

## Case Report

# A Case of Chronic Schizophrenia with Emergent Dementia: Successful Medication Reduction and its Explication

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## Abstract

The emergence of dementia during the treatment of schizophrenia is a problem that occurs in many patients. Despite the appearance of strong cautionary language on the product labels of antipsychotic drugs, advising clinicians to avoid the use of these medications in the setting of dementia, there is no specific guidance for the management of dementia in schizophrenia. Here, we report the case of successful antipsychotic drug reduction in a 63-year-old male with paranoia and severely impaired cognition. We explain possible explanations and the implications of this result.

## Introduction

Throughout the history of medicine, there has been great confusion about the characterization and management of psychotic features in dementia, and/or cognitive deficits in psychosis. In 1893, the term dementia praecox was introduced as a specific disease entity by German psychiatrist Emil Kraepelin. Kraepelin's label – which emphasized deficits in attention and memory in the context of delusions (paranoia), abnormal movement (catatonia), or disorganized thoughts (hebephrenia) – predicted a chronic and progressively deteriorating course [1,2]. When, in the 1950s, dementia praecox was eventually replaced by the word, schizophrenia, this expectation of cognitive decline continued.

Following the identification of premature mortality in elderly demented patients who participated in randomized controlled trials of antipsychotic drugs (a problem later confirmed by naturalistic and observational studies), the U.S. Food and Drug Administration attached Black Box Warnings to the labels of dopamine blocking drugs [3-5]. However, no guidance was issued with respect to the management of dementia which emerges in the course of treating chronic or recurring psychosis. The purpose of this case report is to present an example of successful medication reduction in the latter scenario, and to briefly consider the treatment implications of this result.

## Case Report

Prior to our involvement with this case, a 63-year-old male with a longstanding history of schizophrenia and remitted alcoholism had undergone two recent medical admissions to the hospital: first, for the stabilization of starvation ketosis caused by the delusion that his food and medications were being poisoned; second, for acute delirium

and ataxia which were likely precipitated by antipsychotic drug treatment [6-8]. A workup for dementia in the previous admission had included an MRI of the brain which displayed cortical atrophy, moderate ventriculomegaly, and (by our review) marked deep white matter hyperintensities, consistent with Fazekas stage three changes. The patient was discharged to his residential care home on one psychotropic medication (olanzapine 5 mg bid).

Four weeks later, the patient presented to the emergency room with the recurrence of failing hygiene and the belief that his food, beverages, and medication were being poisoned. He was admitted to the psychiatric unit, where initial examination was notable for poor grooming and thin body habitus. The patient was edentulous and appeared fifteen years older than his chronological age. The initial treatment team prescribed olanzapine 5 mg bid and added Vitamin D3 1000 IU qd. The patient initially declined all medications and demonstrated limited acceptance of fluids and food.

By hospital day #3, members of the nursing team noticed deficits in short-term and long-term memory, including an inability to recall the names of staff members; an inability to recall his age or birthdate; and an inability to recall what he had eaten for breakfast. Though he remained alert and calm, he was disoriented to date, identifying the year as 1934.

On hospital day #4, the authors of this case report assumed care of the patient concurrent with a rotation in treatment teams. We administered the St. Louis University Mental Status Examination, on which the patient scored 3 out of 30 possible points (oriented to date and year, but unable to perform any other elements of this screening test). This reflected severe deficits in attention, memory, spatial orientation (apraxia), language (aphasia), and executive functioning.

Based upon a reported history of several months of steady cognitive decline, severe enough to impact baseline social functioning, the authors prioritized a working diagnosis of dementia. Consultations were requested from physical therapy (recommending close supervision as the patient's "path" would deviate due to poor attention) and speech therapy (recommending soft foods due to mild dysphagia). The nursing team attended to the patient's hygienic needs: trimming nails; shampooing hair; assisting with clean clothing.

A revised dementia workup was undertaken, ruling out syphilis (RPR was negative), anemia (iron and ferritin levels were within normal limits), and nutritional deficiencies (normal levels of B12, B6, B1, folate, zinc, and copper; Vitamin D 25-oh was 38 ng/mL).

Olanzapine was discontinued due to its anticholinergic effects. Risperidone (1 mg bid) was prescribed to prevent neuroleptic withdrawal symptoms. Other treatments were revised to include memantine (5 mg at bedtime), B12 (1 mg daily), Vitamin D3 (increased to 4000 IU daily), selenium sulfide shampoo (for dry scalp) and chlorhexidine gluconate mouth wash (for halitosis/gum health).

By hospital day #5, the patient remained vague, confused, and hypersomnolent. However, his paranoid delusions subsided. He continued to be free of auditory or visual hallucinations, thought blocking, or other features of psychosis.

By day #8, he demonstrated consistent compliance with medical treatments. He was eating well and participated regularly in scheduled activities on the unit. The patient was oriented to self, date, and place, but was unaware of his cognitive limitations (anosognosia). Deficits remained in the domains of memory (inability to identify his diagnoses, recite the events which had led to the admission, identify his treatments, or recall the names of his doctors); speech (illogical mumbling, poor verbal fluency), and executive functioning (inability to organize instrumental activities of daily living, inability to attend to hygiene without supervision). We believe that the severity and persistence of these problems, which continued despite the resolution of paranoia, supported the ascendancy of dementia as the primary condition in this case.

With the consent of his conservator, the patient was discharged back to his residential care home due to his continuing inability to independently coordinate food, clothing, shelter, medical care, or finances. Follow-up was planned with psychiatry, primary care, and neurology – the latter, to confirm our working diagnosis of dementia due to multiple etiologies. Discharge medications included: risperidone 1 mg po twice a day, Vitamin D3 4000 IU po daily, B12 1 mg po daily, and memantine 5 mg po at bedtime.

## Discussion

Upon admission, the patient exhibited signs of poor grooming and hygiene, as well as paranoia regarding his food and medications. As we were not convinced that his delusions were entirely attributable to the historical diagnosis of schizophrenia, we considered a broad differential etiology of cognitive and psychotic symptoms.

Past diagnoses had included alcohol dependence, from which the patient had been entirely in remission for at least one year. This history raised the specter of Wernicke Korsakoff syndrome as a contributing

problem. Thiamine levels were within normal limits during the previous and recent admissions, ruling out Wernicke encephalopathy. The presence of Korsakoff dementia with psychotic features remained a possibility. Creutzfeldt-Jakob disease, which may emerge with or after Wernicke Korsakoff syndrome, was considered but ruled out, as our patient lacked ataxia, hallucinations, or myoclonus [9]. A recent brain scan via MRI had demonstrated ventriculomegaly, cortical atrophy, and deep white matter hyperintensities: the latter, consistent with small vessel disease. These findings suggested a strong component of vascular dementia. Risk factors in our patient included a history of smoking, alcoholism, and years of exposure to psychotropic medications.

With respect to schizophrenia, our patient had been placed under the conservatorship of a relative for approximately two years prior to our encounter, and concurrent with his placement into a residential care home. However, based upon collateral information, severe cognitive deficits had emerged only within recent months and had not been typical of the patient's presentation.

Several epidemiological investigations have highlighted an increased risk of dementia in patients diagnosed with schizophrenia [10-12]. Like others, though, we are not convinced that cognitive decline is a necessary component of the schizophrenic condition [13,14]. Neither are we convinced that the syndrome known as schizophrenia – nor the dementia which may appear in its course – are correctly diagnosed in many patients. It is far from clear how often past cases of dementia praecox, or modern cases of schizophrenia, have reflected undiagnosed manifestations of infections affecting the central nervous system -- such as viral encephalitis, tuberculosis, neuroborreliosis, neurosyphilis, or various hepatides; nutritional deficiencies; genetic anomalies; endocrine imbalances; autoimmune conditions (including paraneoplastic or non-paraneoplastic limbic encephalitis); seizure disorders; or unrecognized toxidromes [15-19].

Based upon similar environmental and behavioral risk factors, the organic precursors of cognitive decline in schizophrenia appear to be no different than those which occur in the general population [20]. A notable exception occurs with respect to the anatomic and physiologic effects of dopamine blocking drugs. A strong line of research evidence, involving autopsy and biomarker studies, links the old and new antipsychotic drugs to the neurodegenerative changes associated with Alzheimer's disease [21-27]. Research has also implicated the same pharmaceuticals in cerebrovascular disease [28,29]. Causal mechanisms may be inferred from studies in lab animals and humans in which investigators have detected drug-induced mitochondrial disruptions, enhancement of oxidative stress, perturbations of the blood brain barrier, disturbances of metallochemistry, alterations in tau phosphorylation, dysregulation of microglia, and induction of insulin resistance [30-36].

We believe that the iatrogenic risk of drug-induced dementia is often overlooked in psychiatric patients, but particularly among those who have been diagnosed with schizophrenia. The present case demonstrates the benefits of realigning diagnosis and treatment in a middle-aged man with cognitive decline. We are mindful of the fact that other professionals have published positive results in which pharmaceutical dose reductions have benefitted patients with similar histories [37,38].

By continuously reorienting our patient; by attending to his physical and nutritional needs; by establishing a warm, caring rapport; and by reducing antipsychotic medication, we were able to facilitate substantial clinical improvement. While in the USA, governmental drug product labels advocate the cautious use of antipsychotics in the setting of dementia; our case implies that it is equally prudent to heed this advice in the treatment of dementia in schizophrenia.

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