

trimethoprim-sulfamethoxazol combination (co-trimoxazole). Sulfamethoxazol was not implicated in the reaction.

Our patient was a 27-year-old man with a personal history of Klinefelter's syndrome who was awaiting inguinal hernia surgery; therefore, we were asked to study allergy to anesthetics and other drugs. A year before, he had taken Bronquidiazina (co-trimoxazole) as treatment for respiratory infection (Bronquidiazina contains 80 mg,

trimethoprim and 400 mg sulfamethoxazol). Thirty minutes after oral intake of the first tablet, he

developed generalized erythema, maculopapular rash, pruritus, and tachycardia. These

An anaphylactic reaction after skin prick test with trimethoprim.

symptoms subsided within a few hours.

The patient was studied in our allergy department. Skin prick tests with trimethoprim (20 mg/ml) and sulfamethoxazol (20 mg/ml) were performed, resulting in a positive skin prick test to trimethoprim with a 38-mm wheal with pseudopods, as well as pruritus, sickness, and hypotension. The patient required treatment with epinephrine. The skin prick test with sulfamethoxazol was negative.

We carried out a histamine-release test with trimethoprim and sulfamethoxazol, using the automated fluorometric method of Siraganian and Hook, with the Autoanalyzer II of Technicom. This test was positive (maximum of 16%) with trimethoprim and negative with sulfamethoxazol.

Two controls did not react to any of these tests.

The clinical findings and the results of the studies performed in our patient indicated an IgE-mediated mechanism as the underlying cause of his reaction to trimethoprim.

Skin prick testing may be considered very safe. Since minor adverse reactions occur in a maximum of 0.49% of the tested patients, the risk of anaphylaxis is very low (1). An anaphylactic reaction to skin prick test with

trimethoprim indicates a patient highly sensitive to this drug.

From a clinical standpoint, our case stresses the importance of the *in vitro* tests in the diagnosis of drug allergy because they are safe. However, the sensitivity of these tests is low. To our knowledge, there are seven reported cases of immediate-hypersensitivity reactions to trimethoprim (2–5). All of them were investigated for specific IgE against trimethoprim, and only four showed positive RAST to this drug (2, 4, 5). The histamine-release test was also performed in three cases, with a negative result (3). We would like to highlight the importance of testing trimethoprim and sulfamethoxazol independently to try to identify the offending drug in the reaction, in order to determine the appropriate therapy, and because anaphylaxis to trimethoprim may be more common than previously thought.

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Suspected allergy to lamotrigine

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Key words: lamotrigine; serum sickness-like disease.

● LAMOTRIGINE is a novel antiepileptic drug, and its most frequently reported adverse events are central nervous system-associated side-effects and rash (1). We report a patient with serum sickness-like illness while on lamotrigine therapy. To our knowledge, an association of lamotrigine monotherapy with serum sickness-like illness has not been previously reported.

An 8-year-old boy with refractory atypical absence epilepsy was started on lamotrigine monotherapy with a dose of 1.2 mg/kg, as his sodium valproate therapy had been recently discontinued. Within 2 weeks, a full dose of 5 mg/kg was reached; he was taking no other medication. On day 25 of therapy, he felt unwell and was admitted to the emergency department with complaints of pruritic generalized urticarial rash, high fever, arthralgia, and myalgia. His examination revealed a fever of 39°C, and he had bilateral cervical, inguinal, and axillary multiple nontender lymphadenopathies, the largest being 4×3×3 cm at the left cervical region. He also had urticarial rash. He was hospitalized, and over the next 48 h, his fever of 39°C persisted and rash disseminated over the whole body. His left cervical lymphadenopathy enlarged to 6×5×5 cm. He did not have mucosal invasion, organomegaly, or arthritis. The laboratory tests were as follows: Hb 12 g/dl, white blood cells 6900/mm³, platelet count 260 000/mm³, differential count of peripheral blood cells – 60% neutrophils, 40% lymphocytes; IgM antibody titers of HSV-1, rubella, CMV, toxoplasmosis, EBV and Hb S antigens, anti-Hb c IgM, and HAV (IgM) were all negative. Complement 3 and 4 levels, erythrocyte sedimentation rate, and anteroposterior chest radiograph were all

within normal limits. Kidney and liver function tests were considered to be normal.

A tentative diagnosis of serum sickness-like illness due to lamotrigine was made, and intravenous methylprednisolone 1 mg/kg was started and lamotrigine gradually discontinued. On day 7 of methylprednisolone therapy, the rash faded and disappeared, and the fever subsided. After 2 weeks of hospitalization, the patient was discharged while on vigabatrin and valproic acid combination therapy. Twenty days later, he underwent placebo-controlled oral rechallenge at the clinic with a starting dose of 50 mg lamotrigine given in four divided doses. On day 1, he did not have any reaction. On day 2, after 2 h, the cumulative dose of 75 mg was reached, and he developed an increasing urticarial rash with pruritus of face, chest, hands, and legs. However, hypotension, angioedema, and wheezing did not develop. Since many drugs associated with serum sickness might

lead to the development of anaphylaxis, we immediately stopped the challenge.

The occurrence of urticarial rash, high fever, and generalized lymphadenopathy 3 weeks after the start of the lamotrigine therapy; the regression of the symptoms with discontinuation of the drug and with methylprednisolone therapy; and, finally, the dose-related rash observed during the challenge test proved that our patient had serum sickness-like disease induced by lamotrigine. Currently, nonprotein drugs appear to be the most common cause of serum sickness-like reactions (2). Recently, a 36-year-old epileptic man was reported, after lamotrigine 300 mg/day add-on therapy, to have severe hypersensitivity syndrome with febrile maculopapular exanthema, edema of the face, desquamation of the distal extremities, generalized lymphadenopathy, and hepatomegaly (3). He was treated with oral

corticosteroids, and later developed transient alopecia and onychodystrophy. The lymphocyte transformation test with lamotrigine was twice positive in this patient. Along with the patient with hypersensitivity defined above, our patient presents further conclusive proof of the severe hypersensitivity syndrome or serum sickness-like illness induced by lamotrigine, especially as monotherapy. Although the most common side-effect of lamotrigine is rash, close monitoring of such patients is necessary.

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Anaphylactic shock induced by intraurethral use of chlorhexidine

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Key words: anaphylactic shock; chlorhexidine; drug allergy; hypersensitivity.

● ALTHOUGH the antimicrobial properties of chlorhexidine gluconate are well known, few clinicians know that chlorhexidine has been associated with hypersensitivity reactions such as anaphylactic shock, a rare but life-threatening complication. As chlorhexidine is now widely used, the

reporting of a well-documented case of anaphylactic shock caused by this drug should be of interest to practicing physicians.

A 64-year-old man with a history of dysuria was scheduled for transurethral resection of the prostate (TURP). His medical history was remarkable for the presence of recurrent eczema of the face. One year before, he had experienced two episodes of malaise and macular rash during urethral dilation and cystoscopic examination performed under local anesthesia. A case of lidocaine hypersensitivity was suspected. Therefore, general anesthesia was preferred for TURP in order to avoid lidocaine use. Anesthesia was induced by propofol, and tracheal intubation was facilitated with vecuronium. Eighty minutes later, the patient developed macular rash with severe hypotension (systolic blood pressure: 70 mmHg). A hypersensitivity reaction was diagnosed, and the patient responded promptly to intravenous administration of epinephrine (1:1000, 1 ml), hydrocortisone (100 mg), and saline fluid. The patient was kept under observation for 2 days and made a complete recovery.

Blood analysis revealed a significant increase in tryptase concentration of 68.3 mg/l (reference level: <12.5 mg/l), reflecting activation of the mast cells. Other laboratory results were as follows: hematocrit 43.5%, white blood cell count 7470/μl (eosinophils 6%), platelets 239 000/μl, and total IgE antibodies 199 UI/ml (<100 UI/ml). As no lidocaine was used during TURP, a reaction to latex or to anesthesia agents was suspected. *In vivo* and *in vitro* tests were performed with the substances associated with the period of anesthesia: vecuronium, propofol, and latex. Cutaneous sensitivity was evaluated by skin prick testing and intradermal testing; vecuronium was tested at a dilution of 4 mg/ml for the prick test, and 40, 4, and 0.4 mg/ml for the intradermal test. Histamine acid phosphate and 0.9% normal saline were used as positive and negative cutaneous test controls, respectively. The response to these