Düşünen Adam The Journal of Psychiatry and Neurological Sciences 2015;28:181-182
DOI: 10.5350/DAJPN2015280214

Carbamazepine-Induced Probable DRESS Syndrome

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Date of receipt / Geliş tarihi: April 29, 2015 / 29 Nisan 2015

Date of acceptance / Kabul tarihi: May 25, 2015 / 25 Mayıs 2015

Dear Editor,

Carbamazepine (CBZ) is a widely used drug in psychiatric practice. The most severe adverse reaction with CBZ occurs as part of a generalized hypersensitivity reaction, known as drug reaction with eosinophilia and systemic symptoms (DRESS). We report here a case of a young adult who presented with probable DRESS. Clinicians should be aware of such an association, as cessation of the offending drug is an essential part of management.

A 27-year-old male adult with antisocial personality disorder was admitted to our psychiatry service. Recently he had experienced severe marital conflicts with his wife and subsequently had homicidal thoughts towards his wife, which was why he presented to the emergency room and was recommended hospitalization. Past history revealed that he had demonstrated a pattern of antisocial behavior since age 15, he had frequently changed jobs, and a year earlier he had attacked his wife with a knife. He had no previous medical history, initial laboratory findings (hemogram, blood chemistry values and urinalysis) were normal. To reduce his impulsivity, CBZ 400mg/day and quetiapine 300mg/d were started. CBZ was increased to 800mg daily at day 4, and to 1200mg daily at day 8. At day 13, the patient's body was covered in a maculopapular rash and he was febrile (39°C). Initial investigations revealed an inflammatory reaction and liver dysfunction. C-reactive protein was 65 (normal range <5) Liver transaminase levels were mildly elevated, aspartate transferase 103 IU/l, alanine transferase 146 IU/l. Serological tests for hepatitis A and B were negative. Initial full blood count showed severe thrombocytopenia (9700 µL) and eosinophilia ($0.6x10^3/mm^3$). Serum amylase, urea, and electrolytes were normal. Urinalysis by dipstick showed protein 1+ and occult blood 3+. The patient was diagnosed with a probable case of DRESS syndrome based on clinical and laboratory findings, and his CBZ was immediately stopped. He was placed on broad-spectrum antibiotics for possible sepsis. Parenteral methyl prednisolone treatment at a dose 60mg/day was started. At day 3, his

platelet counts rose to 27.000 and to 76.000 at day 4 and 203.000 at the end of the first week. Fever and rash disappeared in 7 days and symptoms completely resolved. Laboratory tests were normal in 10 days.

DRESS syndrome is a severe idiosyncratic drug reaction characterized by a papulo–pustular or erythematous skin eruption, fever, lymphadenopathy and involvement of organ systems. The clinical symptoms of DRESS are not immediate and usually occur 2–8 weeks after first administration of the drug (1). Aromatic anticonvulsants (CBZ, phenytoin and phenobarbitone) are amongst the drugs most likely to cause DRESS syndrome. As DRESS syndrome has been very rarely reported related to quetiapine treatment (2), and our patient had already used quetiapine in the year before admission and had not experienced any side effects, we thought that DRESS syndrome was associated with CBZ. Many idiosyncratic reactions have been reported with CBZ, including DRESS syndrome, and they are mostly believed to have an immune etiology (2). Diagnosis is largely clinical, based on knowledge of the temporal relationship between the onset of a drug and symptoms, and exclusion of other conditions. DRESS syndrome can be difficult to differentiate form other diseases which present with trombocytopenia. In our case, differential diagnosis included drug-induced thrombocytopenic purpura, as severe trombocytopenia is not common in DRESS syndrome. The lack of lymphadenopathy and atypical lymphocytes and eosinophilia (>$0.7x10^3/mm^3$) are other findings that were incompatible with DRESS. However, the presence of organ involvement (mild hepatitis), fever, and skin rash covering >50% body surface area and skin rash type suggesting DRESS along with the rapid resolution were findings supportive of DRESS. The RegiSCAR score, diagnostic criteria developed by The European Registry of Severe Cutaneous Adverse Reactions to Drugs and Collection of Biological Samples to assist the diagnosis of drug hypersensitivity syndrome, was determined as 4, which suggested probable DRESS syndrome (3). Steven Johnson Syndrome (SJS) has also to be considered as a differential diagnosis of DRESS syndrome, as in both syndromes clinical manifestations typically occur within 2 to 6 weeks after initiating drug therapy. In our case, the mucosal membranes of the oral cavity and eyes were not affected, which was a differential clinical feature, as these areas are commonly affected in SJS.

The DRESS syndrome must be recognized promptly and the causative drug withdrawn. Earlier withdrawal of the offending agents is associated with a better prognosis (4). Supportive and symptomatic treatments are indicated; corticosteroids are often used.

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