Case Presentation

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42 years old male with a 20 years history of Schizophrenia. He was admitted to inpatient psychiatric unit for 2 weeks with complains of auditory hallucinations and paranoid delusions. He had specific delusion that FBI had implanted a chip in his neck when he had surgery at a military hospital at age 19 years. He wanted to get that chip out and he was looking for surgeon who would perform surgery.
Past History: He was admitted to psychiatric units for more than 10 times and had two suicide attempts a few years ago. He was admitted involuntary 3-4 times.

Medication history: A thorough review of his medication history was done. He had been treated with Haloperidol for several years, which was discontinued as he developed tardive dyskinesia type symptoms. He also had trials of Risperidone, Olanzapine and Quetiapine at maximum therapeutic dosages. He was compliant with his treatment and medication was given to him under supervision of his board and care staff.
Substance abuse history: 20 years history of cigarette smoking, 1-2 packs per day. Had used alcohol, cocaine and methamphetamines when he was in his 20s and 30s. Had attended court ordered substance abuse program at age 34 years and he is clean and sober since then. He is attending AA/CA meetings regularly.
Hospital course: He has treatment resistant Schizophrenia, which was not responding to first and second generation antipsychotic medications.

We planned to start a trial of Clozapine, which is reserved for treatment resistant psychotic disorders.

After medical work-up, Clozapine was started at 25 mgs per day orally and titrated to 450 mgs per day (225mgs twice a day).
Clozapine induced agranulocytosis can be life threatening, and as per FDA protocol, we monitored his cbc and differential on a weekly basis.

His hallucinations and delusions subsided and he was able to tell us that his thoughts of implanted chip may have been his imagination, but he was not sure. He didn’t have any auditory hallucinations.
He was discharged to his board and care with a weekly outpatient follow-up for labs and medication refills.

2 weeks after his discharge form the hospital, he was missing from his board and care and later on the same day, he was found by the police running on streets showing bizzare behaviors. He was yelling at people and trying to take the imaginary chip out of his neck.
He was seen in the ER, his drug screen was negative and there was no evidence of alcohol ingestion.

His basic lab work was normal and he was stabilized in the ER with haloperidol and lorazepam and later transferred to a locked inpatient psychiatric unit.
His clozapine level was sub therapeutic at the time of admission.

He was stabilized again on clozapine in next 2 weeks.
Most of the inpatient psychiatric unit are non smoking now and patients are given nicotine patches during their stay on the units.

Our patient started smoking cigarettes when he was discharged from the unit.
Clozapine is substrate for P450 1A2 and tobacco is inducer of 1A2.

Several case reports have been published with smoking induced decrease in clozapine level.

Bondolfi et al published a paper in Therapeutic Drug monitoring in 2005. They have found three fold increase in clozapine level in a patient who was admitted to a non smoking psychiatric unit.
Van der Weide et al have published a study in Pharmacogenetics in 2003. Recently, a single nucleotide polymorphism identified at position 734 of the CYP1A2 gene, was reported to affect the inducibility of the enzyme. Because this polymorphism in relation to smoking behavior may be relevant in treatment with clozapine. They studied the effect of CYP1A2 genotype on clozapine clearance and dose requirement in a group of 80 smoking and non-smoking schizophrenic patients on long-term clozapine therapy. Clozapine serum concentration and CYP1A2 genotype had been determined routinely

- In smokers, the clozapine serum concentration corrected for dose (C/D ratio) was on average 2.5 times lower compared with non-smokers, indicating an enhanced clearance.
- They didn’t find effect of polymorphism on clozapine level.
Meyer JM have published a study in Journal of Clinical Psychopharmacology in 2001 and they examined 11 patients at a state hospital who were stabilized on clozapine and analyzed their clozapine levels before and after nonsmoking policy was instituted.

They found a mean increase of 72% in serum levels after smoking cessation in this population.
Dosage adjustment based on smoking behavior would be of value in order to lower the incidence of non-therapeutic serum drug levels and, consequently, intoxication or inadequate antipsychotic response.