SESSION 3
COMBINATION THERAPY

CASE-BASED BREAKOUT WORKSHOP

Jacqueline is a 32-year-old female working as a paramedic with an eight-year history of ileocolonic Crohn's disease (CD). She was on azathioprine soon after diagnosis, then transitioned to methotrexate. Adalimumab was commenced 5 years ago but the concomitant methotrexate was subsequently stopped at her request after 1 year of combination therapy. Her CD has been 'controlled' with 40 mg of adalimumab every 2 weeks as monotherapy for the last 4 years. She reports increasing symptoms over the last 6 months, during which time she had the initial COVID vaccine, the second dose and most recently a booster COVID dose.

She currently has three semi-formed bowel movements (BMs) per day and abdominal cramps and feels fatigued.

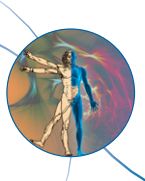
Her investigations revealed:
- WBC: 8.0 x 109/L
- Hb: 98 g/L
- CRP: 7 mg/L
- Alb: 34 g/L
- Fecal calprotectin: 2671 mcg/g
- Stool C and S negative
- *C. difficile* negative

Decision Node 1

- Is any of the above attributable to the COVID vaccine?
- What management strategies would you consider at this time, if any?
- Would you dose optimize the adalimumab and how?
- Do you check an adalimumab level and why?

You advise Jacqueline that the frequency of adverse effects to the COVID vaccine in individuals with IBD is similar to that reported in the general population, and of note, IBD patients on biologic therapy were less likely to experience an adverse effect.

You decide to check an adalimumab level while on 40 mg every other week, which returns at 12.3 mcg/mL. Bowel ultrasound reveals prominence of the terminal ileum and sigmoid. After discussion with the patient, you decide to dose escalate to 40 mg weekly for three months, then re-evaluate accordingly. Unfortunately, her symptoms progress and she requests to change therapies. Jacqueline also mentions new perianal discomfort.



Decision Node 2

- What other investigations do you request?
- What therapeutic options can she consider next?

Colonoscopy reveals moderate inflammation with occasional ulceration in the terminal ileum, the descending colon and the sigmoid without rectal involvement. Perianal examination is non-contributory, but digital rectal examination reveals moderate hemorrhoids, which you believe are contributing to her perianal discomfort.

Jacqueline declines any further anti-TNF therapy after reading reports of waning antibodies to COVID and is not reassured by her recent booster COVID vaccination. She requests a 'gut-specific' option that will not affect her 'immune system'. Intravenous induction and subcutaneous maintenance doses of vedolizumab are provided. She states she is far less fatigued and has an overall improved sense of well-being at her 3- and 6-months follow-up appointments.

Jacqueline reports she has been wearing a pad because of blood and 'pus' leakage from her 'hemorrhoids'. MRI demonstrates a small trans-sphincteric tract leading out to the gluteal skin corresponding to an updated perianal physical examination.

You increase the vedolizumab dosing to q4w for 6 months. There is further improvement in her bowel frequency and abdominal pain, and she achieves mucosal healing as evidenced by colonoscopy. You had hoped there may be some effect on her perianal disease, but the discomfort worsens, with the development of complex branching perianal fistulae.

Decision Node 3

- What are your current therapeutic options?

You ponder whether to go back to an anti-TNF, add an anti-TNF to the existing vedolizumab, reintroduce an immunomodulator, switch to ustekinumab, or wait for approval of the new IL-23 selective agents or JAK inhibitors. While you are scratching your head over these complex decisions, Jacqueline calls your office about a new skin rash on her neck, behind her ears, and on her lower limbs.

Decision Node 4

- What do you do next?
- Does it matter in which order you use the different therapeutic options?
- Can you go back to a previously used mode of action, should you combine two agents that have worked incompletely but may work synergistically, or should you just try something new for which there is a relative paucity of data to help this specific case?

Select Recent References

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