Review

Small Bowel Diverticulosis and COVID-19: Awareness Is the Key. A Case Series and Review of the Literature

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Small Bowel Diverticulosis and COVID-19: Awareness Is the Key. A Case Series and Review of the Literature

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Abstract: Small bowel non-Meckelian diverticulosis is a rare condition with only few published cases despite being described over 200 years ago. In the midst of the COVID-19 pandemic, studies suggested that a lot of patients may experience gastrointestinal manifestations. Intestinal symptoms could worsen the inflammation and infection associated with small bowel diverticulitis. Here, we present two cases: one with inflammation and rupture in a COVID-19 patient and the other as an asymptomatic detection. Furthermore, we provide a mini-review of the literature to emphasize the importance of considering this entity in the differential diagnosis of an acute abdomen.

Keywords: Small bowel non meckelian; Diverticulitis; COVID-19

Introduction

Small bowel non-meckelian (SBNMD) diverticulosis is an uncommon disorder with a prevalence ranging from 0.06% to 4% [1–4]. While diverticula are more commonly found in the colon, they can also occur in the small bowel. It typically occurs in the 6th and 7th decade of life, with a significant majority of 80% being over 40 years old at the time of the diagnosis [4]. Multiple jejunal diverticula, especially in the proximal site, are detected in 80% of cases. The remaining 15% of diverticula are located in the ileum while the remaining 5% occur in both the jejunum and ileum [5]. Both are usually smaller in size multiple and isolated. From a pathological point of view, SBNMD are deemed 'false,' in contrast to Meckel's diverticula located on the anti-mesenteric site [1,2]. The wide range of atypical symptoms, such as vague abdominal pain, flatulence, diarrhea, and melaena, in combination with its rare occurrence, can lead to delayed diagnosis and extreme mortality rates [6,7]. Complications frequently occur with colonic diverticula, which are commonly described. These complications include inflammation, perforation, bleeding, and obstruction. The primary diagnostic tool that we use is abdominal computed tomography (CT) [4].

On the other hand, SARS-CoV-2 virus (COVID-19), primarily targets the respiratory tract through its affinity for ACE2 receptors. These receptors are also prevalent in intestinal cells, leading to symptoms affecting both the respiratory and gastrointestinal systems. COVID-19, affects the bloodstream, causing hyperactivity in platelets and cytokine storms. This can result in damage to the gut barrier and changes to the gut microbiota. Additionally, intestinal vessel thrombosis can occur, leading to malabsorption and malnutrition. These negative effects can increase the severity of the disease and have both short and long-term consequences, including gut inflammation and worsening of inflammatory bowel diseases [8,9].

Management of SBNMD, typically includes a combination of conservative and surgical interventions. The specific treatment approach depends on the rupture's severity, complications, and the patient's overall condition. Every stable patient with localized inflammation and without any radiologic sign of perforation is treated conservatively with bowel rest and broad-spectrum IV antibiotics. If the patient does not show clinical improvement within 48-72 hours or if generalized

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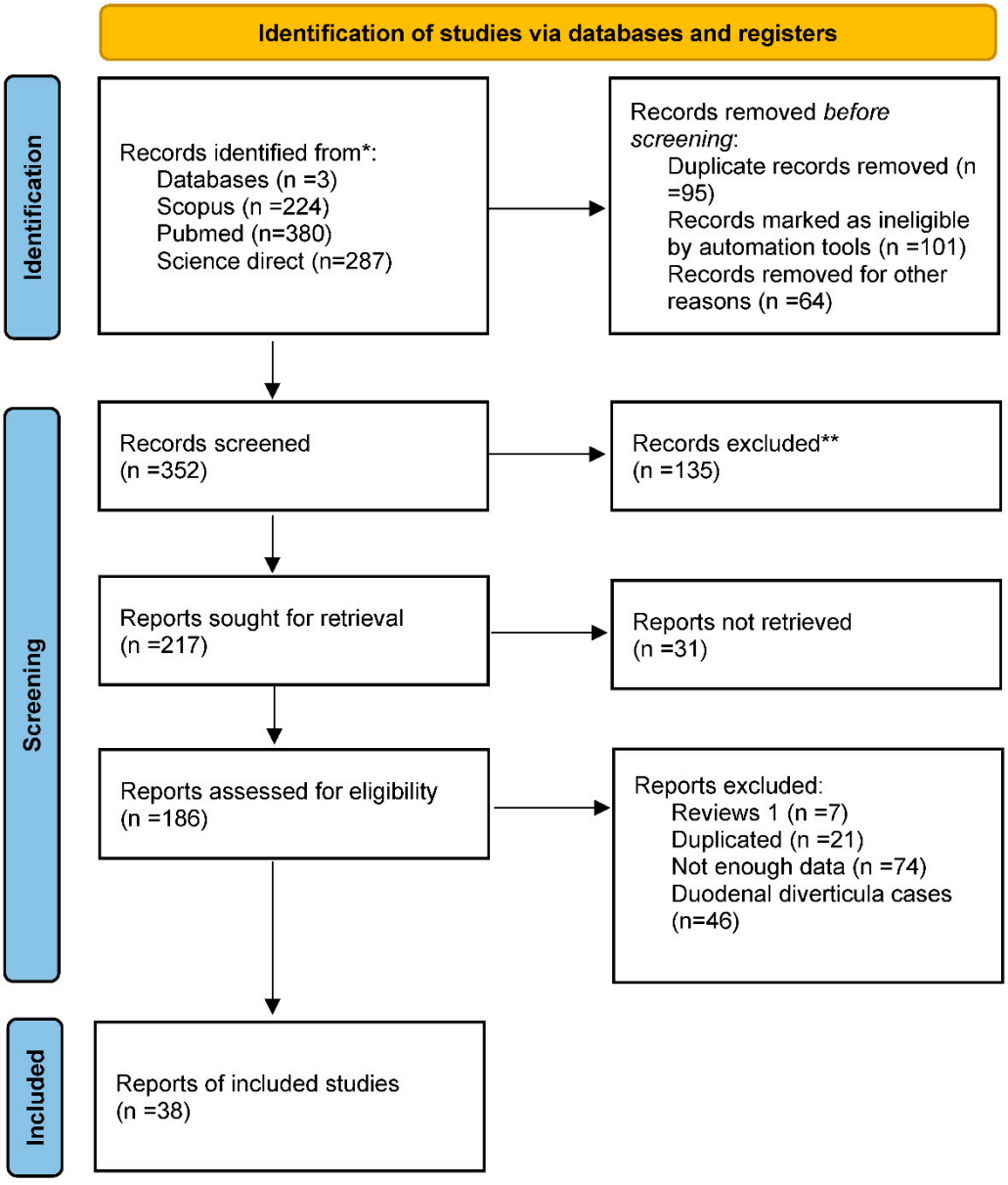
peritonitis or perforation is detected, an exploratory laparotomy may be necessary, which involves small bowel resection with anastomosis [5–7].

Herein, we present two cases of SBNMD, one with rupture in COVID-19 positive patient and one incidentally discovered. In addition, a review with a statistical analysis of all the cases reported in past literature, discussing the most common clinical features, was performed. Also, we proposed the role of laparoscopic surgery as a therapeutic option in disease management.

Materials and methods

A literature review was performed using PubMed, Scopus, and Science Direct. The search terms employed were “small bowel diverticulosis,” “jejunal diverticulitis,” and “Ileus diverticulitis.” Since 2010, 352 articles have been published.

Among these, 217 well-documented papers were identified. There were no restrictions on the age of the articles included in this review. One hundred eighty-six articles were in English, while 31 were in other languages. All these studies were carefully studied. We had only full texts, case reports, and case series articles in the final assessment. We finally selected 38 articles (41 patients), and a database with the patients' characteristics was created and shown in Prisma chart below.



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The database included sex, age, diverticula location, symptoms, diagnostic methods, treatment management, and complications. The cases that fulfilled all these seven criteria were included in the statistical analysis. Two additional cases were added from clinical experience of the authors of this article. Thus, a total of 43 patients were included in the statistical analysis. After obtaining ethical approval and participant consent, personal data were removed, and all clinical data were collected. Descriptive statistics were used to express the results appropriately. Means, medians, and SD were used for continuous variables and frequencies for categorical variables. Statistical significance was set at p <0 .05. Statistical analysis was performed using SPSS version 25 (SPSS Inc., Chicago, IL, USA).

Case report

Case 1

A 45-year-old man presented to our emergency department, complaining about abdominal pain, particularly on the left side, that had been ongoing for 48 hours. Clinical examination revealed abdominal distension and tenderness. Laboratory results showed mildly elevated white blood cell count (9.93 × 10^9/L) and neutrophilia (88%). During the preoperative examination, it was discovered incidentally that the patient has contracted COVID-19 infection. An emergency CT scan of the abdomen revealed free air, fluid collection in the left abdomen, and two small bowel diverticula in the jejunum with local phlegm (**Figure 1a**). From patient past medical history, there is no record of diverticula except experiencing upper gastrointestinal bleeding 11 years ago. Additionally, the patient had a history of cardiac arrest and pacemaker implanted since 15 years.

Informed written consent was obtained from the patient, and he was taken to the operating theater for exploratory laparoscopy, where a ruptured part of the jejunum was found (**Figure 1b**). A partial small bowel laparoscopic enterectomy was carried out with primary side-to-side intracorporeal anastomosis with an endoscopic linear stapler and PDS 2-0 running suture. The patient was discharged from the surgery without drainages and was receive clear fluids in the afternoon after the surgery. He was mobilized six hours after surgery. Throughout the hospitalization period, remained stable, and on the third postoperative day, they were discharged. Patient follow fast-track post-operative protocol (ERAS), which includes mobile communication and visits from a specialist nurse.

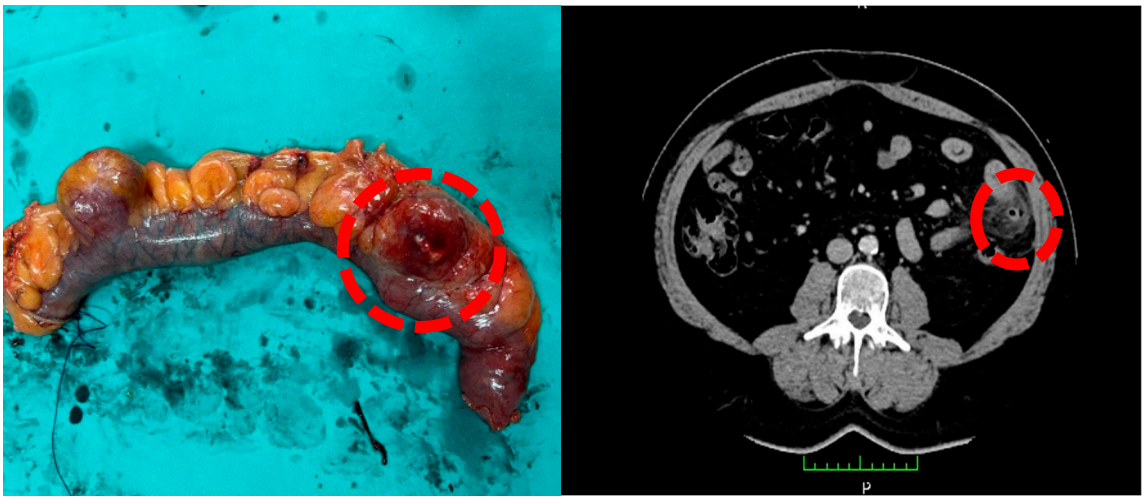

Figure 1a. Case 1 ruptured jejunum diverticula. 1b: Abdominal CT, showed repture non meckelian diverticula.

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Case 2

A 75-year-old man presented to our department due to a rectal tumor of 9cm from the anal verge. The patient underwent an operating theater for a scheduled low anterior resection. During the operation, multiple jejunal diverticula were identified (**Figure 2**). Upon further examination, it was determined that these diverticula were not inflamed, therefore obviating the necessity for their removal.

Figure 2. Incidentally identified SBNM Diverticula.

Results

After conducting a literature review, we have determined the characteristics of jejunal diverticula based on various factors, including sex, age, length, location of the diverticula, significant symptoms, type of procedure, survival rates, and potential complications categorized by Clavien-Dindo classification [2,4–7,10–44].

Regarding sex, 62.79% were male (27 patients), whereas 37.20% were female (16 patients). The ratio between men and women was 2:1, suggesting a male predominance in the reported population. Our Database is shown below (**Index 1**).

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Year	Author	Country	Disease location	Number of cases	Age / Gender	Treatment
2017	Marcano		Jejunal	1	71/Male	Conservative
2019	Almaki		Jejunal	1	65/Male	Open Surgery
2019	Aispuro		Jejunal	1	86/male	Open Surgery
2019	Saritas		Jejunal	2	36/Female	Open Surgery
			Ileus		75/Female	Open Surgery
2020	Ghandour		Jejunal	3	71/Male	Open Surgery
			Jejunal		69/Male	Open Surgery
			Jejunal		55/Male	Conservative
2020	Kunishi		Jejunal	1	41/Male	Conservative
2020	Leigh		Jejunal	1	59/Female	Open Surgery
2020	Ramzee		Jejunal	1	69/Male	Open Surgery
2020	Sammartino		Jejunal	1	91/Male	Open Surgery
2020	Yeung		Jejunal	1	83/Male	Open Surgery
2021	Aiyekbeni		Jejunal	1	70/Male	Conservative
2021	Anjum		Jejunal	1	70/Male	open Surgery
2021	Chung		Jejunal	1	69/Female	open Surgery
2021	Duggan		Jejunal	1	78/Male	Open Surgery
2021	Giufrida		Jejunal	1	54/Female	Open Surgery
2021	Hardon		Jejunal	1	37/Female	Open Surgery
2021	Khsiba		Jejunal	1	76/Female	Conservative
2021	Kim		Jejunal	1	65/Female	Conservative
2021	Mendo		Ileus	1	73/Male	Open Surgery
2021	Rajaguru		Ileus	1	74/Male	Open Surgery
2021	Vayzband		Jejunal	1	71/Male	Open Surgery
2021	Watanabe		Distal Jejunal	1	72/Male	Open Surgery
2022	Abdelihamil		Jejunal	1	69/Female	Open Surgery
2022	Beti		Jejunal	1	83/Male	Open Surgery
2022	Coelen		Jejunal	1	85/Male	Open Surgery
2022	Elfanagely		Jejunal	1	79/Female	Conservative
2022	Glasser		Ileus	1	57/male	Open Surgery
2022	Imasato		Jejunal	1	76/Female	Open Surgery
2022	Karna		Jejunal	1	89/Female	Embolization
2022	Lutaya		Jejunal	1	89/Female	Open Surgery
2022	Massoir		Jejunal	1	84/Female	Open Surgery
2022	Matli		Jejunal	1	41/Male	Conservative
2022	Scheesee		Jejunal	1	85/Male	Open Surgery
2022	Pajtak		Jejunal	1	88/Female	Open Surgery
2022	Prough		Jejunal	1	65/Male	Open Surgery
2022	Walter		Ileus	1	59/Male	Open Surgery
2023	Bangeas		Jejunal	2	45/Male	Laparoscopic
			Jejunal		73/Male	Conservative

Based on our database (**Index 1**), it appears that diverticula are typically found in the Jejunum, as illustrated in **Figure 3** (31 patients, 72.09%), with only 8 patients found in the proximal ileus (18.60%) and 4 patients in distal ileus (9.30%).

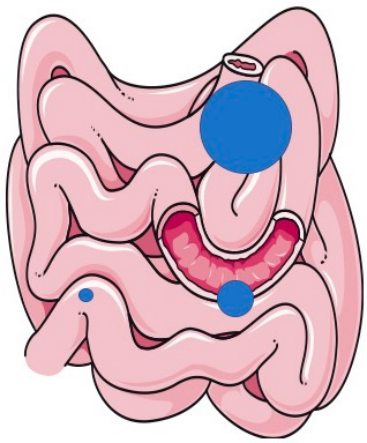

Figure 3. SMNMD localization.

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The age distribution is shown in ***Figure 4***, from which it is concluded that jejunum diverticula most frequently appeared in the age ranges of 64-72, 73-81, and 82–91 years. Median age of the 43 cases (100%) was 71 ± 14.40 years, ranging from 36 to 91 years. The distribution of age among male and female patients was compared, and it was found that the age at which the tumor appeared did not differ statistically between males and females (70.12± 13.27 and 70± 15.99 years, respectively, p= 0.98).

Symptoms of SBNMD were also evaluated and shown in ***Figure 5***. Symptoms were characterized as inflammatory without rupture (***1***) (16 patients, 37.20%), perforation (***2***) (18 patients, 41.86%), bleeding (***3***) (1 patient, 2.32%), (***4***) obstruction (6 patients, 13.95%) and non-specific/Random (***5***) (2 patient, 4.65%).

Out of 43 patients, only 8 (18.60%) received conservative treatment, while the majority (35 patients, 81.40%) required surgical intervention. Diverticula were discovered accidentally in 2 patients (4.65%) without signs of inflammation, and no interventions were performed. Concerning the type of procedure, open laparotomy was performed in 33 (94.28%) out of 35 patients. On the other hand, only two patients (5.71%) underwent the laparoscopic approach.

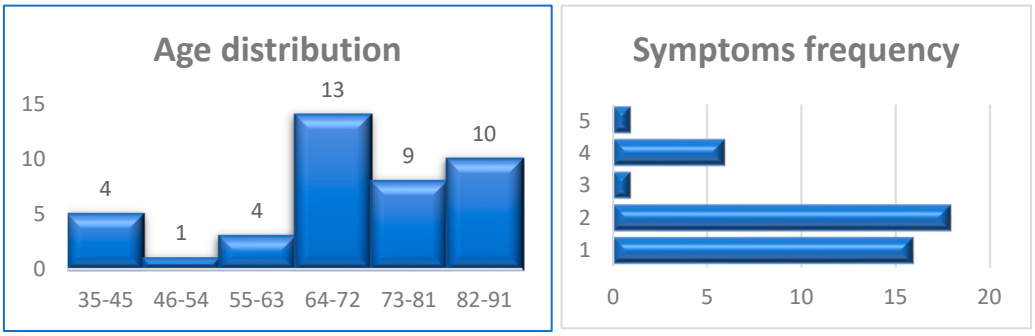

Figure 4,5: Age distribution and Diverticula symptoms.

Median hospitalization was 7 ± 2.37 days, ranging from 3 to 16 days, depending on the treatment option. Hospitalization periods were found to be prolonged for patients who underwent open surgery or were treated using conservative methods.

Regrettably, one patient (2.85%) succumbed to their illness during the post-operative period, while the remaining patients experienced an uncomplicated and stable state of health.

Discussion

Jejuno-ileal diverticulitis, a condition involving inflammation of the diverticula in the small intestine, was initially identified by Sommering in 1794 and further researched by Sir Astley Cooper in 1804 [1]. Due to its low prevalence, there have been only a few reported cases since then. Pathophysiology still needs to be fully understood. These are false diverticula of the small intestine, similar to colonic diverticula, where the mucosa and submucosa protrude through the muscular wall. We assume that an elevated intraluminal pressure combined with bowel wall weakness causes these cases. While they are usually asymptomatic, they can lead to life-threatening outcomes when complicated [2,5,8,11].

In the case of uncomplicated SBNMDs, no specific symptoms can lead to the diagnosis. These patients usually complain of abdominal pain, which sometimes radiates in the back, nausea, emesis, fever, and constipation. Due to the greater frequency in the elderly population, where many other health issues or previous surgical history can co-exist, diagnosis could be challenging [2,5,7,27–34].

Numerous reports have emerged during the COVID-19 period regarding inflammation and bowel ruptures. This is a matter of concern, and we should examine these reports closely to determine the root cause of such incidents and identify measures to mitigate them in the future. In some studies, it seems that Gut enterocytes have been determined to be a significant target of the COVID–19 virus. The virus can enter the cells of the ileum, colon, and esophagus by using Angiotensin-converting enzyme 2 receptors and transmembrane serine protease 2 (TMPRSS2) as a mediator [8,9]. This can

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lead to gut inflammation and exacerbation of inflammatory bowel diseases, causing negative effects that can worsen the disease severity in both the short and long term [9].

A comprehensive patient history must be obtained to rule out other conditions such as appendicitis, cholecystitis, colonic diverticulitis, pancreatitis, bowel obstruction, or foreign body perforation [3,4,8–20,24,34]. An abdominal X-ray can help detect perforation or obstruction but cannot establish a diagnosis on its own. The surgeon must maintain a heightened level of suspicion to ensure the procedure's accuracy and safety. This involves being vigilant and attentive to any potential risks or complications that may arise during the surgery.

Currently, the gold standard imaging study for abdominal scans still involves using CT scans with both oral and intravenous contrast. Due to the rarity of the disease, there are instances in the literature where the diagnosis was not clearly established before the exploratory intervention but only during exploratory laparoscopy. In our cases, the preoperative CT scan was exact for the site and the number of the ill-defined diverticula [28–40].

As mentioned before, inflammation is the most common complication, followed by perforation. First-line treatment for uncomplicated cases involves IV antibiotics and bowel rest strategies. An annual monitoring protocol, including a clinical examination and CT scan of the abdomen, is necessary in case of accidental detection. Prior history-based clinical suspicion is also important [4,28,35,40–45].

Surgical intervention must be undertaken without delay in cases of sepsis, instability or severe comorbidities following perforation. These complications could be severe and lead to serious difficulties if not addressed promptly. The type of procedure (open or laparoscopic) does not seem to play an important role and appears to be determined by the surgeon's preference and center experience. If a patient has a good performance status, surgeons could perform an exploratory laparoscopy and proceed with a conversion procedure (Laparotomy) if needed. The length of bowel resection is also a matter of discussion. There are cases in the literature where the extreme length of bowel disease does not make wide resection feasible [40,43–45]. Most surgeons resect only the complicated diverticular disease and leave the uncomplicated diverticula behind. Based on summarized publications, we create an algorithm in order to manage jejunum diverticulum (**Figure 6**).

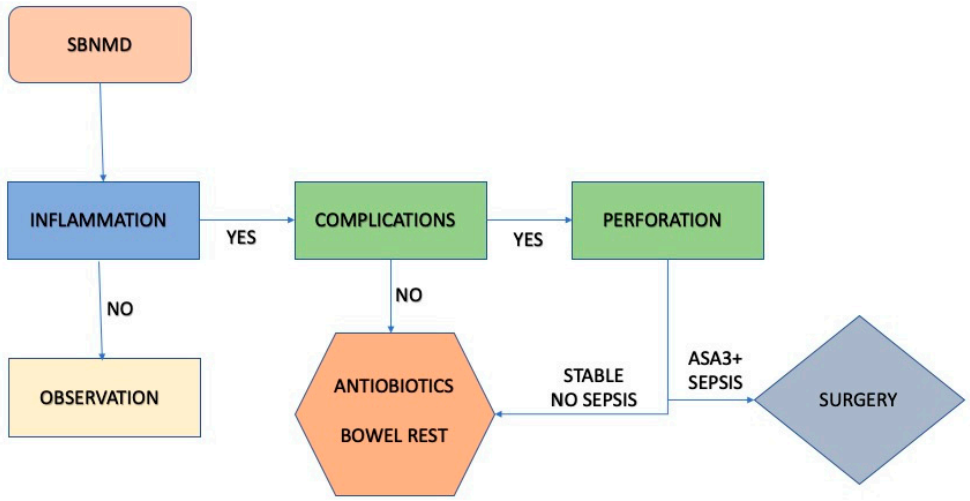

Figure 6. Suggested strategy of SBNMD treatment.

According to our algorithm, in the first case, the patient was hemodynamically stable but had comorbidities (ASA3). CT scan revealed free abdominal air caused by perforation of one of two jejunal diverticula. The decision was made to perform surgery on the patient without delay. An

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exploratory laparoscopy was our first choice, while laparoscopic lavage is seen as an acceptable and safe alternative in selected patients [45]. The patient has no previous abdominal operations and no neglected fasciitis. We recognized the phlegmon and the two complicated diverticula at about 10cm from each other. An enterectomy was made with primary anastomosis. The specimen was about 15cm long, so there was no risk of intestinal failure and small bowel syndrome disease (SBS).

In the second case of accidental detection, we decided on an annual monitoring protocol with clinical examination and CT abdomen.

Conclusion

Small bowel non-meckelian (SBNMD) diverticulosis remains a challenging clinical entity, and the surgeon should have a high index of suspicion. While surgical intervention has been the traditional treatment approach, further advancement in diagnostic tools may offer less invasive and potentially more effective options. Strong evidence-based guidelines are needed to guide clinicians in the diagnosis, management and follow-up of patients with SBNMD. Improving our understanding of this rare condition will lead to better outcomes and quality of life for our patients.

Author Contributions: P.B. was responsible for designing and supervising the study, collecting the data, and writing the manuscript. P.B., N.K., T.C., A.G., and V.P. contributed to writing the manuscript. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The study was conducted by the Declaration of Helsinki. Ethical review and approval were waived for this study due to the study's retrospective design.

Informed Consent Statement: All patients are required to sign a consent form and be provided with complete information regarding their medical condition, including the proposed treatments, potential risks, and benefits.

Data availability statement: Datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

SBNMD: Small Bowel non-meckelian diverticulosis
CT: Computed Tomography
SPSS: Statistical package for social science software
SBS: Short Bowel Syndrome

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