Advances in IBD: An Update for Patients

Speaker: Dr. Maria Abreu
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Goals of webcast

- Understand purpose of Advances in IBD conference
- Review clinical research discussions from 2013 program
- Review the work in progress to advance IBD care
- Review CCFA resources, for more information
Overview of Advances in IBD Conference

What is it? When?
• Advances in Inflammatory Bowel Diseases: Crohn’s & Colitis Foundation’s Clinical and Research Conference
• Educational event for healthcare professionals and researchers who study and manage patients with inflammatory bowel diseases
• 2013 Conference took place December 12-14 in Florida
• 1,892 medical professionals attended the 2013 conference

Purpose:
• Meet educational needs of healthcare professionals
• Clinicians and researchers share information
Clinical Perspectives in IBD
Mimics of IBD: Is it Crohn’s Disease?
Small intestine mimics:

- Tuberculosis, Yersinia-bacteria that can affect the gut
- Growths or tumors (neoplasms)
- Drugs:
  - Non-steroidal anti-inflammatory drugs (NSAIDs)
  - Serotonin-angiotensin receptor blockers (SARBs)
- Celiac disease
- Inflammation of the small intestine (e.g. Meckel’s diverticulum)
- Tissue growths outside of uterus (endometriosis)

Courtesy of Sunanda Kane, MD “Mimics of IBD,” 2013 Advances in IBD Conference
Mimics of IBD:
Is it Crohn’s or Ulcerative Colitis?

Colon mimics:

- Effect of colonoscopy prep on the bowel (prep effect)
- Normal colon
- Bacterial, viral, or fungal infections (Example: C difficile, cytomegalovirus)
- Growths caused by other diseases (Example: Kaposi’s sarcoma, lymphoma)
- Solitary rectal ulcer syndrome (SRUS)- ulcer(s) in the rectum
- Drugs-ipilimumab
- Segmental colitis associated with diverticular disease (SCAD)

Courtesy of Sunanda Kane, MD “Mimics of IBD,” 2013 Advances in IBD Conference
Mimics of IBD: Is it Crohn’s or Ulcerative Colitis?

Perianal mimics:

- Trauma: obstetric or GI surgery
- Infections: tuberculosis, lymphogranulomatosis venereum (LGV)
- Insufficient flow of oxygen-rich blood to intestines (ischemia)
- Growths or tumors

Courtesy of Sunanda Kane, MD “Mimics of IBD,” 2013 Advances in IBD Conference
Mimics of IBD: What to Consider?

- Consider alternative when high-dose prednisone does not work
- Always think about infection, ischemia or tumor growth process
- Conditions can overlap, can have two entities at once

Courtesy of Sunanda Kane, MD “Mimics of IBD,” 2013 Advances in IBD Conference
Diagnostics

Use of Endoscopy in Crohn’s Disease

- Initial diagnosis
- Evaluating extent and severity
- Biopsy
- Monitoring abnormal growths/development
- Dilation
- Monitoring inflammation of innermost layer of intestines (mucosal healing)
- Post-operative disease monitoring

Source: “Misuse of Endoscopy in Crohn’s disease” Douglas C. Wolf, MD, FACG, 2013 Advances in IBD Conference,
Diagnostics

Misuse of endoscopy in Crohn’s disease

- Evaluating inflammation without biopsies
- Insufficient biopsies, or biopsy in incorrect area: e.g., should biopsy edge of ulcer (not center)
- Performing full colonoscopy when less invasive testing will be sufficient
- Not screening for strictures before a capsule endoscopy
- Performing colonoscopy or capsule endoscopy for suspected Crohn’s disease without enough criteria

Source: “Misuse of Endoscopy in Crohn’s disease” Douglas C. Wolf, MD, FACG, 2013 Advances in IBD Conference,
Diagnostics

Use of endoscopy in ulcerative colitis

- Diagnosing ulcerative colitis
- Evaluate disease extent
- Assessment of activity/healing
- Evaluating abnormal growth or development (dysplasia)
- Diagnose or control bleeding
- Used to evaluate pouch
- Endoscopic ultrasound
- Video capsule endoscopy

*Slide courtesy of Gary R. Lichtenstein, “Use and Misuse of Endoscopy in Ulcerative Colitis,” 2013 Advances in IBD Conference*
Diagnostics

Misuse of endoscopy in IBD

• Failure to consider possible mimics of IBD, including ulcerations
• Ulcers (such as aphthous ulcers) may be confused with other entities (C. diff)
• Biopsy is important in diagnosis
• No inflammation in innermost layer of colon (mucosal healing) during remission
• Not examining tissue to predict future probability of flare
• Need to treat individuals with potential for aggressive behavior with aggressive therapy
• Post-operative disease monitoring
• Surveillance for abnormal cell growth (dysplasia)- mostly raised, not flat
Surgery: Laparoscopic Ileocolic Resection

- Removal of the last segment of small intestine (ileum) and the first segment of the large intestine (colon)

- Short term results
  - Fast recovery
  - Minimal scarring
  - Complications are low (<10%)
  - Can use medication to prevent recurrence
  - Loss of small bowel is generally small (typically 20–25 cm)
  - Quick return of quality of life

- Long term results
  - Lower incisional hernia
  - Less adhesions

Source: “A Patient with Severe Crohn's Disease, an Ileal Stricture and Proximal Dilation” Phillip Fleshner, MD, 2013 Advances in IBD Conference
Evaluating Pain

- Inflammation, strictures/ adhesions/ fistulas, bacterial overgrowth, neurobiological/ psychological, psychosocial
- IBD is associated with psychopathology, functional pain, and stress responses
- Maximize treatment of underlying inflammation
- Need personalized behavioral interventions that can improve coping
- Pain medications as second line therapy
- Better identification of risk factors for psychological stress can lead to prevention strategies

*Slide courtesy of Eva Szigethy, “Evaluating Pain in IBD,” 2013 Advances in IBD Conference*
Special considerations: Pediatric IBD

- In treatment, it is important for physicians to consider the impact of biologic therapy on pediatric patient outcomes.
- There is lack of clinical trial data in children, therefore many lessons are taken from adult trials in treatment.
  - Only 1 FDA approved biologic for children (Remicade).
- Drug toxicities are different though drug metabolism is not hugely different.
- There is increasing comfort within pediatric GI professional community with early introduction of biologics.
- More research needed on microbiome and dietary influences in pediatrics.
- Markers of remission in pediatric IBD such as mucosal healing and fecal biomarkers still a subject of debate.
Shared Decision-making

- Explaining decisions in common terms
- Put risks and benefits in perspective
- All risks are not looked at the same way by patients
- Shifting risk-benefit ratio: if patients are on successful therapy, their risk/benefit assessments may change.
- Absolute risk vs. relative risk
Basic science of IBD
Genetics: 163 confirmed loci

**Common pathways:**
- Leprosy
- Microbacterial susceptibility
- Other immune-mediated disease

**CD genes**
- 30 CD specific loci
- NOD2
- PTPN22

**UC genes**
- 23 UC specific loci

**MHC**

110 IBD loci

**Genes in common**

Genetics

• Overlap of genes in UC and CD
  • patients with indeterminate colitis
• Gene variation - functional changes
• Systems biology - what pathways are linked together?
• Genes involved in mycobacterial diseases
  • Susceptibility to mycobacteria or primary immune deficiency syndromes.
• CCFA research in genetics
Microbiome and IBD

- Microbiome includes bacteria, fungi and viruses living in intestine
- Question still being researched: Is Crohn’s disease a mycobacterial disease?
- Bacteria has been studied through sequencing (speaker to define in talk)
- Microbiome currently studied through stool and mucosa (each has different microbacterial populations)
Microbiome and IBD

- Scientists are looking to study the microbiome in different environments
  - Bacteria in lumen of colon
  - Bacteria in mucosa
- Scientists considering connection between diversity in the microbiome and inflammation
- Look at metabolic genes expressed by bacteria
- Diet and the microbiome - more studies needed
- CCFA research in microbiome
IBD Pathogenesis

Crohn’s disease-like

Colonization (bacteria, viruses, fungi, worms)

Crohn’s activating infections

Crohn’s-specific genes (Nod2)

Core genes regulating inflammation, epithelial barrier, autophagy, etc.

Ulcerative colitis-like

Loss of protective flora

UC-specific genes
A look at the future of IBD

Therapy advances: Crohn’s disease

- Treating Crohn’s- need trials in early CD.
- How do we define early disease?
  - If use within 18 months, there is already structural damage.
  - Early CD- before there is evidence of structural damage. We can predict worse prognosis by:
    - Deep ulcerations
    - Smoking
    - Extensive disease
A look at the future of IBD

Therapy advances: In the pipeline

- **Vedolizumab** studied in Crohn’s and UC
  - Blocks new lymphocytes from being recruited to intestine
- **Ustekinumab**
  - Patients who have not been responsive to anti-TNFs
  - Dosing recommendations and side effects are to be examined
- **Tofacitinib**
  - Approved for rheumatoid arthritis
  - Looks promising in ulcerative colitis
  - Phase 2 study
  - Dosing recommendations and side effects are to be examined
A look at the future of IBD

Therapy advances: Ulcerative Colitis

- Two new drugs approved in 2013 for UC
  - Golimumab -- subcutaneous
    - Don’t have comparative effectiveness studies to compare to other anti-TNF agents
    - Studies found that serum levels do impact effectiveness.
  - Budesonide -- colon release
    - New colon release formulation for UC
    - Also used in ileum and right sided colonic Crohn’s disease with an ileal release preparation.
    - Effects almost as potent as steroids without systemic side effects
- In the pipeline: Vedolizumab
  - Targeting gut
  - FDA approval expected in May
A look at the future of IBD...

The Future is Bright
CCFA Resources

- Irwin M. and Suzanne R. Rosenthal IBD Resource Center (IBD Help Center)
  - Provides disease management information and resources
  - Phone: 1-888-694-8872    Email: info@ccfa.org
- Educational webcasts: [www.ccfa.org/resources/webcasts](http://www.ccfa.org/resources/webcasts)
- Connect with other patients
  - CCFA Community website: [www.ccfacommunity.org](http://www.ccfacommunity.org)
  - Support groups and Power of Two (peer mentors): [www.ccfa.org/chapters](http://www.ccfa.org/chapters)
  - GI Buddy: online tracking tool and mobile app
SAVE THE DATE  (New Webcast)

What’s Best for Me? Treatment Options in IBD

Thursday, July 17\textsuperscript{th}, 2014
8:00 PM - 9:00 PM EST

Speaker:
David T. Rubin, MD, FACG, AGAF
University of Chicago Medicine
Chicago, Illinois
Your Feedback is Important!

www.ccfa.org
Questions?