Skin Can Flag Drug Hypersensitivity Syndromes

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SAN ANTONIO — A high level of clinical acumen is crucial to the early diagnosis of serious hypersensitivity reactions to antiepileptic drugs, Dr. Adelaide A. Hebert said at a meeting sponsored by Skin Disease Education Foundation.

Erythema multiforme is a major concern for patients with anticonvulsant hypersensitivity, said Dr. Hebert, professor of dermatology and pediatrics at the University of Texas, Houston.

If a patient presents with anticonvulsant hypersensitivity syndrome, as it is often called in the literature, check the medication's chemical structure before switching him or her to a different agent. "Cross-reactivity among aromatic anticonvulsant medications may be as high as 75%," Dr. Hebert said at the meeting.

There are no reports of drug hypersensitivity with levetiracetam, so it is a notable exception among antiepileptic drugs. "I have asked my neurology colleagues why everyone is not put on Keppra [levetiracetam]. They tell me it does not work well for all patients and it's a third-tier, more expensive agent."

Although the rest of the anticonvulsants carry some risk, the aromatic anticonvulsants are most often involved in hypersensitivity syndromes, especially phenobarbital, phenytoin, and carbamazepine.

Phenobarbital can cause morbilliform reactions, urticaria, erythema multiforme, photosensitivity, and purpura.

Up to 10% of patients taking phenytoin will have a cutaneous reaction. A lupuslike reaction can occur or it may exacerbate preexisting lupus, Dr. Hebert said.

Some atypical cutaneous effects are reported with carbamazepine hypersensitivity, such as unusual bruising and oral ulceration. Photosensitivity, urticaria and Stevens-Johnson syndrome are other risks.

In one recent study, investigators assessed genetic susceptibility to carbamazepine hypersensitivity (Pharmacogenet. Genomics 2006;16:297-306).

Another high-risk anticonvulsant is lamotrigine (Lamictal). Although it has no aromatic ring, "this does not mean lamotrigine does not carry its own risks," Dr. Hebert said. Serious cutaneous eruptions, which may be life threatening, occur more often in children than in adults (1 in 100 pediatric patients versus 1 in 333 adult patients). "Not many medications cause such a high frequency," she said.

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DR. HEBERT

About 10% of patients will develop erythema and a maculopapular eruption, usually within the first 2-8 weeks of lamotrigine use. A history of rash related to another antiepileptic and age younger than 13 years were predictors in one study (Epilepsia 2006;47:318-22).

Initiate lamotrigine at the lowest possible dose and increase slowly. Caution is advised when it is combined with valproic acid since this triples lamotrigine's half-life. A lamotrigine-associated eruption is more likely with this combination, especially as the lamotrigine dose increases over time.

Valproic acid on its own can cause erythema multiforme and Stevens-Johnson syndrome. Alopecia, petechiae, photosensitivity, and pruritus are other possibilities. It can also cause diaphoresis.

With any hypersensitivity reaction, discontinue the drug, get liver function tests and a complete blood count with differential, measure creatine levels, and do a urinalysis. Administer corticosteroids if the reaction is severe, Dr. Hebert advised.

Management of anticonvulsant hypersensitivity syndrome includes avoidance of all aromatic anticonvulsants or other causative medications. Aromatic anticonvulsants include felbamate (Felbatol), fosphenytoin (Cerebyx), and primidone. Cross-reactivity can be avoided by choosing a nonaromatic agent such as ethosuximide (Zarontin), gabapentin (Neurontin), tiagabine (Gabitril), or topiramate (Topamax). "It is a very good idea to also talk to a family member about this [cross-reactivity] and the risk of future hypersensitivity reactions," Dr. Hebert said. SDEF and this news organization are wholly owned subsidiaries of Elsevier. ■

Pages 22a—22d