INTERNAL MEDICINE

□ CASE REPORT □

# DRESS Syndrome with Cerebral Vasculitis

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## Abstract

DRESS (drug rash with eosinophilia and systemic symptoms) syndrome is a severe reaction triggered by drugs that manifests as pyrexia and eosinophilia with involvement of the skin and internal organs. We herein describe the case of a patient who developed hyperuricemia after receiving treatment for tuberculosis, then took allpurinol and developed DRESS syndrome with a contextual coma and right hemisyndrome. This report describes for the first time the presence of vasculitic cerebral involvement in a patient with DRESS syndrome. The cerebral vasculitis responded to treatment, showing clinical and instrumental remission. In cases such as this, allergic cerebral vasculitis should be considered in the differential diagnosis because it can be treated if recognized early, thus leading to remission without the development of any sequelae.

**Key words:** DRESS, vasculitis, allopurinol, cerebral involvement

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## Introduction

DRESS (drug rash with eosinophilia and systemic symptoms) syndrome, also called drug-induced hypersensitivity syndrome (DiHS), is an acute drug reaction that is estimated to occur in 1/1,000-10,000 drug exposures. It presents with a cutaneous rash caused by leukocytoclastic vasculitis, fever, hypereosinophilia and multiorgan involvement, including the lymph nodes, kidneys, lungs, heart and liver (1-3).

The signs and symptoms usually begin two to six weeks after therapy onset (4).

The pathogenesis is not completely understood. There is evidence that increased formation of free radicals alters detoxification pathways in association with the subsequent activation of aberrant immunological processes (5).

Many drugs are associated with the development of this acute reaction, including anticonvulsants (carbamazepine, phenytoin, phenobarbital), minocycline, allopurinol, dapsone, abacavir and nevirapine. Some drugs generate typical clinical pictures in preferential target organs. For example, liver involvement is frequently observed in patients with DRESS caused by phenytoin, while allopurinol often causes nephritis (6). To our knowledge, cerebral vasculitic reactions associated with DRESS syndrome have never been reported.

## Case Report

We herein describe the case of a 31-year-old Caucasian man admitted to our Division for drowsiness, fever, right hemiplegia and a diffuse skin rash. During the previous month, he had been diagnosed as having pulmonary tuberculosis and began treatment with rifampicin, isoniazid, ethambutol and pyrazinamide. Hyperuricemia appeared after one month; therefore, allopurinol was prescribed. After two weeks, widespread erythroderma and hyperpyrexia (39.3℃) without chills appeared. For this reason, the patient was admitted to our Division, where common viral and bacterial infections were ruled out. During hospitalization, the patient developed worsening of his clinical status with coma and right hemisyndrome with marked pyramidal signs and gaze palsy to the right. At the same time, hot and widespread erythroderma appeared with extensive infiltration and an "orange peel" appearance. The findings of heart, pulmonary and abdominal examinations were normal. The axillary, inguinal and laterocervical lymph nodes were enlarged. On neurological examination, the patient exhibited drowsiness with responses to pain, weakness of the upper and lower right limbs with Babinski's sign, hyperreflexia with extension of reflexes and gaze palsy to the right. On blood tests,

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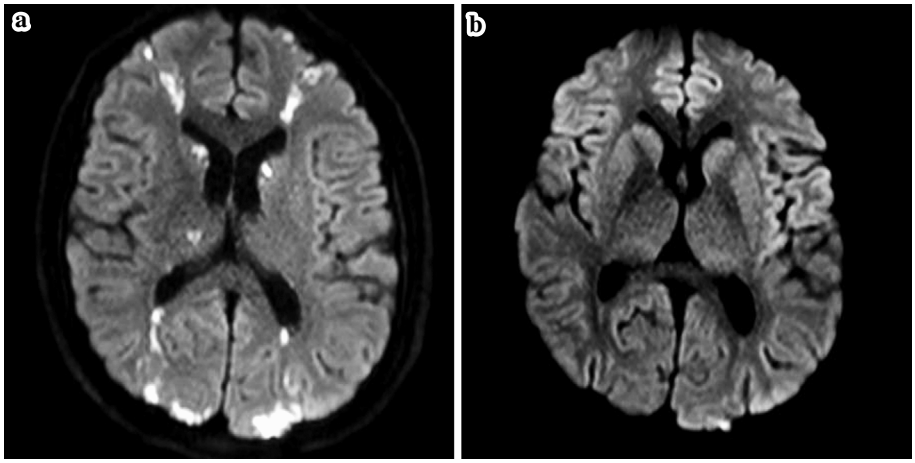


**Figure.** **a. Numerous small areas of altered signals were visible in the following regions: left corti-co-subcortical occipital-parietal, right posterior parietal, temporal, bilateral, bilateral caudate, right thalamic, right frontobasal, bilateral frontal convexity and anterior and in both semi-oval centers. Most of the lesions were distributed not only in the vascular territories of the border, but also in the posterior circulation, the middle cerebral and right anterior cerebral arteries and at the level of the perforating branches. In large part, these changes were already visible on FLAIR images. b. The vasculitic lesions were significantly reduced and appear to be fully resolved.**

the white blood count (WBC) was increased (24,929/μL) with an increased neutrophil count of 16,700/μL and an eosinophil count of 4,000/μL. The patient's renal function and electrolytes were in the normal ranges, although cholestatic hepatitis was present (AST: 43 U/L, ALT: 183 U/L, GGT: 392 U/L, ALP: 715 U/L). PCR tests of viral DNA (HHV6, Epstein-Barr virus, HHV7 and cytomegalovirus) were negative. The patient underwent a brain magnetic resonance (MR) scan, which demonstrated the presence of many supratentorial lesions that were hypointense on T1-weighted images and hyperintense on T2-weighted images. Fluid attenuated inversion recovery (FLAIR)-weighted sequences showed contrast enhancement from 1 mm to 2 cm with diffuse cortical, subcortical and white matter involvement (Figure a). Therefore, the lesions were suggestive of cerebral vasculitis. The clinical manifestations were very severe (plegia and coma), and the presence of vasculitic lesions on MR (which did not show typical caliber changes in the distal branches of the circle of Willis) excluded a diagnosis of reversible cerebral vasoconstriction syndrome (7). Allopurinol was discontinued, and high-dose steroid therapy with methylprednisolone at a dose of 1 g IV was administered for five days, then tapered and administered orally. Rapid resolution of the patient's neurological impairment and erythroderma was observed with normalization of the eosinophil count. MR imaging of the brain repeated after three months showed complete resolution of the vasculitic lesions (Figure b). After complete steroid discontinuation, patch and skin prick tests were performed to identify the drug that had triggered the allergic reaction, and a reaction to allopurinol was detected. Following the acute phase of the illness, the anti-tuberculosis therapy was reintroduced with no allergic reactions.

The definitive diagnosis was DRESS (the RegiSCAR and Japanese consensus group criteria were satisfied) with brain vasculitic involvement triggered by allopurinol.

## Conclusion

The clinical picture suggested DRESS syndrome triggered by allopurinol. In addition to the typical manifestations of this condition, we observed vasculitic-like cerebral involvement with acute and life-threatening neurological distress. Therefore, we identified a new possible target for DRESS multiorgan involvement that was reversible with prompt delivery of high-dose steroid therapy.

This case is important because the eventual possibility of neurological acute disability due to cerebral vasculitis must be considered in patients with DRESS syndrome since it can be reversed completely with timely treatment.

**Established Facts:**

DRESS syndrome is a systemic allergic reaction triggered by drugs that can affect the skin, lungs, kidneys, liver, lungs, heart and lymph nodes.

**Novel Insights:**

DRESS syndrome may involve the brain, manifesting as acute and severe symptoms such as coma and emisidrome hemisyndrome that resolve the same time as other manifestations of the disease if treated appropriately.

**The authors state that they have no Conflict of Interest (COI).**

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