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Atypical Presentations of Crohn's Disease

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Consultant: AbbVie, Clinical Area – IBD

Advisory Board: Pfizer, Clinical Area – IBD

Outline

- Case #1: Josie
- Typical presentation of CD
- Case #2: Wendy

Case #1: “Josie”

- 24 y.o. female referred to Neurology at JH by local neurologist, for Lyme vs MS, in March 2010, because of her c/o ongoing extremity numbness L>R, one episode of bells palsy, treated for Lyme.
- ROS:
  - 5 lb. weight loss, alternating diarrhea and constipation, inability to sleep, ringing in her ears, fatigue, chest pain, joint pain in her knees and her wrists, neck pain, low back pain, trouble concentrating, skin rash, and weakness in her left arm and leg. She also reports muscle twitching and loss of muscle bulk.
- Past Medical History:
  - Significant for toxoplasmosis in her right eye that presented when she was a sophomore in high school. She is legally blind in that eye

- Seen by Rheum at JH March 2010
  - Ordered: labs, MRI, referral to neuro-optho, rheum
- But referred to me by neurology for possible Whipple's Disease (sx: weight loss, diarrhea, joint pain)
- June of 2010: GI
- Cc: She reports long history of "bad stomach."
- Reports constipation since 2006, requiring the use of occasional milk of magnesia. More recently, she has developed diarrhea alternating with normal stools alternating with constipation.
- She reports diarrhea approximately 50% of the time up to 11 stools per day. No nighttime symptoms, no urgency or tenesmus, no obvious blood in her stool.
- She reports previous to 2006, she had a bowel movement usually twice a day.

- Workup: upper endoscopy and colonoscopy. This revealed a normal appearing colon and upper digestive system. However, biopsies of her terminal ileum revealed ileitis.
- A capsule endoscopy also revealed lesions at the ileum consistent with ileitis.
- Blood work normal CRP & sed rate.
- Treated with Budesonide 9 mg daily.

- Saw Neurologist again in June: Labs revealed a low normal vitamin B12 level at 232 (normal MMA and homocysteine level)
- “Given that her low normal vitamin B12 level could be related to a malabsorption syndrome from her Crohn's disease, was treated with monthly B12 supplementation with 1000 mcg subcu/IM injections”

- September: GI: some N/V, RLQ pain, diarrhea and weight loss. Says numbness better on B12 injections but symptoms return 1 week prior to next injection
- Neurology thinks B12 Deficiency may be the cause of paresthesias
- Return December: Start Remicade, but needed clearance from Neuro…..

Update…..

- Was started on Remicade 5 mg/kg: Induction, then maintenance at same, Q 8 weeks
- Stopped B12 inj end of 2012 d/t high levels
- Dec 2017: IFX level 2, no antibodies, so infusion increased to 10 mg/kg Q 6 weeks
- Repeat level 2018: 7.8
- Pregnancies 2016, 2018, miscarriage 2020 between 8-12 weeks
- Re started B12 inj 2020
- Remains on Remicade 10 mg/kg Q 6 weeks, doing well

Typical Presentation of Crohn's Disease

- Diarrhea
- Abdominal pain
- Other: Weight loss, fever, N/V, rectal bleeding
- Extraintestinal manifestations in 6-35%
- Perianal disease – 4-10%
- Average lag time to diagnosis = 26 months (2 months UC)

Neurologic Presentation of Crohn's Disease

- Not very common, but are they just not reported?
- Neurological complications of IBD are one of the most under-reported EIMs in IBD (Hoekstra et al, BMJ Open Gastro 2020;7:e000526)
- But both UC And CD can manifest both in the peripheral and central nervous system
- Zois et al (Journal of Crohn's and Colitis (2010) 4, 115–124): neuro manifestations in IBD range from 0.25-35%
- Peripheral neuropathy is one of the most frequently reported neuro complications
- Causes: malabsorption & nutritional deficiencies; infections (as complication of immunosuppression); SE of medications (cyclosporine, sulfasalazine, biologics, Metronidazole); thromboembolism; immune abnormalities

Case #2: “Wendy”

- Labor Day weekend, 2020: email from nursing school classmate @ her daughter, does she have Crohn’s??
- At age 21, had sore throats and fevers; Strep -, Tonsillectomy May 2019. Moved to Balto for grad school
- Continued to have ST, fevers
- I agreed to see her. Apt set for end of Sept (video and then in person visit)

- Aug 2020, had same, plus pain in “butt cheek”, and labia while out of town……
- Saw Gyn, dx with Bartholin cyst, put on Keflex & Bactrim
- Anorectal pain worsened and presented to JH ER end August:
  - Has significant pain sitting to go to the bathroom
  - Had some pain with BM but used a laxative and pain improved
  - Denies fevers/chills, dysuria, hematuria, vaginal discharge
  - Denies blood in stool
- CT: showed perineal abscess 3.4 x 5.8 x 6.3cm.
  - Had a drain placed by IR which Drained 50 cc initially.
    - Drain removed a few days later
    - Had MRI pelvis that was normal
    - Off Abx, but throat ulcers returned

- Video then F2F Visit in mid September:
  - Noted for 20 pound wt loss since January, some fatigue
  - Ordered MRE, EGD, colonoscopy, labs
  - Labs: Low vit D, otherwise WNL
  - MRE: 1. Involuting fluid collection with fistula tract visualized in the left ischiorectal fossa, however, no direct anorectal communication visualized on this exam. 2. No MR evidence of Crohn's disease

Early October

- ? Return of abscess, treated with Cipro & Flagyl
- Then had return of ST and “throat ulcers”, treated with oral viscous budesonide

Nov 2020

- EGD: normal
- Colonoscopy: IMPRESSIONS: 1. The distal most 2-3cm of the TI were notable for erythema, small erosions, biopsied. More proximally the TI was normal, biopsied; 2. The anal canal and rectum were normal without any evidence for inflammation, fistula or fissure, biopsied; 3. The colon mucosa was otherwise normal; multiple random biopsies were performed using cold forceps 4. Pending biopsies, findings could support diagnosis of mild Crohn's.

Biopsies:

1. Small Intestine, Duodenum (Biopsy):

Normal duodenal mucosa.

2. Stomach (Biopsy):

Antral and oxyntic mucosa with inactive chronic gastritis. No Helicobacter pylori organisms are identified.

3. Small Intestine, Terminal Ileum (Biopsy):

Small intestinal mucosa with active chronic ileitis (ulceration, cryptitis, crypt distortion, villous attenuation).

4. Colon, Right and Transverse (Biopsy):

Normal colonic mucosa.

5. Colon, Left (Biopsy):

Normal colonic mucosa.

6. Rectum (Biopsy):

Normal colonic mucosa.

Note: Sections demonstrate ulcerative active chronic ileitis. The differential diagnosis includes infection, medication-related injury (NSAIDS), and inflammatory bowel disease (Crohn's disease). The findings would support a clinical impression of Crohn's disease if infectious and medication-related causes are excluded clinically.

Questions Re: Biologics

- Why is a biologic for Crohn's the best treatment?
- What the advantages and disadvantages of taking them?
- How long does one stay on a biologic?
- How do you know when you are in remission?
  How long does it take?
- Does the biologic increase the risk of cancer?
- What about pregnancy? Does it affect fertility?
- Do they make a fistula worse?
- What about steroids?
- What about other medications, like mesalamine? Azathioprine? Methotrexate?

- She agreed to start Infliximab
- Referred to colorectal surgeon
- MRI pelvis: IMPRESSION:
  Grade 4 transsphincteric fistula arising at 12 o'clock extending to the left ischioanal fossa where there is an associated abscess which extends along the left gluteal cleft

- Dec: Has EUA, Incision and drainage of perirectal abscess; Fistulotomy (< 1 mm sphincter, muscle incised)
- Jan: Abscess returned: MRI and EUA ordered by surgeon
  - MRI: IMPRESSION:
    - Grade 4 transsphincteric (NEW) fistula arising at the 2 o'clock position extending to the left ischioanal fossa with an associated large abscess which extends along the left gluteal cleft measuring up to 5.9 cm which is increased in size compared to prior examination
  - Has EUA and seton placed
    - Lots of pain so hospitalized over night

March 2021

- IFX increased after induction, to 10 mg/kg Q 6 weeks
  - Insurance denial, so OK for 10mg/kg Q 8 weeks
- MRI pelvis: grade 4 transsphincteric fistula arising at 2 o’clock position, extending to left gluteal cleft with interval decrease in size of associated abscess. Presence of left seton in this anal fistula tract

June

- Insurance demanding non-medical switch to biosimilar
- Colonoscopy to assess mucosal healing: WNL!
- Repeat IFX level = 15
- Colorectal surgeon leaves JH

Currently…..

- Had seton removed by another colorectal surgeon in July
- No recurrence of abscess or fistula
- Now on biosimilar of IFX, still 10 mg/kg Q 6 weeks

Perianal Fistulizing Crohn's Disease

- 23% of patients with CD develop a perianal fistula(s) in the first 2 decades after diagnosis, especially with rectal and colonic involvement
- 10% of patients with CD, a perianal fistula is the initial manifestation of CD, and the formation of a perianal fistula may precede the onset of intestinal CD by several years
- Unfortunately, perianal fistulizing CD is notoriously difficult to eradicate
  - 37% of patients experience refractory disease despite medical and surgical intervention
  - Up to 20% undergo a proctectomy

Lightner A. *Dis Colon Rectum.* 2020; 63: 1023–1026.

Oral & Pharyngeal presentations of CD

- Tonsillitis, pharyngitis typically precede the onset of more typical manifestations of CD by 2 years
- Case studies report presentations include:
  - Tonsillitis, may be purulent
  - Pharyngitis
  - Accompanied by: fevers, lymphadenopathy
  - Path can include granulomas

Other Atypical Presentations of Crohn's Disease

- Extra intestinal manifestations
  - arthropathies
- Hidradenitis suppurativa (HS)
  - Treat with anti-TNFs
- Gyn manifestations
  - Vaginal ulcers: must R/O Bechet's

Gyn Manifestations of CD

- Vulvar lesions most common
- May be a fistula (direct or contiguous spread) or “metastatic” (distant spread) presentation of CD
- Usually solitary painful ulcer, may have abscess
- Biopsy is necessary (granulomas)
  - R/O Bechet's
- Treat medically: Metronidazole, infliximab

Andreani et al International Journal of Surgery 8 (2010) 2–5

Conclusion

- Atypical presentations of CD are not common, but do exist!
- If someone is referred to you with no GI symptoms, consider atypical presentations and complete a work up
  - And may need to be repeated annually
- Management of atypical CD is similar to that of typical CD