Refractory Schizophrenia in the Elderly Patient and the Role of the Primary Care Provider

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Abstract

Schizophrenia is a psychiatric disorder usually diagnosed early in life and involves chronic and/or recurrent psychosis. It is rare that it manifest itself after the age of 40 (9). Regardless of age of onset, it requires a multi-specialty approach that is not always available in all regions (3). It ranks among the top 10 illnesses contributing to the global burden of disease by the World Health Organization (1). Schizophrenia has a prevalence of 7 per 1000 people in the adult population with an incidence of 3 in 10000, affecting about 24 million people worldwide (4). More than half of the population with schizophrenia is not receiving appropriate care (4). Due to the shortage of primary mental health providers, primary care providers need to be more adept at properly treating schizophrenia and other psychiatric illnesses.

Case Report

67 year old white female who initially presented with loss of interest, depressed mood, poor concentration, and poor sleep with memory loss and confusion. Review of systems significant for loss of appetite, fatigue, weakness, headache, hearing loss, neck pain, neck stiffness, cough, diarrhea, nausea, vomiting, painful urination, backache, joint pain, decreased memory, dizziness, anxiety, insomnia, and depressed mood. Her past medical history includes insomnia, depression, hypothyroid, hyperlipidemia and tobacco

abuse. Allergies to Topamax and medications include Metronidazole 250mg, promethazine 25mg and Zofran 4mg for nausea, Flexeril 10mg for chronic neck pain, levothyroxine 50mcg for hypothyroidism, Effexor XR 150mg for depressive symptoms, and Ambien 10mg for insomnia. Surgical history includes cholecystectomy and appendectomy. Due to her initial presentation she was started on Aricept to help with her memory and tramadol for her headaches and neck pain.

Three weeks later the patient came in for a follow up visit with a new complaint of auditory hallucinations. She reports that she is hearing the voice of her niece at the house next door calling out for help. It was reported by the patient's daughter that the niece in question lives in a different town. Since the patient was just recently started on Aricept, it was felt that this may be the cause of her hallucinations, so it was discontinued and she was started on Namenda 10mg. At her next appointment the hallucinations had not improved and her other symptoms have worsened. She became paranoid, believing that she was being recorded and was still hearing the same voice. Due to worsening symptoms at that time she was started on Seroquel XR 300mg and referred to psychiatry for further treatment. Also because of her headaches a CT of the head was performed to begin to rule out any organic cause for them or her psychiatric symptoms. We reviewed the results of her CT at her next visit, it showed only mild cortical atrophy. However her hallucinations had increased. She and her daughter reported that due to the hallucination that she assaulted another person and was being prosecuted. As she lives alone the family was fearful for her continued safety since she was becoming more agitated by the voices. At that point, It was felt that she needed inpatient psychiatric evaluation & treatment. She was sent to Bristol Regional Medical Center Emergency room for mental

health evaluation. It was felt that she would benefit but she become agitated and refused to be admitted to psychiatric services. The patient's daughter called and we started her on Risperdal 2mg daily and was titrated up to 4mg daily, as well as being set up for outpatient psychiatry. She felt no improvement with the Risperdal so it was increased even further to 4mg twice daily. At the following visit she reported that her hallucinations had progressed even further. It was felt that she would benefit from starting treatment with a psychiatrist. After evaluation she was diagnosed with Bipolar disorder type 2, but showed no clinical signs of a dementia like illness. Her hallucinations progressed even further as she began to not only hear her niece's voice but the additional voices of two men, one who is a neighbor. Due to the continued escalation, after discussion with the patient and her daughter, it was felt in her best interest to move in with her daughter. Her medication was also adjusted, Risperdal was increased to 8mg twice daily and Depakote 250mg twice daily was added to her medication regimen. MRI of the brain was performed, showing no acute intracranial abnormality. After moving in with her daughter, the patient noted improvement in the voices. She stated that they never quit talking, but that they became quieter and easier to ignore. She had continued to follow up with outpatient psychiatry and continued her medications. She showed continued improvement in her psychiatric symptoms until her death a few months later.

Diagnosis

The diagnosis of schizophrenia is made using the criterion set forth in the Diagnostic and Statistical Manual of Mental Disorders, version IV-TR. For a period of

one month the patient must manifest two or more of the symptoms in category A: delusions, hallucinations, disorganized speech, gross disorganization or catatonic behavior, or negative symptoms. If the delusions are bizarre or hallucinations consist of a voice keeping a running commentary on the person's behavior or thoughts or two or more voices conversing with each other, then only one of the above symptoms is required. The patient will also demonstrate signs of social or occupational dysfunction, which may be problems at work, with interpersonal relationships, or self-care a great level below the previously achieved level of function. There should be continuous signs of the disturbance for at least 6 months with the problems from category A present for at least one month, or less if successfully treated. Patient should be evaluated for schizoaffective and mood disorders and these should be ruled out as a cause of the patient's mental disease. As a practitioner you should also rule out substance abuse and any general medical condition as being the cause of the patient's symptoms. It should also be considered if the patient's disorder could be related to an autistic disorder or other pervasive developmental disorder (5). Characteristic symptoms of schizophrenia are known as the "first-rank symptoms." These are auditory hallucinations, specifically voices arguing or giving instructions or commenting on one's actions, somatic/thought passivity experiences (delusions of being controlled, thought echo, thought withdrawal, thought insertion, thought broadcasting, and delusional perception (linking a normal sensory perception to a bizarre conclusion).

A. Two or more of the following, each present for a significant portion of time during a one month period
    a. Delusions
    b. Hallucinations

c. Disorganized speech (e.g., frequent derailment or incoherence) d. Grossly disorganized or catatonic behavior e. Negative symptoms, i.e., affective flattening, alogia, or avolition Only one symptom is required if delusions are bizarre or hallucinations consist of a voice keeping up a running commentary on the person's behavior or thoughts, or two or more voices conversing with each other.
B. Social/occupational dysfunction. – for a significant portion of the time since onset of the disturbance, one or more major areas of functioning such as work, interpersonal relations, or self-care are markedly below the level achieved prior to the onset (or when the onset is in the childhood or adolescence, failure to achieve expected level of interpersonal, academic, or occupational achievement).
C. Duration – continuous signs of the disturbance persist for at least 6 months. Must include at least one month of symptoms (or less if successfully treated) that meet Criterion A and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or two or more symptoms listed in criterion A present in an attenuated form (odd beliefs, unusual perceptual experiences)
D. Schizoaffective and Mood Disorder Exclusion: Ruled out because of either (a) no Major Depressive Episode, Manic Episode, or Mixed Episode have occurred concurrently with the active-phase symptoms or (b) if mood episodes have occurred during active-phase symptoms, their total duration has been brief relative to the duration of the active and residual periods.
E. Substance/general medical condition exclusion – the disturbance is not due to the direct physiological effects of a substance or a general medical condition.
F. Relationship to a Pervasive Developmental Disorder – If there is a history of Autistic Disorder or another Pervasive Developmental Disorder, the additional diagnosis of Schizophrenia is made only if prominent delusions or hallucinations are also present for at least one month (or less if successfully treated).

Hallucinations

There are several different kinds of hallucinations that can manifest in schizophrenia. Auditory hallucinations are the most common form in schizophrenia with an estimated prevalence between 40-80% (1). Auditory

hallucinations usually are voices but can also be different sounds. The patient may feel as though the voices are coming from within their head or an exact external location (1). These are also the most affected by treatment. It is described by patients as turning down the volume but not going away so that they are able to more easily deal with them.

Visual hallucinations are sometimes described as fully formed people or body parts but they are not usually present in that way. They most often manifest as glowing orbs or flashes of color. Somatic hallucinations are physical contact perceived by the patient. They can be of simple touch, sexual intercourse, or pain. Olfactory and gustatory hallucinations are much less common than the other types but are occasionally reported by some patients (1).

Delusions

Defined as a fixed, false belief, present in approximately 80 percent of people with schizophrenia, often as an explanation of their hallucinations due to impaired incite (1). Delusions are either bizarre or non-bizarre. Bizarre delusions have no possibility of being true while non-bizarre delusions are plausible. Content is categorized as grandiose, paranoid, nihilistic, and erotomanic. Paranoid delusions are the most clinically significant as their presence may cause the patient to be uncooperative with treatment and less likely to seek evaluation in the first place.

Disorganization

This can manifest as thoughts or behaviors. Behaviors are observable and somewhat more obvious while thoughts are more complex. Following the patient's speech pattern is the easiest way to identify disorganized thoughts. A person with disorganized thoughts may have a disjointed, disconnected speech pattern, most commonly tangential and circumstantial. More severe thoughts may become evident with speech patterns such as derailment, neologisms, and word salad.

Tangential Speech	Increasingly further off topic without appropriate responses
Circumstantial Speech	Focus drifts but returns back to topic
Derailment	Sudden switches of topic without any logic
Neologisms	Creation of new words
Word Salad	Order of words have no sensible meaning

Negative Symptoms

Negative symptoms are either primary or secondary. Primary symptoms are also referred to as deficit symptoms because they represent a loss of normal function. They include affective flattening, alogia, apathy, asociality, and anhedonia. Primary symptoms are harder to treat and more closely related to functional disability. Negative symptoms are independent of positive symptoms. Secondary symptoms are due to other manifestations of schizophrenia or its treatment.

Cognititve Impairment

Certain areas of cognition are affected by schizophrenia: processing speed, attention, working memory, verbal learning and memory, visual learning and memory, reasoning/executive functioning, verbal comprehension, and social

cognition. When given neuropsychological testing, patients with schizophrenia score one to two standard deviations lower than control patients (6). Cognitive impairments may be some of the first signs of schizophrenia, even before positive symptoms.

Course

The course can be described using onset, symptom presentation, and outcome. This can be further broken down by abrupt vs. insidious onset, continuous vs. intermittent symptoms, and poor vs. non-poor outcomes.

Treatment Considerations

Treatment of schizophrenia focuses on managing the acute symptoms as well as long term maintenance therapy.

The acute phase is defined as the first episodes of psychosis as well as when patients with a prior history of schizophrenia have a relapse of psychotic symptoms. Treatment in this phase is aimed at reducing the severity of the symptoms. Anti-psychotics are first-line treatment for schizophrenia and are shown to reduce positive symptoms.

Drug	Usual dose (mg/day)	Initial dose (mg/day)	Max dose (mg/day)	Route
First Generation Antipsychotics				
Chlorpromazine	400-600	25-200	2000	PO, IM
Fluphenazine	2-15	2-10	30	PO, IM, depot
Haloperidol	2-20	2-10	30	PO, IM, depot
Loxapine	20-80	20	250	PO
Perphenazine	12-48	8-16	64	PO
Thiothixene	10-20	5-10	30	PO
Thioridazine	15-30	4-10	40	PO
Trifluoperazine	15-30	4-10	40	PO
Second Generation Antipsychotics				

Aripiprazole	10-30	10-15	20	PO, ODT, IM
Clozapine	150-600	25-50	600	PO
Olanzapine	10-30	5-10	40	PO
Quetiapine	300-750	50	1200	PO
Risperidone	2-6	1-2	8	PO, ODT
Ziprasidone	120-160	40-80	240	PO

Antipsychotics should be started at a lower dose and titrated up to an effective dose as quickly as can be tolerated by the patient. Resolution of symptoms can occur in several days or take up to 6-8 weeks. The most rapid improvement is often during the first two weeks after which improvement will slow, but continue non the less. Patients may find that they are more able to ignore their hallucinations or delusions. Each drug should be tried for two to six weeks before determining whether it is successful. A second antipsychotic can be added if suboptimal response to a single drug (8).

The goal of maintenance therapy is to minimize symptoms and functional impairment, avoid relapses, and promote recovery and reintegration into the patients normal life (8).

Role of the Primary Care Provider

Due to the shortage of primary mental health providers in many areas it falls on the primary care physician to provide the majority of treatment for many patients (3). Even in areas where mental health providers are available it is often difficult to get patients with schizophrenia to agree to see another doctor after having already formed a relationship with their primary doctor.

Conclusion

It is important that, as primary care physicians, we are aware of the presenting symptoms of schizophrenia and be able to properly begin treating it once diagnosed. The doctor-patient relationship plays a vital role as well in the recovery of any patient with a

mental disorder, whether it is schizophrenia, depression, or any other. When mental disorders manifest in the elderly it requires a multifaceted approach, the primary care provider to provide more frequent visits and the patient's family give support in the form of socialization at home, as sometimes the most effective treatment is not medication.

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