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TREATMENT RESISTANT AND VERY EARLY ONSET SCHIZOPHRENIA: A CASE REPORT FROM OMAN

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Abstract

We report here a case of very early onset schizophrenia (VEOS) who presented with atypical features, had poor response to a number of antipsychotic medications and had neutropenia with initial exposure to clozapine. She, however, was re-challenged with a lower dose of clozapine and there was a good improvement in her psychotic symptoms.

Introduction

Schizophrenia is a chronic illness characterized by abnormal beliefs, perceptions and emotional states. Both DSM-5 and ICD-10 are very similar in terms of diagnostic criteria and neither of them have different criteria for children and adults[1]. However, experts in the field of child and adolescent psychiatry have highlighted two subgroups: Early Onset Schizophrenia (EOS, onset of illness before 18 years of age) and Very Early Onset Schizophrenia/Childhood Onset Schizophrenia (VEOS/COS, onset of illness before 13 years of age). Both EOS and VEOS are relatively rare[2]. Early onset schizophrenia (EOS) is a less common condition as compared to adult-onset schizophrenia[1] .The prevalence of EOS is low, with variable estimates, depending upon the setting, sampling method and the methodology of the studies.It varies from 1 in 30,000 children aged under 13 years[2], 1.4 per 10,000 for those aged under 15 years and 1 in 10,000 in those aged under 18 years[3].

Another study showed that about 4.7 percent of patients with schizophrenia had the onset of their illness at or before 18 years of age[4].Undoubtedly, early-onset schizophrenia is a serious disorder with a propensity to cause serious morbidity and reduced longevity[5]. Prognosis is significantly worse than in adult-onset schizophrenia. Some studies have also shown that patients with early-onset schizophrenia have a longer duration of untreated psychosis (median 26.3 weeks) compared to those with adult-onset illness (median 8.7 weeks) [6]. Duration of untreated psychosis (DUP) among other factors, leads to a worse prognosis, compared to adult-onset schizophrenia[7, 8,9,10].

Therefore, prompt diagnosis and well-tailored management plans are of immense importance.Antipsychotics are the mainstay of pharmacological treatment of early-onset schizophrenia[11]. A number of antipsychotics, including risperidone, olanzapine, aripiprazole, haloperidol, palliperidone and quetiapine have been approved by the United States Food and Drug Administration (FDA) for use in children aged 13 years and above[12].
However, choosing the right antipsychotic is a challenge for this age group, having to take into account not only the efficacy but also the short and long-term side effects as well as the issue of compliance (or rather, risk of non-compliance)[12] .

Clozapine has also been shown to be effective and safe for use in cases of early-onset schizophrenia, when other antipsychotics have not been adequately effective[13].As in adult-onset schizophrenia, patients with early-onset should also have a comprehensive multidimensional management plan, incorporating pharmacological as well as psychosocial interventions, with the help of a multi-disciplinary team[11].

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A case history

A girl presented at 13 years of age with frank psychosis and severe impairment of functioning. She was treated with Olanzapine (up to 20 mgs/daily), Haloperidol (oral, injectable and long-acting injectable, up to 25 mgs daily), Risperidone 3 mgs/daily), quetiapine (up to 200 mgs daily), lithium, sodium valproate, ECT (17 sessions in total) and Clozapine at different times over the next three years period. However, there was only a small improvement in her symptoms, with persistent psychosis, social withdrawal, aggression and poor self-care. The trial of clozapine was stopped after three days because of neutrophil count falling below 1000/mm. However, in view of poor response to subsequent treatment with other antipsychotics, ECT and mood stabilizers, she was re-challenged with Clozapine at a slower rate of dose escalation. This was successful in terms of almost complete resolution of her positive symptoms and significant improvement in her negative symptoms, without further worsening of WBC count or any other significant side effects.

Discussion

For patients presenting with a non-affective psychotic disorder, the duration of untreated psychosis (DUP; the time between the onset of positive psychotic symptoms and the initiation of appropriate treatment) varies widely, from a few weeks to several years. Number of studies reported that a longer DUP is associated with poorer clinical outcomes.[14]

Prospective studies have come to similar conclusions. Loeble and his colleagues found that, in a population of patients hospitalized with a first episode of schizophrenia and treated with a standard medication protocol, the duration of illness before treatment was significantly associated with time to remission as well as the extent of remission[15].

The treatment of schizophrenic patients who fail to respond to adequate trials of neuroleptics is a major challenge. Clozapine, an atypical antipsychotic drug, has long been of scientific interest, but its clinical development has been delayed because of an associated risk of agranulocytosis.

Atypical (second-generation) antipsychotics are considered standard treatment for children and adolescents with early-onset schizophrenia. However, the superiority of second-generation antipsychotics over first-generation antipsychotics has not been demonstrated.

There are few randomized, controlled trials comparing treatments for early-onset schizophrenia and schizoaffective disorder. First-generation antipsychotics, such as haloperidol and loxapine, have shown efficacy, but younger patients may be at higher risk for extrapyramidal side effects and less responsive to these agents than adults. Among second-generation antipsychotics, recent randomized, controlled trials found that olanzapine, risperidone, and aripiprazole have shown efficacy in the acute treatment of adolescents with schizophrenia. Risperidone and aripiprazole have been approved by the U.S. Food and Drug Administration (FDA) for the treatment of adolescents with schizophrenia. Clozapine, a second-generation antipsychotic, was found to be superior to both haloperidol and olanzapine in youth with treatment-resistant schizophrenia. However, clozapine's side effect profile limits its use to patients who have tried and failed other antipsychotics[11]. Further, while neutropenia is a serious and potentially life-threatening condition, mild to moderate neutropenia should be followed by a re-challenge with clozapine, with a smaller starting dose and a slower rate of dose-titration[11].

A poor response to antipsychotic medication may be an enduring feature of the illness manifested by patients at the initial episode of illness, or develop over the course of the illness in the context of successive episodes. Thus, there may be two forms of treatment resistance (one that is present at the onset of the illness and thereafter, and one that evolves as the illness progresses), or just one form that develops at various times in the illness course[16].

Finally , therapeutic nihilism on part of the treating clinician is a real risk in management of EOS and VEOS It is important that clinicians be aware of it and they should try to follow the internationally accepted treatment guidelines and treatment pathways is treating these cases.

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