OLGU SUNUMU CASE REPORT

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Fatal DRESS Syndrome Without Eosinophilia After Coronary Artery Bypass Grafting

Koroner Baypas Ameliyatı Sonrası Eozinofili Olmadan Ölümcül DRESS Sendromu

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ABSTRACT Drug reaction with eosinophilia and systemic symptom (DRESS) is a life threatening adverse drug reaction. A 58-year-old female patient presented to our hospital with nausea and vomiting 2 weeks after elective coronary artery bypass grafting (CABG). She had used metoprololol, asetilsalycilic asit and furosemide after the operation. Blood tests showed neutropenia, low eosinophil levels, elevated liver biomarkers. Our case had fever, a morbilliform rash, bone marrow failure and hepatitis. Clinical (fever, exanthema, facial oedema) and laboratory (pansitopenia with liver and pulmonary involvement) findings raised the suspicion of DRESS and the patient was started on 1 mg/kg intravenous (IV) prednisone daily and IV immunoglobulin (IVIG) at 2 g/kg. She died on the the seventh ICU day. DRESS syndrome is a fatal drug hypersensitivity reaction with cutaneous and systemic involvements. Multidisciplinary care is important for a successful treatment.

Keywords: Coronary artery bypass grafting; DRESS syndrome; eosinophilia

ÖZET DRESS sendromu (Drug reaction with eosinophilia and systemic symptom), hayatı tehdit eden bir ilaç reaksiyonudur. Elli sekiz yaşında kadın hasta elektif koroner arter baypas ameliyatından 2 hafta sonra bulantı ve kusma ile hastanemize başvurdu. Operasyon sonrası ilaç olarak metoprololol, asetilsalisilik asit ve furosemid kullanmıştı. Kan testlerinde nötropeni, düşük eozinofil düzeyleri, karaciğer biyobelirteçleri artış görüldü. Hastada ateş, morbiyal döküntü, kemik iliği yetmezliği ve hepatit vardı. Klinik (ateş, ekzantem, yüz ödemi) ve laboratuvar (karaciğer ve pulmoner tutulumlu pansitopeni) bulguları, DRESS şüphesini artırdı ve hastaya günde 1 mg/kg intravenöz (IV) prednizon ve IV immünglobulin (IVIG) 2 g/kg başlandı. Hasta, yoğun bakımdaki 7. gününde ex oldu. DRESS sendromu, kutanöz ve sistemik tutulumlarla seyreden ölümcül ilaç aşırı duyarlılık reaksiyonudur. Multidisipliner bakım, başarılı bir tedavi için önemlidir.

Anahtar Kelimeler: Koroner baypas cerrahisi; DRESS sendromu; eozinofili

DRESS syndrome (Drug reaction with eosinophilia and systemic symptom) is characterized by the presence of at least three of the following: fever, rash, eosinophilia, atypical circulating lymphocytes, lymphadenopathy and hepatitis.[1] The estimated frequency of DRESS syndrome varies between 1/1000-1/10000, and the mortality rate prediction is 10%.[1] The diagnosis of DRESS should be kept in mind when a skin rash, fever, hypereosinophilia and organ involvement is present. Liver is the most commonly affected organ. Cutaneous manifestations generally occur between 2 and 6 weeks after the first dose of culprit drug.[2] Besides the systemic glucocorticoid therapy, intravenous immunoglobulin therapy is essential for life-threatening forms.

Herein, we report a case of severe DRESS syndrome secondary to bypass surgery

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CASE REPORT

A 58-year-old female underwent elective coronary artery bypass grafting (CABG) with two vessels in our hospital. Her medical history was otherwise normal. The patient was discharged on postoperatif day 6 after CABG on metoprololol, asetilsalycilic asit and furosemide. Two weeks later, she was readmitted with nausea and vomitting.

On admission, laboratory results showed normal hemoglobin level (12.3 g/L), mild neutropenia (white cell count, 3.27/L), low eosinophils (0 x 0*3/UL), high C-reactive protein (4.4 mg/L), and hepatic dysfunction (alkaline phosphatase, 164 U/L; alanine aminotransferase, 459.6 U/L; aspartate amino- transferase, 861.2 U/L). Blood pressure was 140/90 mm Hg, pulse rate was 96 beats per minute and temperature was 37°C. Abdomen ultrasonography was normal. Echocardiography was normal with the ejection fraction of 50%. After two days, a maculopapular rash appeared on the face and also there was associated fever (39◦C) and lethargy. Empirical antibiotic and antiviral treatments initiated while awaiting culture results. Multiple cultures (sputum, blood, and urine) were negative. Serology for common viruses were all negative.

Her rash worsened in the next two days, the rash turned to erythroderma, erythematous rash was on the trunk and extremities, a facial dermatitis and a widespread maculopapular rash on the arms, trunk and lower extremities had begun, hypoxia and dyspnea started, fever persisted, and she developed pancytopenia (Figure 1, Figure 2). Malignancy was excluded by bone marrow biopsy.

The patient was transferred to the intensive care unit (ICU) and given specific treatment (systemic glucocorticoids and intravenous immunoglobulins). She was intubated because of hypoxia and dyspnea.

Laboratory results showed anemia (hemoglobin, 8.7 g/L), deep neutropenia (white cell count, 0.10 10*3U/L), high C-reactive protein (24 mg/L), thrombocytopenia (30 10*3/UL). Her condition rapidly worsened with hemodynamic instability and the patient died on the seventh ICU day. The consent form was obtained from the patient's legal representative.

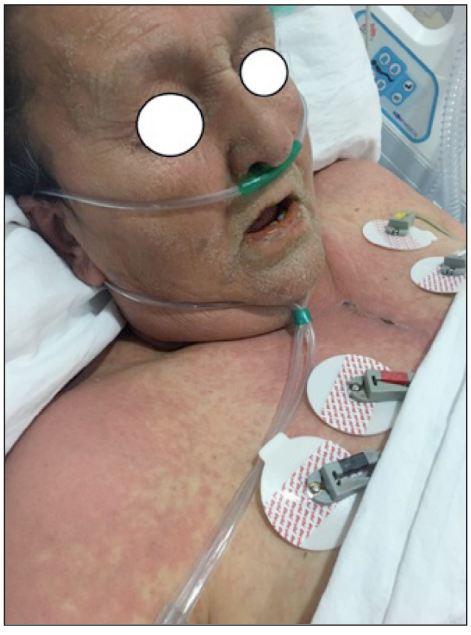

FIGURE 1: Facial edema and morbilliform eruption.

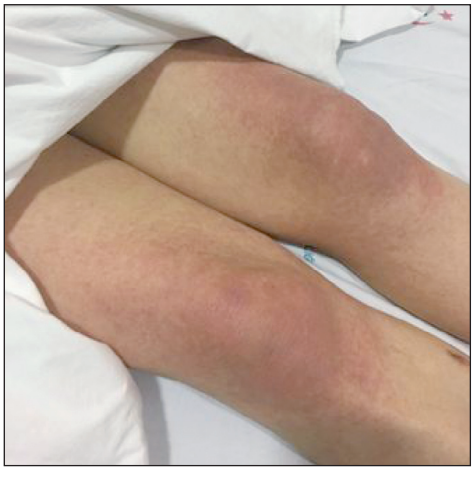

FIGURE 2: Morbilliform eruption on lower extremities.

DISCUSSION

DRESS syndrome begins acutely within two months of the start of treatment and includes a serious skin rash associated with fever, lymphadenopathy, hematological abnormalities, and multiple organ involvement.[1] Anticonvulsants, sulfonamides and gold salt are the most frequently blamed drugs.[1]

The hematological system is often affected. Approximately 30% of cases have an eosinophilia (> 2.0

x 109 eosinophil/L). Hyperosinophilia probably plays a role in visceral involvement.[2] To our knowledge, this is the first case of DRESS syndrome without eosinophilia and after a big surgery.

Corticosteroids are the first line treatment and should be started at the beginning of DRESS syndrome. 1.0 mg/ kg/day of prednisolone is the first line therapy. Emre at al.[3] reported full remission with systemic corticosteroids in eleven patients. In patients with fatal systemic symptoms such as bone marrow failure or fulminant hepatitis, intravenous immunoglobulin (IVIG) at 2 g/kg over 5 days should be added to the treatment.[3] We used IVIG for three days in our patient. Then she died.

Pancytopenia, leukocytosis, coagulopathy, gastrointestinal bleeding, pre-existing chronic renal insufficiency, and multiple comorbidities are poor prognostic indicators.[4]

Two scoring systems according to diagnostic criteria have been developed. Our patient was a probable case of DRESS with a RegiSCAR score of 5.[5] Firstly potentially serious conditions must be excluded (infections, malignancy, autoimmune disorders, connective tissue disease).

Eshki et al. reported that 11 of 15 patients with severe DRESS syndrome had multiorgan failure. Lee et al.[6,7] reported that the liver was affected in 80% of cases in a study of 25 patients. Ichai et al.[8] reported an overall mortality of 40% in a series of 16 patients with severe and steroid resistant liver injury. Pulmonary involvement may also be present. Our case had fever, a morbilliform rash, bone marrow failure, hepatitis and pulmonary failure. The non-antibiotic sulfonamide, furosemide causing DRESS was reported twice before.[9,10] Our patient used furosemide too, but we have no proof that if the culprit drug was that.

Diagnosis of DRESS syndrome is difficult to establish, suspicion is the first step and it is so important to diagnose early and withdraw the offending drug. Multidisciplinary care is important for a successful treatment. When other symptoms exist, DRESS can be considered even without eosinophilia.

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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: *Mihriban Yalçın, Celali Kurt;* ***Control/Supervision:*** *Hilayda Karakök Güngör;* ***Data Collection and/or Processing:*** *Mihriban Yalçın;* ***Analysis and/or Interpretation:*** *Celali Kurt;* ***Literature Review:*** *Mihriban Yalçın, Hilayda Karakök Güngör;* ***Writing the Article:*** *Mihriban Yalçın;* ***Critical Review:*** *Hilayda Karakök Güngör.*

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