IBD: A Management Challenge

Inflammatory bowel disease (IBD) remains among the great management challenges for gastroenterologists and surgeons. The traditional framework for classifying and selecting treatments for patients with IBD is often based on symptoms rather than underlying pathophysiology. Now, the more frequent goal is to achieve mucosal healing rather than following symptoms alone.

IBD physicians, surgeons, and scientists at UPMC are meeting these new challenges on many levels, including:

• Participation in the NIDDK IBD Genetics Consortium (Richard Duerr, MD, PI)
• Multiple clinical and translational trials (Miguel Regueiro, MD, PI)
• Provision of psychology-based pain and disease management training (Eva Szigethy, MD, PhD, PI), through the Visceral Inflammation and Pain (VIP) Center
• The Gastrointestinal Dermatology Clinic led by Lisa Grandinetti, MD (see Page 2)

Ongoing efforts are under way to develop “personalized medicine” approaches and new models of health care that are more effective and less invasive.

Advanced patient care is dependent on open communication and discussion among expert physicians. In addition to traditional educational involvement in peer-reviewed journals and national meetings, UPMC IBD physicians and surgeons coordinate a weekly interactive, multidisciplinary IBD video case conference. Nearly a dozen IBD groups from academic institutions meet regularly to discuss their toughest cases.

The IBD Center at UPMC continues to evaluate complicated referral patients from around the United States and from international sites. All of our physicians and surgeons would be delighted to collaborate on approaches to evaluate and treat patients with complex IBD, or to render a second opinion on a complicated case.

We hope you enjoy this IBD-focused issue.

David C. Whitcomb, MD, PhD
Giant Eagle Foundation Professor of Cancer Genetics
Professor of Medicine, Cell Biology & Physiology and Human Genetics
Chief, Division of Gastroenterology, Hepatology, and Nutrition
Richard H. Duerr, MD, Receives Endowed Chair

Richard H. Duerr, MD, has been named the University of Pittsburgh’s Inflammatory Bowel Disease Genetic Research Chair. Dr. Duerr is a professor of medicine, human genetics, and clinical and translational science for the University’s Division of Gastroenterology, Hepatology, and Nutrition. He serves as the division’s co-director, as well as scientific director for the UPMC IBD Center.

The inaugural lecture celebrating Dr. Duerr’s endowed chair occurred May 7, 2013, at the University of Pittsburgh School of Medicine. His presentation, SNPping Away at the Etiopathogenesis of Inflammatory Bowel Disease, discussed his career in IBD genetics. Dr. Duerr leads one of six genetic research centers that comprise the NIH/NIDDK Inflammatory Bowel Disease Genetics Consortium.

UPMC Inaugurates Gastrointestinal Dermatology Clinic

Approximately 30 percent of gastrointestinal patients, specifically those diagnosed with inflammatory bowel disease (IBD) or celiac disease, have a concomitant dermatologic disease. Recognizing this, the UPMC department of Dermatology coordinated the region’s first-ever Gastrointestinal Dermatology Clinic. The clinic’s goal is to improve the quality of life for patients with dermatologic issues unique to their GI conditions.

Led by assistant professor of dermatology, Lisa Grandinetti, MD, MMS, this clinic demonstrates the coordinated, multidisciplinary expertise available at UPMC. GI experts from the IBD Center partner with Dr. Grandinetti and the Department of Dermatology to provide dermatologic care to ostomy patients and those diagnosed with IBD and other GI conditions. See if you can solve Dr. Grandinetti’s case unknown on Page 6 of this issue.

The clinic will be open on the first Monday of each month, and patients must be referred by a UPMC gastroenterologist. Referring physicians may contact the Gastrointestinal Dermatology Clinic at 412-647-4200.

The UPMC Inflammatory Bowel Disease (IBD) Center, part of the division of Gastroenterology, Hepatology, and Nutrition, is one of the largest IBD subspecialty groups in the United States. Our IBD physician team includes the following:

- Jana G. Al Hashash, MD
- Leonard K. Baidoo, MD
- Arthur M. Barrie III, MD, PhD
- David G. Binion, MD
- Richard H. Duerr, MD
- Wendy M. Elliott, PhD (VIP Center)
- Janet R. Harrison, MD
- Miguel D. Regueiro, MD
- Marc B. Schwartz, MD
- Jason M. Swoger, MD, MPH
- Eva M. Szigethy, MD, PhD (VIP Center)
- Gregory Thorkelson, MD (VIP Center)

The IBD Center and the Visceral Inflammation and Pain (VIP) Center are located in the Oakland section of Pittsburgh, and additional satellite clinics serve patients throughout the southwestern PA region. For additional information about the UPMC IBD Center, visit www.upmc.com/IBD or call 412-624-7692.

Affiliated with the University of Pittsburgh School of Medicine, UPMC is ranked among the nation’s best hospitals by U.S. News & World Report.
TNF-α Antagonists and Psoriasiform Events

By Julia B. Greer, MD, MPH, and Miguel D. Regueiro, MD

Crohn’s disease (CD) is a chronic inflammatory disease of the gastrointestinal tract that often leads to stricturing and penetrating complications. Many patients have a relapsing and remitting course, and as many as 70% of patients require at least one resection. Current treatment guidelines focus not only on achieving clinical remission in CD but also on mucosal healing, both of which correlate with fewer hospitalizations and surgeries. The latest advancement in the treatment of Crohn’s disease are biologic response modifiers known as tumor necrosis factor alpha (TNF-α) antagonists. These agents have helped numerous CD patients enter a stage of remission.

Currently, three TNF-α antagonists have received Food and Drug Administration (FDA) approval for the induction and maintenance of remission for patients with CD: infliximab (Remicade®, Janssen Biotech, Horsham, Pa.), adalimumab (Humira®, Abbott Laboratories, Abbott Park, Ill.), and certolizumab (Cimzia®, UCB, Atlanta, Ga.). Infliximab also was approved for the treatment of ulcerative colitis (UC) in 2005, and adalimumab was approved for UC care in 2012. This class of medication also is used in the treatment of other autoimmune diseases, such as rheumatoid arthritis, ankylosing spondylitis, and psoriasis. Due to their high penetration of use, coupled with relatively recent regulatory approval, ongoing surveillance for additional safety signals is particularly important for this class of medications. Paradoxically, these medications which treat psoriasis and psoriatic arthritis may also confer a risk of developing psoriasiform lesions, such as plaque psoriasis or palmo-plantar pustulosis. We recently investigated this relationship by evaluating reports in the FDA Adverse Event Reporting System (AERS). The FDA uses AERS to monitor for new adverse events and medication errors that might occur with marketed products, but it does not list the primary indication for which the medication was used, and reporting is voluntary. Estimates are that only 1% to 10% of all true adverse reactions are captured. Data in AERS is de-identified.

We examined data from AERS beginning January 1, 2004, through September 30, 2011, reviewing adverse event reports for the TNF-α antagonists infliximab, adalimumab, and certolizumab. We also examined primary “control” drugs including the non-CD drugs, propranolol and lithium, due to their recognized association with developing psoriasis, as well as the non-biologic CD drug, mesalamine. We calculated proportional reporting ratios (PRRs) for psoriasis adverse events for TNF-α antagonists versus control drugs.

From more than 13 million reports in AERS, the biologic group included 5,432 reports with psoriasis listed (infliximab=1,789; adalimumab=3,475; certolizumab=168) compared to just 88 psoriasis reports for the control group (propranolol= 24; mesalamine=24; lithium=40). Compared to control drugs, the psoriasis PRRs for TNF-α antagonists included infliximab (6.61), adalimumab (12.13), and certolizumab (5.43) (P<0.0001). The aggregate “class” PRR for all TNF-α antagonists versus control drugs was 9.24 (P<0.0001). Similar results were observed when psoriasis reports were compared among TNF-α antagonists and other drugs used to treat CD, including azathioprine, 6-mercaptopurine, methotrexate, corticosteroids, and ciprofloxacin, as well as the antimarial drug, hydroxychloroquine. Therefore, the FDA AERS data suggest increased incidence of psoriasiform lesions due to the use of TNF-α antagonists, which should not be mistaken for an extra-intestinal manifestation of CD.

While its incidence is low, we have been seeing TNF-α antagonist induced psoriasis more frequently in the UPMC Inflammatory Bowel Disease Center clinics. The psoriasiform lesions resolve upon cessation of the TNF-α antagonist, although CD often recurs. Fortunately, most cases of psoriasis related to TNF-α antagonists do not require discontinuation of the medication. We have successfully used topical steroids or dapsone for mild psoriasis while more severe psoriasiform lesions respond to methotrexate. Although published evidence is lacking, we feel that some patients may benefit from a lower dose of TNF-α antagonist. If the psoriasis is severe and refractory to treatment, our experience has shown that switching to a different TNF-α antagonist is safe.

References


Dr. Greer is an assistant professor of medicine with the Division of Gastroenterology, Hepatology, and Nutrition. She has written two health-related cookbooks, The Anti-Cancer Cookbook and The Anti-Breast Cancer Cookbook: How to Cut your Risk with the Most Powerful Cancer-Fighting Foods.

Dr. Regueiro is a professor of medicine and serves as the associate chief for education for the Division of Gastroenterology, Hepatology, and Nutrition. He is the co-director and clinical head of the UPMC Inflammatory Bowel Disease Center.
Crohn’s Disease in the Malnourished Pregnant Female: A Case Presentation and Review of Literature

By Jennifer Seminerio, MD
Chief Gastroenterology Fellow

A 40-year-old female patient presented with longstanding Crohn’s disease (CD). She was diagnosed at age seven with disease in both the small and large intestine. She had required six prior operations due to small bowel stricturing disease as well as rectal CD. She had been previously treated with prednisone, budesonide, metronidazole, mesalamine, azathioprine, 6-mercaptopurine, infliximab, and, currently, was receiving adalimumab. When the patient transferred care to the UPMC IBD Center she was suffering from postprandial pain and severe protein and calorie malnutrition with a loss of 33% of her ideal body weight. Deficiencies in zinc, iron, and vitamins A, E, D, and B₁₂ were identified, and she required transfusions and intravenous iron replacement for severe anemia. A CT scan revealed an anastomotic stricture with dilated proximal small bowel and active disease. She was initiated on total parenteral nutrition (TPN) which was started cautiously to avoid refeeding syndrome. She received additional intravenous thiamine, potassium, and phosphorus, and her adalimumab was continued with a plan for surgical correction of the bowel obstruction once nutritional parameters were optimized.

The patient rapidly improved. Within six months, she regained 35 pounds and had returned to work. As the patient’s health improved, her menstrual cycle returned and surgery was postponed when she became pregnant.

The patient was referred to maternal fetal medicine for co-management between gastroenterology and IBD surgery during pregnancy. TPN, vitamin B₁₂, iron gluconate infusions, intravenous vitamins, and adalimumab were continued during pregnancy. TPN was administered through a dedicated single lumen Hickman catheter. Blood glucose was monitored closely to avoid gestational diabetes due to the increased intravenous dextrose load in the TPN, and intravenous lipids were used cautiously to address the increased metabolic demands of pregnancy, as well as to avoid potential hepatotoxicity.

The patient delivered a healthy baby girl at 38 weeks gestation at the weight of 5 pounds, 6 ounces. She will continue on TPN throughout the operative period.

The common age range for Crohn’s disease diagnosis coincides with the peak age for reproduction. Women with quiescent CD have normal fertility rates, but women with active disease often experience greater difficulty getting pregnant. Pregnancy outcomes in women with active CD show increased rates of fetal loss, pre-term delivery, and low birth weight. Women in remission at the time of conception exhibit no

continued on Page 5
Crohn’s Disease continued from Page 4

increased risk of disease exacerbation during pregnancy, while those with active disease demonstrate persistent activity in two-thirds of cases. For these reasons, patients with active disease are encouraged to achieve remission prior to becoming pregnant, although poor pregnancy outcomes are rare in IBD. In general, continuing medical therapy with steroids, 5-ASA agents, purine analogs, and anti-TNF agents is recommended for pregnant women with CD, although methotrexate is absolutely contraindicated due to its teratogenicity.

Individual decisions on whether or not to start or continue IBD medications in pregnancy are made on a case-by-case basis among the patient, gastroenterologist, and obstetrician. Surgical intervention should be avoided during pregnancy if possible, but, when necessary, should be performed during the second trimester.

TPN during pregnancy was first prescribed in the 1980s. Published guidelines recommend TPN for debilitating disease that increases nutritional demands and precludes enteral feeding such as severe, refractory IBD. There are few published reports on use of TPN in pregnant patients with underlying IBD. The average increase in maternal caloric intake should be 200 to 400 kcal/day and special attention should be made to optimize the intake of zinc, selenium, and omega-3 fatty acids. The use of TPN during pregnancy has demonstrated good maternal and neonatal outcomes, as measured by adequate maternal weight gain and fetal growth.

References


Lisa Maria Grandinetti, MD, MMS
Assistant Professor of Dermatology
Director, Dermatology Residency Program

A 55-year-old female with a ten-year history of Crohn’s disease presented with a several-day history of a rash occurring bilaterally on her dorsal forearms. The lesions were tender but non-pruritic. They were preceded by a fever of 102°F and severe left knee pain. A biopsy of the skin lesion was performed.

Compare your answer to Dr. Grandinetti’s on Page 5.

Upcoming Events in Pittsburgh, Pa.

PancreasFest 2013
Acute Pancreatitis: Risk Stratification, Early Management, and Role of Nutrition
July 24 to 26, 2013

GI Post Graduate Course:
Advancements in Liver, IBD, and GI Cancers
October 24 and 25, 2013

For more information about upcoming events sponsored by the Division of Gastroenterology, Hepatology, and Nutrition, please contact joj2@pitt.edu.