Gastroduodenal Crohn’s Disease

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Case Presentation

- 41 M with history of gastroduodenal CD since 1997
  - Initial presentation: abdominal pain, nausea, vomiting, early satiety
  - CT abdomen: 10/97 thickened irregular loops of distal small bowel.
  - Normal colonoscopy.
  - Upper endoscopy: ulcers in the distal duodenum, periampullary area, duodenal bulb and gastric antrum
    - Acute/chronic inflammation with purulent exudate. No infection
    - Treated with prednisone 60 mg with minimal response
    - SBFT: mild distention of D1, nodular D2, 8 cm stricture in D3 and extensive inflammation with narrowing, pseudodiverticula in jejunum
- Duodenojejunostomy/gastrojejunostomy (1/98)
  - J4 inflamed, firm, contracted, consistent with CD

Postoperatively:
- Prednisone continued with taper
- Azathioprine, mesalamine, omeprazole
  - Continued until 2004
- Pt. stopped medication due to diarrhea, which resolved with cessation of meds
- Did well for 1 year until he developed early satiety, bloating, nausea, vomiting, 10 lb weight loss. 1 BM per day
- Presents to UCSF for further management

PMH:
- BCG vaccine
- 1992: left lateral leg ulceration with black mark, treated with Chinese herbs
- Keratitis at same time as leg lesion
- Oral apthous ulcers

Allergies: None

Medications: tums, Chinese herbs, no nsaids

SHx: Taiwanese, computer engineer, married, no tobacco, etoh or drug use

Fhx: no IBD or CRC
• Physical Exam:
  – Weight 126.6 lbs
  – Thin, no distress
  – Abdomen: soft, nontender, nondistended, midline incision
  – Otherwise normal

What Diagnostic Tests Would you Order at this Point?

Laboratory Tests
- WBC COUNT 9.2 x10E9/L 3.4-10
- HEMOGLOBIN 13.6 g/dL 13.6-17.5
- HEMATOCRIT *40.8 PERCENT 41-53
- PLATELETS 434 x10E9/L 140-450
- ALBUMIN *2.7 g/dL 3.4-4.7
- SEDIMENTATION RATE 5 mm/h 0-10
- VITAMIN B12 804 ng/L >243
- FOLATE, RBC 1102 ug/L >487
- C REACTIVE PROTEIN *12.5 mg/L <6.3

UGI/SBFT
- Normal contours and motility of the esophagus.
- Mild, nonspecific fold thickening of the gastric fundus and antrum.
- Deformity of the third duodenum
- A long strictured segment of proximal jejunum beginning at the ligament of Treitz, measuring approximately 17 cm.
- Numerous diverticula affect the duodenum and jejunum.
- Spot images of the terminal ileum appear within normal limits.
Colonoscopy

- Normal mucosa found throughout colon.
- Multiple shallow ulcers in the ileum.
- Pathology:
  - Ileum, biopsy: Chronic ileitis
  - Colon, biopsy: Active colitis with cryptitis
  - No dysplasia or granulomas are noted.

Upper Endoscopy

- Esophagitis was found in the lower esophagus.
- Surgical gastrojejunostomy noted in the body of the stomach. The anastomosis was patent, though somewhat narrowed.
- Normal appearing mucosa was found in the body of the stomach.
- Multiple ulcers were found in the mid jejunum consistent with severe Crohn's ulcers to 15 cm from the anastomosis. The scope did not pass further, but no strictures were seen.
The patient returns to the office to review tests.

- He has lost 7 lbs in the last 3 weeks and continues with the same symptoms
- He states he is intolerant of 6mp/azathioprine and mesalamine and does not want to go back on these
- What medical or surgical regimen would you consider for him?
• Therapy with infliximab is considered
  • A PPD placed was strongly positive
    – He has a history of a BCG vaccine as a child
    – Chest X-ray is negative
• Should he start INH or is this from his BCG?
• Should he go on a low dose immunomodulator?
• Do you worry about infliximab use in the setting of a known symptomatic stricture?

• He is restarted on a PPI. He was noted to be HP positive and
  received 2 weeks of antibiotics
  • Infliximab and INH are started in conjunction
    – 200 mg of hydrocortisone is given prior to each infusion
  • After 2 infusions, he presents to the office
    – He notes improved appetite, but continued nausea, early satiety
    – Reglan 10 mg QID is added as well as oral supplemental nutrition
  • After 3 infusions, he did not have a response and he has an infusion
    reaction on the 4th infusion that resolves with solumedrol and
    decreasing the rate of infusion
    – He felt the 2 weeks of antibiotics were the only thing that improved his
    symptoms
    – Prednisone was started as he felt he has been responsive to this in the
      past
    – Referral made to colorectal surgery

• The patient travels frequently to Asia for
  business and does not return for 2 months
  – On prednisone he has an improvement in his
    symptoms of N/V and discontinues reglan, and gains
    20 lbs.
  – He visited a surgeon in Beijing who noted on SBFT
    that the contrast material passes from his stomach,
    through the pylorus into the duodenum, through his
    duodenojejunostomy and back up through his
    gastrojejunostomy into the stomach
  – He remains reluctant to undergo further surgical
    intervention

• One month later, he has lost 8 lbs and appears
  very frail. He is unable to drink more than 1 can
  of Ensure per day
• Medications: infliximab, rabeprazole, INH, B6
• Labs:
  – WBC COUNT 4.7 x10^9/L 3.4-10
  – HEMOGLOBIN 6.7 g/dL 13.6-17.5
  – HEMATOCRIT 22.9 PERCENT 41-53
  – PREALBUMIN 6 mg/dL 20-37
  – ALBUMIN 1.7 g/dL 3.4-4.7
  – SEDIMENTATION RATE 8 mm/h 0-10
  – C REACTIVE PROTEIN 8.3 mg/L <6.3
• The patient was admitted to the hospital
  – Blood transfusion
  – Total parenteral nutrition
• What further medical or surgical therapy would you consider at this time?

Surgical Intervention
• Takedown of gastrojejunostomy.
• Takedown duodenojejunostomy.
• Partial resection of the jejunum.
• Excision of the third and fourth portion of the duodenum.
• New Roux-en-Y gastrojejunostomy and duodenojejunostomy.

Follow-up
• The patient presented to the office 2 months later doing well
• He had gained 35 lbs since his surgery and had no further episodes of obstruction, nausea or vomiting
• He and his wife adopted a child from Taiwan
• Medications:
  – Infliximab 5 mg/kg every 8 weeks
  – INH 300 mg until 12/06
  – Proton pump inhibitor
• Repeat EGD planned for 12/06

Gastroduodenal Crohn’s Disease
Incidence

- Gastroduodenal CD: 1-5% of all CD pts
- Endoscopic data: higher incidence 7-76%
  - Oberhuber, Gastroenterology 1997:112:698-706
- Maybe more common in patients with combined ileal and colonic disease
  - (Lanets, Seidman. Pediatrics 1989)
- Isolated gastric CD (~14 cases, 1989) or duodenal CD w/o distal disease rare

Definitions

- Noncaseating granulomatous inflammation of stomach or duodenum w/ or w/o obvious CD elsewhere in GI tract
- Documented CD elsewhere in GI tract and diffuse inflammatory change in stomach or duodenum consistent with CD
- Focal gastritis in H pylori negative patient.

Onset of Gastroduodenal Disease

- **Nugent & Roy**
  - 89 patients (largest)
  - Onset of GD disease:
    - 46 (52%) distal first
    - 27(30%) simultaneous
    - 16 (18%) GD first
    [9/16 later distal dx]

- **Yamamoto**
  - 54 patients
  - Onset of GD disease:
    - 30 (56%) distal first
    - 19(35%) simultaneous
    - 5 (9%) GD first
    [3/5 later distal dx]

Disease Distribution

- **National Coop CDT**
  - 535 pts
  - 1% gastric
  - 8% duodenal
- **Nugent & Roy**
  - Duo/antral (60%)
  - Duodenal alone (40%)
- **Yamamoto**
  - Duo/gastric (22%)
  - Duodenal alone (78%)
  - bulb (37%)  
  - Bulb+2nd (13%)
  - 2nd (11%)
  - 2nd+3rd (4%)
  - 3rd+4th (13%)

Symptoms

**Nugent & Roy**
- Upper abd pain (79%)
- Wt loss >10 lbs (64%)
- N/V (61%)
- UGIB (17%)
- Pancreatitis (2/3 on AZA)
- Gastroparesis

**Yamamoto**
- Upper abd pain (70%)
- N/V (50%)
- Weight loss (28%)
- Diarrhea (22%)
- Hematemesis (7%)
- Anemia 1 (2%)

Radiographic Features

- 83/89 (93%) abnormal radiography
  - irregular mucosal thickening, edema, ulceration, nodularity, cobblestoning, aphthoid lesions
  - gastroduodenal stenosis
    - Kantor (string) sign, fissures, pseudodiverticula
    - Ram’s horn sign (funnel shaped antrum): stenosis
    - Free perforation, fistulas rare

Endoscopic Features

- 67 patients, 62/67 abnl (93%)
  - granular, friable, nodular mucosa
  - superficial ulceration
  - aphthoid, linear, stellate, serpiginous ulceration
    - not round or oval like PUD
  - diminished distensibility
  - stenotic pylorus
  - thickened folds

Pathology

- Granulomas: High PPV, low sensitivity
  - 9-15% of patients
- Focal acute inflammation [27-81%]
  - Riddell: 56% pts (31% stomach, 40% duo)
  - Nugent: Acute/chronic inflamm. 65% (41/63)
  - Tanaka: 76% patchy inflammation
- Mashako (J Ped G+N, 1989)
  - 13/31 (42%) children UGI disease by EGD/bx
  - 9 (29%) CD confirmed by EGD; colon bx NDx
Endoscopy

- 75 CD: 28 ‘staging’ UGI sx; 200 controls
- HP +: 33% CD, 34% controls
- 71.4% (36/50) HP(-) CD pts: Focally enhanced gastritis
- Granulomas in 11/75 (15%) CD patients
- 76% of HP(-) CD pts and .8% of controls have either granulomas or focal gastritis.

Oberhuber, Gastroenterology 1997;112:698-706

Complications

- Obstruction, pyloric stenosis: (most common)
  - 54 pts: stricture (76%)
  - ulceration (7%)
  - fistula (4%)
- Common Bile Duct Obstruction: (2 cases)
- Free perforation: (1 GD perforation recorded)
- Upper GI bleeding:
  - Yamamoto 1/54 GD, Nugent 1/89 GD
  - Pardi: 1/31 IBD/GIB had GD. Endoscopic therapy

Yamamoto, Scand J Gastro 1999;34:1019-1024

Complications

- Adenocarcinoma
  - Duodenal: 1 case adenoca in duodenal CD
  - Gastric: Rare
    - Felt gastric adenocarcinoma is not increased in patients with CD
      - (Ekborn 1655 CD, 12 Gastric cs)
    - Most cases of gastric adenocarcinoma in CD are not associated with the presence of gastric Crohn’s

Gastroduodenal Fistula

  - Duodenal fistulas: 16/6313 CD pts (i=0.25%)
  - 4/16 had GD disease
  - 9 colonic, 5 ileal, 2 biliary, 1 jejunal, 1 ileotransverse colostomy, 1 cutaneous
  - 14/16 surgical tx, 1 recurrence
- Usually not associated w/ underlying GD dx
  - Yamamoto (1998): 0/14 GD fistulas
  - Jacobson (1985): 0/6 GD fistulas
  - Goldwasser (1980): 0/23 GD fistulas
- Therapy
  - Simple excision and closure of fistula
  - Wolff: reinforce duodenal repair with Gerota’s fascia or Omental patch
Outcome

- Median f/u 10 years: 80 pts
- 49 pts treated medically: 42 did well
  - steroids, H2 blockers, SAS, AZA
  - 4 deaths: 3 died result of distal CD, 1 lung ca
- 33 pts (37%) surgical [26/30 good results]
  - 23/33 gastroduodenal obstr., 9 pain, 1 GIB
  - 11 gastroenterostomy, 11GE-vag, 4 Bill-vag, 3 Bl-vag,
  - 8 reoperation: obstruction, GIB, pain, stasis

Medical Therapy

- Medical therapy beneficial in ulcerating disease, fistulizing, not obstructive disease
  - Corticosteroids: Nugent 1989, Yamamoto 1999
  - H2 antagonists: some relief, anecdotal
  - PPI: Case reports, Valori (90), Bianchi (91)
  - Tacrolimus (0.15-0.29 mg/kg/d): Sandborn (1997)
    - 1 case of GD Crohn's. Good immediate response
    - d/c 4 weeks side effects: bridge to AZA/MTX tx
  - Infliximab
    - Case reports in the literature describe benefit
    - One report noted duodenal obstruction following infusion

Endoscopic Therapy

- Endoscopic balloon dilation of pyloric or postbulbar stenosis (10-20 mm balloons)
- 5 pts obstructive GD Crohn's
- Symptomatic relief in all 5
- 3/5 recurrent obstructive sx. over 4.2 years
- Serial dilation q 3-4 mos w/o complications or need for surgical intervention.

Outcome

- 54 pts with gastroduodenal CD.
- Stricture (41) ulceration (4) fistula (2)
- 33 (61%) required surgery
  - obstruction (30), fistula (2), bleeding (1)
  - bypass(16), strictureplasty(10), gastrectomy (4)
  - 11 reoperations: obstruction (9), stomal ulcer(2)
Surgical Therapy

- **Strictureplasty**
  - Concern for recurrence
- **Pyloroplasty**
- **Bypass procedures (gastrojejunostomy, Roux-en-Y duodenojejunostomy)**
  - blind loop syndrome
  - marginal ulceration

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**Surgical Therapy**

- 22 pts underwent surgery for GD Crohn's (Lahey Clinic)
  - Indication: obstruction 77%, pain 18%, GIB 5%
  - Operation: 64% duodenal bypass
    - Gastroenterostomy: 4
    - Gastroenterostomy/duo resection: 1
    - Gastroenterostomy/duo resection 1: duodenojejunostomy: 1
    - Vagotomy/antrectomy (Bill) 2: pyloroplasty: 1
    - Resection 3rd duodenum: 1
  - Mortality: 1 pt (4.5%)
  - 50% morbidity
    - Major: 32%(9): duo fistula, CBD transection, GOO, pneumonia, abscess, GIB, DVT, MI
    - Minor: 5 pts
  - 3 pts surgery duodenocolic fistula
    - 1 wound dehiscence, 1 pelvic abscess
    - 1 death with long-term flu from complications CD

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**SUMMARY**

- More common than thought (5% vs 75%)
- Granulomas, focal acute gastritis
- Usually accompanied by distal Crohn's
- Obstruction most common complication
- GD fistula usually arises from distal site
- Increasing role for medical therapy
- Surgical intervention often needed

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**Gastroduodenal Crohn’s Disease**

- **Mild-Moderate disease**
  - Proton Pump Inhibitor
- **Moderate - Severe disease**
  - Anti-TNF α therapy for induction and maintenance
  - AZA/6MP or MTX for maintenance
  - AZA failure
  - AZA/6MP or MTX
  - Tacrolimus Therapy
  - Experimental Agent

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**Annual Endoscopic Surveillance**