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Stevens-Johnson syndrome with overlapping features of DRESS syndrome: A report of two cases

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Abstract

Stevens-Johnson syndrome and drug reaction with eosinophilia and systemic symptoms are severe cutaneous adverse reactions to drugs that are generally considered distinct entities. In addition to identifying the offending medication, distinguishing between these diagnoses is important, as they have differing treatment regimens and prognoses. Distinction between severe cutaneous adverse reactions, particularly in the early stages of disease, can be difficult, and overlapping conditions have been reported in the literature. We present two cases of severe cutaneous adverse reaction, one following initiation of carbamazepine and the other lamotrigine, with extensive mucosal involvement and epidermal detachment, initially diagnosed as Stevens-Johnson syndrome. Despite the use of cyclosporine and repeated doses of etanercept, both cases evolved to have significant edema of the face and extremities, palmar and plantar involvement, and rapid response to systemic corticosteroids, which is more in-keeping with drug reaction with eosinophilia and systemic symptoms. We aim to help clinicians gain awareness of Stevens-Johnson syndrome/drug reaction with eosinophilia and systemic symptoms overlap which may aid diagnosis and guide treatment.

Keywords

Stevens-Johnson syndrome, SJS, toxic epidermal necrolysis, TEN, drug rash with eosinophilia and systemic symptoms, DRESS

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Introduction

Stevens-Johnson syndrome (SJS) and Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) are severe cutaneous adverse drug reactions (SCARs) that are generally considered distinct entities. In addition to identifying the offending medication, distinguishing between SCARs is important, as these drug eruptions have different treatments and prognoses.

Distinction between SCARs, particularly in the early stages, may be difficult and few overlapping conditions have been reported.[1–3] We present two cases of SCAR in which patients diagnosed with SJS had an atypical clinical course, demonstrating some clinical features consistent with DRESS.

Case report

Case 1

A 46-year-old woman presented with a 1-day history of bilateral periorbital edema, conjunctival injection, oral erosions, mild facial edema, and vulvar vesicles. She progressed over the next several hours, developing a pruritic, erythematous morbilliform eruption on the trunk with a positive Nikolsky sign as well as worsening oral erosions. She was afebrile with neither lymphadenopathy nor eosinophilia. The patient was started on carbamazepine 32 days prior and was diagnosed clinically as having early SJS with a severity-of-illness score for toxic epidermal necrosis (SCORTEN) of 1. She did not meet the Registry of Severe Cutaneous Adverse Reactions (RegiSCAR) criteria for DRESS.

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Over the next 2 days, the patient's morbilliform eruption progressed to affect the entire body including extensive involvement of the palms and soles without target lesions. She also had a progression of her mucosal involvement with worsening bilateral conjunctivitis and periorbital swelling, odynophagia, dysphagia, erosions, and ulcerations of the oropharynx and vulvovaginal regions.

The patient's infectious workup was negative. Skin biopsy was consistent with an erythema multiforme-like reaction or early SJS with vacuolar interface dermatitis, basal cell hydropic degeneration, and apoptotic keratinocytes, mild dermal perivascular lymphocytic infiltrate, and rare eosinophils.

After receiving etanercept 50 mg subcutaneously once as well as 2 days of oral cyclosporine 5 mg/kg/day with continued clinical worsening, her cyclosporine dose was increased to 2.3 mg/kg/day intravenously, and she was given a second dose of etanercept. After a further 3 days of treatment, cyclosporine was discontinued and she was switched to methylprednisolone 1 mg/kg/day intravenously. Rapid clinical improvement was noted and after 3 days of IV methylprednisolone, she was switched to an oral prednisone taper. The patient was closely followed by ophthalmology, otolaryngology, and gynecology for site-specific treatments, including amniotic membrane replacement for severe ocular involvement.

Case 2

A 22-year-old woman presented with a 1-day history of periorbital and new-onset lip swelling with tender oral erosions, conjunctival injection, eye pain, and a morbilliform eruption on the body, particularly affecting the face and hands, including pseudo-vesicular papules on the palms. She was febrile with no lymphadenopathy. The patient had started lamotrigine 21 days prior to her presentation. The differential diagnosis of her presentation included a viral eruption versus early SJS with a SCORTEN of 0. The patient's infectious workup was negative. Skin biopsy was not performed.

On day 1 she received etanercept 50 mg subcutaneously and oral cyclosporine 5 mg/kg/day. Her condition worsened with further skin lesions on the face, back, chest, hands, and feet. Nikolsky was positive and there was prominent oral involvement with lip swelling and erosions on the buccal mucosa and tongue. She received intravenous immunoglobulin 2 g/kg on day 2 and oral cyclosporine 5 mg/kg on days 2 and 3. On day 4, she had decreased oral intake due to epiglottic pain and more widespread skin lesions with worsening facial swelling. She was given another dose of etanercept, 50 mg subcutaneous, and her cyclosporine was switched to liquid form, 1.5 mL PO twice daily (6 mg/kg/day). On day 5, enlarged lymph nodes >1 cm were noted in the cervical chain. Cyclosporine was discontinued and IV methylprednisolone was administered on day 5 (2.5 mg/kg; 125 mg) with marked improvement in facial swelling and skin pain and further doses were given on days 8 and 9 (2 mg/kg; 100 mg) with a switch to oral prednisone taper on day 10 with continued clinical improvement. The patient received an amniotic membrane transplant and was treated for erosive vulvar involvement with topical clobetasol and sitz baths. She never had increased eosinophils.

Clinical images for clinical comparison of both cases can be seen in Figure 1.

Discussion

There are significant implications for the correct identification of a SCAR; the impact of a diagnosis of SJS/toxic epidermal necrolysis (TEN) is notably different than a diagnosis of DRESS, with differing first-line therapies. Though DRESS can have several longer-term, predominantly autoimmune sequelae, SJS/TEN nearly always has long-term sequelae. SJS has a significantly higher mortality rate ranging from 20% to 25%,[4] compared to a 5% mortality typically associated with DRESS.[1,4] However, rare cases with overlapping classical features of more than one SCAR can arise, making definitive diagnosis difficult.[1,4]

There have been few case reports of confirmed overlapping SCARs, particularly overlapping DRESS/SJS in the literature.[1–4] The pathophysiology of overlapping SCAR phenotypes is unclear. Both SJS/TEN and DRESS are considered type IV hypersensitivity reactions mediated by T-cells. CD8 cytotoxic T-cells predominate in SJS/TEN with dominant cytokines, including perforin/granzyme, Fas-ligand (Fas-L), and tumor necrosis factor (TNF)-alpha, whereas DRESS typically involves CD4 cells with cytokines including eotaxin and IL5.[4,5] It is postulated that there can be overlaps or combinations of T-cell activation, explaining ambiguities and overlapping clinical features in SCARs.[4,5]

Both patients initially presented with significant mucosal involvement as well as epidermal detachment, leading to a clinical diagnosis of SJS, with anticonvulsant triggers. However, both patients evolved to develop atypical clinical courses for SJS with features classically associated with DRESS including significant edema of the face, extensive palmar and plantar involvement, limited improvement on cyclosporine and repeated doses of etanercept, and improved response on systemic corticosteroids. Though neither patient fulfilled RegiSCAR criteria for "probable" or "definite" diagnoses of DRESS, both patients had overlapping phenotypical features of SJS and DRESS, impacting treatment selection. In both cases, the treatment center's standard of care for SJS/TEN was initiated upon presentation, with several days of cyclosporine and etanercept tried and unsuccessful in managing their mucocutaneous eruptions. It is unknown, but likely recommended, to assess for autoimmune sequelae, such as thyroiditis, in these overlap cases.

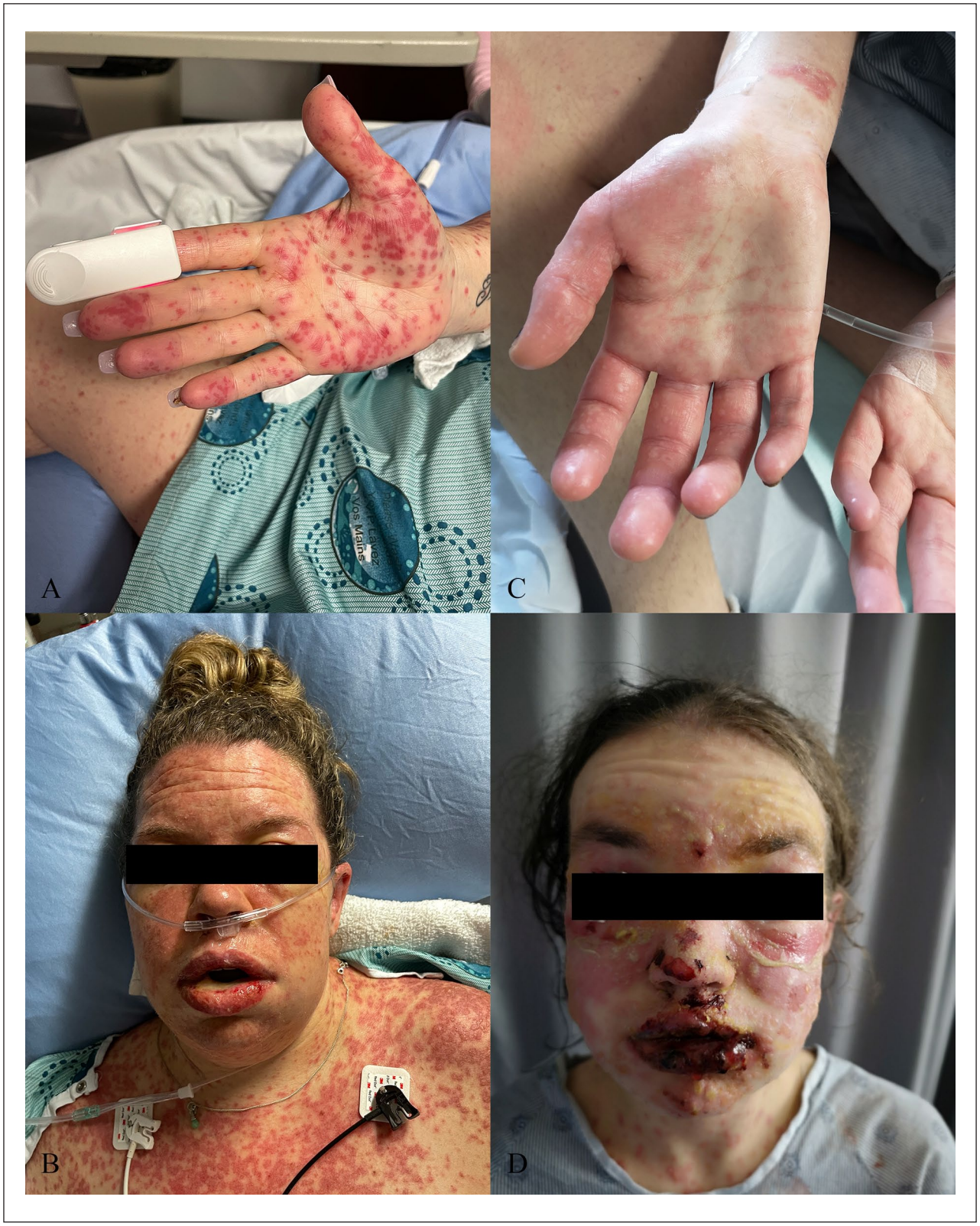

Figure 1. Case comparison of two cases with overlapping features of Stevens-Johnson syndrome and drug reaction with eosinophilia and systemic symptoms. (a) Case 1 palmar lesions; (b) Case 1 facial swelling and oral mucosal involvement; (c) Case 2 palmar lesions; (d) Case 2 facial swelling and oral mucosal involvement.

SJS with clinical features of DRESS syndrome is an uncommon and poorly understood entity. By reviewing these cases, we aim to expand the literature on overlapping DRESS/SJS to help clinicians gain awareness of this entity which may aid in diagnosis and guide treatment options. Our cases suggest that corticosteroids may be the treatment of choice if features of DRESS become evident.

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Patient consent

The authors obtained written consent from patients for their photographs and medical information to be published in print and online with the understanding that this information may be publicly available. Patient consent forms were not provided to the journal but were retained by the authors.

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