Rash With Fever May Signal Drug Hypersensitivity

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VIENNA — The triad of high fever, rash, and organ involvement occurring in a patient who has recently begun a new drug treatment may signal drug hypersensitivity syndrome, Dr. Nikolai Tsankov said at the 16th Congress of the European Academy of Dermatology and Venereology.

This condition is a severe idiosyncratic reaction to certain medications that can cause skin, liver, kidney, lung, and hematologic disturbances. The skin eruption typically is a red maculopapular rash, but can also manifest as bullae, pustules, and even as toxic epidermal necrolysis (TEN).

Mortality has been estimated at 8%, increasing to 18%-40% when hepatic involvement is present, said Dr. Tsankov of the department of dermatology and venereology, Sofia Medical University (Bulgaria). This reaction is most commonly seen with the anticonvulsants phenytoin, phenobarbital, and carbamazepine, but has also been seen with minocycline, sulfonamides, and various other medications.

Immediate withdrawal of all suspected medicines is the first rule of management, said Dr. Tsankov. He described three patients with drug hypersensitivity syndrome and TEN whom he has treated, all with good outcomes.

The first patient was a 32-year-old man with epilepsy who had been taking valproic acid, but switched to lamotrigine. After 8 days he developed symptoms including fever up to 104 degrees, painful lymph nodes, tachycardia, and positive Nikolsky's sign. His liver enzyme and creatinine phosphate levels also were increased.

The second patient was a 20-year-old man with a 10-year history of alcohol abuse who began treatment with carbamazepine and diazepam, and 3 days later developed weakness, joint pain, fever, and a widespread red maculopapular rash as well as hemorrhagic bullae on his soles and palms. He also developed tachycardia, tachypnea, and wet crepitations, as well as elevations in liver enzyme and eosinophilia levels.

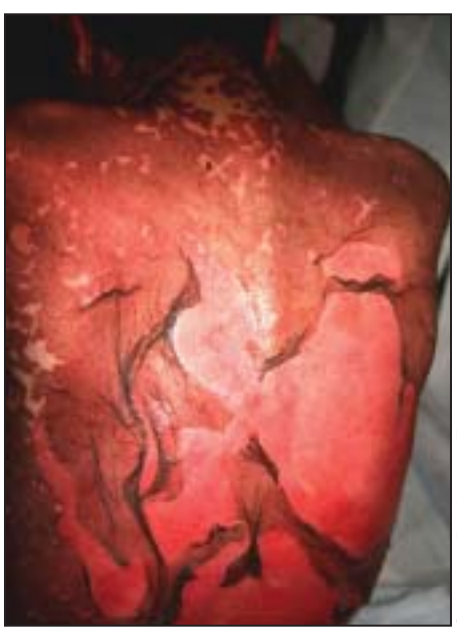
The third patient was a 32-year-old man with hemorrhagic colitis who began treatment with sulfasalazine. After 13 days, a papular rash appeared on sun-exposed areas of the skin, followed by hemorrhagic crusts and blisters. Nikolsky's sign was positive. His erythrocyte sedimentation rate was elevated, and leukocytosis and eosinophilia were present.

Following the cessation of the culprit, the three patients received intensive supportive care, broad spectrum antibiotics, and corticosteroids. Within approximately 4 weeks, all three men showed resolution of symptoms and reepithelialization.

The use of corticosteroids in this situation is controversial; some suggest that systemic corticosteroids should be contraindicated in TEN. Although they do appear to arrest the progression of TEN, the immunosuppressive effects of these drugs also increase the risk of infection, which is often associated with a lethal outcome (Am. J. Clin. Dermatol. 2000;1:349-60).

On the other hand, Dr. Tsankov said in an interview, drug hypersensitivity syndrome is not only a toxic but also an immunologic reaction. "As immune response modifiers, systemic corticosteroids could ameliorate the symptoms of drug hypersensitivity syndrome, especially with severe systemic involvement," he said.

It's important to note that cross reactivity can occur among the three main aromatic anticonvulsants, so a patient who experiences a hypersensitivity reaction to one must avoid all three, he said. Moreover, first degree relatives also should be cautioned because they may be susceptible. ■



COURTESY DR. NIKOLAI TSANKOV

Drug hypersensitivity syndrome can manifest in severe widespread rashes.