

Atypical Intralymphatic T-Cell Proliferation during DRESS Mimicking Intravascular Lymphoma: Case Report

Ihssan Elouarith^{1*}, Ahmed Jahid¹, Fouad Zouaidia¹, Zineb Loubaris², Karima Senouci², Zakia Bernoussi¹, Kaoutar Znati¹

¹Pathology Department, Ibn Sina Hospital Faculty of Medicine and Pharmacy, Mohammed V University, 10100 Rabat, Morocco

²Dermatology Department, Ibn Sina Hospital, Faculty of Medicine and Pharmacy, Mohammed V University, 10100 Rabat, Morocco

DOI: [10.36347/sjmcr.2023.v11i12.009](https://doi.org/10.36347/sjmcr.2023.v11i12.009)

| Received: 02.11.2023 | Accepted: 04.12.2023 | Published: 08.12.2023

*Corresponding author: Ihssan Elouarith

Pathology Department, Ibn Sina Hospital Faculty of Medicine and Pharmacy, Mohammed V University, 10100 Rabat, Morocco

Abstract

Case Report

Drug-induced hypersensitivity syndrome or drug reaction with eosinophilia and systemic symptoms (DRESS) is a severe drug-induced reaction that represents a life-threatening condition. The histopathologic appearance of the skin biopsy is nonspecific but may exceptionally show an atypical intralymphatic lymphocytic infiltrate, and mimic an intravascular lymphoma. Through this article, we will report an exceptional case of a patient presenting with skin lesions pointing to a dress, but whose histological appearance, in the presence of adenopathy during physical examination, can lead, by mistake, to the diagnosis of an intralymphatic lymphoma. We aim to highlight the various diagnostic indices allowing the distinction between these two entities, including the immunohistochemical study, the search for the TcR clonal rearrangement and the anatomico-clinical correlation.

Keywords: DRESS. Atypical intralymphatic CD30+ T-cell proliferation. Immunohistochemistry, TcR clonal rearrangement.

Copyright © 2023 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution **4.0 International License (CC BY-NC 4.0)** which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION

Drug reaction with eosinophilia and systemic symptoms or DRESS is a severe drug eruption which may be responsible for multivisceral involvement. The diagnosis is based on a set of clinical and biological diagnostic criteria. The histological aspects are highly variable and nonspecific. We report the case of a young patient whose skin biopsy posed a problem of differential diagnosis with an intravascular lymphoma.

CASE REPORT

We report the case of a 39-year-old patient, recently diagnosed with gout and treated with allopurinol. After about a month from the start of treatment, the patient consulted in our structure after the appearance of a macular, erythematous-scaly exanthema, having started in the trunk and upper limbs, subsequently extending to the lower limbs. It is associated with an edema of the face, without involvement of the mucous membranes, or fever. The physical examination of the patient also objectified a right, mobile and painless inguinal lymphadenopathy. The biological assessment objectified an impaired renal function. The liver assessment was normal.

A skin biopsy of these lesions was performed. The histological study focused on a skin tissue made of an epidermis showing spongiosis lesions with rare apoptotic keratinocytes and overcoming a parakeratotic hyperkeratosis. The dermis is oedemato-coagulative and comprises vascular structures seat of a lymphoid cell population increased in size and provided with nuclei increased in size, irregular and nucleolated in places. In view of this histological aspect, and the adenopathy found during the clinical examination, a lymphoma was strongly suspected, hence the realization of an immunohistochemical study. The latter confirmed the T cell phenotype by anti CD3, CD4, CD5, CD7 and CD8 antibodies with absence of phenotypic gap. Some cells were positive for anti CD30 antibodies. On the other hand, the lymphatic nature of the colonized vessels was confirmed by anti D2-40 antibodies. There was no clonal TcR rearrangement.

In view of the confrontation of these clinical and histological data, a diagnosis of DRESS was made. The patient was put on symptomatic treatment. Close patient follow-up was favourable, with complete disappearance of the skin lesions.



Figure 1: Clinical appearance of lesions

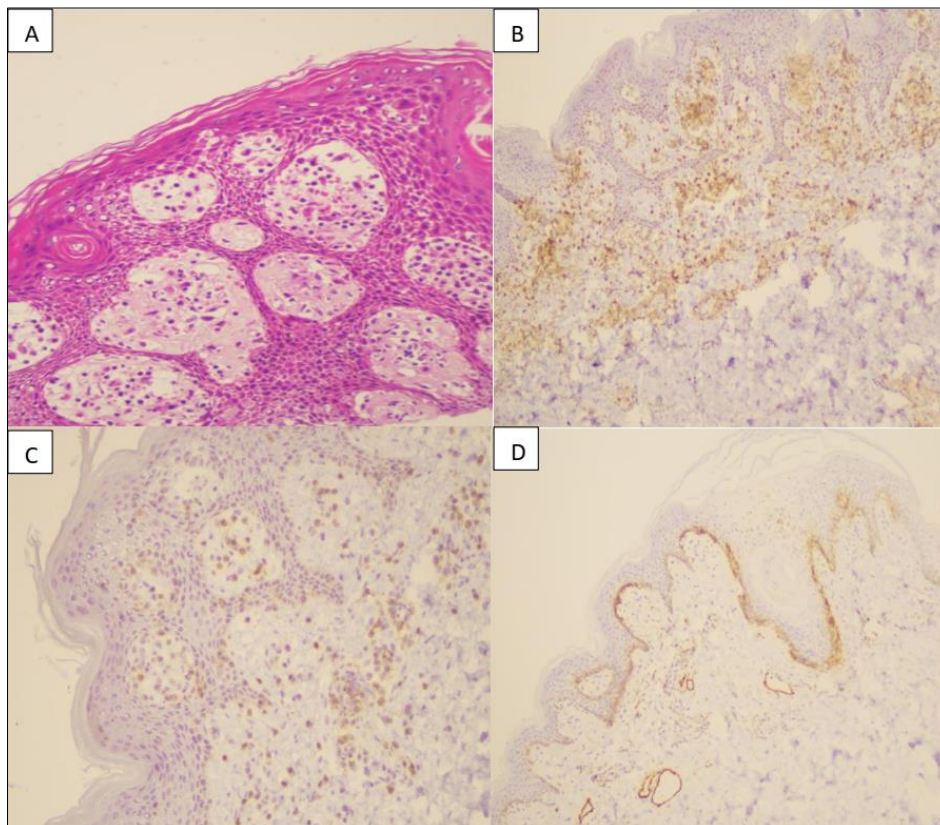


Figure 2 : (A) Histological image showing a histological appearance with an atypical lymphoid infiltrate in the lymphatic vessels of the dermis Hex400 (B): Intravascular lymphocytes show positive labeling by anti-CD30 x100, (C) Anti CD30 antibody marks scattered cells x200 (D)the wall of the lymphatic vessels is labeled by anti-D2-40 x40.

DISCUSSION

Drug hypersensitivity syndrome or drug reaction with eosinophilia and systemic symptoms (DRESS) is a severe drug eruption characterized by skin reactions and systemic involvement [1, 2]. In 1934, this syndrome was first described following the introduction of phenytoin in children [3], and it was only until 1996 that Bocquet *et al.*, proposed the nomenclature of systemic drug hypersensitivity with eosinophilia to be able to distinguish this form of toxidermia from other forms without eosinophilia [4].

The incidence of DRESS syndrome is estimated between 1 / 1000 and 1 / 10,000. However, its value varies according to the drugs involved [2].

More than 50 drugs can be associated with DRESS syndrome. The drugs most implicated are antiepileptics, including phenytoin, phenobarbital, carbamazepine, and lamotrigine. Allopurinol, sulfonamides, dapsone and certain antiretrovirals such as nevirapine and abacavir can also be associated with this syndrome [5-7].

The pathogenesis of DRESS syndrome is still incompletely understood and represents a source of controversy. Based on various observations, different mechanisms have been proposed to be involved in the pathogenesis of DRESS and especially the activation of an inflammatory reaction mediated by T cells responsible for liberation of cytokines including IL-6 and tumor necrosis factor [5-9].

An association with the reactivation of certain viruses of the herpes family such as HHV-6, HHV-7 and EBV has been revealed by studies. It typically occurs after 2-3 weeks from the onset of DRESS symptoms [10].

Genetic factors have also been reported to be involved in the pathogenesis of DRESS after studies revealing on the one hand the high frequency of DRESS in certain geographical areas as is the case of DRESS induced by carbamazepine in Europe and China [16], On the other hand, some studies have demonstrated the frequency of dress in patients with certain HLA haplotypes. For example, the association of abacavir and allopurinol DRESS syndromes respectively with HLA-B*5701 in Chinese [9], and HLA-B*5801 in Portuguese patients [11].

Clinically, patients most often present with fever, macular exanthema, facial edema and polyadenopathy [5-7]. Skin involvement is inconsistent. It usually presents as a maculopapular rash, sometimes itchy and most often progresses to erythroderma [6, 7]. Visceral damage can be observed and can sometimes be serious and lead to multi-organ failure [12].

These symptoms usually appear between two to six weeks after the introduction of the causative drug. A shorter interval has been described in the event of reintroduction or for certain drugs in particular quinolones [7-13].

The biological assessment can show abnormalities in the blood count characterized by leukocytosis with lymphocytosis and eosinophilia in 70% of cases [14]. Other biological abnormalities, such as elevated levels of LDH and ferritin have been observed [9].

Scoring systems based on a number of clinical and biological diagnostic criteria have been developed to facilitate the diagnosis of DRESS syndrome and eliminate other differential diagnoses [15].

Histologically, DRESS syndrome presents with non-specific and highly variable histological signs. Histological study of skin biopsies performed in patients with DRESS, may show various morphological features, including spongiotic dermatitis, erythema multiforme or histological features of toxic epidermal necrolysis [16]. It may also present as a variant of exanthema reactions drug-induced, with a frequent but not constant presence of eosinophils and apoptotic keratinocytes [17].

Many studies highlighted the presence of atypical lymphocytes in cutaneous biopsy during drug reaction, mimicking lymphoproliferative disorders, in particular lymphomatoid papulosis, transformed mycosis fungoides and cutaneous localization of systemic lymphoma.

The intralymphatic localization of this atypical but reactive inflammatory infiltrate is rarer than its interstitial dermal localization, and poses a differential diagnostic problem with intravascular lymphomas [18].

The immunohistochemical study plays a major role in the confirmation of the benign and reactive nature of this lymphoid infiltrate and therefore the elimination of the diagnosis of intravascular lymphoma.

In addition to its role in confirming the T phenotype of atypical cells with the presence of scattered CD30+ cells, immunohistochemistry, allow the confirmation of the intralymphatic localization of the atypical infiltrate thanks to anti-D2-40 antibodies, as opposed to its localization in the blood vessels in the case of lymphoma [19].

In addition to these immunohistochemical data, the absence of TcR clonal rearrangement and the correlation with the clinical characteristics also allow this differentiation [18].

Very few cases of benign atypical intralymphatic T-cell proliferations have been described in the literature in various cutaneous and non-cutaneous disorders such endometrial polyp [18]. According to our research, there is only one published case in the literature on the association of a benign atypical CD30+ intralymphatic T-cell proliferation with drug rush [18].

CONCLUSION

Faced with clinically and biologically diagnosed DRESS, the presence of an atypical intralymphatic lymphoid infiltrate in a skin biopsy represents an exceptional but possible aspect, and should not lead pathologists to wrongly diagnose intravascular lymphoma. An immunohistochemical complement, the search for the TcR clonal rearrangement and a comparison with clinical and biological data are essential.

Acknowledgements: Not applicable

Conflict of Interest: No conflicts of interest

Funding Statement: This study was not funded

Ethical Approval: Not applicable.

Consent for publication: Written consent has been obtained from the patient and the patient's family for the publication of this case report.

Guarantor: Elouarith Ihssan

REFERENCES

- Thielen, A. M., Toutous-Trellu, L., & Desmeules, J. (2008). Les toxidermies médicamenteuses. *Rev Med Suisse*, 4, 1671-5.
- Cacoub, P., Musette, P., Descamps, V., Meyer, O., Speirs, C., Finzi, L., & Roujeau, J. C. (2011). The DRESS syndrome: a literature review. *The American journal of medicine*, 124(7), 588-597.
- Silbert, I. B., & Epstein, J. W. (1934). The treatment of chorea with phenyl-ethyl-hydantoin : A study of 28 cases. *Arch Pediatr*, 5, 373-82.
- Bocquet, H., Bagot, M., & Roujeau, J. C. (1996, December). Drug-induced pseudolymphoma and drug hypersensitivity syndrome (Drug Rash with Eosinophilia and Systemic Symptoms: DRESS). In *Seminars in cutaneous medicine and surgery* (Vol. 15, No. 4, pp. 250-257).
- Pichler, W. J., Wendland, T., Hausmann, O., Schnyder, B., Fricker, M., Pichler, C., & Helbling, A. (2011). Syndrome DRESS (Drug Rash with Eosinophilia and Systemic Symptoms). In *Forum Med. Suisse* (Vol. 11, No. 48, pp. 879-884).
- Descamps, V., & Ranger-Rogez, S. (2014). DRESS syndrome. *Joint Bone Spine*, 8, 15-21.
- Husain, Z., Reddy, B. Y., & Schwartz, R. A. (2013). DRESS syndrome : Part I. Clinical perspectives. *J Am Acad Dermatol*, 68, 693.e1-14.
- Choudhary, S., McLeod, M., Torchia, D., & Romanelli, P. (2013). Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome. *The Journal of clinical and aesthetic dermatology*, 6(6), 31.
- Gru, A. A., & O'Malley, D. P. (2018, January). Autoimmune and medication-induced lymphadenopathies. In *Seminars in Diagnostic Pathology* (Vol. 35, No. 1, pp. 34-43). WB Saunders.
- Shiohara, T., Inaoka, M., & Kano, Y. (2006). Drug-induced hypersensitivity syndrome (DIHS): a reaction induced by a complex interplay among herpesviruses and antiviral and antidrug immune responses. *Allergy International*, 55(1), 1-8.
- Gonçalo, M., Coutinho, I., Teixeira, V., Gameiro, A. R., Brites, M. M., Nunes, R., & Martinho, A. (2013). HLA-B* 58: 01 is a risk factor for allopurinol-induced DRESS and Stevens-Johnson syndrome/toxic epidermal necrolysis in a Portuguese population. *British Journal of Dermatology*, 169(3), 660-665.
- De, A., Rajagopalan, M., Sarda, A., Das, S., & Biswas, P. (2018). Drug reaction with eosinophilia and systemic symptoms: an update and review of recent literature. *Indian journal of dermatology*, 63(1), 30.
- Alkhateeb, H., Said, S., Cooper, C. J., Gaur, S., & Porres-Aguilar, M. (2013). DRESS syndrome following ciprofloxacin exposure: An unusual association. *The American Journal of Case Reports*, 14, 526.
- Maniu, C. M., Buss, G., Feldmeyer, L., Spertini, F., & Ribic, C. (2013). Formes sévères d'hypersensibilité médicamenteuse retardée. *Rev Med Suisse*, 9, 803-11.
- Kardaun, S. H., Sidoroff, A., Valeyrie-Allanore, L., Halevy, S., Davidovici, B. B., Mockenhaupt, M., & Roujeau, J. C. (2007). Variability in the clinical pattern of cutaneous side-effects of drugs with systemic symptoms: does a DRESS syndrome really exist?. *British Journal of Dermatology*, 156(3), 609-611.
- McKee, P. H., Calonje, E., & Granter, S. R. (2005). *Pathology of the Skin with Clinical Correlations*, 3rd edn, vol. 1. London: Elsevier Mosby.
- Elder, D. E. (2009). *Lever's Histopathology of the Skin*, 10th edn. Philadelphia, PA: Lippincott Williams and Wilkins.
- Weingertner, N., Mitcov, M., Chenard, M. P., & Cribier, B. (2016). Intralymphatic CD30+ T-cell proliferation during DRESS: a mimic of intravascular lymphoma. *Journal of Cutaneous Pathology*, 43(11), 1036-1040.
- Ferrara, G., Ena, L., Cota, C., & Cerroni, L. (2015). Intralymphatic spread is a common finding in cutaneous CD30+ lymphoproliferative disorders. *The American Journal of Surgical Pathology*, 39(11), 1511-1517.