

Menenjit Tanılı Hastada Gelişen DRESS Sendromu; Olgu Sunumu

DRESS Syndrome in Patient with Diagnosis of Meningitis; Case Report

Gülten Ünlü¹, Semsî Nur Karabela², Emine Dünder³, Kadriye Kart Yaşar²

1Sağlık Bilimleri Üniversitesi, Kocaeli Derince Eğitim ve Araştırma Hastanesi İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji, Kocaeli, Türkiye

2Sağlık Bilimleri Üniversitesi, Bakırköy Sadi Konuk Eğitim ve Araştırma Hastanesi İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji, Kocaeli, Türkiye

3Sağlık Bilimleri Üniversitesi, Kocaeli Derince Eğitim ve Araştırma Hastanesi İç Hastalıkları Kliniği, Kocaeli, Türkiye

ÖZ

DRESS (Drug Rash with Eosinophilia and Systemic Sypmtoms) Sendromu, solid organ tutulumu, cilt tutulumu, hematolojik tutulumu yapan ilaç reaksiyonudur. Tedavi edilmezse mortal seyredebilir. En sık sebep olan ilaçlar aromatik antikonvülzanlardır. Biz bu çalışmada nadir görülen menenjit tanılı hastada gelişen DRESS sendromu olgusunu sunduk. Hastalık sistemik tutulum yapması ve mortal seyredebilmesi nedeniyle erken tanı ve tedavi önemlidir.

Anahtar Kelimeler: DRESS sendromu, eozinofili, menenjit

ABSTRACT

DRESS (Drug Rash with Eosinophilia and Systemic Sypmtoms) Syndrome, solid organ involvement, skin immunity, hematological involvement is the drug reaction. If not treated, it may be mortal. The most common drugs are aromatic anticonvulsants. In this study, we present a rare case of DRESS syndrome with diagnosis of meningitis. Early diagnosis and treatment are important because of the systemic involvement and mortality.

Keywords: DRESS syndrome, eosinophilia, meningitis

İletişim / Correspondence:

Gülten Ünlü

Sağlık Bilimleri Üniversitesi, Kocaeli Derince Eğitim ve Araştırma Hastanesi İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji, Kocaeli, Türkiye

E-mail: cicekgulten@yahoo.com

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INTRODUCTION

DRESS syndrome is a hypersensitivity reaction consisting of drug reaction, eosinophilia and systemic symptoms. Internal organ involvement and cutaneous lesions can be seen. It was first observed in patients receiving anticonvulsant therapy in the 1930s. The incidence of DRESS syndrome is approximately % 0.1-1 and the mortality rate is around % 10 [1]. Severe hypersensitivity reaction develops against the drug or metabolites of the drug. This may be due to the enzymatic defect in the metabolism of the drug. The most common drugs are aromatic anticonvulsants such as phenytoin, carbamazepine, phenobarbital [2]. Clinically; fever, maculopapular-pruritic rash, lymphadenopathy, exfoliative dermatitis, erythema multiforme, erythroderma, hepatitis, myocarditis, pericarditis, nephritis, pancreatitis, encephalitis, thyroiditis can be seen. The most commonly involved internal organ is the liver. In the laboratory, atypical lymphocytosis leukocytosis, eosinophilia, elevated liver enzymes, renal involvement can be seen [3,4]. Its pathogenesis is not yet fully understood. It is thought to be associated with reactivation of Epstein Barr virus (EBV), cytomegalovirus (CMV), human herpesvirus-6 (HHV-6) viruses with detoxification defects, immunological reactions, and slow acetylation [5].

CASE REPORT

A 33-year-old male patient presented to a university hospital outpatient clinic with complaints of fever, myalgia, headache, fatigue, vomiting for two to three days. Azithromycin tb was started. On the same day, he applied to the emergency department of the same hospital. The ECG was evaluated as normal and discharged. One day later, he applied to the emergency outpatient clinic of our hospital. It was learned that he had a history of tick attachment a week ago. Blood tests and cranial CT were normal. He was hydrated at an emergency service. Amoxicillin-clavulanic acid 1000 mg tb 2 × 1 perioral (PO) was started and discharged the same day with the diagnosis of upper respiratory tract infection. One day later, he was admitted to our outpatient clinic for infectious diseases. On the persistence of fever, muscle aches, headache, weakness and vomiting. He had a history of cranial

temporal A-V malformation. White blood cell (WBC): 11.1 (4-10.6 10³ CK / L) hemoglobin (HGB): 14.9 (12-16.8 g / dl), platelets (PLT): 241000 (139-346 10 H / L) CK-MB: 9.05 (0-5 ng / ml), Myoglobin: 662.7 (0-113 ng / ml), Troponin: <0.01 (0.00-0.06 ng / ml), aspartate aminotransferase (AST): 45 (0-35 U / L), alanine aminotransferase (ALT): 18 (0 -45 U / L), C reactive protein (CRP): 121 mg / dl (0-0.5 mg / dl). One day later, the patient, who had seizures in the hospital outpatient clinics, was taken to the intensive care unit and intubated. Fever: 38 ° C, neck stiffness positive, meningeal irritation findings negative. The patient who underwent lumbar puncture was started on antiepileptic phenytoin IV treatment with antibiotherapy and neurology consultation with the diagnosis of meningoencephalitis. Mild blurred, cell count: leukocyte 50 / mm³ erythrocytes: 20 / mm, cerebrospinal fluid (CSF) glucose: 67 mg / dl (40-70 mg / dl), EKT: 105 mg / dl, CSF protein: 422 mg / dl (15-45 mg / dl), CSF LDH: 25 U / L (0-20 U / L) Microscopic examination with Giemsa and methylene blue revealed lymphocytes. CSF HSV 1-2 DNA PCR: negative, CSF Tbc PCR: negative, Nonspecific CSF culture and blood culture flask did not produce CSF culture.

Meningitis / Sepsis Factors Multiplex polymerase chain reaction (PCR) Test CSF Review:

Herpes Simplex Virus type 1 (HSV 1), Herpes Simplex Virus type 2 (HSV 2), Parechovirus, Enterovirus, Epstein Barr Virus (EBV), Varicella Zoster Virus (VZV), Mumps Virus, Measles Virus, Human Herpesvirus 6, Human Herpesvirus 7, Human Herpesvirus 8, Cytomegalovirus (CMV), Staphylococcus aureus, Haemophilus influenzae, Streptococcus pneumoniae, Streptococcus agalactiae, Neisseria meningitidis, Borrelia burgdorferi sensu lato, Borrelia miyamotoi, Escherichia coli K1, Cryptococcus neoformans sensu lato, Cryptococcus gattii sensu lato, Listeria monocytogenes tests were negative.

The patient had a history of tick attachment a week ago and within a few days creatine kinase (CK) values began to increase. BOS leptospira PCR: negative (CSF) Borrelia burgdorferi Ig M: negative (serum) Borrelia burgdorferi Ig G: negative (serum)

Serum: Anti CMV IgM, Ig G: negative, Anti toxoplasma IgM: negative, Anti Toxoplasma Ig G: positive Anti-Rubella Ig M: negative, Anti Toxoplasma Ig G: positive, EBV VCA Ig M: negative, EBV VCA Ig G: positive. Brucella agglutination: negative, Hbs Ag, Anti HCV, Anti HIV tests were negative. Staf in a single vial of hemoculture in the ICU during the fever period. haemolyticus Intensive care follow-up After 4 days of conscious, partial operation, patients with hallucinations, glasgow coma scale (GCS): 15, liquid diet was started. Antiepileptic treatment was started in the ward with neurology consultation.

Contrast Brain: No nasal septum deviation was detected. Contrast-cranial MRI: Arteriovenous malformation of the right temporoparietal junction with arterial and venous vascular structures approximately 3x2 cm in size was observed. There was a slight thickening in the dura near the right temporal lobe, and a contrast enhancement in the postcontrast examination. (Figure 1).



Figure 1. Cranial AVM malformation-dural thickening

Cranial diffusion there was no signal change in the intracranial neural parenchyma in favor of acute ischemia in MR imaging. Ceftriaxon and vancomycin (continued daptomycin) intravenous (IV) treatments were completed on 14th day and her fever was 36.5 °C on the 4th day. Acyclovir treatment and antiepileptic treatment were arranged as tablets and discharged from the service. One day after his discharge, the patient was hospitalized at the third week of antibiotherapy and antiepileptic treatment with diffuse skin rash and periorbital edema. (Figure 2-3).



Figure 2. Back and chest skin lesions



Figure 3. Skin lesions on the legs and arms

The erythematous, progressive maculopapular rashes were required for skin and neurology consultation drug reaction? The preliminary diagnosis of acyclovir and phenytoin was stopped. Levetiresetam treatment, fluid hydration treatment was started. Skin biopsy from the leg region was evaluated nonspecificly in the pathological examination. In the differential diagnosis of vasculitis, p-ANCA, c-ANCA, ANA, AMA, anti ds DNA autoimmune markers were negative. Laboratory findings (in the second deposit with rash) WBC: 4600 (4-10.6 10^3 g / L), Hemoglobin: 12.7 g / dl (12-16.8 g / dl), PLT: 248000 (139000-346000 ile / L), Sedimentation: 37 mm / h (0-15 mm / h), Eosinophil ratio: 13.7% (0.5-11%), D-Dimer: 1272.5 (0-500 ng / ml), TIT: Bld +++, erythrocyte: 59, leukocyte: 3 , CK: 3789 mg / dl, AST: 58 (0-35 U / L),ALT: 49 (0.45 U / L), gammaglutamyltransferase

(GGT): 186 (12-64 U / L), alkaline phosphatase (ALP): 48 (40-150 U / L), lactate dehydrogenase (LDH): 318 (125-245 U / L), Calcium: 7.9 (8.2-10.6 mg / dl), Albumin: 3.2 (3.5-5 mg / dl). During follow-up, generalized eosinophilia, periorbital, facial edema, myositis developing, microscopic hematuria, costovertebral pain sensibility (+/-), hypoalbuminemia and hypocalcemia developed, side pain, severe back, abdominal pain, liver function tests deteriorated, CRP, sedimentation values The patient was evaluated according to RegiSCAR scoring system with liver, renal involvement, blood eosinophilia and skin involvement due to phenytoin use and was followed up with a total of 6 points with the hypothesis of DRESS (eosinophilia and systemic symptoms) (Table 1).

Table 1. RegiSCAR Diagnostic Criteria for DRESS (eosinophilia and systemic symptoms) Syndrome

Findings Score	Score			Comment
	-1	0	1	
Fire \geq 38.5 °C	N/U	Y		
Lymphadenopathy		N/U	Y	> 1cm and \geq 2 in different region
Eozinofili \geq 0.7x10 ⁶ /L or \geq 10% WBC <10 ⁶ /L		N/U	Y	Score 2, \geq 1.5x10 ⁶ /L olursa, veya \geq 20 WBC<4X10 ⁶ /L olursa
Atypical lymphocyte		N/U	Y	
Rash on the skin $>$ 50% Body surface DRESS-like rash	N	N/U B	Y Y	\geq 2 symptom: purpuric lesions, facial edema, psoriasiform desquamation
Support of skin biopsy	N	Y/U		
Organ involvement		N	Y	Score 1 for each organ involvement, maximum score: 2
Rash resolution \geq 15 day	N/U	Y		
Exclusion of other causes		N/U	Y	ANA, HAV, HBV, HCV, Mycoplasma, Chlamydia, blood culture tests if at least three of the negative: score 1

Y: Yes, N: No, U: Uncertain
Total score:
<2 points: -
2-3 points: Probable diagnosis
4-5 points: Possible diagnosis
> 5 points: Definitive diagnosis

Prednisolone was monitored by increasing intravenous (IV) therapy for three days. The laboratory and clinical findings of the patient whose general condition improved were improved and the rash was regressed and the patient was discharged with levetiresetam 500 mg tb 2x1 po treatment. Electroencephalography (EEG) was evaluated as normal cerebral bioelectric activity. (Day 14 of the treatment) ECG Review was normal. In the clinical follow-up, he developed abdominal pain with severe right side pain. Microscopic hematuria developed. There was no growth in urine culture. Abdominal ultrasonography (USG) in the contracted view of the gallbladder, cholecystitis? It was evaluated. The height of ALT, AST, LDH improved. In the lower and upper abdominal computer tomography (CT), millimetric calculi were observed in the lumen of the gallbladder. Cholecystitis was not considered. His eosinophilia developed during her hemogram examination. Peripheral blood smears revealed eosinophilia and atypical lymphocytes. (Figure 4).

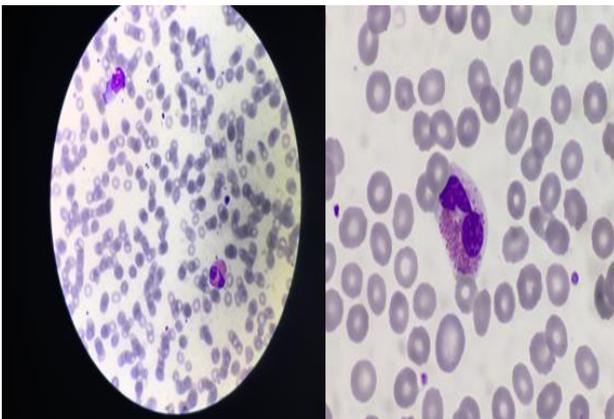


Figure 4. Peripheral blood smear examination

DISCUSSION

Careful clinical and laboratory observation are important in the diagnosis of DRESS syndrome. In the differential diagnosis, infectious mononucleosis, antiretroviral syndrome and systemic lupus erythematosus may be similar. A combination of various symptoms, findings and laboratory results can be compared to combining puzzle pieces for this hypersensitivity syndrome.

Anticonvulsants (carbamazepine, phenytoin, phenobarbital), antibacterial drugs (Amoxicillin, ampicillin, azithromycin, levofloxacin, minocycline,

vancomycin, piperacillin tazobactam), anti-tuberculosis drugs, antiretrovirals (Abacavir, nevirapine), hepatitis C drugs (Boceprevir, telaprevir), antipyretic / Field drugs (Acetaminophen, diclofenac, ibuprofen), sulfonamides (Dapsone, trimethoprim-sulfomethoxazole, sulfosalazine), others (allopurinol, imatinib, omeprazole) are the main drugs. After starting the drug, symptoms usually occur within 2-6 weeks, and the clinical condition may persist for a long time. In our patient, the symptoms started 3 weeks later. The most common cause of mortality is the insufficiency of liver, the most commonly involved internal organ. Histopathological findings of DRESS syndrome rashes are non-specific. Intervention dermatitis is the most common histopathological appearance. In the treatment, it is important to discontinue the drug, to use systemic corticosteroid and to provide supportive treatment. TNF- α inhibitors are new treatment options [9,10].

In conclusion, DRESS syndrome is a hypersensitivity reaction that may be associated with rash, fever, lymphadenopathy, eosinophilia, atypical lymphocytosis and internal organ involvement after drug use. In drug reactions, the findings should be evaluated carefully and should be kept in mind in the differential diagnosis of rash.

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