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Case Report

Carbamazepine-induced DRESS syndrome in a child: Rapid response to pulsed corticosteroids

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Abstract

DRESS syndrome is an idiosyncratic reaction to drugs, which can occur in both adults and children. To date there is no agreed upon criteria for its diagnosis; there is even less consensus on its management. We report the case of a 14-year-old boy with carbamazepine induced DRESS syndrome, predominantly involving the liver. He responded rapidly to high dose pulsed intravenous corticosteroids.

Keywords: DRESS syndrome, carbamazepine, corticosteroids

Introduction

The term DRESS syndrome, or drug reaction with eosinophilia and systemic symptoms, was first coined by the French group, Bocquet etal in 1996, initially with the 'R' of the acronym denoting 'rash' [1]. The name was changed because of the discovery of variable skin involvement in this condition [2,3]. Previous names for the same condition include drug-induced pseudolymphoma, anticonvulsant hypersensitivity syndrome, and hypersensitivity syndrome [2]. The evolving nature of its nomenclature may be the direct manifestation of the non-existent universal defining diagnostic criteria. In general, DRESS syndrome embodies a severe idiosyncratic reaction to drugs, including skin eruption, fever, hematological abnormalities, and internal organ involvement [1-4]. Notable clinical statistics include an estimated incidence of 1 in 1000 to 1 in 10 000 exposures, a delayed onset of 2-6 weeks post-exposure, and a mortality of about 10% [3-6].

Case Report

We report a 14-year-old boy who was admitted by the pediatrician with 3-week history of generalized mildly pruritic erythema, with associated systemic symptoms of lethargy, fevers and chills, nausea, and anorexia. Clinical examination revealed fever (of 39.1°C), jaundice, palpable hepatomegaly, and facial swelling with cervical lymphadenopathy. Specific skin findings included widespread erythematous eruption, xerosis with mild exfoliation, angular cheilitis, and aphthous ulceration (Figure 1 and 2).

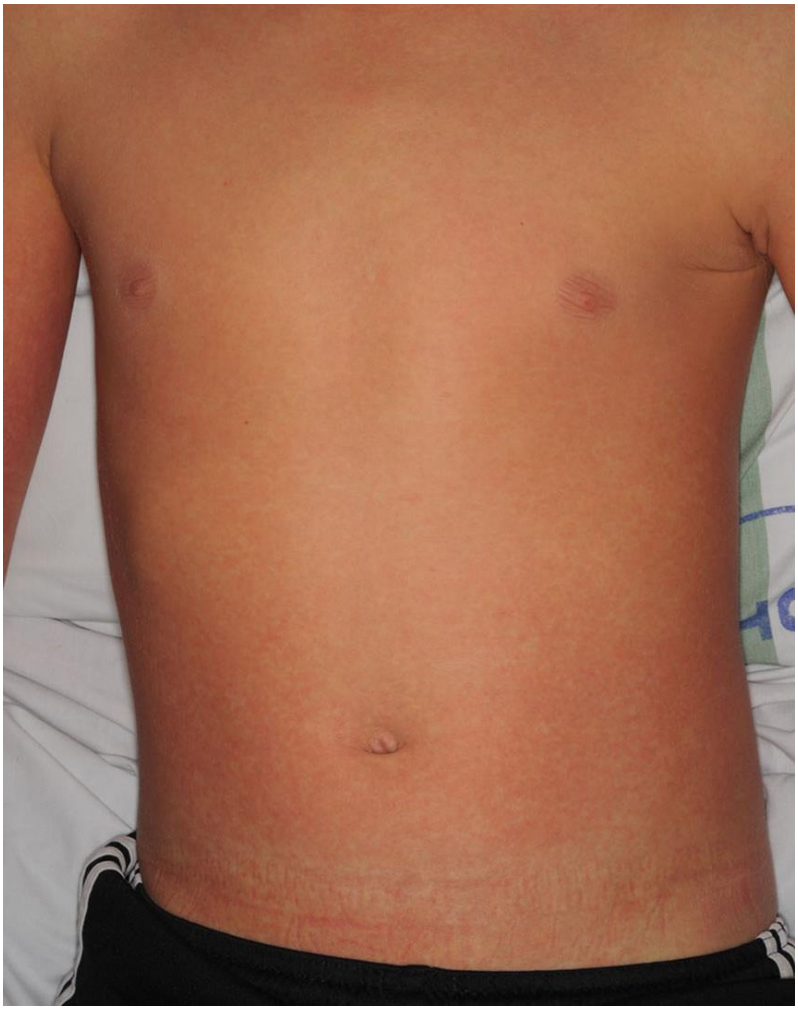

Figure 1. Generalized erythema with jaundice

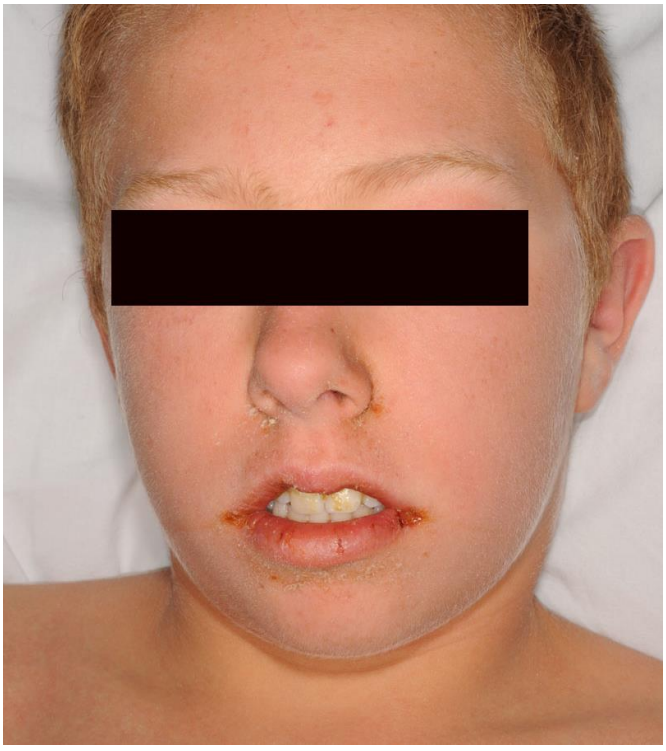

Figure 2. Facial erythema, swelling, jaundice, with angular cheilitis

On further history, the patient had several seizures in the last few years, owing to a traffic accident, and had been started on carbamazepine 2 weeks prior to the onset of symptoms. The provisional diagnosis made by the Dermatology team was DRESS syndrome related to carbamazepine.

Laboratory

Full blood examination showed leukocytosis, with lymphocytosis and mild eosinophilia, thrombocytopenia, and mild microcytic anemia. Liver function tests revealed mixed cholestatic and hepatitic changes, which along with a raised INR (1.7) confirmed liver toxicity. Serological tests for hepatitis A,B, C, and Epstein-Barr virus (EBV) were negative. Involvement of other major organs were excluded via chest x-ray, echocardiogram, and urine testing, although subsequent abdominal ultrasound did detect hepatosplenomegaly with no focal lesions, as well as prominent, non-pathological nodes around the pancreas.

An incisional skin biopsy showed a heavy interface pattern with a chronic inflammatory cell infiltrate, basal cell vacuolar change, and lymphocyte exocytosis, which in foci had an epidermotropism-like appearance (Figure 3). The reaction pattern was consistent with DRESS syndrome.

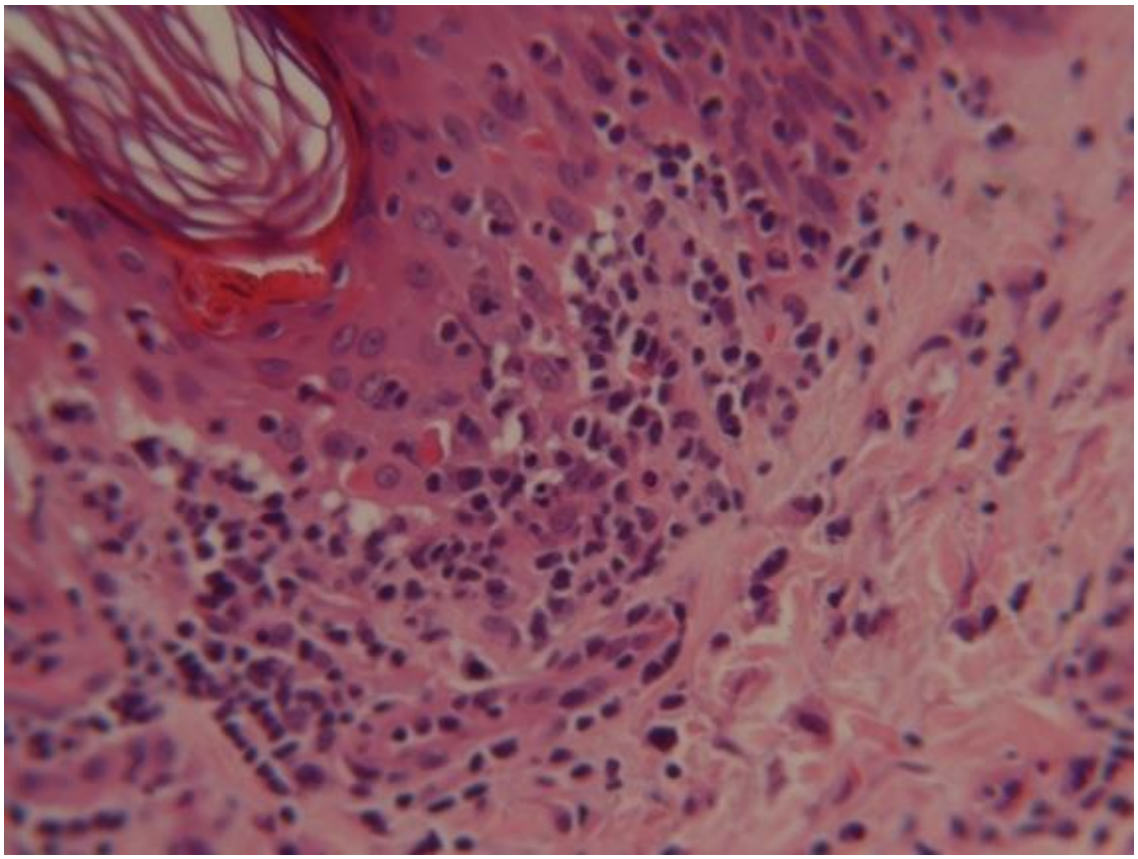

Figure 3. Histopathology (H and E stain), showing interface chronic inflammatory infiltrate, basal cell vacuolisation, lymphocyte exocytosis, and in foci epidermotropism-like appearance

Management in the first week entailed cessation of carbamazepine, bed rest, and general fluid and nutritional support. Topically he was treated with liquid paraffin emollient all over, with fluocinolone acetonide ointment to combat the pruritus. For the cheilitis and aphthae, a topical antifungal and topical antibacterial/corticosteroid combination was used, in addition to chlorhexidine gluconate mouthwash. Despite this, specific liver parameters continued to deteriorate (Figure 4), and from day 7 of admission, he was treated with intravenous (IV) methylprednisolone 1g/day for 3 days, concurrently with oral ursodeoxycholic acid 900mg daily. This led to rapid reversal of both abnormal liver function and clinical symptoms (figure 4). No further systemic steroids were given by mouth or IV, and no rebound of symptoms or laboratory parameters were seen . The patient was discharged to outpatient services 10 days after intervention with the pulsed IV therapy.

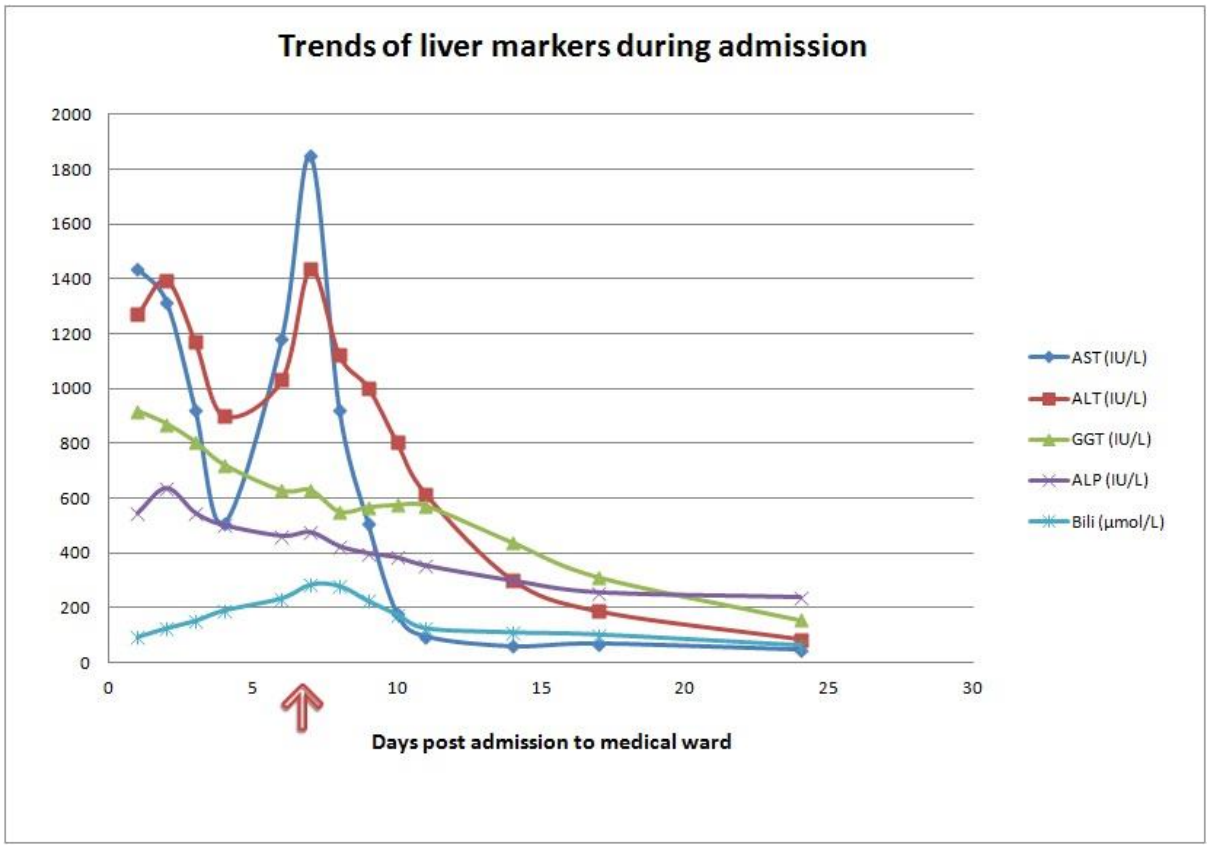

Figure 4. Graph showing commencement of IV methylprednisolone (red arrow) on day 7, with rapid response of major liver function markers

Discussion

As eluded to earlier, the occurrence of DRESS syndrome is rare, with many fewer cases involving children compared to adults in the literature [7-8] . Nonetheless, it is considered to be a true pediatric dermatology emergency owing to its potential threat-to-life [9]. Early recognition of the syndrome and intervention may be the key step to preventing mortality or substantial organ damage.

The drugs implicated in DRESS have numbered at least 44 [4], although as exemplified by our case, the most common culprits are the aromatic anticonvulsants (carbamazepine, phenytoin, phenobarbital), allopurinol, minocycline, sulfasalazine, and abacavir [1,2,4]. In a recent Asian study of 60 DRESS cases, allopurinol and dapsone were found to be the main culprits, eclipsing cases related to anticonvulsants [5]. The increasing number of drugs identified that can lead to DRESS syndrome only adds to the difficulty of drawing valid pathogenetic theories.

Whereas there is no worldwide consensus, the inclusion criteria for DRESS syndrome has been published by RegiSCAR [2]; these criteria have been used in several large studies [4,5]. Our patient's documented findings, fever over 38°C, generalized erythematous rash, jaundice, hepatomegaly, lymphadenopathy, facial edema, cheilitis, mucosal ulceration, hepatitis, cholestasis, lymphocytosis, eosinophilia, and thrombocytopenia, fit very typically with this syndrome [1,2, 5, 10]. Whereas histology is not used in any criteria scheme, our patient's skin biopsy showed dense lymphocytic interface reaction similar to previous descriptions [1].

As for SJS/TEN, the use of corticosteroids in DRESS was controversial previously. More recently both IV and oral forms are becoming more accepted as standard treatment [2,5-7,9]. Reports of dramatic clinical and laboratory response to systemic corticosteroid already exist. Nevertheless, this case further illustrates the potential striking benefits of high dose IV methylprednisolone.

Conclusion

DRESS syndrome can certainly occur in the pediatric population in similar fashion to adults. This case highlights the severity of hepatic damage and the dramatic response to high dose short term IV methylprednisolone.

References

1. Bocquet H, Bagot M, Roujeau JC. Drug-induced pseudolymphoma and drug hypersensitivity syndrome (Drug Rash with Eosinophilia and Systemic Symptoms: DRESS). Semin Cutan Med Surg. 1996 Dec;15(4):250-7. [PMID: 9069593]
2. Walsh SA, Creamer D. Drug reaction with eosinophilia and systemic symptoms (DRESS): a clinical update and review of current thinking. Clin Exp Dermatol. 2011 Jan;36(1):6-11. [PMID: 21143513]
3. Bachot N, Roujeau JC. Differential diagnosis of severe cutaneous drug eruptions. Am J Clin Dermatol. 2003;4(8):561-72. [PMID: 12862499]
4. Cacoub P, Musette P, Descamps V, Meyer O etal. The DRESS syndrome: a literature review. Am J Med. 2011 Jul; 124(7): 588-97. [PMID: 21592453]
5. Chen YC, Chiu HC, Chu CY. Drug reaction with eosinophilia and systemic symptoms: a retrospective study of 60 cases. Arch Dermatol. 2010 Dec;146(12):1373-9. [PMID: 20713773]
6. Tas S, Simonart T. Management of drug rash with eosinophilia and systemic symptoms (DRESS syndrome): an update. Dermatology. 2003;206(4):353-6. [PMID: 12771485]
7. Dewan AK, Quinonez RA. Allopurinol-induced DRESS syndrome in an adolescent patient. Pediatr Dermatol. 2010 May-Jun;27(3):270-3. [PMID: 19804493]
8. Verrotti A, Trotta D, Salladini C, Chiarelli F. Anticonvulsant hypersensitivity syndrome in children: incidence, prevention and management. CNS Drugs. 2002;16(3):197-205. [PMID: 11888340]
9. Kress DW. Pediatric dermatology emergencies. Curr Opin Pediatr. 2011 Aug;23(4):403-6. [PMID: 21670682]
10. Fleming P, Marik PE. The DRESS syndrome: the great clinical mimicker. Pharmacotherapy. 2011 Mar;31(3):332. [PMID: 21361742]