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CASE REPORT

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Amoxicillin and lamotrigine-induced DRESS syndrome: A case report

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Key Clinical Message

This case demonstrated with importance of recognizing DRESS syndrome presenting without the typical eosinophilia due to possible cross-reactivity between amoxicillin and the well-documented inciting medication lamotrigine. Steroid tapering is an effective treatment, but medication avoidance should be stressed to avoid symptom recurrence.

KEYWORDS

allergy, dermatology, immunology: Pathology and laboratory medicine, psychiatry

1 | INTRODUCTION

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is an uncommon, delayed drug-induced hypersensitivity reaction characterized by an extensive pruritic skin rash, lymphadenopathy, and visceral involvement.[1] Hepatitis is a common feature in DRESS syndrome and must be promptly recognized to limit morbidity and mortality. There are several previous reports of lamotrigine-induced DRESS syndrome in the current literature.[2,3] Here we report a case of DRESS syndrome in an 18-year-old female that initially manifested after a three-dose trial of amoxicillin and worsened after increasing her lamotrigine dose.

2 | CASE HISTORY

An 18-year-old Spanish American female with a known mood disorder developed fever, nausea, vomiting, and intermittent abdominal pain and initially presented to an outside hospital. Four weeks prior to admission, she presented to an urgent treatment clinic and was prescribed amoxicillin for suspected tonsillitis. After taking three doses, she developed a faint maculopapular rash on her face that shortly resolved after stopping amoxicillin. Three weeks prior to presentation, she increased her lamotrigine dose to 100 mg daily shortly after stopping amoxicillin and again developed a diffuse maculopapular pruritic red rash over her entire body over the next several days. Her psychiatrist switched her from lamotrigine to aripiprazole after this rash developed but the rash persisted despite discontinuation of lamotrigine. At the time of presentation, the patient was taking aripiprazole 2 mg daily and duloxetine 30 mg daily.

3 | METHODS

Outside records were unavailable to review to verify specific dosages of both lamotrigine and amoxicillin. Three weeks afterward the rash initially appeared, she presented to an outside hospital emergency department with difficulty breathing and worsening rash (Figures 1 and 2). She described difficulty breathing due to swelling on both sides of her neck, consistent with lymphadenopathy, and

FIGURE 1 Right arm showing erythematous maculopapular rash on initial presentation.

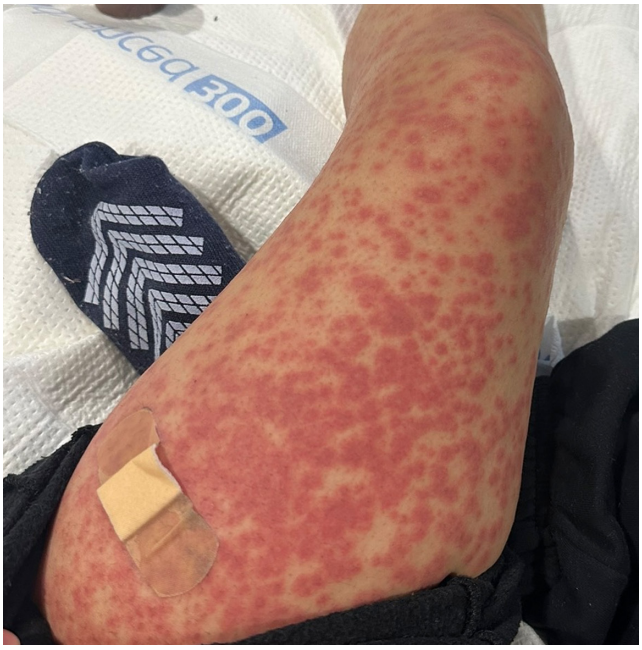

FIGURE 2 Left lower extremity showing erythematous maculopapular rash on initial presentation.

was given an epinephrine injection with subsequent respiratory improvement. Vital signs at the outside hospital were remarkable for fevers up to 101°F, and hypotensive blood pressures from 90/54 to 101/60 at time of transfer to our institution. She was started on oral prednisone 50 mg and transferred to our center for further treatment that same day. Her laboratory tests at the outside hospital and our institution are shown below (Table 1). Labs at our institution did show the presence of atypical lymphocytes. Blood cultures drawn at our institution showed no growth up to day 5. A liver biopsy showed inflammatory infiltrate mixed in nature including plasma cells present within lobules and the portal tracts (Figures 3 and 4). Autoimmune, virology, and liver workups were unremarkable, except for a mildly elevated alpha−1 antitrypsin level at 220 and elevated ANA, speckled pattern 1:320, with a negative anti-smooth muscle antibody (SMA). She was started on oral prednisolone 60 mg, oral diphenhydramine 50 mg and oral hydroxyzine pamoate 100 mg. Her rash darkened to a deep purple shade and coalesced over the next several days. Over the next 5 days, the rash significantly improved, and her general condition was greatly improved. She was discharged on a 16-day taper of oral prednisone 10 mg and oral diphenhydramine 50 mg. The patient was

TABLE 1 Lab values between institutions.

	Outside hospital	Home institution
WBC (10^3/μL)	21.6	18.88
Eosinophils (10^3/μL)	0.6	0.57
Lymphocytes (10^3/μL)	11.3	5.48
AST (U/L)	353	385
ALT (U/L)	407	362
Alkaline Phosphatase (U/L)	320	302
Total Bilirubin (mg/dL)	2.0	1.5

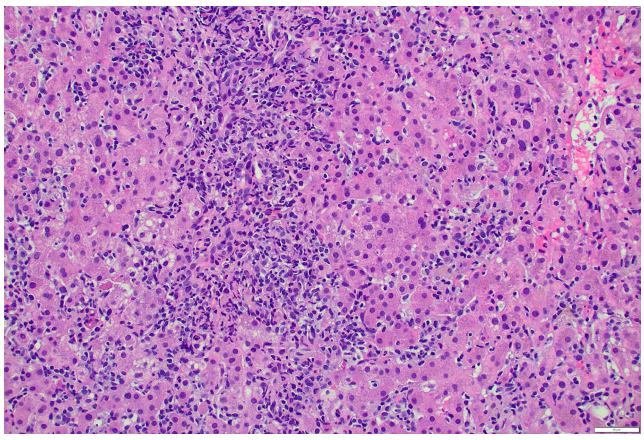

FIGURE 3 Liver biopsy with Masson Trichrome stain at 20× magnification demonstrating inflamed liver parenchyma with acidophil bodies and necrotic hepatocytes. Inflammatory infiltrate is mixed in nature with plasma cells present in both the lobules and portal tracts. Ductular reaction is present within the portal tracts.

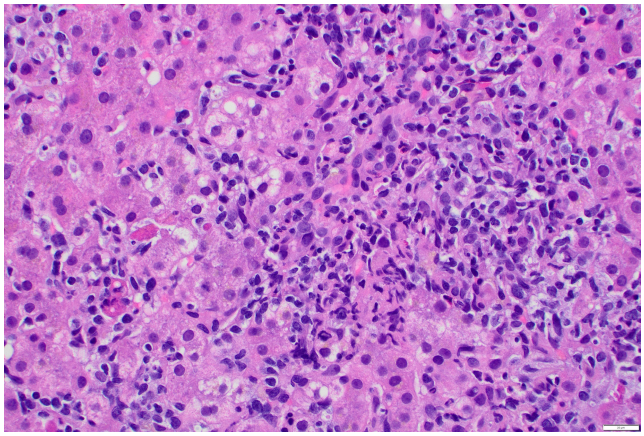

FIGURE 4 Liver biopsy with Masson Trichrome stain at 4× magnification demonstrating inflamed liver parenchyma with acidophil bodies and necrotic hepatocytes. Inflammatory infiltrate is mixed in nature with plasma cells present in both the lobules and portal tracts. Ductular reaction is present within the portal tracts.

seen for follow-up 3 months after discharge with complete resolution of symptoms.

4 | DISCUSSION

This patient presented with 4 weeks of a maculopapular rash, fever, and abdominal pain after starting amoxicillin and increasing her lamotrigine dosage. DRESS syndrome is characterized by a delayed drug-induced hypersensitivity reaction that may have a clear drug trigger in most cases, typically reported as an anticonvulsant, antimicrobial sulfonamides, or allopurinol.[4,5] The RegiSCAR scoring system is used to make a diagnosis of DRESS syndrome with the following criteria (Table 2).[4]

This patient had a RegiSCAR of 6 with the following criteria: fevers, enlarged lymph nodes, presence of atypical lymphocytes, skin rash >50% of the body, presence of edema and infiltration, liver biopsy suggesting DRESS syndrome, internal organ involvement of the liver, resolution in over 15 days, and exclusion of alternative diagnoses. It is important to rule out other potential causes of liver injury, such as viral pathologies, including cytomegalovirus (CMV), autoimmune pathologies, including lupus, and Stevens-Johnson syndrome. The largely unremarkable viral and autoimmune workups made these possibilities less likely. In this patient, the onset of symptoms after initiation of amoxicillin, recent increase in lamotrigine dosage, and clinical improvement after drug discontinuation made alternate diagnoses unlikely.

There is no standardized treatment course, but systemic corticosteroids have been effective in moderate and severe cases with internal organ involvement.[6] Our patient has similar results to other case reports of lamotrigine-induced DRESS syndrome.[2] Other medications including cyclosporine, mycophenolate, cyclophosphamide, and intravenous immunoglobulin have been used as alternatives to corticosteroids, but their outcomes are less common in the literature. Our case differs from others in that the rash did not return during or after the steroid taper, and that a low dose of prednisone taper over only 16 days was sufficient for a complete resolution of symptoms.[7,8] Other cases report a steroid taper over 6–8 weeks to prevent symptom relapse, but this puts the patient at risk of immunosuppression and developing subsequent complications, including opportunistic infections, such as pneumocystis jiroveci pneumonia (PJP) or cytomegalovirus (CMV).[9–13] This shorter steroid taper prevented the use of antibiotic prophylaxis with potentially unnecessary side effects for our presented patient. This is a novel case given the possible cross-reactivity between amoxicillin and lamotrigine. Lamotrigine is commonly associated with DRESS syndrome, but this case differs in that the typical rash occurred after the patient started amoxicillin. The rash worsened after the patient increased her lamotrigine dosage, further suggesting some cross-reactivity between the two medications that lead to her worsening symptoms. This case of possible amoxicillin-induced DRESS syndrome is not as well documented but has been described in one other case.[10] There are documented cases of amoxicillin hypersensitivity after DRESS syndrome, but this presented patient represents a possible predisposition to DRESS syndrome due to amoxicillin.[14,15]

TABLE 2 RegiSCAR scoring for DRESS syndrome.

	Score if not present	Score if present
Fever ≥38.5°	−1	0
Enlarged lymph nodes (>1 cm) at ≥2 sites	0	1
Atypical lymphocytes	0	1
Eosinophilia		
700–1499 cells		1
/≥1500 cells		2
Skin rash extent >50%	0	1
Biopsy suggesting DRESS syndrome	−1	0
At least 2 of the following: edema, infiltration, purpura scaling	−1	1
Internal organs involved		
1 organ	0	1
≥2 organs	0	2
Resolution in >15 days	−1	0
Exclusion of alternative diagnosis	0	1

5 | CONCLUSION

In conclusion, this is a case of a patient presenting with DRESS syndrome after a recent increase in her lamotrigine dosage and after a short course of amoxicillin. A short course of steroids over only 16 days was enough for resolution of this patient's symptoms. This differs in other reports cases with symptom reoccurrence during steroid tapers shorter than 6–8 weeks. This case highlights the crucial importance to recognize potential DRESS syndrome, especially in patients with signs of liver involvement, to minimize risks of acute liver failure and possible liver transplant.

AUTHOR CONTRIBUTIONS

Nicholas Demas was responsible for writing the original manuscript draft and for reviewing and editing. Dr. Mohammad Baseem Shaikh was responsible for reviewing and editing the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors do not have any conflicts of interest to disclose.

DATA AVAILABILITY STATEMENT

Data available upon request from the corresponding author.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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