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Case report-Olgu sunumu
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Neuroleptic malignant syndrome induced acute renal failure: Is mental retardation an additional risk factor?

Nöroleptik malign sendromun oluşturduğu akut böbrek yetmezliği: Mental gerilik ilave bir risk faktörü mü?

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Abstract

Neuroleptic malignant syndrome is a rare but serious complication of neuroleptic treatment. It is a disorder which is usually characterized by muscle contraction and changes in consciousness, extrapyramidal symptoms, hyperpyrexia and blood pressure irregularities that often depend on the use of conventional antipsychotic drugs. In this case report, we discuss acute renal failure induced by neuroleptic malignant syndrome developing on the basis of chronic kidney disease in a patient with mental retardation.

Keywords: Neuroleptic malign syndrome; mental retardation; acute renal failure

Özet

Nöroleptik malign sendrom, nöroleptik tedavinin nadir; ancak, ciddi bir komplikasyonudur. Sıklıkla klasik antipsikotik ilaçların kullanımına bağlı olarak gelişen ekstrapiramidal semptomlar, hiperpreksi, kan basıncında düzensizlikler, genellikle kaslarda kasılma ve bilinçde değişiklikler ile karakterize bir hastalıktır. Bu olgu sunumunda mental gerilik olan bir hastada kronik böbrek hastalığı zemininde gelişen ve nöroleptik malign sendromun oluşturduğu akut böbrek yetmezliğini tartışmaktayız.

Anahtar sözcükler: Nöroleptik malign sendrom, mental gerilik, akut böbrek yetmezliği

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Introduction

Neuroleptic malignant syndrome (NMS), was first described by Delay et. al in 1960 and was defined as a serious and one of the life-threatening side effects of the antipsychotic medication [1]. Patients with high fever and muscle rigidity are in the foreground. Autonomic dysfunction (sweating, tachycardia, labile blood pressure), changes in consciousness, high creatine phosphokinase (CPK) levels, leukocytosis, low iron or potassium levels, and non-specific EEG changes are among the other diagnostic features [2, 3]. Pathophysiology of NMS is fully elucidated, but it has been suggested that the central dopaminergic hypoactivity plays a major role [4, 5]. Clinical studies support that the use of high drug doses, parenteral drugs and more potent drugs are facilitators of NMS [6, 7]. Other potential risk factors are the use of concomitant medications such as lithium or metaklopromid, discontinuation of dopamine agonists, anticholinergic drugs or

benzodiazepines, presence of organic brain syndrome, extrapyramidal disorders, iron deficiency and dehydration [8]. In the literature, especially mental retardation is reported as a risk factor for recurrent NMS [9]. The frequency of NMS is about 0:02 to 2:44%, and 10% of cases result in death category [10-12].

Case report

Forty-year-old woman with frequent epileptic seizures, high fever (39°C), convulsions, decreased urine output, nausea and vomiting complaints in the last 3 days was admitted to the emergency department. Her past medical history revealed the presence of febrile illness, both physical and mental retardation and, the use of epileptic drugs for 32 years. Upon admission to the emergency room, she had used oxcarbazepine 300 mg / day, phenytoin 200 mg/day and clonazepam 2 mg/day. Physical examination revealed clear consciousness, agitation, blood pressure of 160/100 mmHg, fever at 37°C and generalized tonic-clonic seizure, respectively.

Laboratory investigation showed BUN: 156 mg/dL (5-25 mg/dL), creatinine: 16.6 mg/dL (0.4-1 mg/dL), Na: 140 mmoL/L (136-148 mmoL/L), K: 3.1 mmoL/L (3.6-5.1 mmoL/L), Cl: 100.6 mmoL/L (101-111 mmoL/L), venous bicarbonate: 16 mmoL/L (22-29 mmoL/Ll), uric acid: 9.4 mg/dL (2.6-8 mg/dL), LDH: 419 IU/L (98-192 IU/L), ALT: 25 IU/L (5-54 IU/L), AST: 41 IU/L (5-40 IU/L), GGT: 172 IU/L(70-50 IU/L), CPK: 3709 IU/L (26-140 IU/L), total protein: 6.2 g/dL (6.1-8.4 g/dL), albumin: 2.6 g/dL (3.5-5 g/dL), phosphorus: 6.8 mg/dL (2.4-4.5 mg/dL), calcium: 6.6 mg/dL (8.4-10.5 mg/dL), PTH: 305 pg/mL (15-65 pg/mL) Hb: 6.5 g/dL, WBC: 10800/mL, platelet: 280000/µL, arterial blood gas analysis, pH: 7, PCO2: 23 mmHg, PO_2: 47 mmHg, HCO3: 5.8 mEq/L, respectively. The complete urine examination showed proteinuria (+ +), glucose (++), ketones (-), and it was measured 5 g/day of micrototal protein level and 1g/day of microalbumin levels for 24-hour urine. Autoantibodies levels including ANA, anti-dsDNA, p-ANCA, c-ANCA, antiGBM and C3 and C4 were normal limits.

The patient was admitted to the depertment of nephrology with diagnosis of acute renal failure (ARF), and emergency dialysis therapy was applied. She was given 0.2 mg/kg IV diazepam during epileptic seizure and her oxcarbazepine doses was increased to 1200 mg/day by the proposals of neurology department for epileptic seizures. She was also examined by psychiatry because of agitated behaviors and, was given alprazolam 0.5 mg/day and citalopram 20 mg / day. Fever reached 38.5°C on 3th day of hospitalization. Staphylococcus aureus was isolated from the patient's blood culture, and hemodialysis catheters were thought to be the source of infection. Ampicillin-sulbactam was started 3 g/day according to the result of the culture-antibiogramme, and fever disappeared within 48 hours, and it didn't rise again. The intermittent hemodialysis treatment was continued according to the patient's daily BUN, creatinine, electrolytes and blood gas results. After eight sessions of hemodialysis, blood creatinine level fell down to 5 mg/dL, and remained stable around this level. The size of both in renal ultrasonographic examination were small and parenchymal echogenicity was increased (Grade 3). Thus, there was no need for renal biopsy. On the basis of these findings, the patient was diagnosed as acute renal failure from chronic renal disease due to NMS. The patient continuously needed hemodialysis treatment during the next follow-up, and was included in three days a week regular hemodialysis program.

Discussion

Diagnostic criteria for NMS were determined in 1985 by Levenson. While major criteria are fever, rigidity and high CPK level, the minor criteria are defined as tachycardia, tachypnea, sweating, blood pressure alterations, leucocytosis and changes in consciousness [13]. Three major criteria (fever, rigidity and CPK elevation) and 3 minor criteria (blood pressure changes, leucocytosis, changes in consciousness) were present in our patient.

Neuroleptic malignant syndrome is common among young or middle aged adults, and usually it occurs within the first 10 days following the use of antipsychotic drugs, but also may occur at any stage of treatment as well [14, 15]. The use of antiemetics, electrolyte disturbances (especially hypokalemia), environmental humidity and winter seasons (rarely) play a role in the etiology [16]. Doğan et al. [17] detected hypokalemia in one of their 3 cases. They reported appearance of NMS accompanied by the use of metoclopramide and pointed out the relation between winter season in the geographic region and the development of NMS because each of 3 patients were subjected to intense cold environment. The NMS cases arise by antidepressants such as amoxapin, venlafaxin and central nervous system stimulant drugs like methylphenidate as well as neuroleptic according to the publications [18-20]. Also, Pınar et al. [21] have reported a case with NMS due to poisoning by the herbicide called trifluraline. Martinez at al. [22] have reported NMS after phenytoin treatment of epilepsy in a 9-year-of child. In addition, the relatives of our 40 years old patient also mentioned the use of same long-term treatment (300 mg/day oxcarbazepine, phenytoin 200 mg/day, clonazepam 2 mg / day).

Other risk factors described for the NMS are the use of lithium, dehydration, nutritional deficiencies, high-dose and long-term use of antipsychotic drugs with the use of antipsychotics, history of previous NMS, the presence of organic brain disease and previous treatment of electroconvulsive therapy [23-25]. Our patient frequently had a febrile illness in her infancy, and mental retardation determined by psychiatric evaluation. This also supports the possible organic brain disease which is a risk factor for NMS as described above. Moreover, two patients with mental retardation was diagnosed with NMS by Turan et al. [26] Only in one patient high fever, convulsions and dullness were observed after initiation of haloperidol and biperiden therapy. The clinical status improved subsequently after hospitalisation and the initiation of appropriate treatment. Besides the history of difficult birth, family conversations also unveiled that she had the febrile illness and convulsions when she was 3 month. In other case, mistakenly applied larger dose fluphenazine treatment resulted in the beginning of contractions, shivering, sweating, high fever and difficulty in swallowing after 5 days. This hospitalized NMS case who developed ARF due to uric acid nephropathy during treatment was reported to receive hemodialysis treatment for 2 times. They have reported that NMS symptoms and ARF improved after the treatment described above. After meeting the family of the patient, history of frequent exposure to febrile disease during infancy and childhood was also noted. The detection of mental retardation in both cases suggests that mental retardation may be a risk factor for NMS [26]. Renal biopsy specimens of another case with NMS demonstrated uric acid crystals which play a major role in the pathogenesis of acute renal failure due to rhabdomyolysis [27].

In another case report, Diamond et al. [28] claimed that organic brain disease and mental retardation may be risk factors in a case of NMS leading to a coma induced by injection of fluphenazine in a 16-year-old adolescent with mental retardation, such patients ought to be followed-up in a more strict fashion. In the literature, mental retardation especially has been reported to be a relative risk for recurrent NMS. Mortality and morbidity rate are high among the NMS patients with mental retardation [29]. Acute renal failure develops in 16% of all cases of NMS and mortality increases by approximately 50 % [30, 31].

In conclusion, a long-term neuroleptic medication use was the risk factor for the development of the NMS in our case. However, the existence of mental retardation may be an another additional risk factor as suggested by the literature above.

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