Introduction

Serotonin syndrome (SS) is a life-threatening, undesirable drug reaction caused by over activation of central and peripheral serotonin receptors due to high serotonin levels. Olanzapine, a second-generation antipsychotic agent, is an antagonist of serotonin receptor. Despite the effect of serotonin antagonism, it is reported that olanzapine may paradoxically trigger serotonin syndrome. In this case report, we present a patient with SS due to chronic olanzapine use accompanied by bullous drug reaction.

Case Report

A 27-year-old male presented to the emergency department (ED) with altered mental status. It was learned from his family that the patient had come home in a dazed state and gone to sleep directly, but he could not be awakened on the day he was brought to the ED by ambulance. The patient had been using valproic acid and olanzapine for five years due to bipolar disorder. The patient was monitored and 0.4 mg of naloxone was given intravenously (IV). Appropriate fluid, electrolyte and anti-
Serotonin syndrome is a combination of symptoms caused by over activation at central and peripheral serotonin receptors secondary to high serotonin levels. It is usually easy to skip the diagnosis because of mild symptoms attributed to the general side effects of drugs. The findings may range from mild constitutional symptoms to a life-threatening complex syndrome. In mild cases, tachycardia, tremor, mydriasis, sweating can be seen and usually no fever is observed. In moderate severity syndrome, hyperthermia (>40°C), hyperactive bowel sounds, horizontal ocular clonus, agitation can be seen. In severe cases, hyperthermia (exceeding 41°C), hemodynamic instability, muscle rigidity and delirium are seen. Hyperreflexia, rigidity and clonus are more prominent in the lower extremities.

In the literature, SS is reported as a diagnosis of exclusion. There is no diagnostic test to confirm the presence of the syndrome. The most important diagnostic stage is the clinician’s suspicion. In the history, the initiation of a serotonergic drug, the dose change or the addition of other drugs should be questioned. Although many diagnostic criteria are described, Hunter Serotonin Toxicity Criteria (HSTC) has the highest sensitivity and specificity rates. According to the HSTC, in addition to the use of a serotonergic drug, presence of one of the following criteria is efficient for the diagnosis; spontaneous clonus, inducible clonus plus agitation or diaphoresis, ocular clonus plus agitation or diaphoresis, tremor plus hyperreflexia, hypertonia plus temperature above 38°C plus ocular clonus or inducible clonus. Patients with peripheral hypertonus and trunk rigidity are at great risk for possible respiratory failure. Nonspecific abnormalities may also be observed in the laboratory results.

Neuroleptic malignant syndrome (NMS), malignant hyperthermia, anticholinergic toxicity, sympathomimetic drug intoxication, encephalitis, heat stroke and central hyperthermia should be considered as the differential diagnosis. SS that is accompanied by hyperreflexia usually develops in 24 hours, however NMS which is accompanied by bradireflexia, has a slower onset that may extend to weeks. Anticholinergic toxicity is associated with hyperthermia, altered mental status and mydriasis, urinary retention and decreased bowel; but increased muscle tone and reflexes are not expected. An increase in end-tidal carbon dioxide level, widespread rigidity and hyporeflexia are observed in malignant hyperthermia, which may develop after exposure to inhalation anesthetics and depolarizing muscle relaxants. In other differential diagnoses, neuromuscular activation findings that was observed in SS are not expected.

In a patient who is thought to have SS, all serotonergic agents should be discontinued and supportive treatment should be initiated. In most cases, symptoms are resolved within 24 hours. Affective sedation may be achieved with benzodiazepines if needed. In severe cases, cyproheptadine, which is a 5HT-2A receptor blocker, may be initiated. Although it provides symptomatic relief in mild to moderate cases, it does not shorten the duration of the recovery phase. The recommended starting dose is 12 mg and a 2 mg maintenance dose may be administered every 2 hours as long as the symptoms persist. Antipyretics are not useful because the fever in SS is dependent on increased muscle activity, not central.

Antipsychotic drugs, olanzapine and risperidone paradoxically both trigger SS and are reported to be used in the treatment of this syndrome. Since olanzapine is a 5HT-2A receptor antagonist, its use in treatment of SS is reasonable, but it is underlined that it may also cause SS in chronic use. Although the underlying mechanism is not clear in the literature, it has been reported that chronic olanzapine treatment may cause different interactions on the basis of receptors and neurotransmitters in each patient.

Conclusion

Because of the widespread use of serotonergic drugs, it is important for clinicians to keep the SS in mind in patients with altered mental status, fever and neuromuscular hyperactivity. However, it should be remembered that early suspicion and early treatment may prevent from mortality and morbidity.
References
