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# Double trouble: a case of DRESS syndrome induced by lamotrigine and subsequent skin reaction to levetiracetam

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**Double trouble: a case of DRESS syndrome induced by lamotrigine and subsequent skin reaction to levetiracetam**

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A 21-year-old female, diagnosed with epilepsy and well-controlled type 1 diabetes mellitus, was admitted to the Department of Rheumatology and Immunology, University Hospital in Krakow due to a severe, pruritic maculo-papular rash covering more than 50% of her skin for the past two days (Figure 1A–C) and a week-long fever reaching up to 39 degrees Celsius. Further examination revealed enlarged submandibular and cervical lymph nodes. In her medical history, lamotrigine was initiated two weeks ago following two recent tonic-clonic seizures, in addition to the previously used valproate (VPA). Laboratory tests revealed: white blood cells (WBC) 8380/uL (reference range (RR): 4000–10000/uL), eosinophils 440/uL (RR: 40–450/uL), alanine aminotransferase (ALT) 37 U/I (RR: 10–35 U/I), aspartate aminotransferase (AST) 35 U/I (RR: 10–35 U/I), ammonia 32.0 umol/L (RR: 11–51 umol/L), N-terminal pro-B-type natriuretic peptide (NT-proBNP) 245 pg/mL (RR: <125 pg/mL) and

C-reactive protein (CRP) 2.81 mg/L (RR: < 5 mg/L). The electrocardiogram showed normal results. Infections with hepatitis B and C viruses, cytomegalovirus, Epstein–Barr virus, and HIV were ruled out. Initially, methylprednisolone (1 mg/kg/day) and rupatadine (10 mg twice daily) were administered, resulting in a gradual improvement in skin lesions. However, from the third day of hospitalization, laboratory tests showed signs of acute hepatic injury (ALT 1046 U/I, AST 907 U/I, ammonia 103 umol/L), leukocytosis (WBC 14850/uL) with elevated percentage of atypical lymphocytes in peripheral smear, and an increase in NT-proBNP to 870 pg/mL. Unfortunately, the exact eosinophil level has not been evaluated due to the presence of atypical lymphocytes, which interfered with the results. Despite the lack of skin biopsy, the diagnosis of drug reaction with eosinophilia and systemic symptoms (DRESS) was established based on the clinical presentation and the results of tests, including the Registry of Severe Cutaneous Adverse Reactions scoring system. Rupatadine was continued, while the methylprednisolone dose was increased to 250 mg intravenously for 4 consecutive days, cyclosporine was initiated at a dose of 4 mg/kg/day. Additionally, hepatoprotective and encephaloprotective treatments were administered. Upon normalization of liver parameters and regression of skin lesions, the patient was discharged home. Unfortunately, 6 days later, the patient was readmitted to the hospital due to the recurrence of a fine-spotted rash covering more than 50% of the skin and a deterioration in well-being despite no reduction in the daily dose of methylprednisolone. Blood tests revealed ALT at 97 U/I, WBC at 12510 /uL, eosinophils at 400 /uL, CRP <1 mg/L. After a neurological consultation, a skin reaction to levetiracetam was diagnosed, and epilepsy treatment was continued with VPA alone. The use of rupatadine, methylprednisolone at a dose of 32 mg with subsequent gradual tapering to discontinuation over the course of one month from discharge, and cyclosporine was also sustained. In the follow-up, laboratory results normalized, and skin changes resolved 1.5 months after discharge from the hospital.

DRESS syndrome is a severe adverse drug reaction characterized by a rash, accompanied by high fever, eosinophilia, and involvement of organs, primarily affecting the liver, heart, lungs, and kidneys [1, 2]. Multiple organ failure, hepatic necrosis, shock, pulmonary hemorrhage and sepsis are the primary predictor of mortality, with a rate that can reach up to 20% [2, 3] The latency phase typically spans 2 to 8 weeks [4]. Roughly 75% of cases are attributed to high-risk drugs, including antiepileptic agents like lamotrigine [5]. Treatment includes discontinuing the medication causing DRESS syndrome, initiating systemic glucocorticoids, cyclosporine, intravenous immunoglobulins, and plasmapheresis [2, 5].

**Article information**

**Conflict of interest** None declared.



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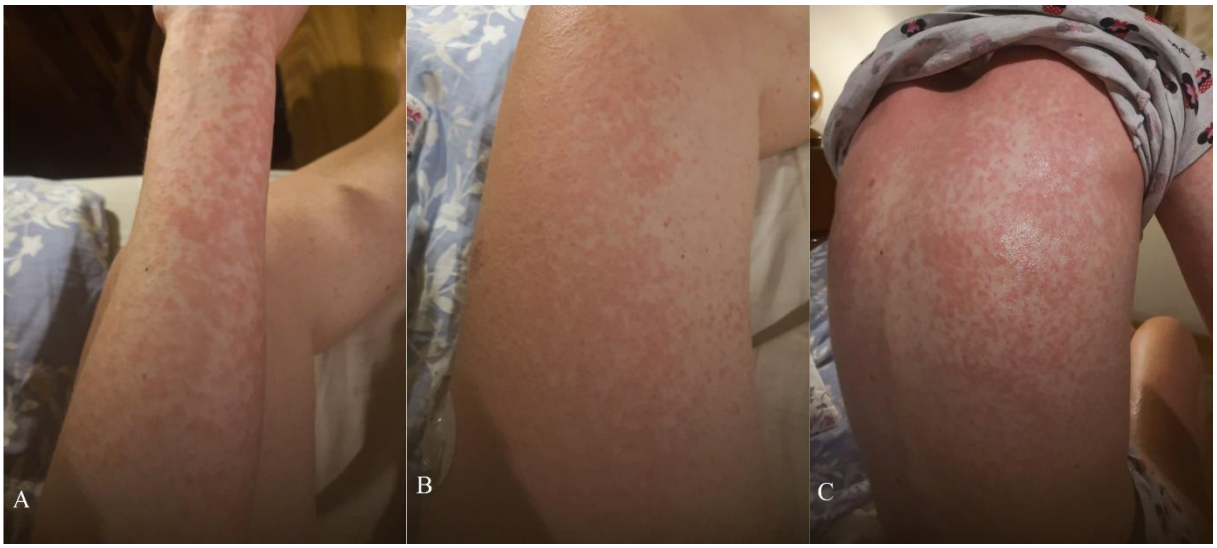


**Figure 1** A – A pruritic maculo-papular rash on the left forearm; B – a pruritic maculo-papular of the left thigh; C – a pruritic maculo-papular rash on the back

**Short title:** DRESS induced by lamotrigine and skin reaction to levetiracetam