IBD in Pregnancy

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CANIBD meeting
Plenary Presentation Objectives

- Discuss the effect of IBD on fertility, pregnancy and fetal outcomes
- Discuss IBD medications and pregnancy
- Discuss the effect of pregnancy and the postpartum period on IBD
Outline

- Case history interspersed with data slides
- Interactive!!! *Shout if you read that properly!*
- Question and answer throughout presentation
- Summary & Take Home Messages
- Final questions (10 mins)
Financial disclosures

- Dr. Cynthia Seow

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Case History

- 29 year old woman with Crohn’s disease is considering pregnancy

- Let’s explore how we would best manage her
  - pre conception
  - during pregnancy
  - post partum?
Why is IBD in pregnancy an important topic?

- 0.5% of the Canadian population suffers from IBD
- Peak incidence of CD and UC: ages 20-40 years
- Women equally likely to be affected as men

Case Presentation – Preconception

- 29-year-old woman with ileocolonic and perianal Crohn’s disease.
- Medications:
  Azathioprine (150 mg PO daily)
  Infliximab (5 mg/kg every 8 weeks).
- 5 loose bowel movements per day.
- Her abdomen is soft, slightly tender in the right lower quadrant and has no active perianal disease.

She is concerned about whether and when she can get pregnant.
Discussion

• **Q1.** How would you counsel the patient regarding the effect of disease activity on fertility and pregnancy?
Preconception counselling and disease optimization

- Fear of medication adverse effects highly prevalent.

- Poor awareness of the harmful effects of IBD flares.

- Contributor to
  - non compliance, medication cessation
  - voluntary childlessness (14-18% IBD vs 6% non IBD)

Effect of IBD on Fertility

- In the absence of surgery, physiologic fertility rates are the same as the general population.
  [Systematic review 11 studies]

- Infertility rates pre vs. post IPAA (20% vs 63%) RR 3.91 (95% CI 2.06-7.44)
  [Metanalysis of 6 studies]

- Consider temporary ileostomy.

Effect of IBD on Pregnancy

23 studies, (n=15,007 IBD: 4,614,271 controls)

Preterm birth
OR 1.85

SGA
OR 1.36

Congenital anomalies
OR 1.29

Stillbirth
OR 1.57

IBD activity during pregnancy

- Disease course depends on disease activity at conception
  - Remission at conception:
    - ~70% remission
    - ~30% active disease
  - Active disease at conception:
    - ~70% persistent activity
    - ~30% improve

IBD activity during pregnancy

- **Active IBD is associated with increased risk of**
  
  - Premature birth (<37 weeks) (up to 3-fold increase)
  - Low birth weight infants (<2500g) (up to 3-fold increase)
  - Miscarriage (active UC) aOR 4.10 (95% CI: 1.2–13.9)
  - Stillbirth (active CD) aOR 4.46 (95% CI: 1.7–11.9)

So how do you achieve this???
Discussion

- **Q2.** What tests should be arranged to assess disease activity?

- **Q3.** Would you order different tests if she was pregnant?
Disease activity assessment

- Full objective assessment best done **pre conception**
- Biomarkers - validity during pregnancy
- Radiology (sonography or MRI)
- Endoscopy
  - Timing
  - Medications
  - Fetal heart rate monitoring

Case Presentation – Preconception

- Harvey Bradshaw Index (HBI): 7
- Hemoglobin (Hb): 105 g/L
- White blood cell (WBC) count: $4.6 \times 10^9$/L
- Platelet count: $235 \times 10^9$/L
- Ferritin: 10 pmol/L
- C-reactive protein (CRP): 25 mg/mL
- Fecal calprotectin (FCP): 1000 µg/g
- **Magnetic resonance enterography**: 10 cm thickened distal ileum
- **Colonoscopy**: Distal ileal ulcers, mild right-sided colonic disease
• **Q4.** Is she in remission and would you change her management?
Case Presentation – Pregnant

- The patient was dose-escalated to 5 mg/kg infliximab every 6 weeks.
- She declined corticosteroids but accepted iron infusions.
- She achieved clinical remission at the 8-week mark.
- She returns to your office 6 months later, indicating she is ~8 weeks pregnant.

- She would like to stop her azathioprine and infliximab now that she is feeling better.
Case Presentation – Pregnant

- HBI: 4
- Hb: 110 g/L
- WBC: 4.6 x 10^9/L
- Platelet count: 235 x 10^9/L
- Ferritin: 75 pmol/L
- CRP: 5.7 mg/mL
- FCP: 175 µg/g
**Discussion**

- **Q5.** Is she now in remission? How will you monitor her disease activity during pregnancy?

- **Q6.** How would you counsel her about ongoing use of azathioprine and infliximab?

- **Q7.** What adjustments, if any, should be made to the dose and timing of her medications?
Disease optimization throughout pregnancy

- Consultation with an obstetrician, preferably one affiliated with a high risk obstetrics program.

- Ongoing management by GI: **Women overestimate the harmful effects of medication** and underestimate the harmful effects of IBD flares during pregnancy.
Women on 5-ASA, thiopurines, or anti-TNF therapy should **continue therapy** throughout pregnancy.

Thiopurines

- No increased risk of congenital anomalies
- Risk of preterm birth: conflicting evidence (medication vs disease activity)
- Altered maternal thiopurine metabolism during pregnancy
- Neonatal anemia

Anti-TNF therapy

- In general, anti-TNF therapy is associated with a ~2 fold increase in remission rates vs. placebo

Red Light  Green Light

To Stop or not to Stop?

Anti-TNF therapy

- The risk of continuing therapy: Neonatal and cord blood levels (up to 4-fold higher than maternal peripheral blood)

- Consequences?
  - Increased infections with combination therapy not anti-TNF monotherapy
  - Neonatal neutropenia (n=4)
  - Avoid live vaccines in neonates

Anti-TNF therapy

- Anti-TNF therapy is not associated with an increased risk of unfavourable pregnancy outcomes.

OR 1.00 (0.72-1.41)

All adverse events: abortion, preterm birth, LBW, congenital malformations

Anti-TNF therapy

• The risks of stopping therapy:
  • Case selection
  • No increased risk of relapse with 2nd trimester cessation
  • Intrapartum relapse 8-14%
  • Post partum relapse 32%

• Higher rate of unfavourable pregnancy outcomes
• Issues with drug hiatus, relapse, antibody formation.

So what do we do with anti-TNF therapy?

- **Modify** the dosing schedule, minimise drug hiatus
- **Resume** post partum ‘baby out, drug in’!

Additional considerations

- Dose modification not cessation of anti-TNF therapy

- Don’t start de novo thiopurine therapy intra partum

- Steroids vs anti-TNF
  - Past history of response
  - Trimester
    - Comorbidities: gestational diabetes, hypertension, pre-eclampsia

- Other: 5-ASA (DBP vs DBP-free)
**Case Presentation – Pregnant**

- You continue azathioprine and infliximab at the current dosing.

- She is referred to the high-risk obstetrics program at your hospital, where she is monitored with perinatal ultrasounds and assessments for fetal growth.

- She is dependent on the infliximab dosing regimen (q 6 weeks) and is scheduled to receive her last intrapartum infliximab at 34 weeks.
Discussion

Q8. What should the patient be told about delivery method (vaginal delivery versus C-section)?
Mode of Delivery

So, you say having a c-section is taking the easy way out? Is using the jaws of life the easy way to get out of a car?
Mode of Delivery

- Decisions regarding cesarean delivery should be based on obstetrical considerations and not IBD diagnosis alone.

- Exceptions are active perianal Crohn’s disease, IPAA.

- Anticoagulant thromboprophylaxis for C section

Case Presentation – Pregnant

- She is planned for a vaginal delivery given the absence of active perianal disease.

- However, due to slow progression of labour, she requires a cesarean delivery.

- The C-section goes well, and she has no complications.

- The baby weighs 7 lb 3 oz and is healthy!
Discussion

• Q9. What adjustments, if any, should be made regarding her medications after delivery? Should the baby have any special tests?
Post Partum Care

- Continue/resume medications post partum
- Consider neonatal Hb
- Avoid live vaccines within the 1st six months, if exposed to anti-TNF therapy in utero.
Discussion

- **Q10.** She would like to breast feed. How would you counsel her about the use of medications during lactation?
Lactation and IBD

• With the exception of methotrexate, the use of IBD medications should not influence the decision to breastfeed, and vice versa.

• Breastfeeding may be protective against relapse
  - May have a protective effect against the development of early onset IBD in the offspring

Conclusions: IBD and pregnancy

- Optimizing mom’s health is in the best interest of mom and baby
- Ongoing disease reassessment is necessary
- Continue medications throughout pregnancy
The fun has only just begun….

I’m afraid you have what’s known as “children.”

Questions?
Key References

