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Cyclosporine treatment of drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome: a case report and brief review of the literature

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Abstract

Systemic corticosteroids are often considered the treatment of choice in the management of severe drug-induced hypersensitivity syndrome (DIHS), also known as drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome. However, in instances when systemic steroids are contraindicated, when there is an inadequate response to steroids, or when a prolonged course of steroids is not ideal, alternate therapies may be considered. Cyclosporine has been reported as a successful alternative immunosuppressive therapy; however, only a few cases have been reported in the literature. This observational case report presents an instance where cyclosporine was successfully used to treat DRESS syndrome in a patient where systemic steroids were ineffective.

Keywords

cyclosporine; drug reaction with eosinophilia and systemic symptoms; drug-induced hypersensitivity syndrome

Report of a Case

A 59-year-old man with a history of multiple myeloma was admitted to the hospital for a rash and new onset edema of the hands and face approximately five weeks after starting induction chemotherapy and antibiotic prophylaxis with trimethoprim/sulfamethoxazole (TMP/SMX). The patient developed numerous, coalescing, purpuric macules and papules, which covered most of his body (Figures 1a and 1b). The patient also had significant edema of the face and hands. The patient's labs were notable for marked leukocytosis with hypereosinophilia and transaminitis with an alanine aminotransferase (ALT) of 212 and an aspartate aminotransferase (AST) of 54. A punch biopsy taken from one of the lesions and was most consistent with a purpuric drug eruption. A clinical diagnosis of DRESS syndrome was made, his TMP/SMX was discontinued, and he was started on prednisone, 1mg/kg/day. Despite these interventions, the patient's hepatic enzymes continued to rise and peaked with an ALT of 1,765 and an AST of 1,337. The decision was made to start cyclosporine 5

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Abbreviations used in this paper: DRESS, DIHS, TMP/SMX

mg/kg/day for a seven-day course, which resulted in rapid clinical and laboratory improvement (Figures 2a and 2b). The patient's hepatic enzymes continued to trend down and normalized in approximately three weeks.

Discussion

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome, also known as drug-induced hypersensitivity syndrome (DIHS), is fatal in approximately 10% of cases, most commonly due to hepatic necrosis¹. Diagnosis of DRESS relies on recognition of the syndromes' clinical symptoms (edema, rash, lymphadenopathy, fever) and signs of hematologic or internal organ involvement in the laboratory data². Management of DRESS includes withdrawal of the suspected causative agent and supportive care². In cases of internal organ involvement, patients are also frequently prescribed a systemic immunosuppressant, most commonly corticosteroids¹. Instances when systemic steroids are contraindicated, when there is inadequate response to steroids, or when a prolonged course of steroids is not ideal, alternate therapies may be considered. Review of the literature revealed seven other cases demonstrating the use of cyclosporine for the management of DRESS syndrome (see Table 1). In two of these cases, cyclosporine was effective as a first-line agent³; in three others, it was used successfully as a second-line therapy after failed initial management with steroids^{1, 2, 4}. Finally, in two other cases, systemic corticosteroids followed by cyclosporine both failed to resolve refractory DRESS syndrome^{5, 6}. This observational case report presents another instance where cyclosporine was successfully used in the management of DRESS syndrome and supplies further evidence that cyclosporine may provide an effective alternative or compliment to systemic corticosteroid therapy.

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Figures 1a and 1b.
Purpuric eruption on abdomen and right leg of patient following initiation of induction chemotherapy and antibiotic prophylaxis with TMP/SMX.



Figures 2a and 2b.
Appearance of rash three days after initiating cyclosporine.

Table 1.

Case reports of cyclosporine use in the management of DRESS.

Publication Year	Causative Drug	Initial Corticosteroid Therapy	Cyclosporine Dosage	Indication for Cyclosporine	Result
2003 ⁴	Phenytoin	Prednisolone, 40 mg/day, followed by topical clobetasol propionate, 0.05%, for a total of 200 mg weekly	4 mg/kg for approximately 6 months	Steroid-resistant DRESS and iatrogenic Cushing's syndrome	Full resolution; stable 9 months later
2005 ¹	Vancomycin	Methylprednisolone, 100 mg IV, four times daily, followed by tapered dose of prednisone for several weeks	100 mg, twice daily, for 5 days	No improvement with corticosteroid therapy	Full resolution; stable 20 months later
2008 ⁵	Celecoxib and ethambutol	Methylprednisolone, 1,000 mg IV daily, followed by 75 mg prednisone daily Patient suffered relapse 1 week later and was started on Methylprednisolone, 1,000 mg IV daily for another 3 days	Cyclosporine, 100 mg daily, with 60 mg methylprednisolone daily	Relapse	Patient continued to decline despite initiation of cyclosporine and methylprednisolone. Patient was intubated and managed with intravenous immunoglobulin infusion (1 g/kg/day) for 2 days. Patient eventually recovered following prolonged steroid taper.
2012 ⁶	Sulfasalazine	Patient initially managed with co-administration of high-dose dexamethasone with cyclosporine, followed by an unknown tapered dose of prednisone			No resolution; patient's condition continued to deteriorate, and she eventually died of myocarditis approximately 6 weeks after her initiation of sulfasalazine
2016 ³	Carbamazepine	Cyclosporine monotherapy with 100 mg twice daily for 7 days			Full resolution of symptoms
2016 ³	Minocycline	Cyclosporine monotherapy with 5 mg/kg/day for 3 days			Full resolution of symptoms
2017 ²	Mexiletine	100 mg/day prednisolone for 9 days, then 70 mg/day for 6 days, followed-by self-wean by patient	5 mg/kg/day for 7 days, followed by 100 mg twice daily for 14 days and then 150 mg daily for 20 days	Relapse of DRESS and development of steroid-induced diabetes mellitus	Full resolution; stable 6 months later