MEETING OF THE MINDS

FAIRMONT ROYAL YORK, TORONTO

FRIDAY, November 4, 2022

MENTORING in IBD XXIII

THE MASTER CLASS

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Crohn's and Colitis Canada
Crohn et Colite Canada

UNIVERSITY OF ALBERTA

UNIVERSITY OF CALGARY MEDICINE

McGill UNIVERSITY

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UNIVERSITY OF TORONTO FACULTY OF MEDICINE

Advanced Therapies: Go Big or Go Small

Case-based Breakout Workshop

#IBDMinds2022

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Initial Presentation

- MC—referred to a pediatric IBD center at age 16
- At referral he had:
  - One-year history of loose, non-bloody stools, worsening in the prior 6 months
  - Now 5–6 liquid stools/day
  - Associated abdominal cramping around eating and stooling
  - 20 lb weight loss documented over 6 months

Initial Presentation

- At presentation:
  - Height 25th percentile
  - Weight 45 kg (<3rd)
  - Body mass index (BMI) 16.5 kg/m^2
  - Hb 108 g/L
  - Albumin 32 g/L
  - CRP 34 mg/L
  - Fecal calprotectin 2300 ug/g
  - Well advanced into puberty
  - No perianal disease

Initial Presentation

- Intestinal ultrasound
  - Bowel wall thickness (6 mm)
  - Hyperemia in terminal ileum
- Upper endoscopy
  - Erosions and small linear ulcers in gastric antrum, otherwise normal
- Ileocolonoscopy
  - Right colon, transverse colon and descending colon: small and aphthous ulcers on background of mostly normal mucosa
  - Sigmoid and rectum: larger ulcers, not deep, more diffuse inflammation
  - Terminal ileum visualized to 10 cm: erythematous mucosa with linear ulcers

Initial Presentation

- Biopsies
  - Acute and chronic inflammation with granulomas
- MR enterography
  - 25 cm segment in proximal ileum with increased wall thickness
  - Hyperenhancement, diffusion restriction and reduced peristalsis
  - No stricture
  - Terminal ileal segment described as having borderline upstream dilatation of 2.7 cm, but no stricture
- Paris classification
  - Crohn's disease A1b B1 L3L4a

Discussion Point 1

- What treatment would you recommend?

Case Evolution

- In discussion with patient and family
  - Infliximab initiated (5 mg/kg/dose rounded up)
  - Proactive therapeutic drug monitoring

Discussion Point 2

- Would you use combination therapy and MTX or AZA?

Case Evolution

- You decide to use combination therapy
- In addition to infliximab you initiated low dose oral once weekly methotrexate as concomitant therapy
- Trough level prior to 4th dose at week 12 was 12.4 ug/ml
- Infusions continued every 8 weeks
- Symptoms quickly resolved

Case Evolution

- Follow-up over the first 1 ½ years:
  - Patient in continuous steroid-free remission with weight gain of 30 lbs
  - Some increment in height (4.5 cm)
  - Infliximab dosage adjusted with weight gain
  - Serologic and fecal biomarkers quickly normalized and remained normal
  - Fecal calprotectin fell to 198 ug/g after only 2 doses of infliximab, then subsequently to 25 ug/g
  - Intention to verify mucosal healing via repeat ileocolonoscopy thwarted by problems with access (COVID-related)

Case Evolution

- At the 2-year mark:
  - Now in continuous clinical and biomarker remission
  - Asks to stop methotrexate

Discussion Point 3

- Would you be in favour of MTX being stopped?

Case Evolution

- Infliximab trough level 10.5 ug/ml
- Infliximab dosage increased
- Infliximab monotherapy continued
- Patient remained well on infliximab monotherapy until 8 months later

Case Evolution

- Following transfer to adult care, he presented with:
  - Recurrence of abdominal pain
  - Loose stools
  - 5 lb weight loss
  - Elevated CRP
  - Infliximab trough level was undetectable
  - Antibodies to infliximab were in the “high titre” range

Discussion Point 4

- Would you recommend any change in treatment?
- How would you monitor his response to treatment?

Case Evolution

- Treatment switched to adalimumab (160 mg/80 mg followed by 40 mg every other week)
- Concomitant methotrexate recommended
- His symptoms once again respond
  - ADA levels in the 12–13 ug/ml range
- Follow-up colonoscopy 6 months later indicates:
  - Healing of original colonic ulcers
  - Persistence of linear ulcers in terminal ileum

Discussion Point 5

- Would you recommend any change in treatment?

Case Evolution

- In discussion with patient, he indicates:
  - Very happy with the way he feels
  - Administering therapy subcutaneously suits his lifestyle at university
  - Does not wish to change from anti-TNF therapy
  - Agrees to increase dose interval to adalimumab 40 mg weekly
- Follow-up visits become less frequent
  - Continues to administer adalimumab weekly, even when away for a university year abroad

Case Evolution

- Unfortunately, upon return to Canada, he reaches out experiencing increasing abdominal pain
- Adalimumab levels were checked (results later indicated 24 ug/ml)
- He presents to the ER with:
  - Severe abdominal pain
  - Vomiting
  - Evidence of partial small bowel obstruction

Case Evolution

- Symptoms settle with conservative management
- Evaluations confirm:
  - Very mild colonic inflammation (scattered aphthous ulcers)
  - Ulcerated ileocecal valve with stricture precludes intubation of the terminal ileum

Case Evolution

- Laparoscopic surgery planned
- Surgeon resects 15 cm of fibrostenotic terminal ileum
- Another segment of thickened ileum more proximally shows no evidence of proximal dilatation and is left *in situ*

Discussion Point 6

- What treatment would you recommend post-ileal resection?
- Would you use monotherapy or combination therapy?
- When would you reassess the patient?
- Do you think the surgeon should have resected all the disease?