throughout her pregnancy. She had a brief admission at 20 weeks' gestation for an unexplained fever and abdominal pain treated with a 2-week course of steroids for a presumed flare of her CD, without any endoscopic studies or imaging performed. She delivered a normal, full-term male infant vaginally. The patient remains on adalimumab and is breastfeeding her newborn. The baby is now 6 months old with normal growth and development.

The treatment of inflammatory bowel disease in pregnancy is a concern for both patients and their physicians. It is accepted that maintenance of remission of inflammatory bowel disease is associated with a successful pregnancy and that active inflammatory bowel disease has been shown to be a factor associated with poor pregnancy outcomes.[5] Accumulating data support the safety of intentional or inadvertent use of infliximab in pregnancy.[6,7] These data suggest that the benefits of infliximab in achieving response and maintaining remission in mothers with CD may outweigh the potential risk to the fetus from exposure to the drug.

Adalimumab is a category B drug in pregnancy. Small animal studies in pregnant monkeys have not demonstrated adverse effects of adalimumab. There is 1 English language case report describing the successful use of adalimumab started before conception and continued throughout the pregnancy.[8] In this report, the patient also suffered from infliximab-resistant CD, and despite severely active disease at conception and moderate activity in the third trimester, the pregnancy was uncomplicated.

When evaluating medications in women who are pregnant or contemplating pregnancy, it is important to address the safety regarding the ability to conceive, teratogenicity, risk of miscarriage, and complications for the child. This decision should be made on an individual basis. In this case, adalimumab induced and maintained remission of infliximab-refractory CD without any apparent side effects to the mother or child. A registry of women who received adalimumab during pregnancy has been initiated, and physicians are encouraged to report such patients (toll-free 877-311-8972).

Daniel S. Mishkin, MD, CM*
William Van Deinse, MD†
James M. Becker, MD‡
Francis A. Farraye, MD, MSc*
*Section of Gastroenterology
†Prime Care
Biddeford, Maine
‡Department of Surgery
Boston Medical Center
Boston, Massachusetts

REFERENCES

1. Siddiqui MA, Scott LJ. Infliximab: a review of its use in Crohn's disease and rheumatoid arthritis. *Drugs.* 2005;65:2179–2208.
2. Hanauer SB, Sandborn WJ, Rutgeerts P, et al. Human anti-tumor necrosis factor monoclonal antibody (adalimumab) in Crohn's disease: the CLASSIC-I trial. *Gastroenterology.* 2006; 130:323–333.
3. Papadakis KA, Shaye OA, Vasiliauskas EA, et al. Safety and efficacy of adalimumab (D2E7) in Crohn's disease patients with an attenuated response to infliximab. *Am J Gastroenterol.* 2005;100:75–79.
4. Sandborn WJ, Hanauer S, Loftus EV Jr, et al. An open-label study of the human anti-TNF monoclonal antibody adalimumab in subjects with prior loss of response or intolerance to infliximab for Crohn's disease. *Am J Gastroenterol.* 2004;99:1984–1989.
5. Moskovitz DN, Bodian C, Chapman ML, et al. The effect on the fetus of medications used to treat pregnant inflammatory bowel-disease patients. *Am J Gastroenterol.* 2004;99:656–661.
6. Mahadevan U, Kane S, Sandborn WJ, et al. Intentional infliximab use during pregnancy for induction or maintenance of remission in Crohn's disease. *Aliment Pharmacol Ther.* 2005;21:733–738.
7. Katz JA, Antoni C, Keenan GF, et al. Outcome of pregnancy in women receiving infliximab for the treatment of Crohn's disease and rheumatoid arthritis. *Am J Gastroenterol.* 2004;99:2385–2392.
8. Vesga L, Terdiman JP, Mahadevan U. Adalimumab use in pregnancy. *Gut.* 2005;54:890.

Cardiac Involvement in Children with IBD During Infliximab Therapy

To the Editor:

Infliximab (IFX), a chimeric monoclonal antibody against tumor necrosis factor-alpha, has been shown to be effective for the treatment of severe inflammatory bowel disease (IBD) in adults[1] as well as in children.[2,3] Patients who receive IFX may exhibit unwanted adverse effects such as acute and delayed infusion reactions, infections, and serological and clinical autoimmune events. In a large cohort study in 500 consecutive adults treated at the Mayo Clinic, IFX-related infections were found in 8%, including 20 patients with serious infections, whereas infusion reactions occurred in 1.5% of 594 infusions administered to 111 pediatric patients.[4]

In 2003, Kwon et al[5] reported 38 adult patients who developed new-onset heart failure and 9 who exacerbated preexisting heart disease during IFX therapy. Recently, others have reported new-onset heart failure in patients undergoing IFX therapy without previous history of cardiovascular disorders: all of the patients improved after discontinuation of infusions.[6,7] A sudden death was reported to have occurred 18 h after a single infusion in a 64-year-old man without heart failure; at the autopsy, organic causes of death such as myocardial damage, pulmonary or cerebral edema, rupture of aneurysms, pulmonary embolism, and internal bleeding were excluded.[8] All reported patients developing new-onset heart failure upon IFX exhibited normal cardiac parameters before biological therapy. Evaluation of cardiac function has never been described in children undergoing IFX therapy.

We wish to report the preliminary results of a study aimed at evaluating heart function through echocardiography and electrocardiography monitoring in children with IBD during IFX therapy. This study was carried out on 26 subjects. Twelve had IBD (4 females, median age 14.0), 9 with Crohn's disease and 3 with ulcerative colitis; 11 received IFX therapy; 14 age- and sex-matched healthy subjects served as controls.

Doppler echocardiography was carried out to assess ejection fraction, left ventricular diastolic diameter, left ventricular systolic diameter, thickness

of interventricular septum, and posterior wall and the respective *Z*-scores. Computed standard 12-lead electrocardiogram was performed to calculate QT, QT correct interval length, and QT dispersion as bioelectrical risk factors of arrhythmias and sudden death; 10-min EGG monitoring in 2 leads was performed to evaluate sympathovagal balance by time and frequency domain indexes of heart rate variability.

Heart involvement was present in 7 of 12 children with IBD: 2 showed a dilative echocardiographic pattern and 5 a septal hypertrophic echocardiographic pattern (1 of them with a bicuspid aortic valve disease). All of these patients received IFX therapy and 5 also received long-term administration of corticosteroids. No differences were found in heart rate variability indexes as compared with controls, whereas a positive correlation between QT dispersion and LVDD and LVSD was found, thus suggesting an increased risk to develop cardiac arrhythmias. Because of lack of cardiovascular screening, we could not exclude the presence of asymptomatic myocardial disease before IFX therapy.

Our preliminary results suggest that assessment of heart function and structure should be included in the monitoring of children undergoing IFX through prospective studies that must recruit a large patient population. The latter should be stratified in subgroups according to different clinical phenotypes and therapeutic strategies. Currently, electrocardiography and imaging studies, such as ultrasound and magnetic resonance, appear to be the most suitable tools to detect potential bioelectrical instability and structural damage of the heart during IFX therapy.

Maria Barbato, MD
Mario Curione, MD
Franca Viola, MD
Paolo Versacci, MD
Fabiana Parisi, MD
Silvia Amato, MD
Salvatore Cucchiara, PhD
La Sapienza University
Rome, Italy

REFERENCES

1. Rutgeerts P, Van Assche G, Vermeire S. Review article: infliximab therapy for inflammatory bowel disease, seven years on. *Aliment Pharmacol Ther.* 2006;23:451–463.
2. Borrelli O, Bascietto C, Viola F, et al. Infliximab heals intestinal inflammatory lesions and restores growth in children with Crohn's disease. *Dig Liver Dis.* 2004;36:342–347.
3. Mamula P, Markowitz JE, Brown KA, et al. Infliximab as a novel therapy for pediatric ulcerative colitis. *J Pediatr Gastroenterol Nutr.* 2002;34:307–311.
4. Colombel JF, Loftus EV, Tremaine WJ, et al. The safety profile of infliximab in patients with Crohn's disease: the Mayo Clinic experience in 500 patients. *Gastroenterology.* 2004;126:19–31.
5. Kwon HJ, Cotè TR, Cuffe MS, et al. Case reports of heart failure after therapy with a tumor necrosis factor antagonist. *Ann Intern Med.* 2003;138:807–811.
6. Leetmaa TH, Markenvard JD. Dilated cardiomyopathy as a side effect of treatment with infliximab. *Ugesker Laeer.* 2005;167:3699–3701.
7. Boyer JF. New-onset acute heart failure and ventricular tachycardia after therapy with a tumor necrosis factor antagonist. *Clin Exp Rheumatol.* 2004;22:274–275.
8. De'Clari F, Salani I, Safwan E, et al. Sudden death in a patient without heart failure after a single infusion of 200 mg infliximab: does TNF-alpha have protective effects on the failing heart, or does infliximab have direct harmful cardiovascular effects? *Circulation.* 2002;105:183.