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The effect of antipsychotic-induced extrapyramidal disorders on patient's compliance with schizophrenia (a clinical case)

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ABSTRACT

Extrapyramidal disorders are common adverse events in antipsychotic therapy. However, their diagnosis is difficult due to broad differential diagnosis, and often their specific clinical variant is not recognized, and timely intervention is not performed, which leads to severe patient suffering. This affects the quality of life of patients with schizophrenia and leads to their refusal to receive therapy, which aggravates the course of the disease. The article presents a clinical case of a 33-year-old patient at a psychiatric hospital with schizophrenia combined with such rare severe extrapyramidal disorders as antipsychotic-induced tardive dyskinesia and tardive dystonia.

The diagnosis was carried out in accordance with the criteria of the International Classification of Diseases, Tenth Revision (ICD-10). The intensity of clinical manifestations was assessed using the Positive and Negative Syndrome Scale (PANSS), the Abnormal Involuntary Movement Scale (AIMS), and the Barnes Akathisia Rating Scale (BARS). Compliance was assessed using the Method for Measuring Medication Adherence in Psychiatry. Detailed differential diagnosis of tardive dyskinesia and tardive dystonia with akathisia and Huntington's disease was presented. Substantiated treatment strategy and positive clinical dynamics with increased compliance were described.

Key words: tardive dyskinesia, tardive dystonia, schizophrenia, compliance, akathisia.

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Влияние экстрапирамидных антипсихотик-индуцированных нарушений на комплаенс пациента с шизофренией (клинический случай)

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РЕЗЮМЕ

Экстрапирамидные нарушения являются частыми нежелательными явлениями терапии антипсихотиками. Однако с учетом широкого круга и сложностей дифференциальной диагностики часто не распознается их конкретный клинический вариант и не проводится своевременное вмешательство, что приводит к выраженным страданиям пациента. Это влияет на качество жизни больных с шизофренией и приводит к отказу от приема терапии, что усугубляет течение заболевания. В статье представлен клинический случай 33-летнего пациента психиатрического стационара с шизофренией, сочетанной с такими редкими, но тяжелыми экстрапирамидными нарушениями, как тардивная дискинезия и тардивная дистония, индуцированными приемом антипсихотиков.

Диагностика проводилась в соответствии с критериями Международной классификации болезней десятого пересмотра (МКБ-10). Выраженность клинических проявлений оценивалась с помощью Шкалы позитивных и негативных симптомов (PANSS), Шкалы патологических непреднамеренных движений (AIMS), Шкалы оценки акатизии Барнса (BARS). Проведена оценка комплаенса с помощью Метода прогнозирования медикаментозного комплаенса в психиатрии. Представлена развернутая дифференциальная диагностика тардивной дискинезии и поздней дистонии с акатизией и болезнью Гентингтона. Описана мотивированная врачебная тактика и положительная клиническая динамика с повышением комплаенса.

Ключевые слова: тардивная дискинезия, тардивная дистония, шизофрения, комплаенс, акатизия.

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INTRODUCTION

Patient noncomliance with therapy is a common problem in the treatment of schizophrenia, leading to relapses, readmissions, and aggravating long-term events [1, 2]. Treatment noncompliance is one of the reasons for transferring patients to therapy with long-acting antipsychotics, which are mostly conventional neuroleptics [3]. The average rate of noncompliance among patients with schizophrenia is 47% [4]. 32 % of patients discontinue seeing a psychiatrist upon discharge from hospital; and 31% of patients who continue regular sessions with a psychiatrist in the outpatient setting are found to have noncompliance or complete refusal of therapy [5].

Within the first 18 months of treatment, 5% of patients discontinue it completely [6]. About 250 factors affecting compliance have been identified

[7]. A key factor is multiple adverse effects of antipsychotics [8], which cause about half of patients to refuse from antipsychotic therapy [9]. Tardive dyskinesia, dystonia, and akathisia occupy a special place among specific motor side effects of antipsychotics. They aggravate the course of schizophrenia, cause treatment failure, and worsen the quality of life [10].

Tardive dyskinesia is a persistent movement disorder that occurs 1–2 years [11] after taking antipsychotics. It represents chaotic movements of different parts of the body. The specifics of the movements and the part of the body vary and may change over time. The first symptoms of tardive dyskinesia usually include repetitive, uncontrolled, chaotic movements of lips, tongue, and facial mimic muscles. Movements of the extremities, head, neck, and soma, difficult swallowing, and forced body postures may also be present [12]. The quality of life of patients with tardive dyskinesia is reduced by 12.3% relative to patients without it [13], and the presence of tardive dyskinesia complicates treatment of schizophrenia and increases the financial burden on the patient's family [14].

Tardive dystonia is an extrapyramidal disorder, one of the most disabling variants of tardive dyskinesia. It occurs several years after the start of antipsychotic therapy and persists after its withdrawal. In less than 20% of cases, it occurs within the first year of treatment [15]. Tardive dystonia begins in the muscles of face or neck. Generalization of dystonia to the extremities and trunk is observed in a small number of cases. The most frequent form of tardive dystonia is oromandibular dystonia. All of this affects patients' quality of life and leads to refusal of therapy, aggravates the course of the underlying disease, and requires increasing doses of antipsychotics: a pathological circle is formed [15].

One of the types of tardive akathisia is persistent akathisia, which develops 3 months after withdrawal of antipsychotic therapy or when a second neuroleptic drug is added to the treatment [16]. Motor restlessness with predominant localization in the lower extremities (repetitive movements such as crossing and uncrossing the legs, and constant shifting from one foot to the other, walking along a single line) is typical of akathisia and is defined as its objective component. The subjective component is represented in the form of an imperative need for movement, restlessness, and tension. The emergence of tardive akathisia, especially when its severity increases, can be mistakenly interpreted as aggravation of the mental state, and can be the reason for the formation of suicidal tendencies [16]. Timely diagnosis and correction of adverse motor events of antipsychotic therapy are necessary to improve the quality of life, increase compliance, and form long-term remission [17].

The aim of the study was to diagnose and describe the effect of combined antipsychotic-induced extrapyramidal disorders, such as tardive dyskinesia and tardive dystonia, on patient's compliance with schizophrenia.

We used clinical-psychopathological and clinical-catamnestic methods with the analysis of medical records of the patient undergoing inpatient treatment at the Department of Endogenous Disorders of Mental Health Research Institute clinics. The patient was examined and treated according to the national clinical guidelines [18]. Schizophrenia was diagnosed according to ICD-10 criteria [19]. The severity of pathopsychological symptoms was assessed according to the Positive and Negative Syndrome Scale (PANSS) [20]. The severity of pathological involuntary movements was assessed according to the Abnormal Involuntary Movement Scale (AIMS) [21]. The Barnes Akathisia Rating Scale (BARS) was used to diagnose akathisia [22]. Compliance was assessed using the Method for Measuring Medication Adherence in Psychiatry [23].

CLINICAL CASE

Patient A., 33 years old, was admitted to the hospital in January 2020 for managing adverse effects of antipsychotic therapy.

Anamnesis. The patient was born following normal pregnancy and delivery and was not behind his peers in his early development. Since preschool age, the patient had not been socially active and could not adapt in a group of peers. He was often ridiculed and physically bullied at school, then he was transferred to homeschooling. Since the age of 13, he could hardly comprehend tasks and could understand simple instructions only after several repetitions. He could not talk for days, looking at geographical atlas for a long time, freezing over one page. He was first examined by a psychiatrist following teachers' recommendations, but was not subjected to full examination and treatment.

At the age of 15, he began to have fear of men and refused to go out unaccompanied. On the eve

of the school year, he made numerous razor cuts on his forearm and neck. He never sought medical care. At the age of 16, he barely completed grade 11, after which he refused to continue his education. Patient's behavior changed, he stiffened while sitting on a chair in one position, could walk quickly around the room from time to time, raised his legs high, squeezed his hands in front of him with effort, strained his neck and moved his lower jaw forward, and was moody. With suicidal intentions, he took a blister pack of zopiclone, after which he was taken to the Accident and Emergency Unit. Having returned home, he learned of his brother's death; he did not react emotionally, went outside, and ran around the house in silence; he had not thought of his brother since.

He took the recommended haloperidol for 1 month on an outpatient basis, then stopped taking it. He was angry and tense; he declared to his parents that he had no future. At the age of 17, he was first hospitalized to Mental Health Research Institute clinics. His mental state was characterized by behavioral disorders against a background of the flat effect, alogia, and hypobulia. He took zuclopenthixol 25 mg/day, clozapine 237.5 mg/day, carbamazepine 800 mg/day, and trihexyphenidyl 10 mg/day. In the outpatient setting, he was irregularly treated with zuclopenthixol 5 mg/day. Nevertheless, he graduated from a law college.

He did not work in his specialization, he was a mine laborer for about 1 year, constantly complaining of fatigue. At the age of 26, the patient was hospitalized to a psychiatric hospital for medical and social assessment. He was diagnosed with paranoid schizophrenia with a continuous course; the second disability group was registered. As of the moment of admission, visual hallucinations were present. After discharge, he irregularly took the recommended risperidone 6 mg/day for 3 years and lived in parental care. About 2 years ago, he completely withdrew the treatment, his condition worsened again: he became restless, wrung his hands, his statements were stereotypical.

One year before the current hospitalization, the patient began to complain of many thoughts in his head, stereotypically repeating the same phrases. He was repeatedly hospitalized in the clinics of Mental Health Research Institute. His mental condition was characterized by the presence of psychic automatism, expressed by schizophrenia-specific disorders in all spheres of mental activity. However, he refused of therapy on the first day, as the doctor suggested a physical examination. He was discharged with a recommendation to take risperidone 6 mg/day.

While taking risperidone, the patient complained of stiffness in the lower jaw. After 3 months of taking it, involuntary movements in the lower half of the face and mouth appeared for the first time, occurring spontaneously or provoked by a speech act. The patient's speech became indistinct. His mother noticed improvement in speech in the morning after a night sleep. Fearing further deterioration of the patient's condition, his mother reduced the dose of the antipsychotic by half. The patient was prescribed biperiden 2 mg/day by the district psychiatrist. Involuntary movements did not decrease. The patient's mother discontinued all medications and initiated a consultation with a neurologist at Scientific Center of Neurology, where amantadine 200 mg was prescribed. It did not have the expected therapeutic effect: involuntary movements increased. The mental state of the patient aggravated, he became more withdrawn, looked gloomy, refused to leave the house due to a fear of being hit on the head, and kept silent while staring out of the window. He would stand up for no reason, shift from one foot to the other, and the involuntary movements of the mouth persisted. Accompanied by his mother, he was admitted to the Department of Endogenous Disorders of Mental Health Research Institute.

Mental status. The patient looked tidy and neat due to constant care of his mother, who changed his clothes and washed him. The patient was tense and seemed withdrawn and not interested in talking to the doctor. The facial expression was hypomimic. Motor skills were slow, movements lacked plasticity and were robotic in nature. During the conversation, he sometimes swayed his trunk back and forth rhythmically. Gestures were absent. Targeted contact was difficult to establish. Speech was indistinct due to involuntary movements in the mouth area, which were provoked by the speech act. To facilitate articulation, the patient touched his lower jaw, sometimes quickly pulled out his tongue, involuntary eye movements in the form of excessive blinking and eyebrow frown were also noted. He answered questions monosyllabically and stereotypically: "yes", "no", "maybe".

According to information received from his mother, the patient lost 9 kg due to poor appetite, became moody, did not sleep well, feared a hit on

his head, and spent a long time in one pose. He complained of a lot of thoughts in his head; episodically saw pictures and cartoon characters before his eyes; experienced fragmentary sensations of imposing, other people's thoughts. Mood was low. He did not actively express suicidal thoughts and intentions and did not exhibit any suicidal tendencies in his behavior. In the ward, he stayed in his bed or walked back and forth across the ward, raising his legs high, stopping and shifting from one foot to the other.

Data of laboratory tests and examinations by somatic specialists. According to electroencephalography, focal changes, stable interhemispheric asymmetry, epileptiform activity, or paroxysmal activity were not found. According to the magnetic resonance imaging, focal or diffuse changes were not found. The therapist's conclusion: chronic cholecystitis, remission stage. Examination by a neurologist: involuntary opening of the mouth, curvature of the lips and cheeks, forced smile during a conversation; squeezing the eyes or frowning the eyebrows, running the hands across the clothes, stroking the hair, shifting the feet periodically while sitting on a chair. Conclusion: combined manifestation of oromandibular dystonia and tardive dyskinesia.

Psychometric examination data: upon admission, according to PANSS, the total score was 113; total AIMS score was 20; according to BARS, no akathisia was found; compliance score was 29.

Differential diagnosis and substantiation of the diagnosis. Involuntary forced movements [24] had a chronic nature; they appeared against the background of the therapy with the antipsychotic and persisted after its withdrawal. There were no other causes for the condition (it was not a secondary disease of the underlying disease), there was no hereditary burden of dementia in Huntington's disease. Motor acts had a typical localization with involvement of the facial muscles in the form of clenching of the jaws and forced smile, observed during the speech act, sometimes with the use of corrective gestures (touching the jaw).

The patient had stereotyped repetitive tongue movements and expressive movements in the form of excessive blinking and motor acts involving the lower extremities (shifting from one foot to the other, walking back and forth, imitating walking while standing still, jactation). Progression of these manifestations is closely associated with receiving antipsychotic therapy for more than 3 months, and the movements persist even after withdrawal of the drug. There are no organic causes of the disorders [25].

Despite the presence of restless movements of the lower extremities, resembling the objective component of akathisia, the key factor is a lack of the subjective component, namely feelings of inner restlessness, tension, an imperative need for movement, and fatigue associated with it [26]. Irregular antipsychotic therapy, violation of the dosage regime and the frequency of intake, and an increase in the negative symptom complex act as both predisposing factors and aggravating factors for the condition. Progression of negative disorders, among other things, is a consequence of low compliance.

In this case, there is a combined presence of adverse antipsychotic-induced movement disorders: tardive dyskinesia and tardive oromandibular dystonia. There is hereditary burden of schizophrenia on the father's side. The patient's schizoid features became more pronounced in adolescence, apathy and absence of purposefulness in learning increased with the emergence of depressive experiences and subsequent suicide attempt, development of hallucinations and delusions, and mental automatism with microcatatonic symptoms. Further, in addition to hallucinations and delusions, progression of decreased energy potential and social withdrawal with the formation of an emotional-volitional defect were observed.

Definitive clinical diagnosis: paranoid schizophrenia, a continuous course. Combined manifestation of adverse antipsychotic-induced motor disorders: tardive dyskinesia and tardive oromandibular dystonia.

Treatment strategy. According to the modern understanding [27], intake of aripiprazole is less likely to cause tardive dyskinesia compared with other antipsychotics. A daily dose of aripiprazole of 7.5 mg was the drug of choice in this clinical case. The patient was also prescribed a cycle of sessions with a speech – language pathologist and recommended a course of physiotherapy in order to restore speech skills. The patient refused of physiotherapy, as any touching caused him bodily discomfort and mental suffering.

Changes in the condition. Following the sessions with a speech – language pathologist, patient's speech became more distinct, involuntary movements in the oral cavity were provoked only by a

speech act. Upon discharge, the overall PANSS score decreased to 95, the overall AIMS score – to 12, and the Medicaid Compliance Scale score increased to 37. Therefore, positive changes with a decrease in the psychopathological symptoms and pathological involuntary movements and an increase in adherence to the therapy were observed.

CONCLUSION

The clinical case presented a situation in which untimely detection and inadequate attempts to correct antipsychotic-induced tardive dyskinesia and tardive dystonia resulted in a treatment failure, up to withdrawal. Prolonged interruptions in maintenance therapy led to mental deterioration and rehospitalizations, worsened the patient's quality of life, and placed a burden on the family. Diagnosis and correction of combined tardive dyskinesia and tardive dystonia by individual selection of antipsychotics allowed to reduce the severity of their manifestations, increase compliance, and improve the patient's mental state.

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Authors contribution

Rahim E.G. – examination and management of the patient, drafting of the article. Kornetova E.G. – development of case management strategy, drafting of an article. Goncharova A.A. – participation in the examination and treatment of the patient, drafting of the article. A.N. Kornetov – drafting of the article and critical revision of the manuscript for important intellectual content. Semke A.V. – final approval of the manuscript for publication.

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