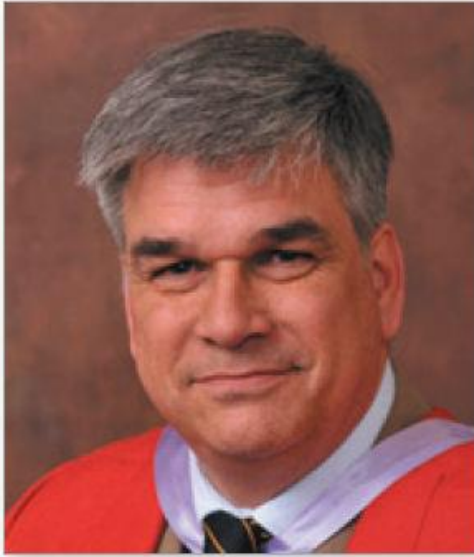




Professor Michael Schultz

Professor

Gastroenterologist and

Head of Department Dunedin School of Medicine

Sunday, August 11, 2019

(Room 10)

8:30 - 9:25 WS #154: Case Studies in Gastroenterology

9:35 - 10:30 WS #164: Case Studies in Gastroenterology (Repeated)

Bloody diarrhea

Michael Schultz

Case

- 19 year old female patient, Miss AB
- Noticed changes in her bowel habit since December 2018
- Developed bloody diarrhoea initially while she was travelling in Australia
- Saw GP in Australia in January 2019
- She had rigid sigmoidoscopy performed. Impression was haemorrhoids, given ultraproct ointment for treatment
- Symptoms did not improve. On going bloody diarrhea but patient continued to carry on with normal life
- Symptoms got worse in April 2019

Case

- Frequency of bloody diarrhea increased, now up to 12 bowel motions per day and Left Iliac Fossa (LIF) pain
- She presented to GP in Dunedin on 10/5/19
- Prescribed Loperamide by GP. Referred to gastroenterology clinic
- Seen in gastroenterology clinic on 22 May 2019
- 6 months history of watery diarrhoea associated with fresh blood and mucous
- Symptoms worse over the past 6 weeks with diarrhea up to 12 times/day including bloody diarrhea up to 6 times/night, worsening LIF pain, weight loss of 3 kg, reduced appetite and feeling generally unwell

History/Examination

- No significant past medical history or family history
- Not on any long term regular meds
- On Loperamide as prescribed by GP recently
- Stopped Ultraproct ointment as no improvement in symptoms
- Tender in Left Iliac fossa and right iliac fossa on abdominal exam
- Temp: 37, Heart rate: 110/min, BP: 110/70

Investigations

- Bloods: Hb 100g/L, Plts 609, WCC 14.5, CRP 136mg/L, Albumin of 17g/L
- Stool PCR and *C. diff.* negative
- Faecal calprotectin > 3000 ug/g
- Abdominal X-ray performed



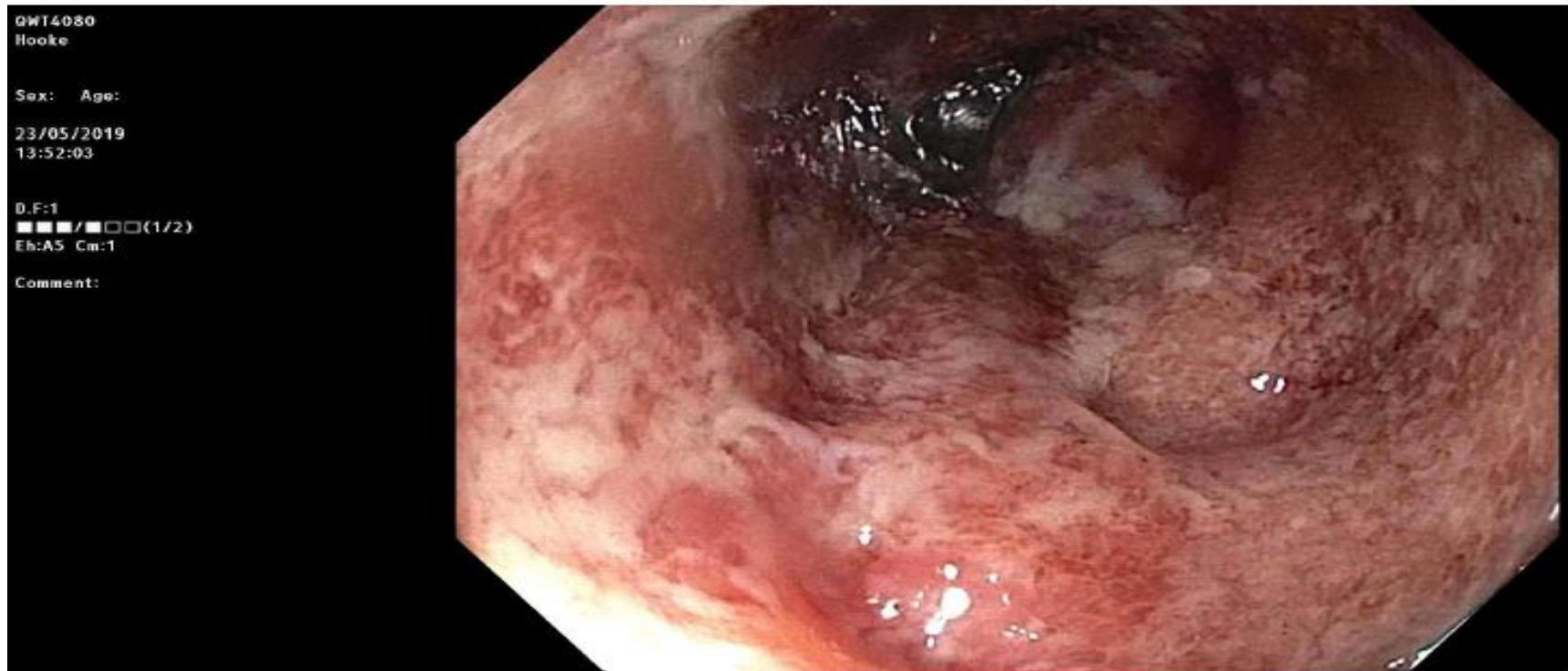
Flexible sigmoidoscopy

Images:



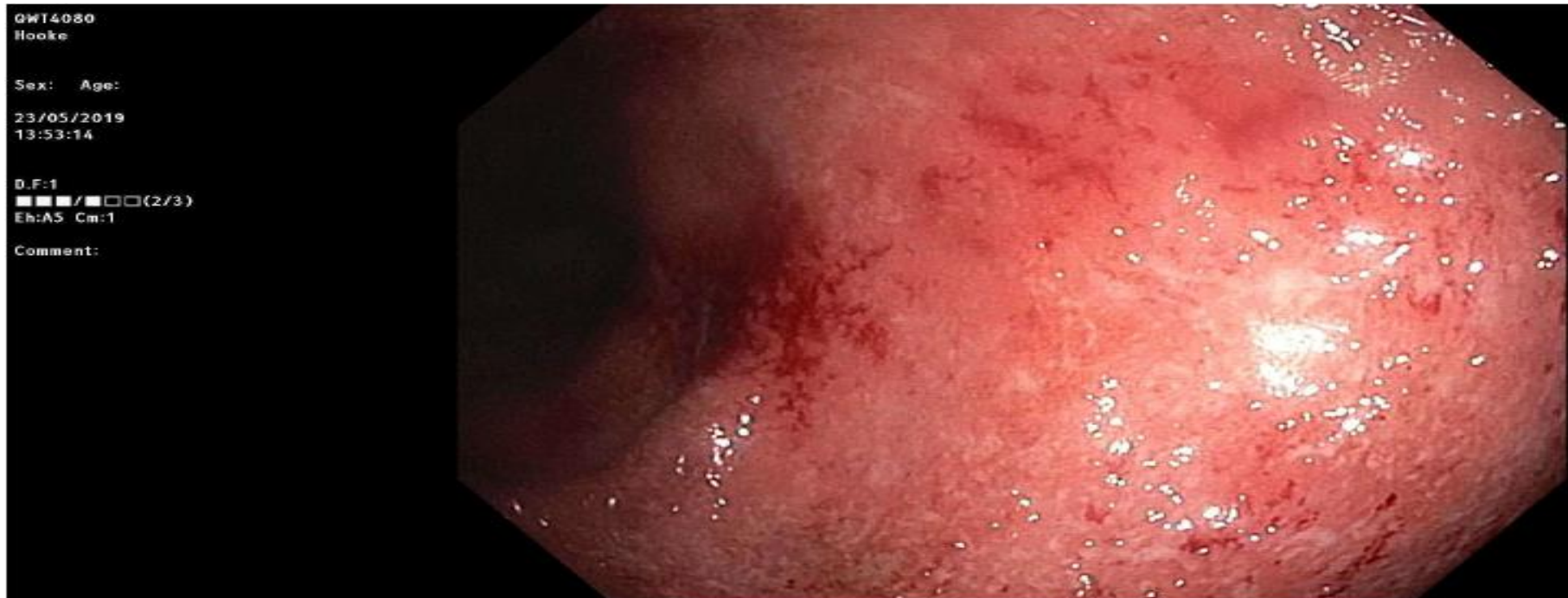
Rectum

Flexible sigmoidoscopy



Sigmoid Colon

Flexible sigmoidoscopy



3

Sigmoid Colon

Flexible sigmoidoscopy

- Severe inflammation characterised by adherent blood, altered vascularity, congestion (oedema), friability, loss of vascularity, mucus and confluent ulcerations was found in a continuous and circumferential pattern.
- Impression was severe acute ulcerative colitis
- Histology later came back showing moderate chronic active colitis

Management

- IV Methylprednisone 60 mg daily
- Clexane 40 mg s/c daily
- Dietician review –low residue diet
- Colorectal surgical team review
- Initial response to IV steroids
- Decrease in number of bloody diarrhoea to 7 to 8 times/day, improved appetite, energy levels
- CRP dropped to 103mg/L on day 1, 40mg/L on Day 2, 31mg/L on day 3

Management

- CRP still > 30, patient still passing 7 to 8 episodes of diarrhoea with PR blood
- She was being considered for escalation of therapy
- Infliximab or Cyclosporin vs Surgery (colectomy)
- IV Steroids continued
- On day 4 symptoms got worse. She was passing up to 9 episodes of bloody diarrhea
- CRP worsened to 56mg/L
- Decision made to escalate therapy as it appeared she had not responded fully to IV steroids

Management

- IV Infliximab (Anti- TNF) infusion commenced on 26/5/19
- 5 mg/kg induction dose
- Steroids stopped following 7 days of treatment
- Patient started to respond to Infliximab treatment
- Frequency of diarrhoea gradually improved to 3 to 4 bowel motions with no blood
- CRP improved from 56mg/L to 7mg/L in next 1 week
- Albumin improved from 17g/L to 24g/L in 1 week
- 2nd dose of Infliximab given on 4/6/2019

Progress

- Patient commenced on Azathioprine at 50 mg od
- Her TPMT level was normal at 260
- Patient discharged on 4/6/19
- On discharge was passing 1 to 2 well formed bowel motion
- IV Infliximab 3rd dose given at week 6 (early July) and plan is to have 8 weekly infusions thereafter
- Patient to continue Azathioprine at 50 mg od
- Normal CRP of 2mg/L, Albumin 33g/L now

Rationale of adding Azathioprine

- Patient on infliximab monotherapy are at increased risk of having the effect of infliximab wear off (secondary non-responder)
- This is due to antibodies developing to infliximab
- Adding Azathioprine will reduce the risk of this antibodies developing

Acute Severe Ulcerative Colitis (ASUC)

- Acute Severe Ulcerative Colitis (ASUC) may be the presenting feature of new onset UC in approximately a third of patients
- It typically presents as an acute on chronic disease and also in a relapsing–remitting pattern but 20%–25% of patients may experience a severe exacerbation (flare) requiring hospitalisation for prompt medical treatment and due consideration for colectomy if medical therapy fails.
- Mortality risk reduces 1 to 2.9 percent with steroids treatment
- Acute Severe Ulcerative Colitis (ASUC) is defined by the Truelove and Witts criteria

Truelove and Witts criteria

	Mild	Moderate 'between mild and severe'	Severe
Bloody stools/day	<4	4–6	≥6 <i>and</i>
Pulse	<90 bpm	≤90 bpm	>90 bpm <i>or</i>
Temperature	<37.5°C	≤37.8°C	>37.8°C <i>or</i>
Haemoglobin	>11.5 g/dL	≥10.5 g/dL	<10.5 g/dL <i>or</i>
ESR	<20 mm/hr	≤30 mm/hr	>30 mm/hr <i>or</i>
CRP	Normal	≤30 mg/L	>30 mg/L

Truelove and Witts Severity Index*



	Mild	Severe	Fulminant
Stools (#/day)	<4	>6	>10
Blood in stool	Intermittent	Frequent	Continuous
Temperature (°C)	Normal	>37.5	>37.5
Pulse	Normal	>90	>90
Hemoglobin	Normal	<75% of normal	Transfusion required
ESR	<30	>30	>30

*Moderate disease includes features of both mild and severe disease.

ESR = erythrocyte sedimentation rate.

Source: Truelove SC, Witts LJ. *Br Med J*. 1955;2:1041-1048.

Acute Severe Ulcerative Colitis (ASUC)

- The immediate objective is to achieve clinical remission as defined by ≤ 3 stools per day without rectal bleeding

Differential diagnosis

- Infectious colitis
- CMV colitis. CMV colitis is associated with poorer outcomes and higher rates of colectomy. Diagnosis via immunohistochemistry (IHC) and PCR from colonic biopsy specimens
- Radiation colitis (radiation therapy to abdomen or pelvic region)
- Ischaemic colitis-acute onset abdominal pain, diarrhoea in pt's with vascular risk factors. Raised venous lactate
- NSAIDS could provoke flare of UC

Investigations

- Stool MC&S, Stool for *C. diff.* to exclude differentials including infectious colitis, *C. diff.* colitis
- Plain abdominal AXR both at presentation and at any time there is clinical deterioration
- AXR- to determine if there is colonic dilation (diameter ≥ 5.5 cm) or toxic megacolon (diameter ≥ 6 cm or cecum > 9 cm and systemic toxicity).
- An erect CXR or a lateral decubitus abdominal film may reveal colonic perforation.
- AXR may provide other vital information. The presence of faecal residue is consistent with uninflamed or normal colonic mucosa. Proximal constipation may be noted in left-sided or distal colitis. It may exacerbate distal disease and paradoxically require laxatives to clear, in addition to treatment of colitis.
- Mucosal islands (or 'thumb printing'), when seen, is a predictor of failure of medical treatment.



Investigations/Endoscopic assessment

- Endoscopic assessment with a limited, unprepared sigmoidoscopy and biopsies with minimal air insufflation should be performed by an experienced operator with biopsies taken to exclude CMV
- A full colonoscopy is unnecessary and may be associated with an increased risk of perforation.
- Validated endoscopic scoring system such as the Mayo endoscopic score to define severity of findings

Management

- Admit to a specialist gastroenterological ward for multidisciplinary care (medical and surgical).
- Anticholinergic, antidiarrheal agents, nonsteroidal anti-inflammatory drugs (NSAIDs), and opioid drugs should be discontinued in patients with severe colitis due to the risk of precipitating toxic megacolon
- Intravenous (IV) corticosteroid therapy in the form of IV methylprednisolone 60 mg/day or IV hydrocortisone 100 mg three to four times a day is the recommended standard
- Methylprednisolone are preferred because they are associated with less sodium-retention and potassium-wasting
- IV fluids with correction of electrolyte imbalance; in particular serum K⁺ as hypokalaemia can predispose to colonic dilatation

Management

- Dietician review with nutritional assessment and optimisation of nutritional status is important for successful outcomes.
- Bowel rest is not recommended in patients as it has no established benefit on disease activity
- Intravenous antibiotics (eg. ciprofloxacin and metronidazole) if high grade fever, peritoneal signs or megacolon.
- There is no role of antibiotics in patients with severe colitis without signs of systemic toxicity

Management

- Patients with acute severe UC are at high risk of venous thromboembolism and patients with IBD have twofold to threefold higher risk of deep venous thrombosis than patients without IBD
- Compression stockings and subcutaneous prophylactic low molecular weight heparin /clexane
- Thromboprophylaxis does not precipitate or exacerbate colonic bleeding

Management

- Overall response to steroids is 67 %
- Patients that respond to IV steroid therapy will then be switched to oral prednisolone (40–60 mg daily with taper over the next 2–3 months).
- Up to a third of patients will fail to respond to intravenous corticosteroids and are termed 'steroid refractory'

Management

- The Travis scores are calculated following 72 hours of steroid treatment to identify patients at risk of failing steroid therapy who require colectomy or second-line medical therapy.
- Stool frequency $> 8/\text{day}$ or stool frequency > 3 day and CRP > 45 at day 3 associated with 85% likelihood of requiring colectomy
- 2nd line medical therapy to be initiated
- Option includes IV infliximab 5 mg/kg or IV Cyclosporin 2mg/kg/day
- If this fails, then surgery (colectomy) is last option

Management

- If medical therapy fails, then surgery (colectomy) is last option
- Colectomy needs to be considered if there is no improvement by days 4–7 with rescue medical therapy and in discussion with the multidisciplinary team.
- Colectomy can treat acute colitis by excising diseased tissue and reduces future risk of recurrence and malignancy.

Conclusion

- ASUC is a medical emergency that requires prompt recognition and hospitalisation
- Intravenous corticosteroid therapy forms the cornerstone of treatment for patients admitted with acute severe ulcerative colitis
- 33% of patients would not respond to IV steroids
- Steroid non-responders by day 3 to be considered for rescue therapy
- IV Infliximab is a good rescue option
- If no response to Infliximab within 4 to 7 days, then multidisciplinary approach to consider surgery
- Delaying or denying colectomy to the patient 'failing' medical treatment may lead to adverse outcomes

References

- Uptodate- Severe acute ulcerative colitis
- Management of Acute Severe Ulcerative Colitis-Medscape
- BMJ-Optimal management of acute severe ulcerative colitis- Saransh Jain, Vineet Ahuja, Jimmy K Limdi.