Neuroleptic malignant syndrome (NMS) is a rare, potentially life-threatening complication which is an unpredictable, idiosyncratic reaction to antipsychotics. In patients receiving traditional antipsychotics, neuroleptic malignant syndrome occurs with an incidence of 0.2–3.3%. However, neuroleptic malignant syndrome also appears in patients treated with atypical antipsychotics, especially Clozapine. A possible cause of neuroleptic malignant syndrome is blockade of dopamine receptors in the nigrostriatal tracts or hypothalamic nuclei. If signs and symptoms of the Neuroleptic malignant syndrome are identified in time, full recovery is possible. This is a report of a female patient with neuroleptic malignant syndrome treated by traditional antipsychotics. As soon as neuroleptic malignant syndrome symptoms were recognized, the antipsychotic drugs were discontinued, symptomatic therapy was initiated and symptoms of neuroleptic malignant syndrome disappeared. However, the patient’s psychotic symptoms persisted and an atypical antipsychotic was administered. During the next few days the psychotic symptoms gradually disappeared and the patient accomplished good recovery.

**Key words:** Antipsychotic Agents + adverse effects; Neuroleptic Malignant Syndrome; Signs and Symptoms

**Summary** – Neuroleptic malignant syndrome is a rare, potentially life-threatening complication which is an unpredictable, idiosyncratic reaction to antipsychotics. In patients receiving traditional antipsychotics, neuroleptic malignant syndrome occurs with an incidence of 0.2–3.3%. However, neuroleptic malignant syndrome also appears in patients treated with atypical antipsychotics, especially Clozapine. A possible cause of neuroleptic malignant syndrome is blockade of dopamine receptors in the nigrostriatal tracts or hypothalamic nuclei. If signs and symptoms of the Neuroleptic malignant syndrome are identified in time, full recovery is possible. This is a report of a female patient with neuroleptic malignant syndrome treated by traditional antipsychotics. As soon as neuroleptic malignant syndrome symptoms were recognized, the antipsychotic drugs were discontinued, symptomatic therapy was initiated and symptoms of neuroleptic malignant syndrome disappeared. However, the patient’s psychotic symptoms persisted and an atypical antipsychotic was administered. During the next few days the psychotic symptoms gradually disappeared and the patient accomplished good recovery.

**Key words:** Antipsychotic Agents + adverse effects; Neuroleptic Malignant Syndrome; Signs and Symptoms

**Introduction**

Neuroleptic malignant syndrome (NMS) is a rare, idiosyncratic, potentially life-threatening complication reported to occur during therapy with both traditional and atypical antipsychotic agents [1,2]. After neuroleptics were introduced for clinical use in 1952 [3], Delay described clinical features of the malignant neuroleptic syndrome for the first time: development of pronounced extrapyramidal symptoms (hyperthermia, „cogwheel rigidity”); tremor, dystonia); hyperthermia (up to 42 degrees C), altered mental status of quantitative (somnolence, spoor, coma) or qualitative type (confusion-delusion clinical picture). NMS also includes a dysfunction of the autonomic nervous system (unstable hypertension, orthostatic hypotension, tachycardia - over 80/min, diaphoresis, hypoxia, incontinence, and salivation). Symptoms of NMS are also associated with abnormalities in laboratory findings such as: leukocytosis (10 – 40.000 with a shift to the left, which is optional) (4 – 6), increase in creatine-phosphokinase (CPK) due to rhabdomyolysis (reference values: 24 – 170 µ/l), electrolytic imbalance associated with hypokalemia, acidosis and increase in transaminases [1,2,4,5].

Over the years, along with the frequent use of psycho-pharmaceuticals of varied actions, articles describing development of NMS as a rare, life-threatening complication associated with adverse effects of antipsychotics, became more frequent as well [2,6,7].

According to current medical literature, the incidence of NMS in different parts of the world is similar (ranges from 0.2 – 3.3% of patients treated with antipsychotic agents), and there are no significant differences in regard to application of traditional and atypical antipsychotics [4,6-8]. It is important and significant to point to the fact that the number of lethal outcomes among patients with NMS has significantly decreased, from 25% prior to 1984, to 7-11% [7] over the last years. It is considered that timely detection of initial symptoms and immediate actions are the reasons for reducing the percentage of lethality in NMS patients. That is why it is of utmost importance to detect initial symptoms and start adequate therapeutic procedures [1–7]. Although there are no significant differences in the incidence of NMS during the use of traditional (TA) and atypical antipsychotics (AA), it has been established that extrapyramidal symptoms are less common in the clinical picture of patients with NMS receiving AA, which is explained by different actions (lower affinity to D<sub>2</sub> receptors in the mn. striate and substantia nigra).

In the literature [2,3] physicians may find factors which may warn them of an increased risk of NMS development. They include the following: rapid increase in the dosage of antipsychotics, dehydration, psychomotor agitation, i.m. application of antipsychotics, organic brain damage (IVC, Parkinson and Wilson’s disease, addicts), fixation over a longer period of time, male gender, younger age (under the age of 50 years), concomitant administration of an-
Side effects of antipsychotic agents

Extreme rhabdomyolysis may be associated with renal insufficiency, deep vein thrombosis, and pulmonary embolism. Complications are mostly due to consciousness disorders, immobilization, impaired swallowing reflex, dysphagia, aspiration pneumonia, dehydration, heart arrest [3,5,7,9].

Due to a serious clinical picture and appearance of life-threatening NMS, it is necessary to inform members of the patient’s family about the course of the disorder and keep detailed medical records.

Case report

This is a report of a 46-year-old woman born in Novi Sad. She is divorced and lives alone. She has secondary education, but has lost her job and only occasionally visits her parents who live in the same place. According to the auto-anamnestic evidence, during puberty and adolescence she sometimes used to abuse alcohol and marijuana. Her first admittance to the Institute of Psychiatry in Novi Sad was in 2002, and she was treated in a Daily Hospital Unit of the Clinic for Affective and Anxiety Disorders. She was discharged with the (F 43.2) diagnosis of prolonged depressive reaction and (F 60.3) borderline personality disorder, according to the ICD-10 Classification of Mental and Behavior Disorders. She was admitted to the Daily Hospital after a series of conflicts in her family. She often fought with her husband and started drinking heavily. Her outpatient treatment lasted for three months, but as there was no improvement, she was admitted for partial hospitalization. She com-
and subfebrile. The laboratory findings were within
normal reference values, extrapyramidal symptoms regressed.

Due to the psychotic clinical picture with paranoid interpretation and risk of repeated agitation, clozapine, an atypical antipsychotic (12.2 mg/day) combined with clonazepam (2.5 mg/day) were initiated.

During the following 10 days, the dosage of antipsychotics was increased to 200 mg/day. The patient reacted positively and psychopathologic symptoms disappeared. She was allowed to spend therapy weekends at home, and they seemed to be more and more successful.

The patient was discharged from hospital at the level of social remission with the recommended outpatient treatment.

Our patient presented with symptoms induced by adverse effects of the antipsychotic therapy - that is NMS, with an only exception of severe leukocytosis. Taking into account that her initial values of leukocytes were low, it may be supposed that timely therapeutic procedures caused only moderate increase of leukocytes, that is that the clinical picture of NMS was not completely developed.

**Discussion**

According to the literature data (1, 3), 79% of patients with NMS make a complete recovery, whereas possible consequences include cognitive disorders, neurological focal deficits, muscle atrophy and contractures.

Since NMS is a very serious complication which commonly occurs during application of antipsychotics and which still has an unpredictable outcome, it is of utmost importance to follow up all side-effects of antipsychotic therapy, such as extrapyramidal symptoms. A timely intervention can prevent development of the complete clinical picture of NMS, and at the same time decrease possible secondary infections and complications of NMS [1,7,9].

**Conclusion**

The presented case of neuroleptic malignant syndrome was most probably induced by administration of an antipsychotic – haloperidol, but possibly by its combination with risperidone. This means that these antipsychotic agents may not be used in this patient due to an extremely high risk from neuroleptic malignant syndrome development. Instead, an atypical antipsychotic was used (clozapine), with different mechanisms of action, and a satisfactory therapeutic effect was achieved – a significant reduction of psychotic symptoms. An outpatient treatment using the same therapy was recommended.

The patient received the following therapy: haloperidol injections 3 x 1 i.m., bensedine 3 x 1 i.m. The same therapy was continued the following day. After the therapy the patient was calmer, cooperative, but some psychopathologic behavior persisted, so she started receiving her therapy per os. Due to shortage of 2 mg haloperidol tablets, risperidone was initiated, but the dosage of antipsychotics was increased to 3 mg per day, and benzodiazepine injections were continued.

On the fifth day of her hospital stay, the patient developed extrapyramidal symptoms including hypertonia (cog-wheel rigidity), associated with severe generalized extrapyramidal tremor, hyperhydrosis and “facies oleosa”. Her state of consciousness varied from somnolence to confusion (psychotic clinical picture). During the same day the patient presented with hyperthermia (37.7 – 38.2 degrees C), labile hypertension (up to 160/100); profuse sweating, tachycardia (up to 120/min), and regular heart rate rhythm.

The laboratory findings revealed increased CPK levels (1540 j/l), hypokalemia (k – 3.3 mmol/l), and increased leukocytosis (3.6 on admission, 6.76 with a tendency to „turn to the left”).

The antipsychotic agent was completely discontinued and bromkriptin was introduced (5 mg/day), as well as infusion solutions, potassium replacement in the infusion, and a urinary catheter was placed (dieresis was over 1500 mg/day). According to the internist’s recommendations, a wide-spectrum antibiotic was added to the infusion. Antipyretic paracetamol was also initiated (3x1), antihypertensive presolol (100 mg 3x0.25) and monopril (20 mg, 2x1). Lorazepam tablets (7.5 mg/day) were given for sedation.

During the next few days the patient was refreshed, fully conscious, but still severely psychotic and subfebrile. The laboratory findings were within...
Neuroleptički maligni sindrom je retka, ali po život opasna komplikacija koja nastaje usled neželjenih dejstava antipsihotičkih lekova. U savremenoj literaturi navodi se inzidenca od 0,2 do 3,3%. Neuroleptički maligni sindrom često nastaje posle naglog povećanja doze konvencionalnih neuroleptika ili u stanju dehidriranosti. Međutim, ovaj sindrom može da se javi i kod bolesnika lečenih atipičnim antipsihotskim medicinama, češće kod primene Clozapine. Patofiziološki mehanizam nastanka neuroleptičkog malignog sindroma objašnjava se jatrogenom blokadom Dopaminskih receptorima (D2) nigrostriatuma, mezokorteksa i hipotalamičkih jedara. Ukoliko se najznačajniji simptomi ovog sindroma (mišićna hipotonija, promene svesti, hipertermija, dijaforeza i sl.) pravovremeno uoči i na njih se promptno reaguje, moguće je potpuni oporavak.

Prikaz slučaja
Ovo je prikaz slučaja bolesnice lečene konvencionalnim antipsihotskim medicinama. Blagovremeno uočeni, antipsihotska terapija je odmah prekinuta, uz uvedena je simptomatska terapija, a simptomati su nestali.

Diskusija i zaključak
Budući da je neuroleptički maligni sindrom komplikacija potencijalno opasna po život, koja nastaje usled neželjenih dejstava neuroleptičkih lekova, neophodno ih je uočiti kod svakog bolesnika, a ukoliko se pojave simptomi neuroleptičkog malignog sindroma, potrebno je odmah prekinuti terapiju antipsihotskim lekima. Ako je neophodno izvršiti zamenu leka, potrebno je da lek ima nizak afinitet prema (D2) receptorima, i da se kombinuje sa simptomatskom terapijom.

Literatura


Sažetak

Ključne reči: Antipsihotici + neželjeni efekti; Neuroleptični maligni sindrom;ZNaci i simptomi

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