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LETTER TO THE EDITOR

DRUG RASH WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS INDUCED BY LAMOTRIGINE THERAPY

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Dear Editor,

Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) is characterized by skin rash, fever, lymph node enlargement and internal organ involvement (e.g. hepatitis, myocarditis, interstitial nephritis, interstitial pneumonitis), eosinophilia and leucocytosis (1-3).

DRESS may be induced especially by aromatic anticonvulsants (e.g. carbamazepine, phenobarbital, hydantoin) and valproic acid, antibiotics (e.g. isoniazid, minocycline) and sulfonamides, although other drugs are implicated as immunosuppressors (e.g. azathioprine and cyclosporine), several antiretroviral agents (e.g. abacavir and nevirapine), diuretics and antihypertensive drugs (e.g. captopril, hydrochlorothiazide and spironolactone) and others (e.g. terbinafine, dapsone, ranitidine, thalidomide, ibuprofen, gold salts, D-penicillamine, sulfasalazine and allopurinol) (4-8).

Recently DRESS has been attributed to the oral skin-care supplement Imedeen (9). An association between 1) human herpes virus (HHV-6) active infection (primo-infection or reactivation) and 2) a DRESS like syndrome due to ceftriaxone have been reported (10-12).

We report the case of a girl of 4 years and 9 months (height 105 cm, body weight 13.5 Kg) affected by Mitochondrial Encephalomyopathy, Lactic Acidosis, Stroke-like episodes (MELAS) (OMIM#540000), who developed skin rash, fever, lymph node enlargement, elevated serum aspartate aminotransferase (AST) levels, eosinophilia and leucocytosis after lamotrigine (LTG) therapy.

The patient was taking several drugs for MELAS treatment: L-carnitine (1000 mg twice a day orally), coenzyme Q10 (25 mg twice a day orally) and L-arginine (500 mg four times a day orally) while furosemide (20 mg twice a day orally), and carvedilol (6.25 mg twice a day orally) were administered for the treatment of MELAS complications. LTG, that was shown to be effective as both add-on and monotherapy for typical absence seizures and generalized tonic–clonic seizures (13) was prescribed by a neurologist at the beginning of seizures which started 2 months and 15 days before admission to our hospital. Valproic acid, a first-choice drug that has been shown to be effective as monotherapy against generalized tonic–clonic seizures and myoclonic seizures (13) was not used because of the high risk of acute liver failure after exposure in mitochondrial diseases.

The patient started LTG at the dose of 5 mg/day and gradually, after 45 days, reached a dosage of 20 mg twice a day, with a reduction in frequency and severity of the seizures. After 4 weeks from the beginning of LTG therapy at the dosage of 20 mg twice a day, the

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patient was admitted to our hospital because of the appearance of: 1) fever (body temperature 40.5°C), 2) diffuse erythema which started on the chest and spread to the entire body within 15 hours, and 3) lymph node enlargement. A blood examination showed a leukocyte count of 19800/mL, an absolute eosinophil and monocyte count respectively of 1270/mL and 1146/mL, hemoglobin 10.6 g/dL, AST 98 UI/l (normal value < 40).

A blood examination performed 48 hours before the onset of symptoms during a routine control, showed a leukocyte count of 14.000/mL, an absolute value of eosinophils and monocytes respectively of 86/mL and 850/mL, hemoglobin 14.2 g/dL and AST 35 UI/l. LTG was suspected to be responsible for the clinical manifestations (fever, rash, lymph node enlargement) and the abnormal laboratory test results (eosinophilia, leucocytosis, > AST). LTG was therefore immediately discontinued and replaced with clobazam (12.5 mg/day orally divided into three doses every 8 hours, each of 5 mg, 2.5 mg and 5 mg) while the other drugs were not discontinued and a treatment with betamethasone was started (0.5 mg every 8 hours with a total of 3 administrations orally). Within 36 hours the eosinophil and leucocyte count declined respectively to 47/mL and 13000/mL, AST to 36 UI/l, the rash cleared without exfoliation and fever and lymph node enlargement disappeared.

The diagnosis of DRESS, without apparent multi-organ involvement, was supported by: 1) the appearance of fever, rash, lymph node enlargement, increased levels of AST, eosinophils and leucocytes after 6 weeks of LTG treatment; 2) disappearance of fever, rash and lymph node enlargement and normalization of laboratory data within 36 hours of LTG suspension. The prompt cessation of LTG treatment immediately (24 hours) after the appearance of fever, rash, lymph node enlargement, eosinophilia and > AST may explain why multi-organ involvement did not occur in this patient.

LTG may induce serious rashes in patients who assume this drug, including Stevens-Johnson syndrome and rash-related death, but the present is, to our knowledge, the first report of DRESS in a child treated with LTG.

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