SHORT COMMUNICATION

What is This Rash?

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A 25-year-old man presented with generalized pruritic rash, fever, sore throat, facial and glandular swelling, right upper quadrant pain, anorexia, and nausea for 3 days. The rash initially erupted on his upper chest, spreading to his face and extremities over 24 h. A month prior he had experienced new-onset seizures, initially prescribed phenytoin 300 mg daily. Two weeks before presenting, phenytoin was discontinued and topiramate (100 mg bid) started. On exam, he appeared mildly ill. Diffuse, blanching, erythematous papules, and fine petechiae covered his face and body, sparing his palms and soles. There was mild facial edema and superficial erosions on his hard palate and mucosa of the lower lip (Fig. 1a, b, c), with tender cervical lymphadenopathy most prominent posteriorly. Labs were notable for WBC 27 K/mm³ (18 % atypical lymphocytes and 9 % eosinophils); PLT 139 K/mm³; liver function tests (LFTs) AST 168 IU/L, ALT 350 IU/L, total bilirubin 4.2 mg/dL (direct 2.9 mg/dL); and urinalysis positive for blood.

These findings were most consistent with DRESS (drug rash with eosinophilia and systemic symptoms). The suspected exposure was phenytoin. The onset of symptoms 1 month after exposure fits the 2- to 8-week delay characteristic of DRESS. Phenytoin is a known culprit [1]. There is scant evidence for topiramate-related DRESS, and published cases all involved other agents associated with DRESS. Since topiramate could not be excluded, it was discontinued and the patient started on levetiracetam. He was given oral corticosteroids and admitted. Biopsy demonstrated morbilliform drug eruption, typical of

DRESS. Hepatitis, measles, EBV, CMV, HIV, and toxoplasmosis were excluded. ANA and cultures were negative. The rash

Fig. 1 A 25-year-old man with generalized rash, glandular and facial swelling, and superficial erosions on his hard palate and mucosa of the lower lip

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persisted but other symptoms improved, including LFTs. He was discharged after 3 days on 60 mg prednisone daily. Three days later, his LFTs had risen again (AST 317 IU/L, ALT 1035 IU/L). He was re-admitted, treated with 12 h of n-acetylcysteine (NAC), and corticosteroids. His LFTs normalized over 1 month. His rash did not resolve until 5 weeks from onset.

DRESS has an incidence of 1:1000 to 1:10,000 exposures. Many aromatic anticonvulsants (phenytoin, carbamazepine, phenobarbital), sulfonamides, and allopurinol are associated with DRESS. The RegiSCAR scoring system classifies the likelihood of DRESS based on the presence of three or more of the following: rash, fever ≥ 38 °C, lymphadenopathy in at least two sites, serologic abnormalities (eosinophilia, atypical lymphocytes, thrombocytopenia), and involvement of at least one organ [2]. Additional suggestive features include duration of rash ≥ 15 days and absence of other causes (i.e., viral hepatitis, mycoplasma, chlamydia, bacteremia, or autoimmune disease). DRESS can be challenging diagnostically since it may occur weeks to months after exposure, and patient's presentation may be consistent with other systemic disorders. The exact pathogenesis of DRESS is unknown. Hypotheses include production of reactive metabolites during drug metabolism (i.e., immunologic responses to abnormal detoxification of arene oxide molecules) and reactivation of herpesviruses (i.e., CMV, EBV, human HHV-6/7). Therapy involves withdrawal of the drug, supportive care, and usually corticosteroids. More serious cases, involving exfoliative dermatitis or severe end-organ damage, require management in an ICU, with possible liver transplant for acute liver failure (ALF). There are reports of treatment with NAC in patients with hepatic injury. Theoretical benefits include inhibition of

hypersensitivity immune response and increased glutathione, involved in the detoxification of several anticonvulsants [3]. Other suggested therapies include plasma exchange, IVIG, and valganciclovir. DRESS carries a 10 % mortality rate, typically from ALF [4]. Early recognition is critical, and DRESS must be considered in patients with morbilliform rash and systemic systems in the setting of exposure. Quality data is required to determine the benefit of treatments, including corticosteroids.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no competing interests.

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