

## CLINICAL VIGNETTE

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# Carbamazepine-induced DRESS Syndrome

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A 63-year-old male with history of trigeminal neuralgia presented to the Emergency Department (ED) for a diffuse rash. He was in his usual state of health until 2 months prior to presentation when he noted onset of a rash over his left flank. Over the next few weeks the rash spread to his abdomen, arms, neck and face. The rash was erythematous and intensely pruritic. He reports that around that time, he had begun taking carbamazepine for trigeminal neuralgia. He had been previously evaluated for his rash and treated with oral diphenhydramine, and topical clotrimazole. At that visit he reported his trigeminal neuralgia symptoms persisted, and his carbamazepine dose was increased from 200mg daily to 600mg daily. His rash worsened over 10 days, so he presented to the emergency department where he was given IV diphenhydramine and oral loratadine. Labs revealed mild leukopenia at 3.8k/uL with 12.6% eosinophils and an erythrocyte sedimentation rate (ESR) of 38mm/hour. His symptoms transiently improved, so he was discharged home. After ED discharge his rash gradually worsened and spread to his face, so he returned to the emergency department four days later.

On repeat presentation to the ED, the patient had temperature of 38.2°C, pulse 112 beats/min, blood pressure, 135/86 mmHg, respirations 20 breaths/min, and oxygen saturation 98% on room air. There was generalized erythroderma and desquamation of skin overlying head, face, back, arms, and legs. There was also posterior auricular lymphadenopathy and periorbital and peripheral edema. Laboratory analysis revealed a normal white blood cell count of 5.68 k/uL, with 34% eosinophils, ALT and AST were mildly elevated at 60 U/L and 44 U/L respectively. Carbamazepine was discontinued, and the patient was started on IV methylprednisolone and IV diphenhydramine. Dermatology was consulted, and they recommended adding topical 1% triamcinolone wraps. The patient was admitted to the Internal Medicine service for carbamazepine-induced DRESS syndrome.

During hospitalization his rash and pruritus improved, and his eosinophils normalized. Labs eventually revealed human herpes virus-6 IgG positivity. He was discharged home on oral prednisone for DRESS syndrome and gabapentin for his trigeminal neuralgia. He was told to avoid carbamazepine in the future. On follow up two months after discharge, his symptoms had completely resolved.

### *Discussion*

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome is a rare, potentially fatal, type IV hypersensitivity reaction that involves a widespread skin eruption, characteristic hematologic abnormalities, and visceral involvement.<sup>1,2</sup> Medications most commonly associated in this condition include anti-epileptics (carbamazepine, phenytoin, phenobarbital and lamotrigine), allopurinol, dapsone, sulfasalazine, and non-steroidal anti-inflammatories.<sup>3,4</sup> The pathogenesis of DRESS syndrome is thought to involve both a drug-induced T-cell-mediated immune response<sup>5</sup> and reactivation of latent herpes virus infections (HHV-6, HHV-7, EBV, CMV).<sup>6</sup>

The symptoms of DRESS syndrome often begin within two to six weeks after initiation of the causative medication. Early presentation commonly includes fever, malaise, and skin eruption.<sup>1,7</sup> The skin eruption typically begins as a morbilliform rash on the face and upper extremities.<sup>8</sup> The rash is commonly accompanied by lymphadenopathy and facial edema.<sup>8</sup> In most cases, the rash progresses to a diffuse, confluent erythema, involving over 50% of the total body surface area (BSA).<sup>8</sup> Laboratory findings often include leukocytosis with increased eosinophil and atypical lymphocyte counts, elevated serum markers of inflammation, and evidence of internal organ involvement. Systemic symptoms can include diffuse painful lymphadenopathy and fatigue. Other symptoms depend largely on the affected internal organs.<sup>3</sup> The most commonly involved organ is the liver in up to 60-90% of cases.<sup>9,10</sup> Liver involvement often presents as a mild and transient elevation of ALT, but rarely, acute liver failure and severe hepatitis can occur.<sup>11</sup> Other visceral manifestations include renal involvement presenting as interstitial nephritis,<sup>12,13</sup> pulmonary involvement presenting with nonspecific cough and dyspnea,<sup>14</sup> and cardiac involvement presenting as eosinophilic myocarditis or pericarditis.<sup>3,15</sup>

DRESS syndrome should be suspected in a patient with skin eruption with a history of new drug exposure in the previous two to six weeks. Laboratory investigations should include complete blood cell count (CBC) with differential, peripheral blood smear, liver function tests (LFTs), and testing for herpesvirus infection.<sup>2,3</sup> The findings of peripheral eosinophilia >700/microL on CBC, atypical lymphocytes on peripheral smear, increased alanine aminotransferase and/or

alkaline phosphatase on LFTs, and positive herpesvirus infection all support the diagnosis of DRESS syndrome.<sup>2</sup> Skin biopsy can also be used to support the diagnosis of DRESS and rule out other causes of cutaneous eruptions.<sup>16</sup>

Given the potentially life-threatening nature of DRESS syndrome, most patients are hospitalized for treatment.<sup>17</sup> Immediate cessation of the offending drug is the mainstay of treatment.<sup>17</sup> Additionally, it is currently recommended that patients receive high or super high potency topical corticosteroids for symptomatic relief of pruritus and cutaneous inflammation.<sup>18,19</sup> Patients may also require fluid, electrolyte, and nutritional support, wet dressings and emollients.<sup>17</sup> Internal organ involvement, if present, is treated with high-dose systemic corticosteroids.<sup>12</sup> Most patients recover completely after weeks or months of treatment.<sup>20</sup>

This case highlights the importance of maintaining DRESS syndrome in the critical differential diagnosis of any diffuse rash, especially with erythroderma. All unexplained rashes warrant a close review of possible offending medications, and when eosinophilia is present the patient should be specifically evaluated for DRESS syndrome.

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Submitted May 23, 2019