CASE REPORT

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Drug Reaction with Eosinophilia and Systemic Symptoms Syndrome That Develops After Hysterectomy Surgery

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ABSTRACT DRESS syndrome, "drug reaction with eosinophilia and systemic symptoms," is a hypersensitivity reaction that can lead to severe organ dysfunction and mortality. Increased reactive metabolites are thought to cause an immunological response due to inadequate detoxification of the responsible drug. The drugs with which the reaction is most frequently observed are anticonvulsants and sulfonamides. It can be fatal with the reuse of some groups of drugs. Early diagnosis of the disease and discontinuation of the responsible drug in the early period of the reaction is essential. Systemic steroids are used in treatment, and intravenous immunoglobulin is used when necessary. We have presented a 43-year-old female patient diagnosed with DRESS syndrome who was using nitrofurantoin because of a Double J catheter.

Keywords: DRESS syndrome; drug hypersensitivity; eosinophilia; fever

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a rare drug hypersensitivity reaction in which hematological abnormalities, particularly fever, lymphadenopathy, hepatitis, eosinophilia, atypical lymphocytes, and other visceral involvement, as well as a diffuse mucocutaneous rash, may be seen. It was first observed in 1959 after using phenytoin and was called pseudolymphoma.[1] Moreover, in 1996, Bocquet et al. defined DRESS syndrome.[2] The mortality is approximately 10-20%, indicating the importance of early diagnosis and treatment.[3] The most common cause of mortality is a liver failure.[4]

Among the drugs that cause DRESS syndrome, the use of anticonvulsants, sulfonamides, allopurinol, dapsone, vancomycin, and, although less frequently, some antibiotics are accused.[5] We aim to explain our approach to our case, who was diagnosed with DRESS syndrome with widespread rash and fever that appeared on the seventh day after nitrofurantoin use in our clinic and to contribute to the literature.

CASE REPORT

Myoma uteri was detected in the examination of a 43-year-old female patient who applied to the gynecology outpatient clinic with a complaint of inguinal pain. In her history, she was using medical drugs with the diagnosis of asthma, and no allergy to drugs was reported. The patient who underwent a hysterectomy operation was followed up postoperatively. Nitrofurantoin antibiotherapy was administered because of having a Double J catheter. On the 7th postoperative day, a fever of 38 °C and an erythematous rash were observed on the forearm, leg, and back, and hemogram, biochemistry, and blood culture samples were taken (Figure 1). Laboratory tests revealed C-reactive protein 88 mg/dL, procalcitonin 0.5 ng/mL, alanine aminotransferase (AST) 161 U/lt, aspartate aminotransferase (ALT) 269 U/lt, eosinophil 530/mm^3, and lymphopenia. Blood culture samples were negative. Dermatology consultation was requested for diffuse skin rash, and DRESS syndrome was considered in the foreground.

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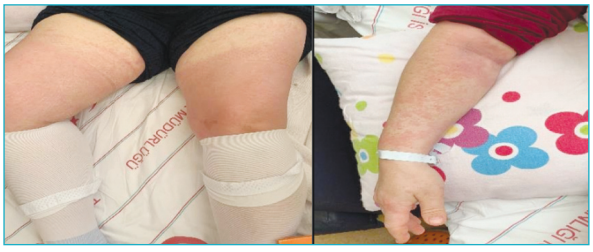

FIGURE 1: Maculopapular lesions and erythematous plaque appearance on the legs and forearms on the seventh day.

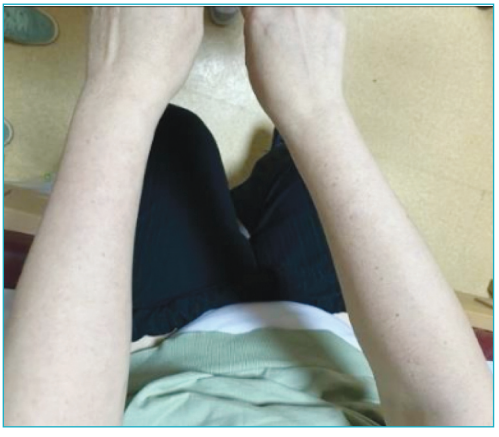

FIGURE 2: Regression of skin lesions in the second week of treatment.

DRESS syndrome was defined as fever, erythematous rash, edema in the fingers and toes, cervical, axillary, and inguinal lymphadenopathy, the elevation of AST and ALT, eosinophilia, and lymphopenia during antibiotic use. The current antibiotic therapy was discontinued, and the patient was treated with 1 mg/kg/day prednol. A punch biopsy was performed on the skin. Histopathological examination revealed dyskeratotic cells in the epidermis, vacuolization in the basal layer, pericapillary lymphocyte, and eosinophil leukocyte infiltration in the dermis and the findings were considered compatible with DRESS syndrome. In the second week of the treatment, the patient's complaints regressed (Figure 2).

Written and verbal consent was obtained from the patient for the case report.

DISCUSSION

Although the etiopathogenesis of DRESS syndrome is not fully known, reactive intermediates released while drugs are metabolized via the cytochrome p450 system are thought to be effective in the clinic. The epoxide hydrolase enzyme usually detoxifies them; however, it is assumed that this enzyme is deficient or dysfunctional in DRESS syndrome.

Although there are different scoring systems for diagnosing DRESS syndrome, the European RegiSCAR criteria by Kardaun et al. are mainly used (Table 1).[6] The presence of three or more findings other than the first two criteria specified in Table 1 is necessary for the diagnosis.

Symptoms usually appear within 2-4 weeks after taking the drug. As skin findings, maculopapular lesions, purpura, vesicle, erythroderma, and lymphoma-like infiltrating lesions can be seen. Facial edema and diffuse lymphadenopathy reaching 1-2 cm in size are often seen in the clinic.[7] Laboratory findings include leukocytosis, eosinophilia, lymphocytosis, monocytosis, neutrophilia, impaired liver function tests.[8]

In DRESS syndrome, liver, renal, pulmonary (interstitial pneumonia), cardiac (myocarditis), and neurological (encephalitis) system involvements can also be seen. The liver is the most affected internal organ and is the most common cause of mortality. Hepatitis often occurs in anicteric form. In more than 70% of those cases, especially ALT elevation is detected. Liver damage can be prevented by discontinuing the offending drug and starting steroid therapy quickly. However, deterioration in the clinical findings can be seen weeks after the treatment of DRESS syndrome. This may be due to early discontinuation of corticosteroid treatment.[9]

TABLE 1: Drug reaction with eosinophilia and systemic symptoms syndrome criteria identified by the RegiSCAR group.

Need for hospitalization
Suspicious drug use that may cause a reaction
Acute skin rash
Fever over 38 C
Lymphadenopathy in at least two areas
At least one internal organ involvement
Blood findings
Less or more than normal lymphocyte count
Eosinophil elevation (in number or percentage)
Platelet count below normal values

In Cacoub et al.'s review of 172 cases, anticonvulsants are the most common causative drugs.[2] Cases of vancomycin, cephalosporin, sulfamethoxazole, and streptomycin have been reported when antibiotics are considered. On the other hand, nitrofurantoin, a 5- nitrofuran derivative, is one of the choices in treating kidney and uncomplicated urinary tract infections in gynecology. Various side effects have been reported with its use. Although there is no evidence, the symptoms in our case occurred due to nitrofuran group antibiotics. The clinical course was similar to the cases in the literature. The first finding was fever, rash, lymphadenopathy, elevated transaminases, and eosinophilia. Skin lesions started regressing on the second day of steroid treatment, and liver enzyme levels returned to completely normal in the second week of treatment.

In the literature, there are also cases of DRESS syndrome with a fatal course. In a case of DRESS syndrome that developed after coronary artery bypass surgery, it had a fulminant course. It resulted in death on the 7th day despite intravenous immunoglobulin (IVIG) treatment on the 3rd.[10] Although corticosteroids are the first-line treatment, IVIG treatment should be added for five days in severe cases of bone marrow failure or fulminant hepatitis. Another critical issue that determines the prognosis is the responsible drug. Yang et al. reported that the mortality rate in cases where aromatic convulsants were responsible was 7.7%.[11] Chen et al. stated that allopurinol-related DRESS cases had the highest mortality.[12] In addition, some publications state that accompanying herpes virus reactivations are effective in poor prognosis. A high rate of human herpesvirus 6 infections was demonstrated in 11 cases of severe DRESS, resulting in multiple organ failure by Eshki et al.[13]

In conclusion, in the presence of widespread maculopapular eruptions, sudden onset fever, and systemic symptoms, drug use should be questioned, and DRESS syndrome should be considered in the differential diagnosis. Early diagnosis of the disease, discontinuation of the causative drug, and initiation of supportive treatment, especially steroids, significantly reduce morbidity and mortality.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Hale Çetin Arslan;* ***Design:*** *Hale Çetin Arslan, Esra Can;* ***Control/Supervision:*** *Esra Can;* ***Data Collection and/or Processing:*** *Hale Çetin Arslan;* ***Analysis and/or Interpretation:*** *Hale Çetin Arslan;* ***Literature Review:*** *Emine Türkmen;* ***Writing the Article:*** *Hale Çetin Arslan, Esra Can;* ***Critical Review:*** *Esra Can.*

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