Successful treatment of steroid-refractory drug-induced hypersensitivity reaction relapse with cyclosporine

Riya Patel MS[1], Eugenie Quan MD[2], Diana Dougherty MD[3], Patrick Rush DO[2], Susan Dorsey MD[2], Mariana Phillips MD[2]

[1]Virginia Tech Carilion School of Medicine

[2]Division of Dermatology, Department of Internal Medicine, Virginia Tech Carilion School of Medicine

[2]Division of Gastroenterology, Department of Internal Medicine, Virginia Tech Carilion School of Medicine

Introduction

- Drug reaction with eosinophilia and systemic symptoms (DRESS), or drug-induced hypersensitivity reaction (DiHS), is a severe systemic drug reaction
- Exact pathogenesis is unknown; however, human herpesvirus 6 reactivation is associated with increased severity and prolonged course [1]
- RegiSCAR scoring system for diagnosis of DiHS includes: fever >101.3^{O} F; enlarged lymph nodes in at least two different areas; eosinophilia; atypical lymphocytes; skin involvement; organ involvement; disease duration >15 days [2]
- First-line therapy is drug withdrawal and systemic glucocorticoids. Cyclosporine (Cys) is a second-line treatment for DiHS with limited evidence [3]
- Most common autoimmune sequelae is Graves disease and type I diabetes mellitus [4]

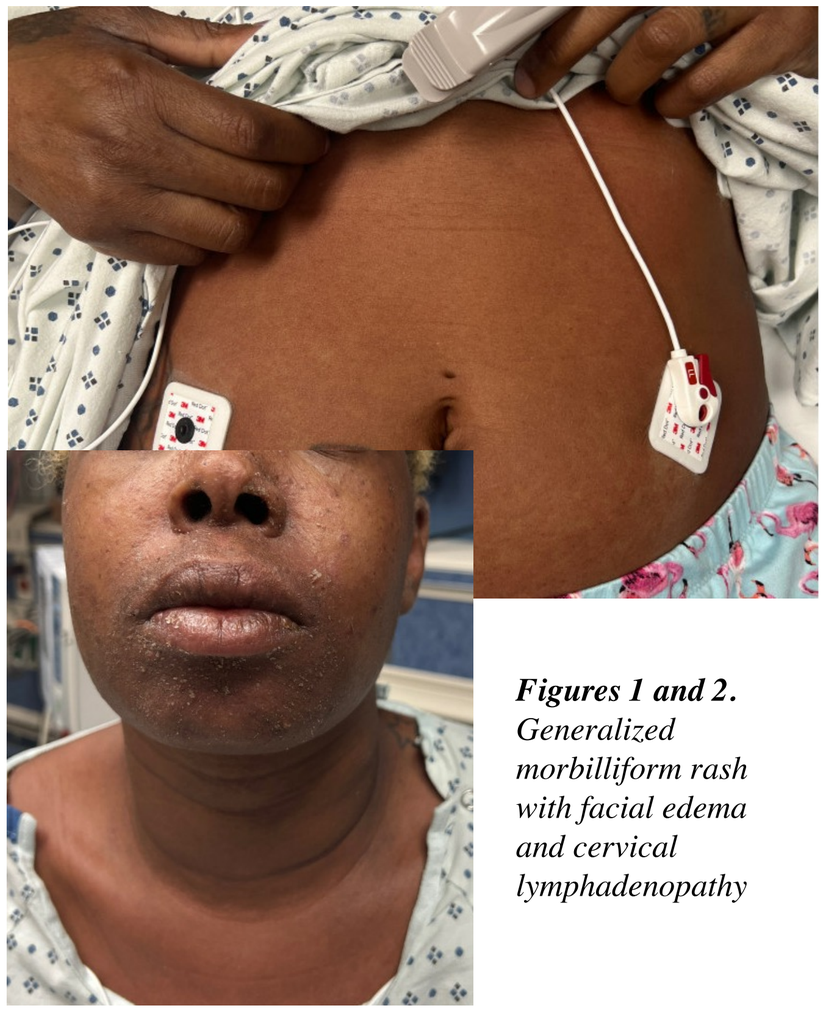
Case Presentation

- 32-year-old woman with history of bipolar disorder presented with diffuse morbilliform rash, facial edema, and cervical lymphadenopathy after starting divalproex, risperidone, and trazodone two months prior (Figures 1 and 2)
- Notable labs on admission included elevated LFTs (AST 170, ALT 318) and eosinophilia
- Hepatitis and autoimmune panels, including ANA, anti-actin, anti-mitochondria M2, and anti-LKM-1, were negative
- Skin biopsy showed vacuolar and superficial perivascular dermatitis with mixed inflammation, compatible with DiHS
- Discontinued divalproex due to suspected cause while risperidone was switched to paliperidone
- Started on prednisone 80 mg daily with LFTs improving to AST 68, ALT 258
- Two weeks after discharge, she was re-admitted with recurring rash and elevated LFTs (AST 324, ALT 645) while on prednisone 70 mg daily
- Work-up was notable for positive HHV-6 DNA PCR, CMV DNA PCR, and mycoplasma urine cultures. Liver biopsy showed acute hepatitis
- Paliperidone and trazodone were discontinued. She was started on methylprednisolone 120 mg (1.5 mg/kg) daily; however, her LFTs continued to worsen to AST 389, ALT 1494

Case Presentation (cont.)

- Cys 200 mg BID (5 mg/kg) was then initiated. Her LFTs continued to worsen to AST 138, ALT 2820; however, two days after starting Cys, her LFTs began to improve. She was discharged on a Cys and prednisone taper
- Two months later, she presented with pruritic erythematous patches on the antecubital fossae, neck, and upper chest after she was tapered off Cys. She was still on prednisone 20 mg daily. LFTs were elevated to AST 1204, ALT 2263
- Work-up was notable for positive anti-actin, anti smooth muscle 1:160, elevated IgG 2403 relative to IgA and IgM. Repeat liver biopsy showed chronic active hepatitis compatible with autoimmune hepatitis
- Differential diagnosis included ongoing liver damage from continued DiSH/DRESS versus secondary autoimmune hepatitis

Figures



Figures 1 and 2. *Generalized morbilliform rash with facial edema and cervical lymphadenopathy*

Discussion

- DRESS/DiSH can have a prolonged course, even after stopping the culprit medication, due to herpes virus reactivation
- All related medications to the culprit medication should be discontinued—risperidone was switched to paliperidone, a metabolite of risperidone, in our case and could have contributed to the patient's first DiHS relapse
- Cyclosporine should be considered as a treatment option for steroid-refractory DiHS
- Improvement may not be seen until several days after initiation of treatment
- Antiviral therapy can be considered if there is concern for viremia or visceral organ involvement; however, immunosuppressive therapy should not be stopped
- Patients should be closely monitored for autoimmune sequelae, including autoimmune hepatitis

Conclusion

This case highlights that cyclosporine may be effective in refractory DiHS associated with latent HHV-6 and CMV reactivation and clinical and laboratory improvement may not be seen for several days after starting the medication.

References

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