# **TNF Blockers May Trigger Demyelinating Disease**

#### BY BRUCE K. DIXON Chicago Bureau

CLEVELAND — Treatment with a tumor necrosis factor- $\alpha$  inhibitor may trigger a demyelinating polyneuropathy with Guillain-Barré-like symptoms, according to MaryAnn Mays, M.D., of the Cleveland Clinic Foundation.

The case in point, presented in a poster at a symposium on the treatment of autoimmune and inflammatory disorders

#### sponsored by the clinic, was that of a 56year-old man with seropositive rheumatoid arthritis who became severely disabled after infliximab infusions were added to his methotrexate therapy.

Dr. Mays, a neurologist, reported in an interview that the patient's rheumatoid arthritis symptoms lessened markedly following his first anti-TNF treatment in 2002, but following an infusion in late 2003, he experienced dizziness and hearing loss that lasted for a week. The symptoms recurred and lasted longer following a third infusion 2 months later.

The next infliximab infusion in April 2004 produced worsening neurologic symptoms, including blurred vision, headaches, dysarthria, hearing loss, ataxia, dysphagia requiring percutaneous endoscopic gastrostomy for nutrition, and progressive weakness, Dr. Mays said.

"Initial evaluation included cerebrospinal fluid WBC of 123, protein 79, and electromyograph consistent with demyelinating polyneuropathy. But the overall pattern was not typical of Guillain-Barré syndrome [GBS]," Dr. Mays said. "He had high white count and normal protein. Auditory evoked potentials showed a right central conduction disturbance. His detrusor urinae muscle did not respond to stimuli, which is typical of GBS. His right Babinski sign was atypical of GBS."

Feyrouz Al-Ashkar, M.D., the lead investigator and a rheumatologist, noted in an interview that by the time the patient was brought to the clinic, he "could not walk, use his hands, lift his head, or feed himself, although he could still breathe on his own."

"He received intravenous immunoglobulin and steroids before we saw him. When he got here, he again received intravenous steroids and another course of intravenous



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DR. AL-ASHKAR

immunoglobulin, and slowly, but surely, he recovered completely," Dr. Al-Ashkar said.

Dr. Mays noted that "the fact that the patient responded well to a second course of intravenous immunoglobulin was further evidence that what he had was a demyelinating polyneuropathy other than GBS.'

According to Dr. Al-Ashkar, the message to clinicians "is that if you start noticing neurologic deficits or other adverse events, especially demyelinating diseases, in patients who are receiving infliximab, this should alert you to stop it and look for another treatment."

Dr. Al-Ashkar wrote that "if neurologic symptoms occur following [TNF] infusion, then evaluation for demyelinating disease, including chronic inflammatory demyelinating polyneuropathy, multiple sclerosis, and GBS, should be pursued.

"In such cases, our experience would suggest that there is potential for worsening of neurologic deficits with each infliximab treatment, and that continuing treatments after onset of neurologic symptoms would be relatively contraindicated," she wrote.

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s and rheumatoid arthritis: Methotrexate is in Pregnancy Category X. See CONTRAINDICATIONS. Nursing Mothers See CONTRAINDICATIONS. Pediatric Use

## **fiatric Use** ety and effectiveness in pediatric patients have been established only in cancer chemotherapy and in polyarticular-course juvenile rheumatoid arthriubished clinical studies evaluating the use of methotrexate in children and adolescents (ie, patients 2 to 16 years of age) with JRA demonstrated safe-/ comparable to that observed in adults with rheumatoid arthritis. (See **CLINICAL PHARMACOLOGY, ADVERSE REACTIONS** and **DOSAGE AND ADMINIS-**Published clinical subules valuating the use of inethorexate in children and apolecomis (e. patient) 24 to 15 years of age) with JAR Annotation and apolecomis (e. patient) 24 to 15 years of age) with JAR Annotation and apolecomis (e. patient) 24 to 15 years of age) with JAR Annotation and apolecomis (e. patient) 46 CHARMACOLOGY, ADVERSE REACTIONS and DOSAGE AND ADMINIS-TRATION.) Geriatric Use of methorexate did not include sufficient numbers of subjects age 65 and over to determine whether they respond differently from youngers subjects. In general, does selection for an elderly patient should be catious effecting the greater frequency of decreased heratic and renal function, decreased foliat stores, concomitant disease or other drug therapy (e. that interfere with renai function, methorexate) or to determine measurements may over scitmate renal function in the defly, more accurate methods (e. creatine dearance) should be considered. Sum methorexate levels may abo be reluiced by foliate supplementation. Show cleany functions of the stores should be considered. Sum methorexate tions, estimatorisma for and function in the defly, more accurate methods (e. creatine dearance) should be considered. Sum methorexate tions, estimatorisma of the reluiced by foliate supplementation. Post-marketing experimes suggests that the occurrence of bone marrow are suppression, tromborytopena, and pneumonitisma y increase with age. See Boxed WARNINGS and ADVERSE REACTIONS.

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common reactions included decreased hematocrit, headache, upper respiratory infection, anorexia, arthralgias, chest pain, coughing, dysuria, for postaxis, fever, infection, sweating, tinnitus, and vaginal discharge.