

DRESS Syndrome: A Mimicker to Behold

Ines Kechaou*, Hamdi Mohamed Salah, Eya Cherif and Lamia Ben Hassine

Department B of Internal Medicine, Charles Nicolle's Hospital. Faculty of Medicine, University of Tunis El Manar, Tunisia

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*Corresponding author: inessekechaou@gmail.com

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Abstract

This is a case of 55 year old woman presented with fever, enlarged lymph nodes, skin rash, mucosal involvement, eosinophilia, kidney injury, hepatomegaly and splenomegaly 14 days after taking Diclofenac. The diagnosis with Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome induced by Diclofenac was made after extensive investigation, which ruled out infectious and neoplastic causes, highlighting the challenge in diagnosing DRESS syndrome. The patient's symptoms resolved after drug withdrawal and corticosteroid therapy. This case emphasizes the importance of thorough medication history to investigate recent drug intake that could contribute to a prompt diagnosis in a patient with a polymorphic clinical presentation that could delay the diagnosis.

Keywords: DRESS syndrome, drug induced eruption, eosinophilia, hypersensitivity, pharmacovigilance.

Introduction

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a rare condition characterized by variable clinical manifestations including fever, rash, hematological abnormalities and multiple internal organs damage.¹ DRESS syndrome diagnosis might be challenging especially when confronted with atypical clinical presentation such as predominant multiple lymphadenopathies mimicking malignant or infectious diseases. DRESS syndrome may also occurs as complication of malignancy treatment, which is a rare condition. Imatinib was the first-line treatment for newly diagnosed Chronic myeloid leukemia (CML) patients,² which rarely induces DRESS syndrome.³ Programmed death receptor-ligand 1 (PD-L1) plays an important role in the progression of malignant disorders⁴ and Anti-PDL-1, in cancer treatment also induce DRESS.⁵ Mortality related to DRESS syndrome ranges between 10 to 20%, stressing both importance and urgency of accurate diagnosis.^{6,7}

We herein report the case of a woman with no medical history of drug hypersensitivity reactions presenting with DRESS syndrome induced by Diclofenac.

Case Report

Fifty-five-year-old woman, with a medical history of asthma, was referred to our internal medicine department for a 2-week history of fever, pruritus and skin rash. She reported intake of Diclofenac for joint pain thirteen days prior to the start of clinical signs. She had no known history of drug hypersensitivity reactions and denied use of other medications.

On clinical examination, we noted: pharyngeal erythema, fever at 39°C, multiple tender cervical lymphadenopathies with a 4cm-sized lateral jugular lymph nodes and multiple occipital lymphadenopathies measuring 2 cm each, palpable centimeter-sized lymph nodes in the inguinal and right axillary regions. Skin examination revealed infiltrated palpable purpura on the lower limbs along with macular, erythematous, pruriginous skin rash affecting both the abdomen and the forearms [Figure 1]. It also revealed blisters on the patient's lip and desquamative lesions of both feet [Figure 2].



Figure 1: Erythematous skin rash affecting the abdomen and the forearms.



Figure 2: Desquamated lesions of both feet.

Routine blood tests highlighted evidence of inflammation with increase in both C-reactive protein (224 mg/L) and ESR (120 mm). Serum protein electrophoresis showed gamma-globulin serum level at 28.2 g/L (8-13 g/l) with no evidence of monoclonal gammopathy. We noted: normocytic non-regenerative anemia (hemoglobin: 11.1g/L, mean corpuscular volume: 82.5fl), leukocytosis: 12700/mm³ with elevated eosinophil count: 1600/mm³. We also noted renal failure: serum creatinine at 213 μmol/L. Liver function tests, calcemia and thyroid function tests were within normal range. Infectious investigations were negative including: blood culture hepatitis B, hepatitis C, HIV, Serology of Epstein Barr virus, cytomegalovirus. Tuberculin skin test and sputum smear were negative. Urinalysis, chest X-ray and echocardiography were without abnormalities. Antinuclear antibodies and negative anti-neutrophil cytoplasmic antibodies were negative. Total IgE serum level was elevated: >500 UI/L (<100 UI/L).

Computed tomography of the neck, chest, abdomen and pelvis confirmed the presence of multiples lymphadenopathies (cervical region, both axillary regions, the abdomen and pelvis), hepatomegaly (20 cm) and an enlarged spleen (15 cm). Histological examination of a cervical lymph node biopsy showed extensive non caseating necrosis with no granulomas. Immunohistochemistry was normal. Culture of lymph node tissues showed no evidence for bacterial growth especially Koch bacillus.

On the fifth day of admission, blisters developed on the patient's tongue [Figure 3]. Given the negativity of investigations, DRESS syndrome was highly suspected. Pharmacovigilance opinion was requested and it favored a drug reaction related to Diclofenac intake. DRESS syndrome diagnosis was retained as the patient had a score of 6 on the RegiSCARs (Registry of Severe Cutaneous Adverse Reactions to Drugs and Collection of Biological Samples) scoring system⁸ (fever≥38.5°C, enlarged lymph nodes, eosinophil count≥1500/mm³, suggestive skin rash affecting more than 50% of body surface area, kidney injury and negative tests for other etiologies) allowing considering it a definite case of DRESS syndrome.



Figure 3: Blisters on the patient's tongue.

Patient was put on corticosteroids 20 mg/day of Prednisone for 10 days. Over the next two weeks, the macular rash as well as the palpable purpura improved until complete regression. Patient no longer had fever and lymph nodes examination noted complete regression. Renal function returned to normal range with an estimated

glomerular filtration rate of 73 ml/min while eosinophil count was also normal. A computed tomography was performed at the three-month follow-up visit, which confirmed the regression of all abnormalities.

Discussion

We report a case of DRESS syndrome secondary to use of Diclofenac with polymorph clinical presentation: fever and enlarged lymph nodes with skin rash appearing at a later date with renal failure and hepatic disorder.

The epidemiological data on the incidence of DRESS syndrome are scarce. However, it's been approximated that the risk to the overall population falls between 1 in 1,000 and 1 in 10,000 drug exposures.⁹

Among anti-inflammatories: Aspirin, celecoxib, diclofenac, ibuprofen, and piroxicam have been incriminated in the occurrence of DRESS syndrome suggest a frequency ranging between 2.3 and 13.2%.^{10,11} Mechanisms underlying DRESS syndrome are yet to be completely elucidated. TGF- β ¹² and interleukin-10 (IL-10) are key regulators of immune homeostasis with anti-tumor effect,¹³ the later showing a significant increase in dress syndrome patients¹⁴ accompanied with increased FOXP3+ T cells in skin lesions.¹⁵

Polymorph skin involvement and mucosal erosions, such as observed in our report, has been observed in various reports.^{1,16-18} The presence of desquamative lesions on the feet is not common and initially raised suspicions of a non-typical paraneoplastic origin, given the presence of hypereosinophilia, lymphadenopathy, and hepatomegaly.

Eosinophilia is common (95%) with a possible delay of one to two weeks after the onset of clinical symptoms, thus requiring frequent monitoring.¹⁹ Enlargement of lymph nodes can be observed in 54% of patients.^{8,18} Lymph node histological examination in our report showed necrosis which has also been reported and did not warrant reconsidering the diagnosis of DRESS syndrome as no histological finding is specific of the diagnosis.^{7,8}

Kidney injury may occur in 12 to 40% of patients.^{8,19} In an 11-year study including 52 patients with DRESS syndrome, liver and spleen enlargement like in our report, was observed respectively in 34.6 and 1.9% of cases.²⁰

Diagnosis of DRESS syndrome was considered certain in our patient according to RegiSCAR scoring system. A long latent period can be observed, usually lasting two to six weeks.¹⁷ In our case, clinical symptoms onset was roughly two weeks after intake of Diclofenac.

Immediate withdrawal of the culprit drug is the corner stone of the management. Corticosteroids are, by far, the most used treatment. It may reduce disease flare-ups and eventually long-term development of autoimmune sequelae.²¹⁻²⁴ Resorting to systemic corticosteroids are usually reserved to severe DRESS syndrome with internal organs damage. In our case, corticosteroids were initiated given the presence of acute renal failure. However, they were quickly discontinued given the favorable clinical evolution with no recurrence. Usage of intravenous immunoglobulin had also yielded successful results.^{17,21}

Conclusion

DRESS syndrome must be considered in patient with a recent medication intake presenting fever, skin rash, mucosal ulcerations, eosinophilia and internal organs involvement. In addition to drug withdrawal, corticosteroids remain a valid therapeutic choice especially in cases of life-threatening internal organs damage.

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