Case Presentations

Uma Mahadevan MD
Sunday November 5, 2007

Making the Diagnosis

Case 1

History of Present Illness

• 24 F who presents with debilitating diarrhea.
• Four years ago suffered from constipation, occasional abdominal pain with stress-associated diarrhea over last 3 years.
• Over last 6 months, symptoms worsened.
  – 3-4 loose BM’s daily, loose, occasional blood on toilet paper, mucus.
  – Sharp stabbing pain
  – Urgency with such severity, afraid to leave the house
• ROS: mild nausea, 5 lb weight loss, but no fever, arthralgias, nocturnal BM’s or incontinence
• PMH: endometriosis, recurrent yeast infection
• All: tagamet, tamaflu → hives
• Meds: OCP, peptobismol, tums, MVI, CA#
• Shx: graphic designer, tobacco quit 1 year ago ½ ppd x 5 years, social ETOH, no drugs
• Fhx: Brother with CD, Great uncle with colorectal cancer
• Physical Exam:
  – thin (92 lbs), otherwise normal
• Laboratory Tests:
  – Normal CBC, lft’s, albumin (4.7), crp, esr, tsh, tissue transglutaminase
• Microbiology
  – Stool culture, O+P, C. difficile negative
• Small Bowel Follow through
  – Normal

Endoscopy
• EGD: normal
• Colonoscopy:
  – There were shallow ulcers and erythema in the distal 5-10 cm of ileum
  – There were patches of hemorrhagic appearing mucosa in the transverse colon.
  – Otherwise the colon was normal.

Ileal Ulceration

Hemorrhagic Appearance
Pathology

- Duodenum, biopsy: No significant pathologic abnormality.
- Stomach, biopsy: Patchy mild chronic inflammation;
- Transverse colon, biopsy: Mild active colitis
- Ileum, biopsy: No significant pathologic abnormality.
- Colon, "random," biopsy: No significant pathologic abnormality.

What Does this Patient Have?

What would you treat her with?
How do you make a diagnosis of IBD?

- Given her family history of CD and the findings on colonoscopy, she was started on budesonide 9 mg per day
- She noted significant improvement with solid stools and reduced urgency
- Lexapro 10 mg per day not tolerated
  - Switched to desipramine, she did not take it.

- Would you do any further testing at this time?
- Prometheus Serology: markers not detected
  - ASCA IgA Elisa 18.9 EU/ml (<20.0)
  - ASCA IgG ELISA 21.2 EU/ml (<40.0)
  - Anti-OmpC IgA ELISA 3.4 EU/ml (<16.5)
  - Neutrophil AutoAb <12.1
  - DNase sensitivity not detected
Crohn’s or Not Crohn’s?

**NOT CROHN’S**
- Normal laboratory tests
- Negative serology
- Unremarkable biopsy results
  - Active colitis

**CROHN’S**
- Family history CD
- Ileal ulcers
- Response to budesonide

3 months later, she complains of severe RLQ abdominal pain, epigastric pain worse with eating
- Presents to local ER, labs-UA normal, sent home
- Presents to PCP, UA normal, pelvic US normal, sent home
- Presents to UCSF ER
  - CT abdomen and pelvis, US gallbladder, EGD normal
  - Labs normal
- Felt to be IBS, severe, desipramine recommended

Making the Diagnosis

Case #2

History of Present Illness

- 42 M with generalized malaise, myalgias, arthralgias (knees, hip)
  - Migratory, worse in morning, resolves throughout day
  - Took ibuprofen as needed
- Rash on back, arms described as “pimples”
- Mild abdominal pain
- No diarrhea, blood per rectum
- PMH: Diverticulitis w/ abscess 1 year ago → sigmoid colectomy, Barrett’s esophagus
- SHx: Tile contractor, married, no tobacco
- Fhx: Mother with ulcerative colitis
- Physical Exam: unremarkable
• Colonoscopy 6/06 outside hospital
  – Patchy erythema in terminal ileum
  – Erythema in ascending colon
• Pathology: reviewed at UCSF
  – Terminal ileum, biopsy: Active ileitis
  – Ascending colon, biopsy: Mild active colitis
  – No chronic architectural changes or granulomas are identified in the terminal ileum or colon biopsies. These findings are nonspecific.
• Labs: WBC = 14.7, otherwise normal (hematocrit, platelets, albumin, crp, esr, tsh)

• He was started on budesonide, with no improvement in symptoms
• He presents to UCSF for diagnosis and treatment
• What does he have?
• What would you do now?

• Budesonide discontinued as having anxiety, insomnia and no benefit
• Sulfasalazine 2 gm per day
• IBD serology
  – All Assays (ASCA IgA, IgG, anti-OmpC, Anti-Cbir1, neutrophil-specific nuclear autoAb) negative individually
  – IBD predicted: Ulcerative colitis

• New testing does not look at positive or negative above a cut point, it is a pattern of all 7 markers
• Is this IBD:
  – Pro: family history, serology
  – Con: use of nsaids, nonspecific pathology, no bowel symptoms
• Referred to Rheumatology, as arthritis most active symptom.
**Refractory Crohn's Disease**

Case #3

**History of Present Illness**

- 39 F with CD referred in 2003 with disease refractory to medical therapy
- Diagnosed in 1998, disease limited to the colon
- Mesalamine agents, budesonide, 6-mercaptopurine, oral methotrexate were tried and not tolerated.
- Good response to prednisone, but unable to taper off for any long period of time
- Infliximab given x 2 with good response, on third attempt, shortness of breath
  - Reintroduce 3 months later. Again tolerate first 2 infusions, but not third. This time no benefit.

**Colonoscopy 8/03**

- Erythematous, friable, ulcerated mucosa from 15-30 cm from the anal verge.
- The remainder of the colon was normal.
- Inflammation was found in the ileum.
- The ileocecal valve was narrowed
- Pathology:
  - Ileum, biopsy: Chronic active ileitis with ulceration and granulation tissue, and epithelial reactive changes
  - Sigmoid colon, biopsy: Chronic active colitis and cryptitis with granulation tissue and ulceration, mild architectural distortion

**Complaints**

- Complained of significant stressors in her life
- Review of Systems:
  - Nausea and vomiting chronically with extensive work up negative
  - Arthritis in lower extremities
  - Headaches
  - Denies anxiety
- PMH: none
- PSH: laparoscopy for endometriosis, tubal ligation
- FHX: no IBD or CRC
- SHX: married, employed, no tobacco, ETOH, drugs
• Started on Methotrexate 25 mg SQ weekly
• No real improvement.
  – Complains of LLQ pain, obstructive symptoms
• Hospitalized with worsening symptoms
• Colonoscopy: 12/03
  – A stricture was noted at 20 cm from anal verge. Balloon dilatation was performed.
  – There was inflammation and narrowing from 15-30 cm from the anal verge.
  – The rectum and remainder of the colon were normal.
  – Inflammation was found in the ileum.

• What would you offer her at this point?
• What are the medical and surgical options?
POSTOPERATIVE DIAGNOSIS:
- Crohn’s disease, severe disease in the last 10-12 inches of ileum as well as significant sigmoid and descending colon Crohn’s disease.

OPERATION: 1/26/04
- Exploratory laparotomy
- Ileocecal resection with primary anastomosis
- Sigmoid and left colon resection with primary colorectal anastomosis
- Diverting loop ileostomy.
  - A rigid sigmoidoscope used to test the anastomosis. No evidence of leak, but given the amount of edema and the difficulty of her tissue in holding the staples, a diverting loop ileostomy created to allow this area to heal properly
- Takedown of loop ileostomy: 3/22/04

Post-operatively, had issues with
- Diarrhea 14-20 BM per day
- Stitch abscess at ileostomy site
- Failure to gain weight (87 lbs)
- Methotrexate continued

What would you do at this point?
- Diagnostic tests?
- Medications?

Colonoscopy 8/04
- The majority of the ileum was normal except immediately proximal to the anastomosis which showed moderate inflammation.
- An ileocolonic anastomosis was noted at 40 cm from the anal verge. The entrance to the ileum was slightly narrowed but larger than the scope.
- There was severe inflammation at the rectum

Endoscopic Images
- Rectum
- Anastomosis
• Prednisone 40 mg per day
• Adalimumab 80 mg loading dose, 40 mg every other week
• Some improvement, but unable to taper off prednisone, so adalimumab increased to every week, methotrexate 15 mg weekly
• Having 4-6 BM per day, 20 lb weight gain, but unable to taper off prednisone 10 mg daily without increased symptoms
  – Back to work

• SBFT 4/05: unremarkable
• Colonoscopy 4/05:
  – There was severe ulceration of the rectum to 10 cm from the anal verge.
  – There was a ileocolonic anastomosis at 40 cm from the anal verge.
  – The intervening colonic mucosa above the rectum was normal.
  – There were two openings at the anastomosis, with one being shallow/blind and the other, lower, being the true opening to ileum.
  – There was ulceration at the anastomosis.
  – There was mild scattered ulcers in the ileum.

Rectal Inflammation
Anastomosis

Summary

• 40 F with severe Crohn’s, status post-resection
  – On adalimumab 40 mg weekly, methotrexate 15 mg weekly
  – Still with cramps, diarrhea, prednisone dependence
  – Insurance refused adalimumab 80 mg weekly
  – Patient refuses ileostomy
  – Now divorced from her husband
• What would you offer her at this point?

Case #4

Refractory Ulcerative Colitis

History of Present Illness

• 17 M with UC diagnosed 8/06.
  – 18 months of diarrhea, abdominal pain, blood
  – Colonoscopy 8/05; pancolitis
    • Biopsies demonstrated acute and chronic colitis, normal ileum
• Mesalamine: increased diarrhea
• Prednisone, antibiotics, azathioprine 100 mg per day
  – No improvement
• Referred to UCSF
• 9-10 BM per day, nocturnal BM
• 15 lb weight loss, some gain now
• PMH: otherwise negative
• Medications:
  – Balsalazide 6.75 gm
  – Azathioprine 100 mg (65 kg)
  – Robinol, protonix
• Family History: unremarkable
• Shx: Student, denies ETOH, tobacco, drugs

• Physical Exam:
  – Thin, otherwise unremarkable
• Laboratory tests:
  – WBC COUNT 12.3 x10E9/L 4.5-13.2 WBC
  – HEMATOCRIT 44.2 PERCENT 38-49 HCT
  – PLATELETS 261 x10E9/L 140-450 PLT
  – AST l*11 U/L 16-41 AST
  – ALT 14 U/L 12-59 ALT
  – BILIRUBIN, TOTAL b*1.8 mg/dL 0.3-1.3 BILT
  – ALKALINE PHOSPHATASE 65 U/L 52-171 ALKP
  – ALBUMIN 3.8 g/dL 3.4-4.7 ALB
  – SEDIMENTATION RATE 5 mm/h 0-10 ESR
  – C REACTIVE PROTEIN 1.7 mg/L <6.3 CRP

Does this patient have active ulcerative colitis?
• What diagnostic tests would you do?
• What medical therapy would you offer him?

Colonoscopy
• Inflammation was found in the ileum with scattered small ulcers, erythema.
• There was frond-like mucosa throughout the colon that may suggest a layer of pseudopolyps.
• An ulcer was found in the cecum.
• There was inflammation with ulceration and extreme friability in the right colon.
Pathology

- Ileum, biopsy: Small intestinal mucosa with prominent lymphoid follicles; no significant pathologic abnormality.
- Right colon, biopsy: Chronic active colitis with inflammatory exudate and changes consistent with healing ulcer.
- Left colon, biopsy: Chronic active colitis with inflammatory exudate and changes consistent with healing ulcer/inflammatory polyp.
- COMMENTS: The right and left colon specimens (Parts B and C) show a background of chronic active colitis. The colonic mucosa demonstrates focal villiform architecture and extensive granulation tissue with re-epithelialization.
  - These mucosal changes are consistent with a recently healed ulcer and could also correspond to inflammatory pseudopolyps.
  - No CMV, HSV or adenovirus.

Ileum

Ulcers in right colon

Pseudopolyps throughout
• What Medical Therapy Would you offer him?

• Increased his azathioprine to 150 mg daily
• Infliximab 5 mg/kg at 0,2,6 weeks
• 8/06 Update:
  – Had 4 doses of infliximab
  – Still having 8-10 BM per day
  – Good appetite, no weight loss
  – Does not wish to consider surgery
  – Laboratory tests are normal