Liver transplantation after DRESS syndrome: a case report and review of the literature

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Abstract

Drug reaction with eosinophilia and systemic symptoms is a quite unusual condition related to drug reaction. A case report of sulfasalazine-induced liver failure is described. The patient was submitted to liver transplantation. Liver transplantation is an option when DRESS is associated with acute liver failure, but the prognosis remains poor.

KEY CLINICAL MESSAGE

This study describes a patient with drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), associated with liver failure.

INTRODUCTION

Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome) is a quite unusual condition related to drug reaction. Several drugs have been linked to DRESS. It is a severe idiosyncratic drug reaction characterised by erythematous or papulo–pustular skin eruption associated with lymphadenopathy, fever, and visceral involvement (hepatitis, nephritis pneumonitis, pericarditis, myocardiitis, and colitis). Leucocytosis, eosinophilia (90%) and/or mononucleosis (40%) also may be seen. Severe acute hepatitis due to sulfasalazine or Trimethoprim-sulfamethoxazole is described in literature, but the occurrence of DRESS and liver failure is rare.

In this study, we report a patient with acute liver failure due to sulfasalazine-induced DRESS, treated with liver transplant.

CASE REPORT

An 18-year-old male patient was treated for toxoplasma retinochoroiditis with sulfasalazine, along one month. The patient had no past history of allergies or drug intolerance. He presented in a local hospital with fever, vomiting, cervical and inguinal nodules, abdominal pain, and macular rash on all body. The patient was transferred to our Transplant Center after onset of jaundice and encephalopathy. He was admitted in intensive care unit with facial edema, generalized scaling exanthema and acute hepatitis. Serological tests for viral hepatitis and all autoimmune antibodies were negative. Laboratory tests showed a total eosinophil count of 3220/mm³ (normal, <500 mm³), high level of transaminases (AST=1303 IU/L; ALT=1768 IU/L, lactate dehydrogenase level of 2274 IU/L (normal, 240 to 480 IU/L), total bilirubin level of 18.47mg/dL, direct bilirubin level of 14.81mg/dL, prothrombin time (PT) international normalized ratio (INR) of 5.18, and Factor V 17%. Abdominal ultrasound examination identified no chronic liver disease. The RegiSCAR⁷
system scored 5 points confirming the diagnosis of DRESS. Skin biopsy observed Interface and spongiotic dermatitis, consistent with drug eruption.

Therefore, the patient was worked up for urgent orthotopic liver transplantation (OLT), which was performed 24 hours after admission. At this time he was under corticosteroids and clinical support, including mechanic ventilation due progressive encephalopathy and dialysis due latic acydosis.

The orthotopic liver transplantation was uneventfull. Even though liver function improved in postoperative period, the patient developed sepsis requiring high doses of vasopressors. Broad-spectrum antibiotics were introduced but patient remained hemodynamic unstable. The patient died at 7th postoperative day. Blood cultures showed growth of *Klebsiella pneumoniae* resistent to carbapenems.

**Liver and Skin histology**

The histology analysis demonstrated massive eosinophils infiltrat compatible with DRESS and the liver explant presented a massive necrose associated a eosinophilis infiltrated (Figure 1 and 2).

**DISCUSSION**

The present report describes an adult patient with DRESS syndrome and liver failure treated with OLT. Liver failure in the setting of DRESS syndrome is quite rare. Few case reports presented patients with DRESS syndrome and high level of hepatic injury (Table 1). In these studies, most of the patients were treated with corticosteroids.\(^8\)\(^-\)\(^29\).

The management of DRESS syndrome is challenging. It is important to withdraw the suspected drug and the delay is associated with poorer outcomes.\(^30\)-\(^32\) Supportive therapy in intensive care unit should be provided to stabilize the patient. Early administration of systemic corticosteroid therapy is generally recommended.\(^33\) Systemic corticosteroid helps to improve in both clinical symptoms and laboratory abnormalities within days.\(^33\) Most of the cases reports of DRESS syndrome with liver dysfunction showed success with corticosteroids treatment (Table 1).

Liver transplantation is an option when DRESS is associated with acute fulminant hepatic failure, but the prognosis remains poor (Table 2).\(^34\)-\(^39\). Besnard et al.\(^34\) reported two pediatric Crohn’s disease patients undergoing liver transplantation after DRESS syndrome induced by sulfasalazine. During follow-up, one of them developed acute rejection and fatal aspergilosis. Song et al.\(^37\) reported living-donor liver transplantation in a 14-years old patient. Patient presented chronic rejection after 25-months follow-up. Amante et al.\(^35\) and Roales-Gómez et al.\(^38\) reported adult patients treated with OLT, with no information concerning long-term follow-up. Mennickea et al.\(^36\) reported an adult patient treated with OLT, with mortality in postoperative period due to massive intrabominal blood loss.

Recent studies support the use of Molecular Adsorbents Recirculation System (MARS) as a rescue for patients with liver failure. Roales-Gómez et al.\(^38\) described MARS use, although patient did not responde well, and patients was eventually submited to OLT. Ng et al.\(^23\) reported a pediatric patient that underwent MARS in the intensive care unit, with satisfactory response.

The present study showed a patient with Sulfasalazine and Trimethoprim-sulfamethoxazole severe reaction. Sulfasalazine and Trimethoprim-sulfamethoxazole carries a significant risk of drug toxicity. Yusuf et al.\(^24\) reported the first case of DRESS syndrome in a child treated for toxoplasma retinochoroiditis. Rare cases of immunoallergic reactions to sulfasalazine, including DRESS syndromes, have been reported, such as the classic “3-week sulfasalazine syndrome” occurring 3 weeks after the first administration.\(^8\)

**CONCLUSION**

DRESS is associated with acute liver failure is a lifethreatening condition. Liver transplantation is an option for the management of these patients, although the prognosis remains poor.

**AUTHORS CONTRIBUTIONS:**
• Igor Lepski Calil³, PhD: (analysis and interpretation of data)
• Rafael Soares Nunes Pinheiro¹, PhD: (acquisition of data and drafting the article)
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• Orlando de Castro e Silva Júnior³ PhD: (final approval of the version to be submitted)

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| Case Report | Patient | Drug | Treatment | Follow up |
|-------------|---------|------|-----------|----------|
| Brooks H et al | 53-year-old man | Sulfasalazine | corticosteroids | Alive |
| Case Report          | Pacient                | Drug                  | Treatment            | Follow up |
|---------------------|------------------------|-----------------------|----------------------|-----------|
| Queyrel V et al.     | 15-year-old woman      | Sulphasalazine        | corticosteroids      | Alive     |
| Mainra RR et al.     | 24-year-old woman      | Trimethoprim-sulfamethoxazole | corticosteroids | Alive     |
| Descloux E et al.    | 45-year-old woman      | Sulphasalazine        | corticosteroids      | Alive     |
| Michel F et al.      | 63-year-old woman      | sulfasalazine         | corticosteroids      | Alive     |
| Teo L et al.         | 49-year-old woman      | Sulphasalazine        | corticosteroids      | Alive     |
| Bejia I et al.       | 46-year-old woman      | Sulphasalazine        | corticosteroids      | Alive     |
| de Aquino RT et al.  | 47-year-old woman      | Sulphasalazine        | corticosteroids      | Alive     |
| Augusto JF et al.    | 77-year-old woman      | Sulphasalazine        | corticosteroids      | Alive     |
| Yeşilova Z et al.    | 38-year-old man        | Sulphasalazine        | corticosteroids      | Alive     |
| Rosenbaum, J et al.  | 11-year-old woman      | Sulphasalazine        | corticosteroids      | Alive     |
| van der Mark SC et al. | 24-year-old woman    | Sulphasalazine        | corticosteroids      | Alive     |
| Piñana E et al.      | 11-year-old boy        | Sulphasalazine        | corticosteroids      | Alive     |
| Lau G et al.         | 34-year-old woman      | Sulphasalazine        | corticosteroids      | Died      |
| Daoulah A et al.     | 56-year-old woman      | Sulphasalazine        | corticosteroids      | Died      |
| Ng CT et al.         | 17 year-old male       | Trimethoprim-sulfamethoxazole | MARS               | Alive     |
| Yusuf IH et al.      | 15-year-old girl       | Sulphasalazine        | corticosteroids      | Alive     |
| Girelli F et al.     | 53-year-old woman      | Sulphasalazine/Amoxicillin | corticosteroids | Alive     |
| Hernández N et al.   | 60-year-old woman      | Sulphasalazine        | corticosteroids      | Alive     |
| Zaïem A et al.       | 45-year-old woman      | Sulphasalazine        | corticosteroids      | Alive     |
| Ferrero NA et al.    | 15-year-old boy        | Sulphasalazine        | corticosteroids      | Alive     |
| Pirklbauer M et al.  | A 53-year-old woman    | Sulphasalazine        | corticosteroids      | Alive     |

Table 1. Reported cases who had diagnosis of DRESS caused by associated Sulphasalazine and Trimethoprim-sulfamethoxazole.
| Case Report       | Patient                | Drug         | Follow up |
|-------------------|------------------------|--------------|-----------|
| Song S et al      | 14-year-old female     | Vancomycin   | Alive     |
| Roales-Gómez V et al | 22-year-old male       | Ibuprofen   | Alive     |
| Present study     | 18-year-old male       | Sulfamethoxazole | Died     |

**Table 2.** Patient diagnosed with DRESS undergoing liver transplantation.

**Caption**

**Figure 1.** Liver Histology. H&E stain. Massive eosinophils infiltrating with extensive necrosis of the liver compatible with fulminant hepatitis.

**Figure 2.** Skin Histology. H&E stain. Massive eosinophils infiltrating compatible with DRESS.
