleagues, for whom the onset of obsessive-compulsive symptoms began abruptly after the successful treatment of a pineal germinoma. In contrast to our case, however, Jonathan had no known basal ganglia involvement. These findings further implicate pineal body dysfunction in the pathophysiology of obsessive-compulsive disorder (OCD).

As noted in our report, through the production of melatonin and subsequent modulation of sex hormones, the pineal gland is a key structure involved in sexual development and regulation of the onset of puberty (1). It is notable that both cases involve adolescent young men. Although it is not clear...
whether pineal involvement in OCD and psychosis has the same pathophysiologic significance, disruption of the pineal body during this developmental stage may lead to common behavioral manifestations in the two cases described. The average age at onset for both OCD and psychotic illness is earlier for men, and the emergence of symptoms in both disorders often closely follows the transition to puberty. Furthermore, both disorders are marked by significant disruption in circadian rhythm and sleep (2), suggesting abnormalities in melatonin regulation. Finally, in addition to the synergistic effects with serotonin noted by De Nadai et al., there is also evidence that melatonin may have antioxidant and neuroprotective effects (3). Disruption of the pineal body may thus have lasting effects in the developing brain, and understanding these relationships may shed light on how hormonal changes are related to the onset of idiopathic psychosis or OCD.

Continued work aimed at determining how a pineal tumor may be etiologically related to both psychotic and obsessive-compulsive symptoms may increase our understanding of factors underlying the complex relationship between these two disorders. Indeed, pineal abnormalities and melatonin continue to be routinely implicated in psychotic illness as well (4). As both OCD and attenuated psychotic symptoms are highly comorbid in the schizophrenia prodrome (5), longitudinal studies of youths at high risk for both disorders are necessary to further develop our understanding of possible common etiologic mechanisms.

References


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Alternative Explanation for fMRI Findings in Social Phobia

To THE EDITOR: In the December 2010 issue of the Journal, Karina S. Blair, Ph.D., and colleagues (1) analyzed the differences in processing unintentional and intentional social norm transgressions comparing patients with generalized social phobia and healthy volunteers. They found that patients with generalized social phobia showed an increased response to unintentional transgressions in the medial prefrontal cortex. The investigators also described increased responses in the amygdala and the insula, arguing that this must be because of a greater general responsiveness to social stimuli in social phobia.

In this study, the authors extensively described how they presented the stimuli and how they analyzed the fMRI results. For example, they excluded alternative explanations of their findings, such as the influence of low mood as measured on the Inventory of Depressive Symptomatology–Self Report scale. However, the authors gave only one example of the stimuli they used, namely, choking and coughing up food (unintentional) and spitting out bad-tasting food (intentional). This example is very likely to be perceived as disgusting, and this makes one wonder whether all of the harmless social norm violations used in this study were disgusting.

There are harmless non-disgusting transgressions, such as wearing two different shoes, which can be done intentionally or by accident. It is unclear from the information provided if these types of stimuli were included in the study, and if so, how many of the 26 stem stories described non-disgusting transgressions. In general, the stimuli used in fMRI studies should be made public, or an extensive description should be offered in order to make replication of the study possible.

However, in this particular study, there is another reason to describe the stimuli more precisely, as an alternative explanation for the findings is possible. Disgust stimuli can activate the insula (2), and there is evidence for increased activation of the insula in response to disgust faces in social phobia (3). Therefore, on the basis of the information provided, increased sensitivity to disgust could explain the difference in insula responses between patients with social phobia and healthy comparison subjects.

References


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Response to Hubbeling Letter

To THE EDITOR: Dr. Hubbeling provides a thoughtful commentary on our recent article on social norm processing in generalized social phobia, making two points that we will consider in turn.

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