A 44-Year-Old Woman with Intrusive Thoughts

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A 44-year-old unmarried woman with a diagnosis of schizoaffective disorder, post-traumatic stress disorder, and more than 20 previous hospitalizations presented to the emergency department with a complaint of “losing it.”

She reported 2 weeks of progressively worsening “voices.” On further questioning, the patient described these voices as her own thoughts intrusively indicating the occurrence of terrible circumstances (loss of her house and the ending of the relationship with her boyfriend). She had insight into the fact that these events were not actually occurring, but she could only briefly reassure herself before these thoughts would again interject and lead to significant worry and distress. She had no previous history of auditory hallucinations. She presented to the behavioral emergency center; inpatient admission was recommended due to the significant impact these symptoms were having on her functioning. Although she was not behaving in a disorganized manner, her distress was so intense she was not able to care for herself.

Due to residual symptoms, 1 month before admission, her outpatient psychiatrist had increased her clozapine dose from 125 mg to 150 mg. Clozapine was noted as the most effective therapeutic intervention in the treatment of her symptoms compared with treatment with other neuroleptics. Her previous antipsychotic medication trials included: ziprasidone; paliperidone; risperidone; quetiapine; and aripiprazole.

She had not been hospitalized for 2 years prior to this admission, despite many prior frequent hospitalizations. At the time of admission, she had been on clozapine for 30 months. She was also taking lisinopril, levothyroxine, insulin, hydroxyzine, and metformin.

The patient described a history of schizoaffective disorder starting at age 19 years during her freshman year of college. In addition to a history of multiple hospital admissions, she reported difficulty functioning effectively in the occupational setting, having received Social Security Disability Insurance for 22 years. However, she reported being an active volunteer at a nursing home within walking distance of the townhouse shared with her boyfriend and owned by her mother.

During the hospitalization, she continued to report symptoms of intrusive, egodystonic thoughts. She described these thoughts as “uncontrollable,” as if her “head was in overdrive.” Her thoughts centered on fears that her boyfriend was going to end their relationship, and the hospital was going to take away her townhouse. She acknowledged these events were not reality-based, but continued to perseverate on these worries.

To relieve her anxiety, she would repeat aloud or in writing that these circumstances “were not true.” She would also call her mother many times a day for reassurance, or ask staff to confirm that these negative events were not going to happen.
Schizophrenia with Comorbid Obsessive-Compulsive Symptoms

At the time of presentation, the differential diagnosis of her symptom presentation included decompensation of her schizoaffective disorder vs. a comorbid obsessive-compulsive spectrum disorder. Her clozapine level was 348 ng/mL and norclozapine level was 171 ng/mL. To target mood stability, her clozapine dose was increased to 200 mg daily. However, after 6 days her symptoms did not improve and citalopram 20 mg was initiated to target obsessionality. One day after starting the citalopram, the patient reported improvement in her anxiety and reported her thoughts were slower.

The remainder of the hospital course was variable with alternating periods of both improved insight and distress. She experienced sedation related to the increased dose of clozapine; therefore, the dose was decreased to 150 mg daily. A second rationale for decreasing the dose was related to the concern that clozapine may have induced obsessive-compulsive symptoms.

DISCUSSION
The relationship between obsessive-compulsive symptoms (OCS) and schizophrenia has long been studied, with an estimated 24% of patients with schizophrenia meeting criteria for obsessive-compulsive disorder (OCD). Comorbid OCD/OCS with schizophrenia has been associated with significantly worse positive and negative symptoms and significantly worse motor dysfunction when compared with patients with schizophrenia without OCD/OCS.

Although the exact relationship remains unclear, explanations for this commonly identified comorbidity include: 1) comorbid OCS and schizophrenia patients may represent a pathophysiological subgroup of patients with schizophrenia; 2) OCS and schizophrenia may share a common genetic predisposition; 3) OCS may be induced by treatment of schizophrenia with atypical antipsychotics; and 4) previously existing OCS may be exacerbated by treatment with atypical antipsychotics.

Use of antiserotonergic atypical antipsychotics has been implicated in association with OCS theoretically related to antagonism of the 5HT2 receptors. Clozapine specifically has been cited in association with OCS in a number of case reports. However, retrospective chart reviews attempting to elucidate a relationship between clozapine and OCS have been mixed. Ghamei and colleagues reviewed 142 patients treated with clozapine and found no cases of de novo OCD secondary to clozapine treatment and no clear worsening of OCD symptoms. However, of the 142 patients in the study, only 41 had a diagnosis of schizophrenia; 52 were diagnosed with schizoaffective disorder.

De Haan and colleagues conducted a retrospective cohort study...
of 121 patients admitted with psychotic disorders, 91 of whom were diagnosed with schizophrenia and 17 with schizoaffective disorder. In this study, there was a significant relationship between the use of clozapine and the worsening or emergence of OCS: 20.6% of patients on clozapine developed OCS compared with 1.3% of patients treated with other antipsychotic medications (typical antipsychotics and risperidone).\(^5\)

In a comparison of patients receiving haloperidol or clozapine, Sa and colleagues\(^3\) did not find a statistically significant difference in the prevalence of OCS in patients receiving haloperidol vs. clozapine. However, they found that patients receiving clozapine had a significantly greater severity of OCS, as measured by the Yale-Brown Obsessive Compulsive Scale (Y-BOCS total score of 21.5 vs. 12.7).\(^3\)

Regardless of whether or not obsessive symptoms are induced or exacerbated by clozapine, the underlying issues of notable comorbidity and the need for effective treatment remain. De Haan and colleagues\(^6\) showed mixed results with use of selective serotonin reuptake inhibitors (SSRIs). A randomized, controlled trial assessing the use of fluvoxamine in the treatment of comorbid OCD in patients with schizophrenia showed improvement in Y-BOCS total and compulsive scale.\(^10\)

In addition, there are case reports describing the use of aripiprazole augmentation in the treatment of clozapine-associated OCS.\(^11,12\) In all nine cases, patients developed OCS or experienced a worsening of OCS after initiating clozapine, and in all cases the addition of aripiprazole (average dose 22.9 mg daily in the study by Englisch and colleagues\(^12\) and 30 mg daily in the study by Vallari and colleagues\(^11\)) was associated with improvement in OCS. Englisch showed a decrease in total Y-BOCS score from 18.7 to 12.43 after initiation of aripiprazol, with a mean observation period of 9.7 weeks.

**CONCLUSION**

Patients with previous psychiatric history warrant re-evaluation when their symptoms differ from previous presentations. With this patient, it was important to differentiate psychotic delusions associated with schizophrenia from egodystonic obsessions associated with OCS. This patient demonstrated insight and recognized the ideas as her own thoughts. She actively worked to resist them, although at times unsuccessfully. Given this patient’s subacute symptom presentation associated with an increased dose of clozapine, her symptoms warranted consideration of pharmacologic side effects.

**REFERENCES**