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CASE REPORT / *OLGU SUNUMU*

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Serotonin Syndrome Due to Overdose Intake of SSRI

Yüksek Doz SSRI Alımına Bağlı Gelişen Serotonin Sendromu

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17. Ulusal Klinik Toksikoloji Kongresi 17-20 Mayıs 2012 Mardin Kongresinde sözel sunu olarak sunulmuştur.

SUMMARY Serotonin syndrome is a drug side effect resulting from serotonergic hyperactivity. The severity of its symptoms can be mild and overlooked and sometimes it may cause life-threatening serious consequences. This syndrome is caused by the administration of one or more drugs having serotonergic activity. This case is a 25-year-old female patient who attempted suicide by ingesting an overdose of her prescription medications: 60 units of 100-mg Faver (Fluvoxamine), 20 units of 50-mg Setral (Setraline), and 10 units of 20-mg Paxil (Paroxetine).

Key Words: SSRI overdose, myoclonus, Serotonin syndrome

ÖZET Serotonin sendromu serotonerjik aşırı etkinlik sonucu oluşan bir ilaç yan etkisidir. Hafif şiddette olup gözden kaçabildiği gibi hayatı tehdit eden ciddi sonuçları olabilmektedir. Serotonerjik etkili bir veya daha fazla ilacın bir arada kullanılması bu sendroma yol açar (Dokuz Eylül). Buradaki olgu 25 yaşında kadın hasta olup intihar amaçlı yüksek doz 60 adet 100 mg Faver (Fluvoxamine), 20 adet 50 mg Setral (Setraline), 10 adet 20 mg Paxil (Paroxetine) almıştır.

Anahtar Kelimeler: Yüksek doz SSRI, myoklonus, Serotonin sendromu

Introduction

Sertraline is a selective serotonin (5-Hydroxytryptamine, or 5-HT) reuptake inhibitor (SSRI) (1). This group of drugs reversibly blocks reuptake of 5-HT in the synaptic range (1). It is effective in the treatment of sertraline depression, obsessive-compulsive disorder, and eating and personality disorders. It is widely reported that sertraline is efficacious and well-tolerated (2). Fluvoxamine acts as an antiobsessional and antidepressant by selectively affecting the presynaptic gaps (3). Like Fluvoxamine and sertralin, paroxetine is also an SSRI.

The therapeutic index of SSRIs is considerably wide. Mortality brought about by SSRIs only is rare (4). Our case is a 25-year-old female patient who attempted suicide by ingesting an overdose of her prescription medications: 60 units of 100-mg Faver (Fluvoxamine), 20 of 50-mg Setral (Setraline), and 10 of 20-mg Paxil (Paroxetine).

Case Report

A 25-year-old female patient diagnosed with obsessive-compulsive disorder and depression was brought to the emergency room of Nusaybin State Hospital after informing her relatives she did not feel well as a result of having attempted suicide a half hour earlier by ingesting an overdose of her prescription medications: 60 units of 100-mg Faver (Fluvoxamine), 20 of 50-mg Setral (Setraline), and 10 of 20-mg Paxil (Paroxetine).

In her physical exam when she was first admitted, her general condition was moderate, with a BP of 160/90 mmHg, a pulse of 150/min. a temperature of 36.5 °C, tachypnea, and sweating. She was conscious and exhibited restlessness and mild apathy and agitation; she was partially cooperative and occasionally established eye contact. She suffered no neck stiffness and showed no signs of meningeal irritation. At irregular intervals the patient was observed to repeatedly

turn her head to face first one side then the other. Her speech was normal, albeit reduced. Jerky eye movements were present in the form of horizontal spasmodic vibrations. Her pupils were slightly dilated and responded weakly to direct and indirect light. In addition, there was clearly no extraocular muscle weakness as spontaneous eye movements in all directions were observed. She had full muscle strength in all extremities. The upper (biceps, stiloradial, and triceps) deep tendon reflexes were slightly increased, while lower ones (patella and Achilles) were lively, with a few cycles of clonus. Myoclonus was present in the lower extremities. The patient's plantar reflexes were extensor responses (Babinski signs). Due to the patient's mental state, it was impossible to evaluate the sensory examination. Examination of the extrapyramidal system revealed mild rigidity in the patient's upper and lower extremities. All other systemic examinations were normal. The hemogram and biochemical parameters of her first laboratory tests were: albumin 5.58 g/dL, Na 147 mmol/L, Cl 113 mmol/L, Ca 11.7 mg/dL, and WBC 12.5 (x10) K/µL; all other values were within normal reference ranges. It was impossible to measure the blood levels of the drugs she had taken. We were likewise unable to measure the patient's blood gases.

The patient was hydrated intravenously in the emergency room. Gastric lavage performed by nasogastric tube revealed residues of 6 unknown drugs. Activated charcoal (1 mg/kg) was administered. Upon completion of initial intervention, the patient was admitted to Intensive Care to be monitored for serotonin syndrome. Activated charcoal treatment was continued in ICU with a second dose (1 mg/kg). The patient was sedated for the first 24 hours with an infusion of Demizolam. I and O were monitored. The patient was treated twice (3 mg and 2 mg) with ampules of Beloc (metoprolol) for tachycardia. In spite of the fact that the treatment administered prevented elevated body temperature, the patient complained of fever; yet her temperature remained between 36.5 °C and 37.2 °C. BP ranged from 98/67 to 160/94 mmHg. The patient's blood glucose level fell to 80 mg/dL, so she was administered 5% dextrose in the 4th hour. Lower extremity myoclonus lasted 16 hours. No abnormality was observed in laboratory parameters. The patient was discharged on the 3rd day of hospitalization in good general condition. Evaluation of the patient on the 2nd and 4th days following discharge revealed no symptoms.

Conclusion

Serotonin syndrome is a toxic condition resulting from postsynaptic serotonin hyperstimulation of neurons (5,6). This side effect occurs most often in patients prescribed single or multiple medications increasing the serotonin level in postsynaptic gaps (6,7). The Hunter serotonin toxicity criteria, the Sternbach criteria, and the Radomski criteria are used for diagnosis of serotonon syndrome (8-10) (Table 1). Serotonin syndrome consists of cognitive behavioral changes, neuromuscular hyperactivity, and autonomic activation. Our reasons for considering serotonin syndrome in this case were the patient's suicidal overdose on SSRIs; coupled with the presence of such pyramidal irritation and extrapyramidal neurologic findings as changes in mental state (fluctuations in consciousness), acute onset myoclonus, ocular clonus, rigidity, increased deep tendon reflexes, Achilles clonus, and Babinski signs, all of which are major symptoms included in diagnostic criteria; as well as the occurrence of autonomic symptoms like tachypnea, perspiration, sinus tachycardia, weak pupil response, dilation of the pupils, and hypertension. In the differential diagnosis, the infectious, metabolic, and toxic causes necessitating this view must also be taken into account (11). In our case, infectious reasons were not considered, most especially because of the multiple overdoses of serotonergic agents specified in the patient's history, but also due to the absence of neck stiffness despite all of these clinical findings, as well as to the presence of a multifocal and quickly improved clinical picture that simultaneously affected the central, peripheral, and autonomic nervous systems, such as the occurrence of pyramidal, extrapyramidal, and autonomic signs coincidental with changes in mental state.

Physical examination and medical history hold an important place in the differential diagnosis of Neuroleptic Malignant syndrome (NMS), malignant hyperthermia, and serotonin syndrome. NMS is an idiosyncratic reaction to antipsychotic drugs like butyrophenones and phenothiazines (12). It is thought to be caused by dopamine receptor blockers. It usually begins with altered consciousness and hyperthermia followed by muscle rigidity. Only dopaminergic drugs cause NMS. It develops after several days, in contrast to serotonin syndrome. Patients improve days or weeks later (12). The onset of and recovery from symptoms of serotonin syndrome, on the other hand, both occur within hours. Whether ingestion of the drug is suicidal or therapeutic, symptoms occur in the first 6 hours in most cases. In our case, too, the myoconus appeared within the first few hours and lasted 16 hours.

Malignant hyperthermia is a syndrome resulting from a genetic predisposition to neuromuscular blockers such as succinylcholine and anesthetic agents like halothane (13). This syndrome occurs within minutes after exposure to anesthetic agents. A hypermetabolic state characterized by muscular rigidity and increased oxygen consumption and carbon dioxide production, metabolic acidosis, and hyperthermia are all characteristic features of malignant hyperthermia (14). We

Table 1. Serotonin syndrome diagnosis criteria

Sternbach criteria (8):

Initiation or dose increase of a serotonergic agent

Exclusion of other etiologies (e.g., infection, substance abuse, withdrawal syndrome, etc.)

Neuroleptic agent must not have been initiated or the dose increased

There must be at least three of the following symptoms:

· Mental status changes (confusion, hypomania)

· Agitation

· Myoclonus

· Hyperreflexia

· Diaphoresis

· Chills / tingling sensations

· Tremors

· Diarrhea

· Incoordination

· Fever

Hunter criteria (9):

After ingestion of or increase in dose of a serotonergic agent, a diagnosis of serotonin syndrome is made in the event of any of the clinical situations listed below:

a. Spontaneous clonus alone

b. Induced clonus + agitation (or excessive perspiration)

c. Ocular clonus + agitation (or excessive perspiration)

d. Tremors + hyperreflexia

e. Hypertonia + fever above 38 °C + ocular clonus (or induced clonus)

Exclusion of other etiologies (e.g., infection, substance abuse, withdrawal syndrome, etc.)

Neuroleptic agent must not have been initiated or the dose increased

Radomski criteria (10):

Following initiation of treatment with, increased dosage of, or addition to an already existing treatment of a serotonergic drug, if either 4 of the below major symptoms or 3 of the major and 2 of the minor symptoms are seen

a. Major symptoms:

· Mental: confusion, mood elevation, semicoma/coma

· Neurologic: myoclonus, tremors, chills/tingling, rigidity, hyperreflexia

· Autonomic: fever, perspiration

b. Minor symptoms:

· Mental: agitation/irritability, insomnia

· Neurologic: incoordination, pupillary dilation, akathisia

· Autonomic: tachycardia, tachypnea/dyspnea, diarrhea, hypertension/hypotension

The clinical features described in the first criterion, must not be signs of an underlying psychiatric disorder existing prior to initiation of serotonergic drugs

Other etiologies (e.g., infections, metabolic or endocrine causes, substance abuse, and withdrawal syndrome) should be excluded.

Before the onset of signs and symptoms listed above, treatment with a neuroleptic drug must not have been initiated or its dose increased.

believe the reason malignant hyperthermia did not develop on our case was because it was averted by early diagnosis and treatment and by the patient's resultant early recovery.

There is no specific antidote or treatment for serotonin toxicity. Early diagnosis and supportive treatment are important. Avoiding the potential drug reaction between two serotonergic drug therapies is a basic factor in prevention of this syndrome (15-17). When initiating treatment of serotonin syndrome, the first priority is to discontinue the medication causing this condition. Nonspecific serotonin receptor blockers such as benzodiazepines, propranolol, chlorpromazine, ciproheptadin, and methysergide may be used in the treatment of serotonin syndrome (18). Although there are cases of overdose on single serotonergic drugs, generally symptoms in every age group – young, elderly, and even neonatals-appear when two or more such medications are taken together, even if each is taken in therapeutic doses (19). In our case, the patient overdosed on three serotonergic drugs; serotonin syndrome was the result.

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