Hallucinations Common in Pediatric Lupus

BY KATE JOHNSON

MONTREAL — Pediatric neuropsychiatric systemic lupus erythematosus has several unique manifestations that are not seen in adult patients, and without precise questioning they could easily be missed, reported Dr. Lim on March 11.

Patients can have visual, auditory, and even tactile hallucinations, but about one-third of them have “preservation of insight,” meaning they know these experiences are not real, said Dr. Lim, a rheumatologist at the Hospital for Sick Children in Toronto. Because they can distinguish between hallucinations and reality, the children respond to their symptoms and do not tell their parents or physicians “because they don’t want to be believed,” she said.

Visual hallucination and distortion are seen in three-quarters of pediatric patients with neuropsychiatric systemic lupus erythematosus (NPSLE), but have not been documented in adults with NPSLE. Dr. Lim said at the annual meeting of the Canadian Rheumatology Association. “They may be looking at a picture on the wall, and it might distort and move in and out at the same time. We find a lot of patients in adults who don’t report things like this without reporting them. Also a lot of them see bugs, or spiders crawling towards them, and that is very frightening,” she said.

Flector® Patch
(diclofenac epoprostenol topical patch) 1.3%

Exa Only

Cardiovascular Risk
• Risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.

INDICATION AND USAGE
• Flector® Patch is contraindicated for the topical treatment of acute pain due to trauma or other causes in patients in whom renal prostaglandins have a compensatory role in maintaining renal perfusion. In such patients, administration of nonsteroidal anti-inflammatory drugs may cause a dose-related decrease in renal blood flow and may precipitate overt renal decompensation.

PRECAUTIONS
• Flector® Patch is contraindicated for the treatment of periarticular acute pain. Flector® Patch should not be given to patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs. Patients with known CV disease or risk factors for CV disease may also be at greater risk.

CONTRAINDICATIONS
• Flector® Patch is contraindicated in patients with known history of GI adverse events.

WARNINGS, Cardiovascular Effects

With long-term treatment of NSAIDs, including Flector® Patch, anaphylactoid reactions may occur in patients with a history of asthma, angioedema, or bronchospasm after exposure to NSAIDs. Patients who have experienced an anaphylactoid reaction that was fatal or resulted in hospitalization or anaphylactic reaction should be discharged under close observation in case of further reactions.

Hematological Effects

Any patient who develops a skin rash or any other sign of hypersensitivity, including angioedema, urticaria, and/or allergic-type reactions after taking aspirin or other NSAIDs, should be discharged under close observation in case of further reactions.

Gastrointestinal Effects

Serious, potentially fatal upperGI adverse events, including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal, are rare. These events may occur at any time during use and without warning symptoms. Diffuse, rather than focal, GI adverse events are seen in about 1% of patients treated for one year. These trends continue with longer duration of use, increasing the likelihood of developing a serious GI event at some time during treatment. NSAIDs should be prescribed with extreme caution in those with a previous history of ulcer disease or gastrointestinal bleeding.

Clinical Trials

As with other NSAIDs, anaphylactoid reactions may occur in patients with a history of asthma, urticaria, or allergic-type reactions after exposure to NSAIDs. Patients who have experienced a serious anaphylactic reaction with one NSAID may be at greater risk with other NSAIDs.

The risk of upper GI toxicity, including serious, potentially fatal adverse events, is higher in elderly patients, usually followed by recovery to the pretreatment state.

In late pregnancy, as with other NSAIDs, Flector® Patch should be used in pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus. Patients’ pre-existing bleeding conditions may be at greater risk.

Renal Effects

NSAIDs, including Flector® Patch, can cause serious kidney adverse events, including kidney failure, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. These events may occur without warning symptoms.

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In an observational study which she presented as a poster at the meeting, Dr. Lim and her colleagues followed a coHORT of children with NPSLE at a single center in South Korea from August 2005 through November 2008. Of a total of 447 children with juvenile SLE, 53 (12%) children and adolescents (46 female) exhibited secondary psychiatric manifestations and cognitive dysfunction. Half of the subjects had psychiatric manifestations at first presentation, and 75% of 260 children (53%) exhibited them within a year of diagnosis. The median age of diagnosis with psychiatric illness was 15.9 years and the median duration of psychiatric symptoms prior to diagnosis was 60 days. Clinical and laboratory measures, imaging features, and treatment regiMEns were evaluated using standardized assessment forms, and all patients were evaluated by an experienced psychiatrist.

The clinical features of lupus-related psychiatric disease were identified and classified according to American College of Rheumatology nomenclature for adult systemic lupus erythematous (SLE) patients. Specifically, a patient needed to fulfill the following three criteria: (1) a recent observed problem with concentration or memory; significant impairment of the patient's academic performance, as indicated by a significant drop in grades; and improvement following treatment. Using this definition, the study reVealed that all patients had significant cognitive dysfunction, said Dr. Lim. “What's more important is that the patients had actually reported these problems. For example, their short-term memory was bad; they couldn't remember what they ate for breakfast, or what their home work was. They also couldn't learn new things; they had word-finding difficulties, and they were also not doing well in school. So you may have had an A student going down to a C.”

She said that 85% of the subjects had concentration difficulties, 77% had memory deficits, 24% had psychomotor slowing, and 21% had decreased comprehension. Two patients also had prominent depressive features. In addition, 75% of the subjects also had psychoses with hallucinations. In 83% the hallucinations were auditory, 75% were visual, and 75% were non-specific.

Visual distortion also was reported in 38% of this psychosis subsist, she said. In all, 42 of the 53 patients underwent magnetic resonance brain imaging, of whom 45% had normal results, 29% had non-specific white matter changes only. Of the 53 subjects, 28 underwent lumbar punctum, of whom 64% had normal results, 29% had elevated total protein, and 7% had an elevated white cell count.

“We're finding is that even among second-line immunosuppressant patients, cyclophosphamide is turning out to be something that is very useful,” commented Dr. Lim. “When we start patients on azathioprine because their symptoms are not responding to prednisone, we may have only mild psychotic symptoms, which we feel that a third actually need to be switched over.” Of the patients with psychosis, 60% (n = 24) also required antipsychotic treatment.

The investigators were able to collect data on response to therapy for some of the patients: Six relapsed and 25 went on to remission (although 3 of these eventually relapsed).

Response was defined as the absence of psychiatric symptoms, or antipsychotic medication use in patients who had a psychosis score of less than 50% of the peak dose for at least 3 months. Remission was defined as the absence of psychiatric symptoms, or antipsychotic medication use in patients who had a psychosis score of less than 50% of the peak dose for at least 3 months.

OverDIAGNOSIS There is a need for more experience with overdiagnosis of Flector Patch. In clinical trials, the maximum single dose administered was one Flector Patch containing 165 mg of diclofenac. There were no serious adverse events.

Across all studies, drug effects occurring due to incorrect use or accidental overdose of this product, the general measures recommended for the treatment of overdose are those indicated for the treatment of non-active ingredient skin.