Seminars in Colon and Rectal Surgery 30 (2019) 100689

Contents lists available at ScienceDirect

Seminars in Colon and Rectal Surgery

journal homepage: www.elsevier.com/locate/yscrs

Diverticulitis in the immunocompromised patient

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ARTICLE INFO

Keywords:
Diverticulitis
Steroids
Immunocompromised
Transplant
Immunosuppression

ABSTRACT

Diverticulitis in immunocompromised patients is of special clinical importance because these patients experience a higher rate of morbidity and mortality than the general population due to diverticulitis. Immunocompromised patients tend to present later than the general population and may have less impressive findings on physical exam and CT scan. They are more likely to fail non-operative management and have more complications after emergent surgery. Just like in immunocompetent patients, the decision to pursue elective colectomy after diverticulitis is individualized to the patient's risk of surgery, co-morbidities, effect on lifestyle, chronic symptoms, or severity of attacks.

Introduction

Diverticula are outpouchings of the colon wall and encompass a wide array of pathology including infection, bleeding, fistula, or perforations. Diverticular disease is common within industrialized nations with an incidence up to 50% in people over the age of 60 years old and increasing further with age.[1] The incidence also appears to be rising in younger populations.[1] Diverticular disease is the 5th most expensive disease in the gastrointestinal system with an estimated annual cost in the USA of over $2 billion.[2] Diverticulitis results from perforation of a diverticulum leading to pericolic inflammation from release of feculent material into the peritoneal cavity. Symptoms include abdominal pain, change in bowel habits, nausea, vomiting, or fevers. Diagnosis is typically confirmed and stratified into uncomplicated and complicated by CT scans.

Diverticulitis can vary widely in severity from localized inflammation to free perforation with peritonitis. The treatment of diverticulitis can be subdivided into non-operative and operative management. The majority of patients can be managed non-operatively with antibiotics and bowel rest. Patients with peritonitis or sepsis typically need operative management. Patients managed non-operatively in the acute setting may opt for elective resection once the inflammation has resolved. In the general population, recommendations regarding elective resection are based on patient symptomology and preference with emerging evidence suggesting elective resection can result in better lifestyle and improved costs.[3]

Immunocompromised patients represent a unique subset of diverticulitis patients. Immunocompromised patients are a diverse patient population including patients with certain malignancies, patients on chronic steroids or immunosuppression for rheumatologic or autoimmune diseases, transplant patients, liver or renal failure patients, or HIV/AIDS patients. Diverticulitis in immunocompromised patients is of special clinical importance because these patients experience a higher rate of morbidity and mortality than the general population due to diverticulitis. The cause of this increase is likely multi-factorial including delay in diagnosis, more severe disease at presentation, and inability to mount an effective immune response. This chapter will explore the scope of this problem, the presentation, the evaluation, as well as the recommended treatments for diverticulitis in immunocompromised patients.

Epidemiology

The number of immunocompromised patients continues to rise, and in the United States it is estimated that 2.7% of US adults are immunocompromised in some way,[4] This population includes 1.1 million patients living with HIV/ AIDS, 11 million with cancer, and approximately 200,000 patients with transplants.[5] The incidence of diverticulitis in the general population is 0.02%, but is estimated to be about 1% in chronic steroid and transplant patients.[5] There are approximately 300,000 annual hospitalizations for diverticulitis, and between 6% and 17% of those patients were immunocompromised.[6]

Immunocompromised patients encompass a wide range in demographics including age, race, and socioeconomic status. Most of the literature on diverticulitis in the immunocompromised population is focused on chronic steroids and transplant patients with little or no studies regarding treatment of patients with HIV/AIDS, primary immunodeficiencies, malnutrition, collagen vascular disease, or malignancies undergoing chemotherapy. In chronic steroid and

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https://doi.org/10.1016/j.scrs.2019.100689
1043-1489/

transplant patients, the general pathogenesis for the development of diverticulitis from diverticula appears to be the same as the general population.

Despite minimal research regarding diverticulitis and HIV, there is a rising number of HIV positive patients developing diverticulitis. A large database study found that these patients tended to be younger and non-white compared to the general population, but there was not an increased incidence of diverticulitis compared to the general population[7] Previous studies examining intrabdominal infections and surgical outcomes in HIV/AIDS patients found that the biggest predictor of survival was a CD4 count greater that 200.[8]

End-stage renal disease patients represent a large demographic of patients. These patients typically have a high incidence of bacterial translocation and impaired gastrointestinal motility. Large database studies demonstrate that the incidence of diverticulitis is 11 times greater in this population compared to the general population.[9] For patients with a relative immunosuppression due to malignancy or chemotherapy, there have been no major epidemiologic studies evaluating the incidence of diverticulitis.

Presentation and diagnosis

Diverticulitis in immunocompetent patients usually presents with stereotypical acute onset of left-sided lower abdominal pain. Typically, patients have additional gastrointestinal symptoms including nausea, vomiting, or diarrhea. A leukocytosis and associated fevers can corroborate the diagnosis. Physical exam is essential for the diagnosis of diverticulitis, and the presence of peritonitis indicates severe disease. Other findings such as fecaluria, pneumaturia, or pyuria could suggest suspicion of a colovesical fistula. Despite these common symptoms, other diseases including inflammatory bowel disease, irritable bowel syndrome, ischemic bowel, malignancy, or gynecologic disorders can mimic the symptoms of diverticulitis.

In immunocompromised patients, the main presenting symptom is abdominal pain (over 90%) and patients typically have a leukocytosis and fevers, though at a decreased rate than the general population.[5] Severe presenting signs such as hypotension are more common in immunosuppressed patients. Despite the similarity of presenting signs between immunocompetent and immunocompromised patients, immunocompromised patients appear to be diagnosed later. This is because immunosuppression, especially in the case of steroids, can mask the symptoms of diverticulitis. Immunosuppression inhibits the normal inflammatory response to a perforated diverticulum. The decreased inflammatory response results in a decreased sensation of pain. This results in patients being less likely to seek care and providers being less likely to investigate with imaging studies due to the indolent symptoms.

The main diagnostic tool for confirmation of diverticulitis is computed tomography (CT). CT scans are 98% sensitive and 99% specific for the diagnosis of diverticulitis when used with intravenous and intraluminal contrast.[3] CT scans can identify the severity of diverticulitis, perforation, or the presence of an abscesses. Stratification of diverticulitis is crucial at determining treatment options. CT scans may show colonic wall thickening, fat stranding, phlegmon, extraluminal gas, abscess, fistula, or stricture.[3] CT scans are helpful at monitoring the progression of diverticulitis following treatment especially in the setting of an abscess. The main disadvantages of CT scans are the radiation dose, and in early diverticulitis it may not be diagnostic.[3]

For immunocompromised patients, CT remains an essential diagnostic tool despite having a lower sensitivity and specificity. Because of the muted immune response, patients have atypical radiographic findings of diverticulitis and may only show extraluminal air, but no pericolic inflammatory changes, fluid, or abscess.[3] Despite these atypical CT findings, it provides the most detailed information that will directly influence treatment. Due to its immense diagnostic capability, providers should have a low threshold for CT scans in immunocompromised patients presenting with abdominal pain.

Treatment and prognosis

In the acute setting, treatment of diverticulitis can be divided into non-operative and operative management. The decision for which type of treatment to pursue is dependent on the patient's clinical status (Fig. 1). For the majority of patients, non-operative management is the optimal treatment. In cases of uncomplicated diverticulitis, patients can be managed as outpatient with oral antibiotics. In complicated diverticulitis, patients are usually admitted and treated with intravenous antibiotics. If an abscess were amendable, a drain can be placed percutaneously. Patients undergoing non-operative management for complicated diverticulitis typically improve but, in some cases require an operation. Operative treatment is undertaken for cases of hemodynamic instability, peritonitis, frank perforation, or failure of non-operative management. Operative management typically consists of an exploratory laparotomy, resection of diseased colon, and washout of the peritoneal cavity. The decision to perform a resection with end colostomy (Hartmann's procedure) or a primary anastomosis is surgeon and patient dependent, though there have been improved results in morbidity with primary anastomosis.[3] Creating a primary anastomosis with a diverting ileostomy is another option, given that ileostomies are more likely than end colostomies to be taken down and have lower complications associated with takedown.[3]

For immunocompromised patients, treatment of diverticulitis in the acute setting can be complex. The success of non-operative management in immunocompromised patients is uncertain with some studies reporting a rate of success of approximately 60%, while others report a much lower rate of 6%.[5,10] For comparison, in the general

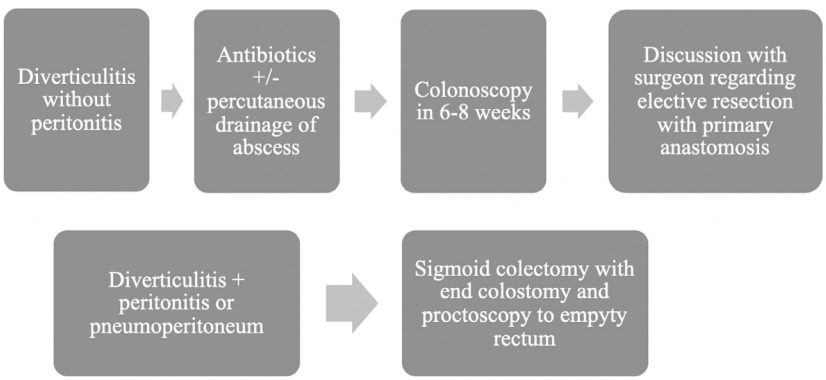

Fig. 1. Algorithm for the management of diverticulitis.

population the rate of success for non-operative management is about 91%.[3] The difference in success between immunocompromised and immunocompetent patients is likely due to the inability of the immune system to quarantine and combat bacteria released from the colonic lumen during diverticulitis.

Regardless of the actual rate of success of non-operative management in immunocompromised patients, the overall rate of operative intervention is clearly much higher. This appears to be especially true in patients on chronic steroids who were found to have higher rates of emergency surgery for diverticulitis compared to patients with cancer, transplants, chronic kidney disease, and other sources of immunosuppression.[11] The higher rate of operative intervention is due to a variety of reasons including delay in diagnosis, weakened ability to fight infection, and more severe co-morbidities necessitating earlier intervention. Perforation is the common reason for surgical exploration in immunocompromised patients. Immunocompromised patients undergo Hartmann's procedure more often than primary anastomosis compared to immunocompetent patients.[12] Even in cases of primary anastomosis, these patients typically are diverted with a loop ileostomy.[12] This is likely due to fear of poor healing of the anastomosis in immunocompromised patients, especially for those that are on steroids.

The outcomes of acute diverticulitis in immunocompromised patients are more likely to be fatal or morbid compared to the general population. Overall mortality of diverticulitis in immunocompromised patients is 19−25%, compared to 4−6% in the general population.[5,13] Post-operative mortality does not appear to differ depending on the cause of immunosuppression.[11] The average length of stay is about 19 days for immunocompromised patients and 13 for immunocompetent patients with diverticulitis.[13] There are significantly more complications in patients who are immunocompromised, with surgical site infections being the most common. Following emergency operations, 51% of immunocompromised patients experience complications compared to 24% in the general population.[13] Elective procedures in immunocompromised patients for diverticulitis appear to have similar rates of complications compared to the general population.[13] Complications specific to immunocompromised patients include Addisonian crisis and impaired wound healing. Addisonian crisis occurs in times of stress when the hypothalamic-pituitary-adrenocortical axis, downregulated from exogenous steroid use, is unable to respond appropriately. These patients can require intensive care for hemodynamic management. Impaired wound healing occurs with chronic steroid use due to the suppression of cellular wound responses resulting in fewer fibroblasts and subsequent collagen synthesis.

All patients after their first episode of diverticulitis require colonoscopy. This should ideally be done after the acute inflammation has resolved, usually within 6- 8 weeks. This is required to rule out malignancy or another process that could masquerade as diverticulitis on CT (ischemia or inflammatory bowel disease).[3] The presence of a mass in addition to wall thickening seen on CT is highly suggestive of malignancy, but absence of a mass does not rule out this possibility.[3]

Of immunocompromised patients who undergo emergent surgery for diverticulitis, 80−90% were experiencing their first episode of diverticulitis.[14] Recurrence rates of diverticulitis after non-operative management is similar between immunocompromised and immunocompetent patients, with about 20% of patients having a subsequent episode.[10] Subsequent episodes of diverticulitis in immunocompromised patients are more common in those with a severe first episode, but there is no increased need for emergent surgery during the subsequent episode when compared to immunocompetent patients.[10] The increased mortality rate from diverticulitis in immunocompromised patients appears to only exist for first episodes of diverticulitis and this increased mortality rates does not necessarily exist for subsequent episodes.[15]

The rationale for elective colectomies for recurrent diverticulitis have changed dramatically over the last 20 years in immunocompetent and immunosuppressed patients. Previously the number of episodes played a large role in recommending a patient for elective colectomy. The idea of diverticulitis being progressive has been challenged with data showing that a larger number of episodes of diverticulitis was not associated with an increase in morbidity or mortality, and that the incidence of recurrent diverticulitis is lower than previously thought.[3] Current guidelines recommend elective resection be considered based on the individual's risk of surgery, co-morbidities, effect on lifestyle, chronic symptoms, or severity of attacks.[3] Immunocompromised patients are slightly unique because non-operative management is less effective, so a lower threshold for surgery is recommended[3]

Recognizing that there is a high mortality rate from diverticulitis in immunocompromised patients and that this occurs during the first episode of diverticulitis, there have been some who advocate for prophylactic colectomies. In particular, transplant patients with a pre-transplant colonoscopy that identifies sigmoid diverticulosis, may benefit from a prophylactic colectomy prior to immunosuppression. There is a dearth of data supporting this treatment strategy. In fact, one study showed that colonic screening prior to renal transplant was ineffective at predicting post transplantation colonic complications.[6] Transplant patients with polycystic kidney disease appear to be at particularly high risk for diverticular disease with studies showing rates of diverticulosis approaching 50% in this population.[17] Despite the high rate of diverticulosis in this population, the rate of perforated diverticulitis requiring surgery appears to be about 2% (and 0.09% in the overall renal transplant population) which does not support the use of prophylactic colectomies prior to transplantation.[17] Some authors have recommended that patients with a known history of symptomatic diverticular disease are considered for colectomy prior to transplantation, but there have been no prospective studies to evaluate the risk and benefits of this approach.

Conclusion

Diverticulitis in immunocompromised patients is a complex clinical problem. These patients present with more mild symptoms delaying their diagnosis, undergo more emergent operations, and have a higher overall mortality with more complications than the general population. Treating these patients requires a strong clinical suspicion and early treatment.

References

1. Weizman AV, Nguyen GC. Diverticular disease: epidemiology and management. *Can J Gastroenterol*. 2011;25(7):385–389. https://doi.org/10.1155/2011/795241.
2. Sandler RS, Everhart JE, Donowitz M, et al. The burden of selected digestive diseases in the United States. *Gastroenterology*. 2002;122(5):1500–1511. Retrieved from: http://www.ncbi.nlm.nih.gov/pubmed/11984534.
3. Feingold D, Steele SR, Lee S, et al. Practice parameters for the treatment of sigmoid diverticulitis. *Dis Colon Rectum*. 2014;57(3):284–294. https://doi.org/10.1097/DCR.0000000000000075.
4. Harpaz R, Dahl RM, Dooling KL. Prevalence of immunosuppression among US adults, 2013. *JAMA*. 2016;316(23):2547–2548. https://doi.org/10.1001/jama.2016.16477.
5. Hwang SS, Cannom RR, Abbas MA, Etzioni D. Diverticulitis in transplant patients and patients on chronic corticosteroid therapy: a systematic review. *Dis Colon Rectum*. 2010;53(12):1699–1707. https://doi.org/10.1007/DCR.0b013e3181f5643c.
6. Regenbogen SE, Hardiman KM, Hendren S, Morris AM. Surgery for diverticulitis in the 21st century a systematic review. *JAMA Surg*. 2014;149(3):292–302. https://doi.org/10.1001/jamasurg.2013.5477.
7. Cronley K, Wenzke J, Hussan H, et al. Diverticulitis in HIV-infected patients within the United States. *HIV Med*. 2016;17(3):216–221. https://doi.org/10.1111/hiv.12304.
8. Sachar DB. Diverticulitis in immunosuppressed patients. *J Clin Gastroenterol*. 2008;42(10):1154–1155. https://doi.org/10.1097/MCG.0b013e3181862ac1.
9. Chang S-S, Huang N, Hu H-Y. Patients with end-stage renal disease were at an increased risk of hospitalization for acute diverticulitis. *Medicine*. 2016;95(39):e4881. https://doi.org/10.1097/MD.0000000000004881.
10. Biondo S, Borao J, Kreisler E, et al. Recurrence and virulence of colonic diverticulitis in immunocompromised patients. *Am J Surg*. 2012;204(2):172–179. https://doi.org/10.1016/j.amjsurg.2011.09.027.
11. Biondo S, Trenti L, Elvira J, Golda T, Kreisler E. Outcomes of colonic diverticulitis according to the reason of immunosuppression. *Am J Surg*. 2016;212(3):384–390. https://doi.org/10.1016/j.amjsurg.2016.01.038.
12. Golda T, Kreisler E, Mercader C, Frago R, Trenti L, Biondo S. Emergency surgery for perforated diverticulitis in the immunosuppressed patient. *Colorectal Dis*. 2014;16(9):723–731. https://doi.org/10.1111/codi.12685.

13. Reshef A, Stocchi L, Kiran RP, et al. Case-matched comparison of perioperative outcomes after surgical treatment of sigmoid diverticulitis in solid organ transplant recipients versus immunocompetent patients. *Colorectal Dis*. 2012;14(12):1546–1552. https://doi.org/10.1111/j.1463-1318.2012.03077.x.
14. Brandl A, Kratzer T, Kafka-Ritsch R, et al. Diverticulitis in immunosuppressed patients: a fatal outcome requiring a new approach. *Can J Surg*. 2016;59(4):254–261. https://doi.org/10.1503/cjs.012915.
15. Biondo S. Age and immunocompromised status in acute diverticulitis. Colorectal Dis. 2012;14(12):1553–1554. https://doi.org/10.1111/codi.12017.
16. McCune TR, Nylander WA, Van Buren DH, et al. Colonic screening prior to renal transplantation and its impact on post-transplant colonic complications. *Clin Transplant*. 1992;6(2):91–96. Retrieved from: http://www.ncbi.nlm.nih.gov/pubmed/10150089.
17. Domínguez Fernández E, Albrecht KH, Heemann U, et al. Prevalence of diverticulosis and incidence of bowel perforation after kidney transplantation in patients with polycystic kidney disease. *Transplant Int*. 1998;11(1):28–31. https://doi.org/10.1007/s001470050098.