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Case Report

DRESS syndrome by sulfonamides, about a case

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ABSTRACT

Among the most feared toxico-dermas is drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome, a rare drug dermatitis that occurs after acute exposure to drugs whose clinical impact is based on multiple organs (skin, liver, kidneys, lungs, heart) and cell lines (eosinophils and lymphocytes). It is an entity with high mortality if it is not identified early, its treatment consists of the immediate suspension of the responsible drug and the administration of steroids, these being the therapeutic protagonists. A 64-year-old male patient with clinical, biochemical and histopathological criteria compatible with DRESS syndrome. It is essential to suspect the clinical course of DRESS syndrome before the appearance of dermatosis with multisystem involvement associated with the use of drugs, emphasis is placed on its early identification and the establishment of timely treatment to modify its prognosis.

Keywords: DRESS syndrome, Sulfonamides, Case report

INTRODUCTION

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome, is a severe pharmacological reaction characterized by eosinophilia plus polymorphous skin lesions, fever, adenopathy's and visceral involvement.[1] There is a wide range of drugs listed as responsible for this pathological phenomenon, where aromatic anticomycials are the most frequent; they have also been observed after the consumption of sulfa drugs, xanthine oxidase inhibitors, glycopeptides, among fifty other drugs plus.[1-4]

It is a condition that in the epidemiological context is rare, occurring in around 10 cases per million inhabitants, with cosmopolitan distribution, affecting any age group, with predominance in the adult population and greater inclination towards the female gender.[1,2]

Currently, the pathological cascade for the genesis and development of this syndrome is not known with certainty, so it has postulated in addition to the pharmacological interaction, phagocytic activation and the release of cytokines mediated by lymphocytes, microbiological invasion (viruses and bacteria) and genetic anomalies, all without reaching a reproducible conclusion.[1,2,5]

It is a disease with a variable prognosis: if an early identification and suspension of the associated drug is made, once the recommended treatment is indicated there is a total remission of all manifestations or on the contrary, lead to multi-organ failure and therefore death. Mortality is close to 10%, with secondary liver failure due to eosinophilic invasion being the culprit almost entirely. For this reason, there is clinical case of 64-year-old received in public hospital in city of Mérida, Yucatán, Mexico.

CASE REPORT

A 64-year-old male patient, originally from and residing in Mérida, Yucatán, with systemic arterial hypertension with no significant hereditary or toxic history. He began four weeks prior to admission with irritative urinary symptoms and intolerance to the oral route, treated with trimethoprim

tablets and sulfamethoxazole for an unknown period. Three weeks laterite debuts with dermatosis characterized by the presence of a mild generalized maculopapular rash that affects the trunk, scalp and all four limbs, which subsequently intensifies together with fever (38°C), oliguria, non-productive cough and progressive dyspnea. He went to hospital general regional, para clinicals were performed that demonstrated leukocytosis 19,000 mm^3 at the expense of neutrophilia 18,300 mm^3, eosinophilia 1500 mm^3, creatinine 4.2 mg/dL, urea nitrogen 40 mg/dL, urea 150 mg/dL, AST 65 U/L, ALT 58 U/L BT 5.3 mg/dL, BI 3.2 mg/dL, BD 2.1 mg/dL, and decompensated metabolic acidosis; your chest x-ray with right micronodular para hilar infiltrate. It was received in hospitalization with a diagnosis of septic shock of pulmonary focus (as part of the health protocol and performed PCR for SARS CoV-2 resulting negative) meriting renal function replacement therapy with placement of angio-access for hemodialysis, as well as vasopressor support and microbial antimob carbapenem type, and physical examination persisted same generalized erythematous lesions, which respected head only (Figure 1-3) as well as hyperemic non-exudative pharyngitis and right axillary adenopathy of 2 cm and left inguinal of 1.5 cm. Assessment was requested by the dermatology service, which considered as a diagnostic possibility DRESS syndrome associated with trimethoprim and sulfamethoxazole, began management with systemic steroid (prednisone 50 mg every 24 hours) and performed saccade biopsy taking obtaining the following histopathological findings (Figure 4-6).

Three days after the intervention, the patient has a higher leukocyte elevation, hemodynamic and ventilatory deterioration that leads to death.

Table 1: RegiSCAR score for DRESS.

RegiScar score	-1	0	1	2	Clinical case
Fever >38.5°C	No	Yes			0
Linfadenomegalia		No	Yes		1
Eosinophilia			$0.7\text{-}1.499\times10^9$	$\geq15\times10^9$	1
Eosinophilia with leukocytes ≥4000			10%-19.9%	≥20%	1
Atypical lymphocytes		No	Yes		1
%SC rash cutaneous		No	>50%		1
Suggestive DRESS biopsy	No	Yes			0
Involve liver		No	Yes		1
Kidney involvement		No	Yes		1
Involve pancreas		No	Yes		0
I involve other organs		No	Yes (heart and lung)		1
Resolution ≥ to 15 days	No	Yes			0
Evaluation of other potential causes: ANA, blood culture, serology for HAV, HBV, HCV, chlamydia, mycoplasmas. If none positive and > of 3 negatives			Yes		1
Total clinical case points					+9

Unlikely case: 2 points. Probable case: 3-5 points. Final case: ≥6 points.

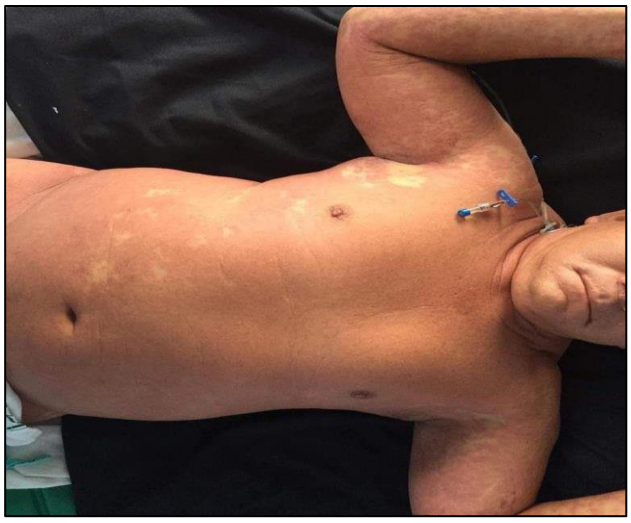

Figure 1: Generalized rash.

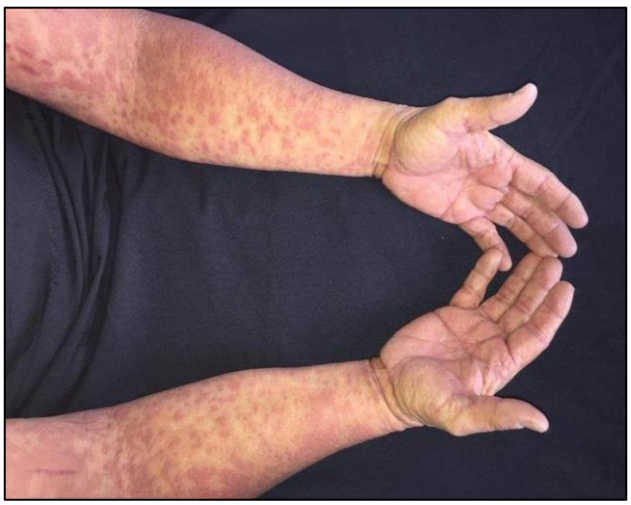

Figure 2: Generalized maculopapular rash in the flexor region of both forearms.

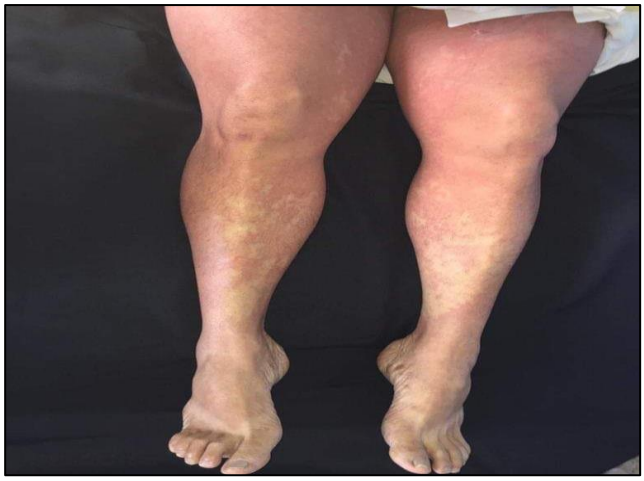

Figure 3: Morbiliform rash on both pelvic limbs.

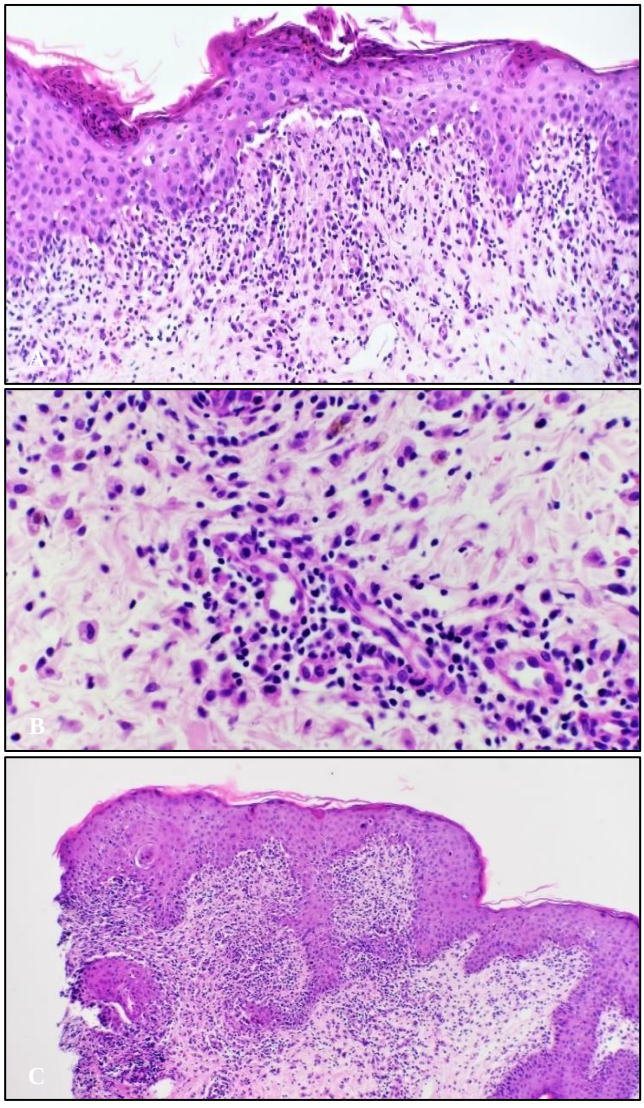

Figure 4 (A-C): Dermatitis of the interface type vacuolar degeneration with superficial perivascular ilphotrated and spongioses consistent with DRESS syndrome.

Figures 4 dermatitis of the interface type vacuolar degeneration with superficial perivascular ilphotrated and spongioses consistent with DRESS syndrome.

They are observed fragments of thin skin with the presence of parakeratotic hyperkeratosis in patches, hypogranulosis, spongiosis, irregular acanthosis, with the presence of elongation of the interpapillary ridges in serrated configuration, numerous cytoid bodies and intraepithelial lymphocytes, interface and vacuolar dermatitis with lymphohistiocytic infiltrate, in band and superficial perivascular without vasculitis data. Some lymphocytes have atypia. There is also erythrocyte extravasation and pigment incontinence. The superficial dermis presents edema, vascular ectasias, endothelial edema and elongation of the dermal papillae with epidermal thinning.

DISCUSSION

Dress syndrome belongs to the family of drug-reactive dermatoses, of a severe nature, an event starring a hypersensitivity reaction type IV of acute presentation.[1]

Among the risk factors most detected in addition to the personal or family history of this syndrome, include the female gender, black race, high temporary estrogenic environment (pregnancy and lactation), chronic alcoholism and use of hepatotoxic drugs. On more than one occasion, attempts have been made to integrate theories that explain the nature of the syndrome and its relationship with various agents, where they suggest both the participation of an immune disruption (affecting lymphocytes and macrophages), anomalies in the processing of toxification with subsequent grouping of reactive metabolites, genetic variations, and even the presence of infectious agents (such as the Herpes 6 virus); all yielding results not conclusive.[1,2,5,6] In most studies it is emphasized that this syndrome usually appears after the administration of a drug, with aromatic anticonvulsants being most frequently observed, followed by sulfonamides (drug involved in this case), glycopeptide-type antibiotics and allopurinol, among many others.[1,2,7-13]

The clinical picture usually begins two to six weeks after the start of consumption of the associated drug. They typically debut with fever (predominant sign), morbiliform rash (up to three-quarters of cases), mucosal involvement, generalized lymphadenopathy, and constitutional symptoms such as asthenia, adinamia, and arthralgia. In some cases it is accompanied by pruritus; however it is not an official rule. Laboratory studies show significant leukocytosis with significant elevation of eosinophils and presence of atypical lymphocytes, both being found in up to 90% of cases.[1,2]

This syndrome does not denote activity only in cutaneous and annexed territory, it also has the potential to invade in turn the liver tissue (which is the most frequent and severe, responsible for most of the unwanted outcomes of the disease) adopting a cytolytic, cholestatic or mixed

behavior.[2,14] Another organ that is also affected is the kidney; manifesting itself with signs and symptoms secondary to hyperazoemia whose clinical behavior adapts in the form of interstitial nephritis, necrotizing granulomatosis and vasculitis.[1,2,15] Less frequently observed is the cardiovascular system, observed in the form of myocarditis that is considered a feared presentation due to the deadly potential even in early stages of the disease. At the pulmonary level, its presentation is varied, adopting an insterticial, pleural pattern or in the form of respiratory distress syndrome. Although it is a very tiny percentage, failures can also be documented at the neurological, gastrointestinal and thyroid levels, so no apparatus and system are exempt.[14]

Of course, this syndrome represents a diagnostic challenge due to the extensive number of systemic manifestations it encompasses and the heterogeneity of the presentation at the level of the skin. For diagnostic approach purposes, a scoring system called RegiSCAR (Registry of severe cutaneous adverse reaction) is used, which was created to qualify the severity of skin adverse reactions, and according to the score obtained catalogs them as "no case", "possible", "probable" or "definitive".[2,16,17] In the patient, more than 8 points were found, which correspond to a definitive case for DRESS syndrome.

It is known that DRESS syndrome is not the only severe pharmacological skin reaction with multi-organ involvement, so it is essential to consider other differential diagnoses, including Stevens-Johnson syndrome, toxic epidermal necrolysis, generalized exanthematic pustulosis and erythroderma; reactions that also require specific pharmacological management.

The initial medical approach consists of immediate discontinuation of the drug by adding systemic steroid to unison, which is indicated mainly when there is cardiac and pulmonary involvement. It is recommended to administer prednisone (or equivalent) at doses of 1 mg/kg/day, for a prolonged period with progressive weaning of dosage when clinical and biochemical improvement is documented; in case of poor therapeutic response, pulses with methylprednisolone, immunotherapy and in certain cases plasmapheresis are used; all in order to avoid sequelae and complications (diabetes mellitus and renal insufficiency).[2,14] Its mortality is high, up to 10% of the cases registered, especially in the context of hepatic involvement, a finding found in the patient, who was also incorporated into hematological, pulmonary, cardiac and renal involvement.[14]

CONCLUSION

The presence of DRESS syndrome associated with trimethoprim and sulfamethoxazole was demonstrated by clinical, laboratory and histopathological criteria in a man of the seventh decade with a history of polypharmacy. The intention of this presentation is to consider this syndrome in patients with acute intake of drugs that debut with erythema and multi-organ involvement without a frequent medical cause that justifies it. If this entity is identified early, the prognosis can be favorable and even remain free of sequelae, so it is important to integrate the pathophysiological substrate of DRESS syndrome with the consumption of the aforementioned drugs since they are considered therapeutic agents of habitual use in all population groups.

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