

Ileum Adenocarcinoma: A Rare Case Report

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ABSTRACT

Background: Ileum adenocarcinoma is difficult to diagnose due to the length of the ileum which makes it difficult for diagnostic tools to enter the ileum. Surgery is the main management of Ileum adenocarcinoma. Poor prognostic factors are determined by old age, distal tumor location, large tumor size, stage, and lymph node involvement. In general, the management of Ileum adenocarcinoma is similar to that of colonic adenocarcinoma. **Case presentation:** A 55-year-old female complained of recurrent abdominal pain mainly in the right lower abdomen. Abdominal distension was found accompanied by darm contour and darm steifung and increased bowel noise. A mass with a diameter of 7 cm was found in the right lower abdomen, contrast-enhanced abdominal CT scan revealed a solid mass in the caecum with post-contrast enhancement, size 6.58x5.76x4.98 cm which extended to the ascending colon and caused dilatation of the Ileum loop. Right extended hemicolectomy followed by end-to-side ileum - colon transversum anastomose followed by 6 series adjuvant chemotherapy. Anatomical pathology results of the resection showed morphological features suitable for Adenocarcinoma, pT3pNx, and pMx with tumor cell-free resection margin. **Conclusion:** The case of Ileum adenocarcinoma is rare, exploratory laparotomy surgery is indicated in patients with high clinical suspicion of Ileum malignancy even though radiologically and endoscopically do not show positive results. Tumor markers are not specific and sensitive for the diagnosis of Ileum adenocarcinoma. Operative management of patients is tailored to the location and extension of the tumor.

Keywords: difficult diagnose; exploratory laparotomy; ileum adenocarcinoma; rare case; surgery

INTRODUCTION

Ileum adenocarcinoma is a rare case of cancer, despite one-third of the length of the gastrointestinal tract being the ileum. Ileum adenocarcinoma is generally treated the same as colorectal cancer, although patient outcomes are inferior [1]. In the United States alone, there were at least 10,590 (2.3 per 100,000) patients diagnosed with Ileum cancer in 2019 [2]. The incidence has been slowly increasing since 1990. Adenocarcinoma is the most common pathology outcome, followed by neuroendocrine cancer, lymphoma, and sarcoma (Gastrointestinal Stromal Tumor and Leiomyosarcoma). Primary tumors mostly grew in the duodenum (60%), jejunum 25-29%, and ileum 10-13%. The median age of patients is 60 years and is predominantly male [1-3].

The etiology of Ileum adenocarcinoma is still not fully understood. There are several theories, one of which is that the contents of the ileum are liquid contents that rarely cause recurrent irritation to the ileum mucosa. This also explains why adenocarcinoma is more common in the duodenum, as the contents of the duodenum are more irritative as they contain a mixture of gastric acid, bile, and pancreatic enzymes.

In addition, the ileum has no storage function, which prevents prolonged transit of germs. Alcohol consumption, smoking, and environmental exposures may lead to an increased risk of Ileum adenocarcinoma. Inflammatory conditions also play a role in the development of Ileum adenocarcinoma. Celiac disease and Crohn's disease are suspected to be one of the causes of Ileum adenocarcinoma. In the case of Crohn's disease, the cancer is generally found in the distal ileum. Patients diagnosed with Crohn's disease have a 21-60-fold risk of developing adenocarcinoma [1,3].

Ileum adenocarcinoma does not have a specific screening tool as cases are rare, resulting in low screening values. This leads to patients presenting generally at an advanced stage, due to delayed diagnosis and non-specific symptoms. Recurrent abdominal pain is a common symptom that patients complain of. Less than half of the patients complained of weight loss, nausea, and vomiting. One-third of patients present with complaints of gastrointestinal bleeding characterized by iron deficiency anemia with negative colonoscopy or esophagogastroduodenoscopy results.

Due to the difficulty of diagnosis, patients usually present with intestinal obstruction (22%-26%) or Ileum perforation (6%-9%) [1,2].

Adenocarcinoma of the ileum is difficult to diagnose due to the length of the ileum which makes it difficult for diagnostic tools to enter the ileum. Several methods can be performed to view the intraluminal of the ileum such as push enteroscopy, video capsule enteroscopy (VCE), and deep small bowel enteroscopy (balloon enteroscopy and spiral enteroscopy). CT Scans and MRIs are only able to detect this malignancy in cases of Ileum obstruction. CT Enteroclysis, performed by introducing contrast into the ileum through a nasogastric tube, is said to have improved sensitivity and specificity for the diagnosis of Ileum adenocarcinoma [3].

Surgery is the main management of Ileum adenocarcinoma. The surgical technique depends on the location of the adenocarcinoma and the stage of the patient. However, despite adequate radical resection and KGB dissection, the 5-year survival rate is still low (about 25%). Previous studies have revealed poor prognostic factors including old age, distal tumor location, large tumor size, stage, and KGB involvement [3]. In general, the management of Ileum adenocarcinoma is similar to that of colonic adenocarcinoma. However, with significant anatomical and molecular differences between Ileum and colonic adenocarcinoma, various studies should be conducted to obtain clinical management guidelines for Ileum adenocarcinoma [1].

CASE REPORT

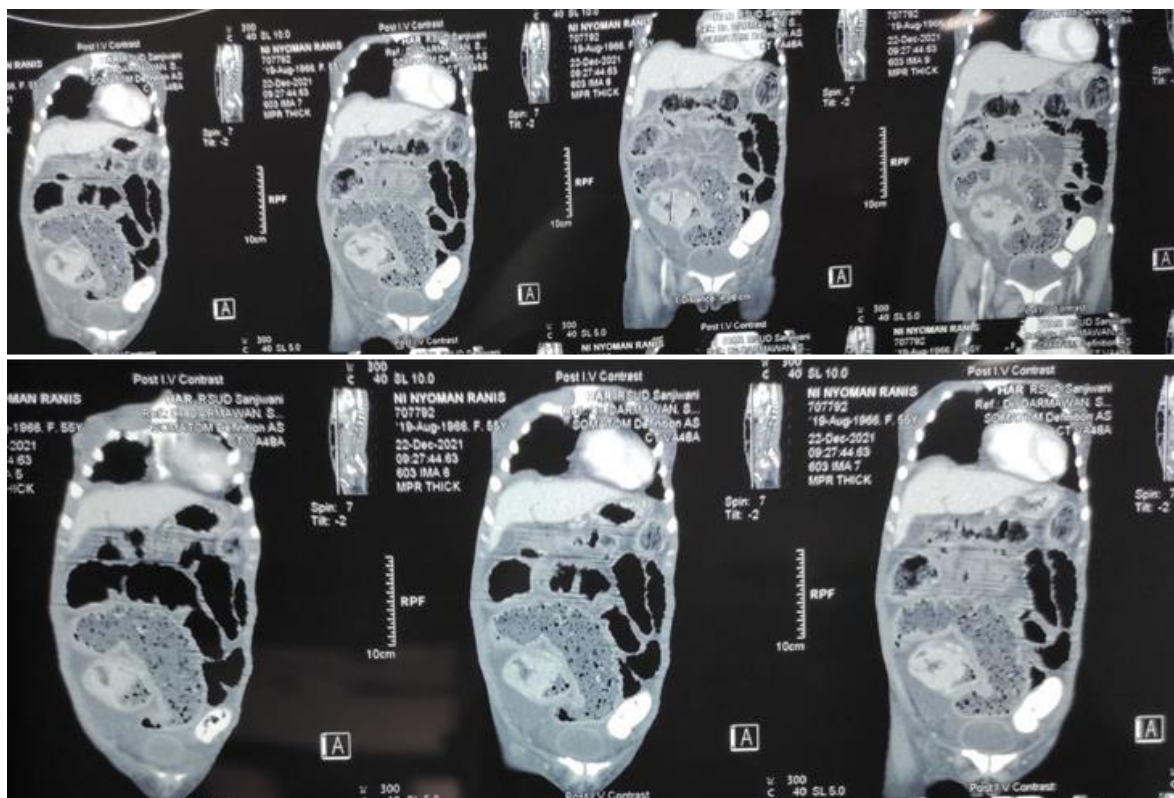
A 55-year-old woman complained of recurrent abdominal pain for the last 6 months, the pain was felt mainly in the right lower abdomen.

The pain is dull and has worsened in the last few days. This complaint was accompanied by flatulence in the last 2 days and could not defecate. A history of weight loss was recognized by the patient, losing about 8 kg in the last 6 years. The history of bloody stools was denied by the patient. The history of abdominal surgery was denied by the patient.

The physical examination revealed a moderate general condition with stable vital signs. Abdominal distension was found accompanied by darm contour and darm steifung and increased bowel noise. A mass measuring 7 cm in diameter was found in the right lower abdomen, the impression was fixed. No defans were found in this patient. There was no mass in the patient's right or left inguinal region. A rectal examination was performed, and no mass was found. From the history and physical examination, it was concluded that the patient with suspicion of diagnosis leads to malignancy in the area of ileocecal junction (caecum tumor) dd periappendicular infiltrate. This patient then underwent a supporting examination.

On laboratory examination, Hb was found to be 10.8 (the previous history of Hb 7.2, 3 colf PRC transfuse had been done in the previous hospital) with normal leukocytes. Liver function and renal function were within normal limits. Albumin 2.4 (with a history of albumin transfusion 2 colf in the previous hospital).

A contrast-enhanced CT scan of the abdomen revealed a solid mass (50.1HU) in the caecum that intensified post-contrast (81.1 HU), measuring 6.58 x5.76x4.98 cm that extended into the ascending colon and caused dilatation of the Ileum loop (Figure 1).



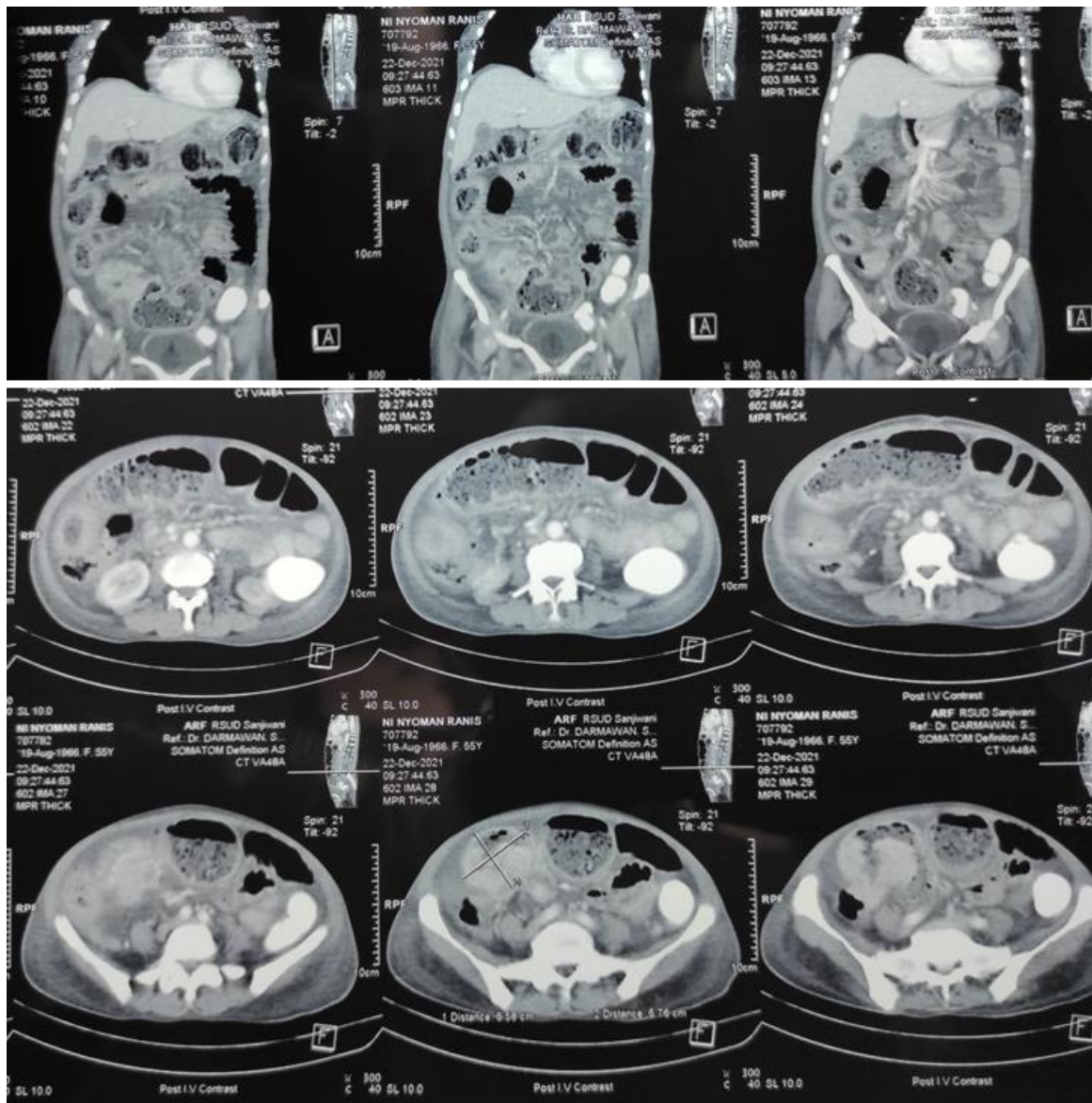


FIGURE 1: Abdominal CT scan.

The patient was diagnosed with caecum tumor susp malignancy and exploratory laparotomy was performed. During surgery, a distal ileum intraluminal mass (10 cm from ICJ) was found

accompanied by ileum adhesion with the ileum as well as with ascending colon. The patient underwent right extended hemicolectomy followed by an end to side ileum - transverse colon anastomosis (Figure 2).

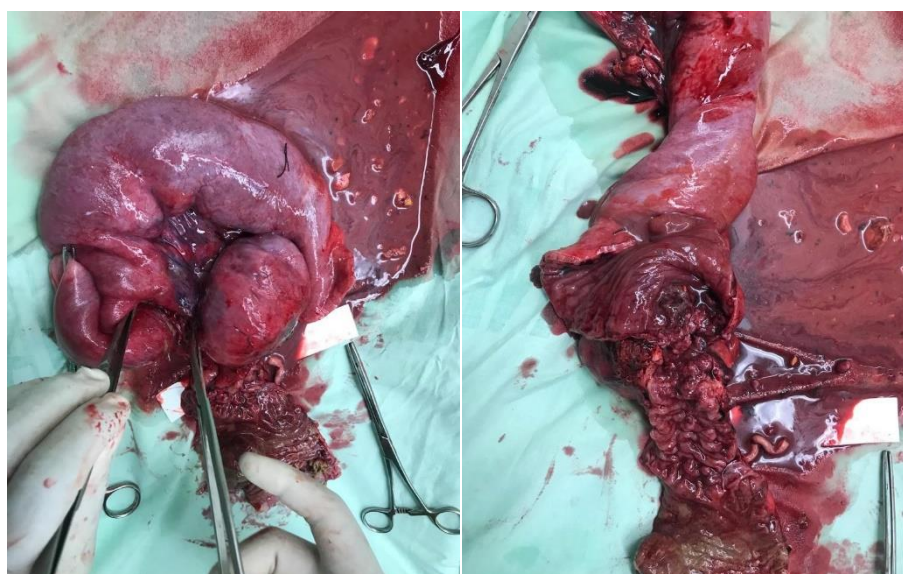


FIGURE 2: Intraoperative finding.

The patient was treated with analgesics, antibiotics, a fasting-phased diet, drain monitoring, and albumin correction with a target albumin of 3. On the seventh day, the patient was discharged in good condition. PA resection results showed morphological features suitable for Adenocarcinoma, pT3pNx, and pMx with tumor cell-free resection margins. The patient returned to the surgical clinic in stable condition and without complaints. The patient then underwent continued therapy in the form of adjuvant chemotherapy scheduled for 6 series.

DISCUSSION

A 55-year-old female with a diagnosis of adenocarcinoma, epidemiology of ileum in male to female ratio of 2:6. In 2018, there were an estimated 10,470 ileum cancer cases in the United States. This constituted an incidence rate of 2.3/100,000 people. These cases also comprised only 0.6% of all cancer diagnoses in the United States that year [4]. In contrast, there were about 145,000 cases of large intestine cancer in the United States that same year. According to 2015 data, the lifetime risk of developing ileum cancer in the United States is about 0.3% [4], some 2-5 times less than that for cancer of the large intestine [5]. While colorectal cancer ranks as the fourth most incident in the United States, ileum cancer comes in 23rd place [4]. Men are more increasingly likely than women to fall ill, with an incidence of 2.6 in 2018 relative to 2.0 for women [5]. African Americans are disproportionately affected, with incidences of 4.2 and 3.5 among men and women, respectively, while Native Americans and Asians were the least likely to be diagnosed with the disease. In the United States, the median age for the first diagnosis was 66 years [4]. The United Kingdom has a comparable rate of ileum cancer diagnoses, with an incidence of 3.1/100,000 among men and 2.2/100,000 among women. Their overall incidence is the same as that of the United States: 2.6/100,000. Interestingly, males in Scotland have a higher incidence than the U.K. average (3.5/100,000), while females have a lower incidence (1.6/100,000) [6]. According to 1998-2002 data, ileum cancers were most common in North America and Western Europe and least common in Asia. In those years, the incidence was 1.4 and 1.0, for men and women respectively, in the United States and Sweden, while 0.7 and 0.4 in Japan [5].

The median age for ileum cancer diagnosis in the United States is 66 [4]. The median age for diagnosis is comparable in the United Kingdom; however, the most common age for incidence in the United Kingdom was 80-84 [6]. The median age for ileum mortality is 72 in the United States [4], while the "peak" age for mortality is 85-89 in the United Kingdom, over a decade greater than the average life expectancy [6]. After around 40 years of age, the risk of ileum cancer begins to increase, and it does not appear to level out until around 90 years old [6]. Males are more likely to be diagnosed with and die from, ileum cancer than females. In the United States, the gender discrepancy in incidence is about 1.3:1 and in mortality about 1.6:1, suggesting lower survival rates among men [4]. Interestingly, in the

United Kingdom, while men are still more likely to be diagnosed, survival rates for men are actually higher than those for women [6]. Differences in diet, carcinogen exposure, and metabolic rate, among others, may underlie the sex difference in ileum bowel incidence and mortality.

The rarity of adenocarcinoma arising in the small bowel is largely unexplained but is most likely due to a combination of several factors. It has been postulated adenocarcinoma of the colon occurs about 50 times more frequently than small bowel carcinomas. Factors that have been suggested as having an important role in reducing tumor formation include: (1) the dilute nature and rapid transit time of small bowel contents which reduce mucosal contact of intraluminal carcinogens compared with those of the colon; (2) a reduced number of bacteria, which has been associated with the carcinogenic effect of broken down bile salts as in the colon"; (3) the alkaline pH of the small bowel exerts a protective effect'; (4) the presence of benzopyrene hydroxylase, which, it has been postulated, detoxifies several carcinogens; and (5) a high concentration of secretory IgA antibodies which may perhaps neutralize oncogenic viruses [3,7-9].

Several conditions are also known to be associated with a higher incidence of primary carcinoma in the small bowel found that adenomas affecting the ampulla contained carcinoma more often than lesions found elsewhere in the duodenum and ileum. Although T cell lymphomas are known to arise in the jejunal mucosa of patients with coeliac disease, there is also an uncommon association with adenocarcinoma in these patients [8].

Neoplasms of the ileum are rare, especially considering the size of the organ. The ileum, also known as the small bowel, makes up some 75% of the length of the alimentary canal (or digestive tract) and accounts for about 90% of its mucosal surface [10]. Nevertheless, cancers of the ileum account for less than 5% of all gastrointestinal (GI) cancer cases [10], and only about 0.6% of all cancer cases in the United States [6]. Despite their rarity, ileum cancers are on the rise in the developed world, with an estimated growth in the incidence of over 100% in the past four decades [11]. The ileum is located between the stomach and the large intestine and is the primary site of the end absorption of nutrients from food, including proteins, lipids, and carbohydrates. It is composed of three distinct regions: the duodenum, jejunum, and ileum. The duodenum is where most of the body's digestive enzymes are released [5], and interestingly, it is also the most common site for cancers in the ileum. Overall, 55-82% of small bowel neoplasms occur in this smallest region of the ileum. Meanwhile, the jejunum accounts for 11-25% of these cancers, and the ileum for the remaining 7-17% [4-7]. Cancers of the ileum are primarily of two etiologies: small bowel adenocarcinoma (SBA) which accounts for 40% of cases, and neuroendocrine tumors, which accounts for another 40%. Gastrointestinal stromal tumors, sarcomas, and lymphomas compose the remaining 20-25 [5,6,10].

The rarity of SBA has made it difficult to characterize the pathogenesis of these two varieties fully; however, the vast differences in incidence suggest that SBA have markedly different pathogenesis, elicited by a different array of mutagens, than colon adenocarcinomas [10].

Patients with small bowel adenocarcinomas present with non-specific symptoms, such as vague abdominal pain, weight loss, nausea and vomiting, bowel obstruction, gastrointestinal bleeding, or anemia, which challenges the diagnosis. So in the initial patient, diagnosis does not indicate the presence of a tumor in the ileum because the complaints and physical examination given are not typical [7,9,11].

The diagnosis of Ileum adenocarcinoma is difficult due to its rarity, diverse and nonspecific clinical presentations, and lack of an agreed diagnostic pathway. Clinical symptoms of Ileum adenocarcinoma are often nonspecific, with abdominal pain being the most common complaint experienced by the patient in this case report. In a retrospective study of 491 cases of Ileum adenocarcinoma between 1970-2005, the most common complaints were abdominal pain (43%), nausea and vomiting (16%), anemia (15%), gastrointestinal bleeding (7%), jaundice (6%), weight loss (3%), and other complaints (9%). Because these complaints are not specific, there is often a diagnostic delay, where the median time from the appearance of symptoms to the establishment of a diagnosis is about 2-8 months [2].

There is no diagnostic protocol for Ileum adenocarcinoma. CT scan is the initial diagnostic step for non-specific abdominal complaints. CT scan is able to detect abnormalities in 80% of Ileum tumors. Upper endoscopy may detect duodenal tumors, while colonoscopy is expected to exclude malignancies in the colon as well as detect tumors in the terminal ileum. Video capsule endoscopy, push enteroscopy, and double balloon enteroscopy can be used to view the intraluminal of the ileum, but these procedures are quite invasive and not available in many places [2,3,12].

Exploratory laparotomy surgery is indicated in patients with high clinical suspicion of Ileum malignancy even if radiologically and endoscopically unremarkable. Tumor markers are not specific and sensitive for the diagnosis of Ileum adenocarcinoma. Operative management of the patient is tailored to the location and extension of the tumor. In this case, an intraluminal mass was found in the distal ileum (10 cm from ICJ) accompanied by adhesion of the ileum with the ileum and ascending colon. The patient underwent a right extended hemicolectomy followed by an end to side ileum - transverse colon anastomosis [2,13].

The results of anatomical pathology of the resection showed morphological features suitable for Adenocarcinoma, pT3pNx, and pMx with tumor cell-free resection boundaries so the patient was carried

out adjuvant chemotherapy planned for 6 series. The proportion of patients receiving chemotherapy doubled during the study period, both for patients with locoregional and metastatic disease. Especially in patients with locoregional disease, the twofold increase is remarkable since non-observational studies addressing the beneficial effect of chemotherapy are lacking. Adjuvant chemotherapy is associated with an improvement of disease-free survival, but not with the improvement of overall survival [14-16]. Recently, a population-based study showed a survival benefit of 16 months (42 vs 26 months) for patients with stage III tumors treated with adjuvant chemotherapy [11]. Locoregional disease chemotherapy was more often offered to younger patients, patients with Ileum or stage III tumors, and patients who were diagnosed in the period 2009-2013. In metastatic disease, however, the doubling of palliative chemotherapy is not surprising, since a survival benefit of several months has already been observed in multiple retrospective studies [10]. In patients with metastatic disease, only a younger age and diagnosis after 2003 were positive predictive factors for receiving palliative chemotherapy. The overall survival rate of all patients with an adenocarcinoma of the small bowel did not improve over time and remained dismal with an overall median survival of 13-14 months. Our results are inferior to the reported overall survival of approximately 20 months in other population-based studies, but these studies were merely conducted before the millennium and might have included neuroendocrine tumors with a more indolent behavior [9,10,13,14,17].

CONCLUSIONS

Adenocarcinoma of the terminal ileum is rare and difficult to diagnose as the complaints are generally nonspecific. Right lower abdominal pain is the most common symptom, but it is non-specific and has many differential diagnoses. CT scans can be used for diagnosis in patients with gastrointestinal problems, especially in the elderly with suspicion of malignancy. However, half the cases of Ileum adenocarcinoma are diagnosed during surgery. Bowel cutting with adequate KGB dissection is still the operative option. The role of adjuvant chemotherapy has not been fully studied. In general, patient outcomes are generally poor and early diagnosis is paramount in patient management.

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DECLARATIONS

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