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Case Report / Olgu Sunumu

Serotonin Syndrome Dueto Linezolid in a Patient Receiving Escitalopram Treatment

Patient Receiving Escitalopram Treatment Esitalopram Tedavisi Alan Hastada Gelişen Linezolide Bağlı Serotonin Sendromu

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Abstract

Serotonin syndrome is a potentiallyfatalconditioncaused by overstimulation of serotonin receptors in the centraland peripheralnervous system. Serotonin syndrome developsdueto the increasedamount of serotonin duetoincreasedserotoninsynthesisorrelease, decreasedmetabolism, inhibition of reuptakeand / ordirectagonistic to serotonin receptors. Intheliterature, rarecases of serotoninsyndromeduetolinezolid have been reported. Inthisreport, wepresent a case of serotoninsyndromedeveloped in a patientreceivinglinezolid therapy fordiabetic foot infectionandreceivingescitalopramtreatment for major depression.

Keywords: Linezolid, escitalopram, serotonin syndrome

Özet

Serotoninsendromu merkezi ve periferik sinir sisteminde serotonin reseptörlerinin aşırı uyarılması sonucu gelişen ölümcül olabilen bir durumdur. Serotoninsendromu, serotoninsentezininin veya salınımının artması, metabolizmasının azalması, geri alımının inhibisyonu ve/veya serotonin reseptörlerine direk agonistik gibi nedenlere bağlı olarak artmış serotonin miktarına bağlı olarak gelişir. Bu sendrom en sıklıkla sorumlu ilacın aşırı dozu ve/veya ilaç etkileşimine bağlı olarak gelişebilir. Literatürde nadir de olsa linezolide bağlı serotoninsendromu vakaları bildirilmiştir. Bu sunumunda diyabetik ayak enfeksiyonu nedeniyle linezolid tedavisi alan, major depresyon nedeniyle esitalopram tedavisi de kullanan hastada gelişen Serotonin sendromu vakası sunulmak istendi.

Anahtar Kelimeler: Linezolid, esitalopram, serotoninsendromu

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1. Introduction

Serotonin is an endogenously produced chemical that allows brain cells and other nervous system cells to communicate with each other. Serotonin syndrome develops due to the increased amount of serotonin due to increased serotonin synthesis or release, decreased metabolism, inhibition of reuptake and / or direct agonistic to serotonin receptors and may lead to the collection of potentially fatal symptoms. Serotonin syndrome has traditionally been described as a combination of autonomic hyperactivity, neuromuscular disorders, hemodynamic changes and consciousness changes (1,2).

Serotonin syndrome can cause symptoms ranging from mild clinical syndrome to death. Approximately 7300 cases of serotonin syndrome have been reported each year and approximately 100 of these patients have mortality (1,2,3).

Serotonin syndrome may occur due to different mechanisms, overdose or combined use of drugs that increase serotonergic activity. Serotonergic drugs that inhibit serotonin reuptake among agents (serotonin reuptake inhibitors SSRIs, tricyclic antidepressants, trazodone, meperidine, dextromethorphan, tramadol), drugs that increase the release of serotonin (amphetamines, opioid analgesics, levodopa), agents that inhibit serotonin metabolism (e.g. monoamine oxidase inhibitors (MAOIs), linezolid, selegiline), post-synaptic serotonin receptor agonists (e.g. buspiron, triptans, carbamazepine) are available. Especially in combination with MAOIs and drugs from the group that inhibits serotonin reuptake use is the most risky group for serotonin syndrome forms (1-4).

2. Case Report

A 65-year-old female patient whom previously diagnosed as major depression and diabet was applied to our infectious diseases polyclinic with with complaints of discharge, swelling, redness and pain in her left foot. On physical examination, her general condition was good, her consciousness was cooperative and her vital signs were stable. In laboratory tests; white blood cell was 8.200 / mm3 (4,50-11,00), C-reactive protein (CRP) was 158 mg/L (5-10), and the erythrocyte sedimentation rate (ESR) was 96 mm/h (0 – 20). There were no pathological findings in other biochemical tests. Wound culture was obtained from the patient and empirically cefazolin 3x1 g iv treatment was started. When methicillin-resistant staphlococcus aureus (MRSA) was grown in the wound culture, cefazolin treatment was stopped and linezolid 2x600 mg IV treatment was started. The drug treatment (metformin and escitalopram) which was used continuously before the patient was continued during hospitalization.

Foot Magnetic resonance imaging (MRI) was performed to investigate the presence of osteomyelitis. While the patient's vital signs were stable, she developed sudden sweating, fever, sinus tachycardia, hypotension, tremor, tachypnea, delirium and confusion on the fourth day of hospitalization. The patient was admitted to the intensive care unit for close follow-up. Cranial CT and MRI were requested. No pathology was detected. The patient underwent lumbar puncture to exclude central nervous system infection. Cerebrospinal fluid (CSF) cell count; glucose, protein and cell counts were normal. No cell was detected in CSF cell count. Hydration started. On the first day of admission to intensive care unit, the patient was intubated due to severe respiratory distress. Blood, urine and CSF cultures were obtained from the patient for differential diagnosis. Meropenem 3x2 gr iv was added empirically until culture results were obtained. Procalcitonin test was requested early detection of possible bacteremia. It was negative.

Neurology and psychiatry consultations were requested as no pathology was detected to explain the change in the patient's state of consciousness. Since no pathological findings were detected by consultations, imaging and laboratory findings, the intensive care physician suspected that the patient might have serotonin syndrome developed as a result of combined use of linezolid and escitalopram as an exclusion diagnosis.

After the patient's Naranjo score (5) was found 6, it was evaluated as a possible adverse event. Linezolid and escitalopram treatments stopped and ciproheptadine (4 mg daily) was started with nasogastric tube. Teicoplanin 400 mg ı.v once a day treatment was started for the diagnosis of diabetic foot infection. Eighteen hours later, the patient showed signs of initial recovery. The patient's vital signs stabilized and the separation process from sedation and ventilation took place 48 hours later. The patient regained consciousness. As there was no growth in CSF, urine and blood cultures, meropenem was stopped. There was no signs of osteomyelitis in the foot MRI. After 2 weeks of hospitalization, the patient was discharged from hospital, with the recommendation of outpatient control with oral fusidic acid tablets, as the improvement of clinical and laboratory findings.

3. Discussion

In the available literature, cases of serotonin syndrome developing in patients using linezolid together with antidepressant drug have been reported. Similarly from our

country, Şahiner et al. (6) had reported a serotonin syndrome case, whom undergoing antidepressant therapy with the serotonin reuptake inhibitor (SSRI) group and after using of linezolid. Samartzis et al. (7) had reported a case of an adverse interaction between linezolid, amitriptyline and analgesic fentanyl in a 68-year-old woman with advanced ischemic peripheral arterial disease and sepsis. Woytowish et al. (8) reviewed the literature and identified 32 documented serotonin toxicity cases, including 3 fatalities due to linezolid plus other serotonergic agents. There are also case reports of developing serotonin syndrome without the need to combine escitalopram with another drug (9,10). There is even a reported case of advanced serotonin syndrome due to the use of quinolone group antibiotics and antidepressant therapy (11).

Serotonin regulates a wide range of physiologic and pathophysiologic processes in human body. So we can say it is much more than a neurotransmitter essential for the modulation of mood. Serotonergic drugs modulate many function of the body (3). On the fourth day of hospitalization, our patient developed sudden sweating, fever, sinus tachycardia, hypotension, tremor, tachypnea, delirium and confusion. Symptoms in our patient's history started after taking linezolid, absence of any neurological disease other than diabetes mellitus tip 2, no other drugs were used, no history of substance use, absence of reproduction in blood, urine and bos cultures, and normal neurological and systemic physical examination were found significant in serotonin syndrome. The present findings in the intensive care unit follow-up suggested serotonin syndrome caused by the interaction of SSRI and linezolid. Like our case report Volpi-Abadie et al. (2) reported similar features of serotonergic syndrome cases. Serotonin syndrome is a diagnosis of exclusion (2). Several diagnostic criteria have been proposed for serotonin syndrome. The recent one is the Hunter Serotonin Toxicity Criteria (HSTC) and the other one is Sternbach Criteria (2). Boyer et al. reported that many clinical conditions may be confused with serotonin syndrome. These patients had a history of serotinergic drug use, the onset of symptoms was less than 12 hours, hypertension, tachypnea, tachycardia and fever above 40 ° C. Pupillary mydriatic, bowel sounds hyperactive, lower extremity muscle tonus increase, hyperreflexia, clonus, agitation or coma are detected (1). In our case according to at least 1 symptom of Hunter criteria -a patient with fever and agitation and according to the sternbach at least 3 criterias- mental state changes, tremor and fever are meaningful for serotonin syndrome caused by linezolid interaction. The common features in all of them are the addition of a serotonergic agent, increasing the dose or adding an agent that increases the blood level of the serotinergic agent, the exclusion of other etiologies, the initiation of neuroleptic drugs or the dose not increased (12,13). This was consistent with the clinical history of our patient. Some nonspecific laboratory abnormalities may be seen in serotonin syndrome: leukocytosis, low bicarbonate level, elevated creatinine level and transaminases (2). But the presented case had no pathological findings in biochemical tests.

Serotonin syndrome may also occur during the use of a low dose or serotonergic drug alone. Mild cases can be overlooked (14). When the studies were examined, it was determined that there were cases of serotonin syndrome that occurred during the use of antidepressants alone and in low doses. Gelener et al. (10) reported a case of serotonin syndrome in a patient who was recommended duloxetine 30 mg / g for migraine. Confusion and hypervigilance occur two hours after the first dose of the drug, vital values of the patient, biochemical parameters and brain imaging methods were obtained normal. Another antimicrobial agent other than linezolid that have interaction with SSRI in the literature is ciprofloxacin. Sarısoy et al. (13) reported 2 cases of serotonin syndrome in which 1A2 enzyme inhibition and increased blood level of duloxetine (hence increased serotonin activity) resulted from the addition of ciprofloxacin to their treatment. In a retrospective study of Taylor et al. (15) 79 patients who had used SSRI and linezolid in the same period in their clinic were included in the study and 4 (6%) emphasized the possibility of serotonergic syndrome. Overall, the suspicion of serotonin syndrome and diagnosis must occur rapidly so treatment can prevent the morbidity and mortality associated with this condition (2).

4. Conclusion

Linezolid is now widely used in our clinical practice with treatment response and a number of advantages. The widespread use of serotonergic drugs, clinicians must maintain a high clinical suspicion for serotonin syndrome; early recognition and treatment of serotonin syndrome can prevent significant morbidity and mortality associated with this condition. Physicians must be astute and aware of the possibility of this life-threatening syndrome. If the diagnosis is unclear, physicians should discontinue any serotonergic agents and start supportive care.

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