Editorial

A Sense of Insecurity

Jeffrey M. Weinberg, MD

The voluntary withdrawal of the psoriasis drug efalizumab from the US market reminds me of one of the first tenets I learned as a medical student and again as a dermatology resident: Any medication can cause any problem at any time. These problems include side effects of which we are aware as well as those, obviously, of which we are not aware.

Efalizumab was withdrawn in April 2009 and has not been available since June 2009 following reports of 3 cases of progressive multifocal leukoencephalopathy (PML) in patients on long-term therapy with the medication.[1] Progressive multifocal leukoencephalopathy is a rare, progressive, demyelinating disease of the central nervous system that usually leads to death or severe disability. It is caused by activation of the JC virus, which resides in latent form in up to 80% of healthy adults, typically only causing PML in immunocompromised patients. The factors leading to activation of the latent infection are not fully understood, though abnormalities in T cells have been described as important for reactivation. Progressive multifocal leukoencephalopathy has been reported in human immunodeficiency virus–positive patients, immunosuppressed cancer patients, transplant recipients, and patients with autoimmune diseases. There are no known interventions that can reliably prevent or adequately treat PML.

Progressive multifocal leukoencephalopathy is new to dermatologists but has been reported with the use of other medications, including rituximab and natalizumab.[2] Efalizumab had been approved in the United States for nearly 5 years when the first case of PML was reported, and approximately 46,000 patients had received treatment worldwide.[1]

On a personal note, I will miss efalizumab. It helped many of my patients and several of them did not want to discontinue their therapy, even after they became aware of the 3 cases of PML. It was difficult to tell them that the drug was withdrawn and we needed to explore other options.

The major question raised by this situation is: How do we integrate this information into our practice behaviors as we move forward? Do we assume that this side effect was medication specific and continue to prescribe systemic agents without change? Do we avoid newer agents with a less-established track record? Do we suddenly develop fears regarding potential unknown side effects of all such medications? Dermatologists generally are conservative by nature, and unexpected fatal side effects of our therapies give us a sense of insecurity. We yearn to know when safe is really safe. Unfortunately, there are no guarantees; some therapies are only safe until they are not.

Obviously there are no simple answers to these questions and each physician will need to address them in an individual manner. The best we can do is educate our patients on the benefits and risks, both known and potentially unknown, of their therapeutic options. We must tell them clearly that medications pose risks, both those risks listed in the package insert and some that may not be there yet. Given this information, it is up to each patient to determine the optimal approach to his/her therapy.

From the Department of Dermatology, St. Luke's-Roosevelt Hospital Center, New York, New York; Beth Israel Medical Center, New York; and Columbia University College of Physicians and Surgeons, New York.

Dr. Weinberg has served on the speakers bureau for Genentech, Inc.

REFERENCES

1. Genentech announces voluntary withdrawal of Raptiva from the U.S. market [press release]. South San Francisco, CA: Genentech, Inc; April 8, 2009. http://www.gene.com/gene/news/press-releases/display.do?method=detail&id=12047&categoryid=4. Accessed August 21, 2009.
2. Carson KR, Focosi D, Major EO, et al. Monoclonal antibody–associated progressive multifocal leucoencephalopathy in patients treated with rituximab, natalizumab, and efalizumab: a Review from the Research on Adverse Drug Events and Reports (RADAR) Project. *Lancet Oncol.* 2009;10:816-824.