OBSERVATIONS

Fulminant Type 1 Diabetes in the Course of Drug Reaction With Eosinophilia and Systemic Symptoms (DRESS) Syndrome

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DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms) syndrome is a life-threatening drug reaction. Its management relies on discontinuation of the culprit drug and treatment with corticosteroids (1).

A 68-year-old Filipino woman was admitted for ketoacidosis (DKA), revealing diabetes. Four months before admission, she had been treated for bronchitis with erythromycin, then moxifloxacin. A transient skin rash occurred. Six days before admission, she was treated with amoxicillin/clavulanic acid for recurrence of bronchitis, and fever and a pruritic skin rash occurred. Four days later, the patient was admitted for drowsiness, tachypnea, and vomiting. She reported no abdominal pain, no weight loss (BMI 20.3 kg/m^2), and no polyuria. Physical examination disclosed facial erythema, palpebral edema, conjunctivitis, generalized maculopapular skin rash, cheilitis, and diffuse lymph node enlargement. Plasma glucose was 31 mmol/L, ketonuria was 4+, plasma bicarbonate was 4.9 mmol/L, and arterial pH was 7.18, leading to the diagnosis of DKA. Liver enzyme concentrations were increased. Serum lipase was normal. HbA_{1c} was 7.9%. The patient recovered within 24 h with treatment with intravenous fluids, insulin, and potassium replacement. Then, good glucose control was obtained with subcutaneous insulin therapy (1.0 IU $\cdot$ kg^{-1} $\cdot$ d^{-1}). On day 3, eosinophilia (1.0 $\cdot$ 10^9/L) was noticed. A mild dyspnea with bilateral crackles, and an increase in *N*-terminal pro-brain natriuretic peptide (1,602 ng/L, $N < 300$) suggested left ventricular dysfunction, that resumed within 2 days. Thereafter, all abnormalities resolved spontaneously except for insulin-requiring diabetes. The diagnosis of definite DRESS syndrome was established (1). Serological tests for hepatitis B and C, human immunodeficiency virus, cytomegalovirus, Epstein-Barr virus, and PCR tests for herpes simplex virus-1 and -2 and for herpes virus 6 (HHV-6) were negative. Antibodies to glutamic acid decarboxylase, islet antigen-2, and zinc transporter 8 were not found. Plasma C-peptide was undetectable.

In patients with DRESS syndrome, diabetes has been described in 11 individual cases, revealed by DKA in 7. In half the cases, as in ours, presentation was consistent with nonautoimmune fulminant type 1 diabetes (FT1D) (2). In all patients, C-peptide was undetectable, including those with autoimmune diabetes, indicating that DRESS syndrome may induce complete β-cell destruction on various pathophysiological backgrounds. The frequency of DRESS-associated diabetes is not known. A recent Japanese survey of patients with DRESS syndrome showed a 0.54% prevalence of FT1D, much higher than in the general population (3). The frequency of autoimmune type 1 diabetes in patients with DRESS syndrome has not been assessed.

The pathogenesis of DRESS syndrome involves T lymphocyte and macrophage activation, and cytokine release that may damage multiple organs and might lead to the occurrence or to the acceleration of autoimmune diabetes (4). Concerning FT1D, it has been suggested that viral infections may trigger an immune reaction to infected β-cells, leading to their accelerated destruction (5). Indeed, reactivation of viral infections, such as HHV6, HHV7, cytomegalovirus, or Epstein-Barr virus, has been frequently reported in patients with DRESS syndrome (1).

Thus, DRESS syndrome may be complicated by the onset of diabetes, revealed by a glycemic crisis, and characterized by severe insulinopenia. Blood glucose concentrations should be carefully monitored in patients with DRESS syndrome.

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References

1. Cacoub P, Musette P, Descamps V, et al. The DRESS syndrome: a literature review. Am J Med 2011;124:588–597
2. Imagawa A, Hanafusa T. Fulminant type 1 diabetes—an important subtype in East Asia. Diabetes Metab Res Rev 2011;27:959–964
3. Onuma H, Tohyama M, Imagawa A, et al. High frequency of HLA B62 in fulminant type 1 diabetes with the drug-induced hypersensitivity syndrome. J Clin Endocrinol Metab 2012;97:E2277–E2281
4. Ben m'rad M, Leclerc-Mercier S, Blanche P, et al. Drug-induced hypersensitivity syndrome: clinical and biologic disease patterns in 24 patients. Medicine (Baltimore) 2009;88:131–140
5. Tanaka S, Nishida Y, Aida K, et al. Enterovirus infection, CXC chemokine ligand 10 (CXCL10), and CXCR3 circuit: a mechanism of accelerated beta-cell failure in fulminant type 1 diabetes. Diabetes 2009;58:2285–2291