Hong Kong College of Physicians
Case Report for Interim Assessment
Specialty Board of Advanced Internal Medicine (AIM)

For AIM Training, case reports should be submitted in the prescribed format together with the application form for Interim Assessment at least EIGHT Weeks before the date of Interim Assessment

Name of candidate (print and sign):
Hospital and Unit: Specialty:
Name of supervisor (print and sign):
Date(s) and place (hospital) of patient encounter: 14th Jan, 2022
Date of report submission: 1st March, 2022

Case report

Note: Failure to follow the prescribed format (including the number of words) results in a FAILURE mark (score between 0 and 4) for the Case Report.

Title:
Just another case of GE?

Case history:

A 37-year-old Filipino was admitted through AED for 1 week's history of gastrointestinal symptoms. She presented with colicky and cramping lower abdominal pain and watery diarrhoea up to 15 times per day. She also started to notice fresh blood in stool, mild weight loss over the course of a few days, and poor appetite. Otherwise, she did not have vomiting and tenesmus. She denied urinary and respiratory symptoms, joint pain, or rash. She had no itching or red eyes. She did not have any haematochezia in the past. She also could not recall any ingestion of undercooked meat/seafood etc. She worked as a domestic helper and did not have recent travel history or contact history of tuberculosis. She did not have any recent use of medications including NSAIDs or traditional Chinese medicine. Before attending AED, she went to a private hospital and was given oral levofloxacin for 3 days with no improvement in her symptoms. She otherwise enjoyed good past health, did not smoke nor drink. Sexual and menstrual history were unremarkable.

Fever of 38 °C and sinus tachycardia of 118 beats/min were noted in AED with stable blood pressure of 120/70mmHg and normal saturation in room air. Physical exam revealed generalized abdominal tenderness but no guarding or rigidity. Initial investigations were performed, including a negative pregnancy test and unremarkable chest X-ray and abdominal X-ray (AXR). Blood tests revealed normal liver and renal function tests but found

Passed at Council Meeting on 24 Oct 2019

leukocytosis of 18×10^9/L, normal hemoglobin level of 14.8g/dL, mildly low albumin of 32g/dL, high C-reactive protein (CRP) of 14mg/dl and Erythrocyte sedimentation rate (ESR) of 55mm/hr. Urine routine microscopy was unremarkable. Stool was saved for further microbiological work up. In view of clinical picture of dysentery, she was started with intravenous ciprofloxacin.

However, she was noted to have persistent diarrhea. White cell count and CRP levels fluctuated but remained high. She also started to experience worsening abdominal pain with increasing abdominal distension without peritoneal signs. Repeated AXR showed dilated large bowels measured up to 8.3 cm (figure 1) and subsequent CT abdomen with contrast was performed and raised the suspicion of toxic megacolon. Gastroenterology team was consulted, and she was initially treated as possible clostridium difficile colitis in view of recent antibiotic usage with intravenous metronidazole, oral vancomycin and intravenous hydrocortisone. In view of indeterminate interferon gamma release assay (IGRA) result and use of steroid, isoniazid was also started.

Stool workup came back with negative multiple PCR, negative diarrheal virus panel and negative CD toxin and culture. Other workups including viral hepatitis B and C, CMVpp65, and thyroid function test were also unremarkable. Sigmoidoscopy was then performed showing extensive severe inflammation from rectum to 20cm sigmoid colon. Biopsy of the sigmoid colon demonstrated benign ulcer with no granuloma and viral inclusion or positive CMV antigen on immunostaining.

She was then monitored for treatment response. Unfortunately, AXR still showed dilated large bowel loops. A diagnosis of acute severe ulcerative colitis was suspected, and intravenous hydrocortisone 100mg every eight hours, mesalazine 2g twice daily and azathioprine 25mg daily were started first. Later, a dose of Vedolizumab 300mg was given in view of lack of clinical improvement (ten days from commencement of intravenous steroid). One day later, CXR revealed free gas under diaphragm, which was confirmed by CT as perforated viscus (figure 2).

Surgical team was immediately consulted and total colectomy with ileostomy was performed. Intraoperative finding showed turbid fluid at the peritoneal cavity over right upper quadrant and a 1cm perforation was noticed at proximal transverse colon, partially sealed off by omentum/ epiploicae. Entire colon from caecum to rectum was severely inflamed, thin and friable. Cut-open specimen showed inflammatory pseudopolyps and severely inflamed colon. Pathology confirmed diffuse ulceration, consistent with ulcerative

Passed at Council Meeting on 24 Oct 2019

colitis.

Post-operatively, hydrocortisone was switched to tapering course of prednisolone. Later, patient further developed per rectal bleeding on post-operation day 12. Sigmoidoscopy revealed two sites of active oozing at 8cm from anal verge and hemostasis was achieved with endoclips. Condition was stabilized and she was fit for discharge after around total one month of hospitalization. Vedolizumab maintenance was arranged 2 weeks later from first dose then 6 weeks and every 8 weeks thereafter, while ileal pouch rectal anastomosis (IPRA) would be arranged later.

Discussion and literature review

Ulcerative colitis (UC) is a chronic immune-mediated inflammatory disease limited to the mucosal layer of the colon. It commonly involves the rectum and extend in a proximal and continuous fashion. In this case, there was absence of rectal involvement, which has been noted in fewer than 5% of adult patients with UC. The pattern of disease activity is most often relapsing and remitting. Majority of patients have a mild to moderate course. However, about 10-15% presents with an aggressive course of disease as illustrated above. The 5- and 10-year cumulative risk of colectomy is 10-15% though rates of early colectomy have declined [1]. Prompt diagnosis and treatment is extremely important to decrease risk of colectomy and hence other morbidities and disabilities. UC is further categorized as extensive colitis (pancolitis), proctitis and left-sided colitis in terms of disease extent, according to the Montreal classifying system [2]. Extensive UC indicates disease involvement extending proximal to the splenic flexure, as seen in this case.

For this case, given her acute symptoms of inflammatory diarrhea, differentials were narrowed down mainly into infectious and inflammatory causes. Treatment was initiated to cover CD given the prior exposure to antibiotics prescribed by the private doctor, not only because CDI can present similarly as infectious colitis but also because CDI is recognized to complicate a significant proportion of patients with UC. It is associated with increased risk of hospitalization, surgery and even mortality among patients with inflammatory bowel disease (IBD) [3]. The diagnosis of CDI is established by either a positive nucleic acid amplification test (NAAT) for CD toxin B gene or a positive stool test for CD toxin(s).

Passed at Council Meeting on 24 Oct 2019

Endoscopically, finding of pseudomembranes on the inflamed mucosal surface are highly suggestive of CDI. In this case, IV metronidazole and oral vancomycin were given before negativity of stool culture and CD toxin was confirmed.

It is equally important to look for extraintestinal manifestations including joint, skin, ocular and hepatobiliary involvement (e.g. primary sclerosing cholangitis) which were absent in this case.

Endoscopic findings in patients with UC are non-specific. Typical findings include a continuously inflamed segment involving the distal rectum and extending proximally with features of inflammation including loss of vascular markings, granularity and friability of the mucosa, erosions, and, in the setting of severe inflammation, deep ulcerations and spontaneous bleeding. Biopsy of the colon is important to establish the chronicity of inflammation and to exclude other causes of colitis e.g. CMV colitis. Furthermore, as toxic megacolon was suspected, a flexible sigmoidoscopy, instead of full colonoscopy, with minimal insufflation of air should be performed to reduce risk of colon perforation and colonic dilation.

Determining the severity of disease is important once a diagnosis of UC is made. There are currently several quantitative disease activity indexes that are available. The Truelove-Witts classification of disease severity comprising six variables (i.e. bowel movements, blood in stool, pyrexia, pulse rate, anemia and ESR) is widely used. Mayo score is another commonly used index to assess disease severity and monitor patients during therapy. It incorporates stool frequency, presence of rectal bleeding, findings on endoscopy and physician's global assessment. The above case could well be classified as at least moderate to severe disease.

Goal of treatment for patients with active UC is to achieve complete mucosal healing. Corticosteroid therapy remained the mainstay of treatment for moderate to severely active UC and acute severe ulcerative colitis (ASUC). In steroid-refractory ASUC, either infliximab or cyclosporin can be used with similar efficacy [4]. Vedolizumab, an anti-integrin alpha 4 beta 7, also demonstrated effectiveness in moderate-to-severe UC [5]. It was chosen to be the therapy of choice in this case as IGRA was indeterminate and there was a risk of reactivation of latent tuberculosis. Patients diagnosed with latent TB prior to anti-TNF should be treated with a complete therapeutic regimen for latent TB [6].

Other treatment for moderate-to-severe UC include azathioprine, other anti-TNF agents (e.g. adalimumab), anti-interleukin 12/23 (e.g. ustekinumab), which demonstrated superiority over placebo in

Passed at Council Meeting on 24 Oct 2019

achieving response and remission in moderate-to-severe active UC [4]. Tofacitinib, an oral small molecule JAK inhibitor, is also used for treating adults with moderate to severe UC who have failed or are intolerant to anti-TNF agent-based therapy. Recently, ozanimod, an oral sphingosine-1-phosphate (S1P) receptor has also established its effectiveness as induction and maintenance therapy [7].

Indications for colectomy in UC include ASUC and chronic refractory UC not responding to traditional medical therapy and colonic dysplasia/cancer. The absolute indications in case of ASUC would include toxic megacolon refractory to medications, perforation, uncontrolled hematochezia and multiorgan dysfunction [8]. This case unfortunately showed inadequate response to medical treatment and was complicated with colonic perforation.

Vedolizumab would be continued as maintenance therapy in this case. A pivotal trial has proven effectiveness of vedolizumab 300mg IV every 8 weeks to maintain remission. A total 40% of patients receiving it maintained remission at 52 weeks compared with 16% of patients who received placebo [5].

Risk of colorectal cancer (CRC) in patients with UC is increased by 1.5-fold to 2-fold compared to general population [9]. Screening and subsequent surveillance colonoscopy to assess for dysplasia in individuals with UC of extent greater than the rectum should start 8 years after diagnosis, and surveillance examinations should be continued every 1-3 years. In this case, our patient underwent a subtotal colectomy with an ileostomy, surveillance examination of the remaining rectum is also performed every 1-3 years. If an ileal pouch anal anastomosis (IPAA) is done to restore gastrointestinal continuity, surveillance pouchoscopy is performed at timing guided by patient's risk for dysplasia. Overall, the incidence of CRC in patients with IBD who have undergone IPAA is low [10].

Passed at Council Meeting on 24 Oct 2019

Tables and figures (where applicable) (no more than two figures)

Figure 1. AXR showing thickened colonic wall, loss of haustrations and colonic dilation.

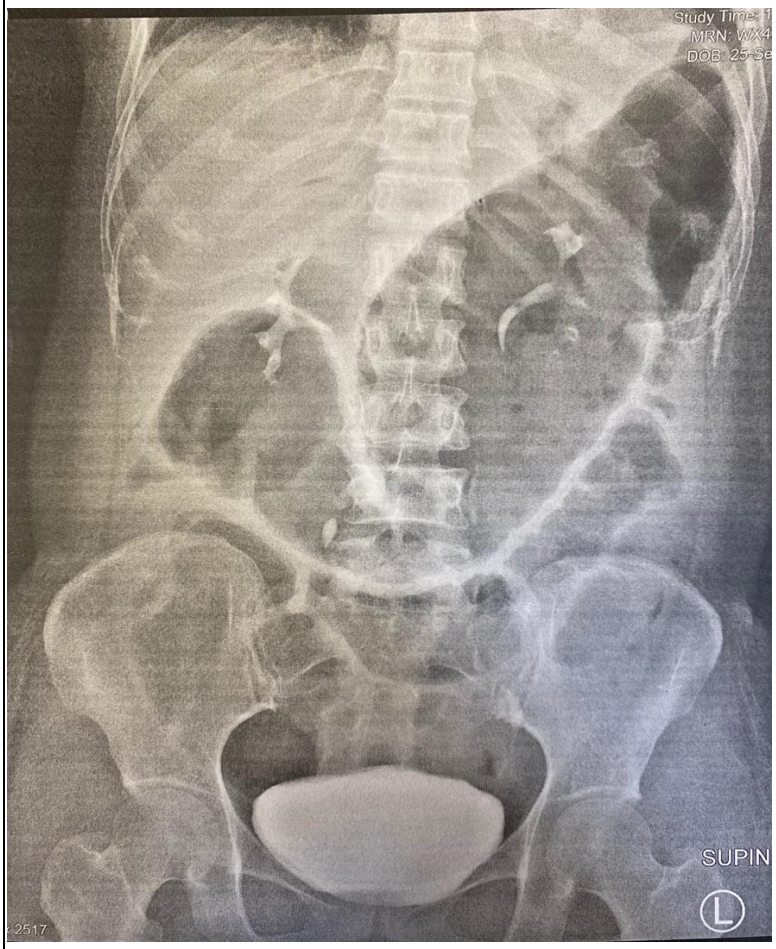
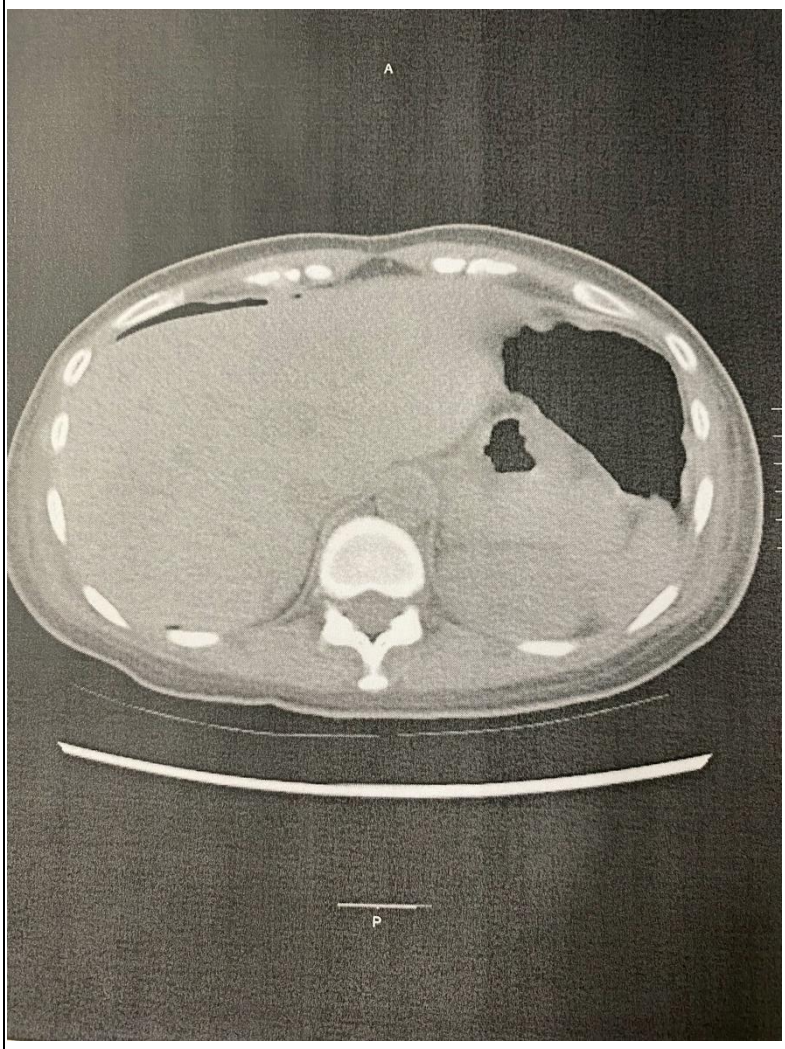


Figure 2. CT confirming free intraperitoneal gas


A
P

Reference (not more than 10)

[1] Mathurin Fumery, Siddharth Singh, Parambir S. Dulai, Corinne Gower- Rousseau, Laurent Peyrin-Biroulet, William J. Sandborn. Natural History of Adult Ulcerative Colitis in Population-based Cohorts: A Systematic Review. Clin Gastroenterol Hepatol. 2018 Mar;16(3):343-356.e3. doi: 10.1016/j.cgh.2017.06.016. Epub 2017 Jun 16.

[2] J Satsangi, M S Silverberg, S Vermeire, J-F Colombel. The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications. Gut. 2006 Jun;55(6):749-53. doi: 10.1136/gut.2005.082909.

[3] A N Ananthakrishnan, E L McGinley, D G Binion. Excess hospitalisation burden associated with Clostridium difficile in patients with inflammatory bowel disease. Gut. 2008 Feb;57(2):205-10. doi: 10.1136/gut.2007.128231. Epub 2007 Sep 28.

[4] David T. Rubin, MD, FACG, Ashwin N. Ananthakrishnan, MD, MPH, Corey A. Siegel, MD, MS, Bryan G. Sauer, MD, MSc (Clin Res), FACG (GRADE Methodologist) and Millie D. Long, MD, MPH, FACG. ACG Clinical Guideline: Ulcerative Colitis in Adults. Am J Gastroenterol. 2019 Mar;114(3):384-413.

[5] Brian G. Feagan, M.D., Paul Rutgeerts, M.D., Ph.D., Bruce E. Sands, M.D., Stephen Hanauer, M.D., Jean-Frédéric Colombel, M.D., William J. Sandborn, M.D., Gert Van Assche, M.D., Ph.D., Jeffrey Axler, M.D., Hyo-Jong Kim, M.D., Ph.D., Silvio Danese, M.D., Ph.D., Irving Fox, M.D., Catherine Milch, M.D., Serap Sankoh, Ph.D., Tim Wyant, Ph.D., Jing Xu, Ph.D., and Asit Parikh, M.D., Ph.D., for the GEMINI 1 Study Group. Vedolizumab as Induction and Maintenance Therapy for Ulcerative Colitis. N Engl J Med. 2013 Aug 22;369(8):699-710. doi: 10.1056/NEJMoa1215734.

[6] Rahier, J.F.; Magro, F.; Abreu, C.; Armuzzi, A.; Ben-Horin, S.; Chowers, Y.; Cottone, M.; de Ridder, L.; Doherty, G.; Ehehalt, R.; Esteve, M.; Katsanos, K.; Lees, C.W.; MacMahon, E.; Moreels, T.; Reinisch, W.; Tilg, H.; Tremblay, L.; Veereman-Wauters, G.; Viget, N.; Yazdanpanah, Y.; Eliakim, R.; Colombel, J.F. (2014). Second European evidence-based consensus on the prevention, diagnosis and management of opportunistic infections in inflammatory bowel disease. Journal of Crohn's and Colitis, 8(6), 443-468. doi:10.1016/j.crohns.2013.12.013

[7] Sandborn WJ, Feagan BG, D'Haens G, Wolf DC, Jovanovic I, Hanauer SB, Ghosh S, Petersen A, Hua SY, Lee JH, Charles L,

Chitkara D, Usiskin K, Colombel JF, Laine L, Danese S; True North Study Group. Ozanimod as Induction and Maintenance Therapy for Ulcerative Colitis. N Engl J Med. 2021 Sep 30;385(14):1280-1291. doi: 10.1056/NEJMoa2033617.

[8] Gaetano Gallo FASCRS, MD, Paulo Gustavo Kotze , MD, MsC, PhD, Antonino Spinelli MD, PhD, FASCRS. Surgery in Ulcerative Colitis: When? How? Best Pract Res Clin Gastroenterol. Feb-Apr 2018;32-33:71-78. doi: 10.1016/j.bpg.2018.05.017. Epub 2018 Jun 14

[9] Olén, Ola; Erichsen, Rune; Sachs, Michael C; Pedersen, Lars; Halfvarson, Jonas; Askling, Johan; Ekbom, Anders; Sørensen, Henrik Toft; Ludvigsson, Jonas F (2020). Colorectal cancer in ulcerative colitis: a Scandinavian population-based cohort study. The Lancet, 395(10218), 123–131. doi:10.1016/S0140-6736(19)32545-0

[10] Lauranne A. A. P. Derikx, Wietske Kievit, Joost P. H. Drenth, Dirk J. de Jong, Cyriel Y. Ponsioen, Bas Oldenburg, Andrea E. van der Meulen–de Jong, Gerard Dijkstra, Marina J. A. L. Grubben, Cornelis J. H. M. van Laarhoven, Iris D. Nagtegaal, andF rank Hoentjen, on behalf of the Dutch Initiative on Crohn and Colitis. Prior Colorectal Neoplasia Is Associated With Increased Risk of Ileoanal Pouch Neoplasia in Patients With Inflammatory Bowel Disease. Gastroenterology. 2014 Jan;146(1):119-28.e1. doi: 10.1053/j.gastro.2013.09.047. Epub 2013 Sep 25.

No of words in Case History and Discussion (excluding references):___1633_____. (should be between 1000-2000)

Declaration

I hereby declare that the case report submitted represents my own work and adheres to the prescribed format. I have been in clinical contact with the case selected. The case report has not been submitted to any assessment board or publication and it is NOT related to my second specialty(ies), if any. My consent is hereby given to the College to keep a copy of my case report, in written and/or electronic, at the College Secretariat and allow the public to have free access to the work for reference.

_____

(signature of Trainee)

Endorsed by Supervisor *

_____

(signature of Supervisor)

* Supervisors must go over the Case Report with the Trainees, advise Trainees whether further amendments are necessary, review the

Originality/ Similarity Report prepared by Trainees, adherence to the required format, sign on the report and remind Trainees on issues related to copyright and plagiarism.