CASE REPORT

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The neuroendocrine tumor of the ileocecal valve presented as an obstructive ileus – a case report and literature review

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Summary

Neuroendocrine tumors of the ileocecal valve are rare, frequently manifesting with nonspecific symptoms that complicate early diagnosis. This report examines a 66-year-old woman with significant comorbidities, including diabetes mellitus and chronic renal failure, who presented to the emergency department with severe cramping abdominal pain, vomiting, and a mild fever. Initial imaging and laboratory tests yielded inconclusive results. However, a CT scan of the abdomen and pelvis revealed a small bowel obstruction at the ileocecal valve, caused by a tumor mass. Given the acute nature of her symptoms, the patient underwent an emergency right hemicolectomy with ileocolostomy. Histopathological analysis confirmed a 4 cm, well-differentiated grade 2 neuroendocrine tumor with lymphovascular invasion, along with metastases in 4 out of 17 examined lymph nodes. The patient had an uncomplicated postoperative course and was discharged on the tenth day in stable condition. This case highlights the need to consider neuroendocrine tumors in the differential diagnosis of bowel obstruction when imaging reveals a mass near the ileocecal region. Early detection and prompt surgical intervention are essential for optimal outcomes. Due to the rarity of neuroendocrine tumors in this anatomical location, this case provides valuable insights into the diagnostic and management complexities they pose. Continuous follow-up with a multidisciplinary team remains essential to monitor for potential recurrence or metastasis.

KEY WORDS: *neuroendocrine tumor, obstructive ileus, chromogranin A, proton pump inhibitors, false positive*

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INTRODUCTION

Despite 100 years of clinical studies, neuroendocrine tumors (NETs) remain poorly understood because of their rarity, tumor heterogeneity, nonspecific presentation, unique indolent biology, and lack of awareness(1). The most common sites are the lungs, small intestine, rectum, and anus(2) . Gastrointestinal neuroendocrine tumors are rare, slow-growing tumors with distinct histological, biological, and clinical characteristics that have increased in incidence and prevalence within the last few decades(3). While NETs can arise in different organs, colonic NETs are exceptionally rare(4). Despite the increasing incidence of colorectal NETs in recent decades, these tumors remain uncommon, accounting for ~20% of all NETs(5). Ileum is the most common location of small intestine NETs, with two-thirds of patients having a tumor in the final 100 cm of the small bowel(6).

NETs account for less than 1% of all colorectal cancers and may be a completely asymptomatic incidental finding unless a patient presents with bowel obstruction or carcinoid syndrome(7). Colonic NETs usually have a high mitotic index, leading to diseases of poor biological nature, and given the delayed nonspecific presentation and the lack of a well-established adjuvant therapy regimen, they are associated with poor overall survival(8). Although surgical management is similar to that of adenocarcinoma of the colon, due to its aggressive nature and rarity, the therapeutic strategy depends on early detection along with timely surgical intervention followed by well-established adjuvant therapy, which is possible with a multidisciplinary team approach(9).

We present a rare case of a neuroendocrine tumor of the ileocecal valve with metastasis in lymph nodes, which caused an emergency presentation of small bowel obstruction at the general hospital with clinical, radiological, pathological, laboratory, and surgical findings. According to our knowledge and review of the literature, this is the first case of a neuroendocrine tumor of the ileocecal valve that caused obstructive ileus. This manuscript has been reported in line with SCARE's 2023 Criteria(10).

CASE PRESENTATION

A 66-year-old female patient presented to the emergency department with abdominal cramps that had lasted for the past 18 hours. The patient vomited yellow-green bitter contents during that period. The highest temperature measured at home was 37.8 °C. Past medical history included diabetes mellitus treated with oral hypoglycemics, chronic renal failure without the need for dialysis, and a cholecystectomy that was performed several years ago due to gallstones. The patient occasionally used Pantoprazole® and Trospium chloride®. For continuous diabetes therapy, she took the oral hypoglycemic Metformin®. Physical examination revealed diffuse abdominal pain with moderate distension. Upon admission to the emergency department, the patient was afebrile; axillary temperature was 36.4 °C, and arterial blood pressure was RR 130/70 mmHg, pulse 106/min, and oxygen saturation 98%.

The patient underwent urgent laboratory and X-ray, ultrasound, and CT diagnostic procedures for the next 60 minutes during a stay in the emergency department.

Laboratory findings revealed leukocytes and erythrocytes, as well as hemoglobin, in the reference range. However, laboratory findings revealed elevated C reactive protein (128.1 mg/L), elevated blood sugar (9.9 mmol/L), slightly elevated total bilirubin (37 umol/L), elevated creatinine (154 umol/L), elevated urea (12.2 mmol/L), slightly elevated alanine aminotransferase (ALT) (65 U/L) and aspartate aminotransferase (AST) (63 U/L), and slightly decreased sodium (132 mmol/L), while other findings were within the reference range.

An X-ray of the thoracic organs and the left profile showed bilateral hilar, perihilar, and parenchymal fibro-adhesive changes. Adhesive changes were also visible in the area of the anterior phrenic costal sinus. The rest of the findings were within the reference range for age without pathological signs. An X-ray of the native abdomen (Fig. 1) standing upright showed no free gas. Some air-fluid levels were formed, with a slightly more pronounced intestinal curve (blue arrows in Fig. 1). In the projection of the gallbladder, metal clips from a previous laparoscopic cholecystectomy were found.

Abdominal ultrasound showed flatulence (Fig. 2). The liver was inhomogeneous and hyper-

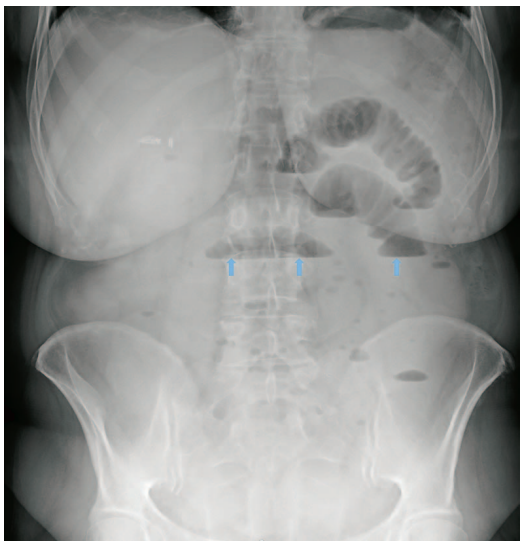

Figure 1. X-ray of the native abdomen

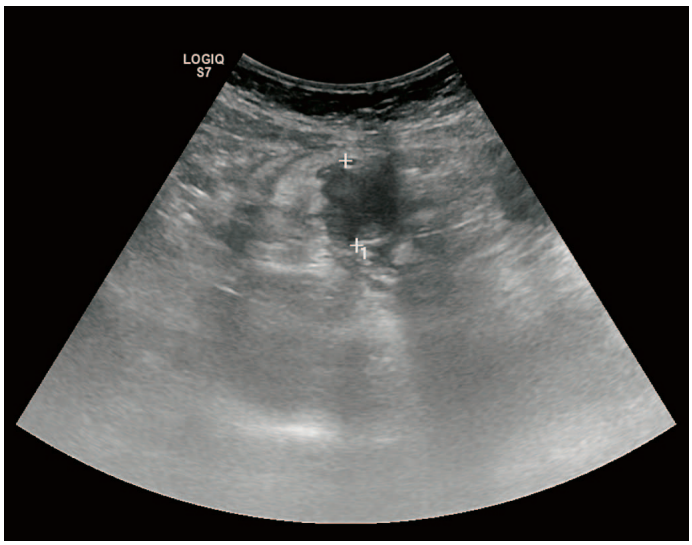

Figure 2. Abdominal ultrasound

echogenic in echo structure, the signs of diffuse liver lesions. Within the hilus of the right kidney, arcuate hypoechoic zones up to about 7 mm thick that correspond to parapyellic cysts or a slightly more pronounced ductal system. Several descending colon diverticula without signs of inflammation. The dilated segments of the small intestine, measuring up to 3 cm in diameter, exhibit thickened walls with more pronounced and active intestinal peristalsis. They are filled with a significant amount of content, indicating a disturbance in intestinal passage. Within individual parts of the small intestine and in the pouch of Douglas, a moderate amount of clear liquid content was found. The wall of the base of the cecum and terminal ileum was thickened, measuring about 27 x 25 mm, with a hypoechogenic content. Along with the described area, a tubular structure about 13 mm thick is partially shown, which may correspond to the inflamed appendix with surrounding inflammatory changes – peritiflitic tumor or partial intestinal obstruction of other etiology with inflammatory changes.

Due to the unclear ultrasound findings and the development of intestinal obstruction, CT of the abdomen and pelvis was performed with intravenous contrast (Figs. 3 and 4). A series of native and post-contrast scans were performed from the pulmonary bases to the aortic bifurcation with prior labeling of the gastrointestinal tract with the contrast agent Gastrographin® (Bayer).

On the shown part of the lung bases, a banded, primarily scarring change is visible on both sides. There are no signs of inflammatory consolidation or stagnation. No pleural effusion. The liver is of average size, has slightly wavy outer contours, and is appropriately post-contrast opacified. Bile ducts of appropriate width. The gallbladder was surgically removed. The pancreas has wavy outer contours, appropriately post-contrast opacified. The spleen is appropriately sized and appropriately post-contrast opacified. There were no expansive formations in the adrenal lodge area. The kidneys have slightly wavy contours, thinned in places, and deformed parenchyma. There are no signs of congestion or lithiasis in the duct system of both kidneys. The kidneys secrete in time. The cyst of the right kidney was about 6 mm in size. Segmentally shown ureters are of appropriate width and location (slightly more pronounced canal system of the right kidney). Ureters of appropriate width. Paraaortic and paracaval area, and in the epigastrium and mesentery, multiple lymph nodes size up to about 14 mm. Gynecological organs of appropriate presentation. The bladder has suitably thick walls with no pathological content inside the lumen. Minor gastric hiatal hernia. Minor umbilical hernia. Perihepatic space and between individual intestinal vortices showed some free liquid content. Thickened wall of the base of the cecum and terminal ileum, within which a denser marginally spiculated zone is

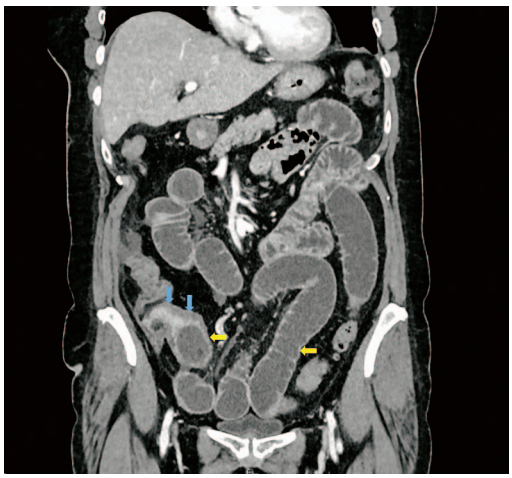

Figure 3. CT of the abdomen and pelvis, performed with contrast

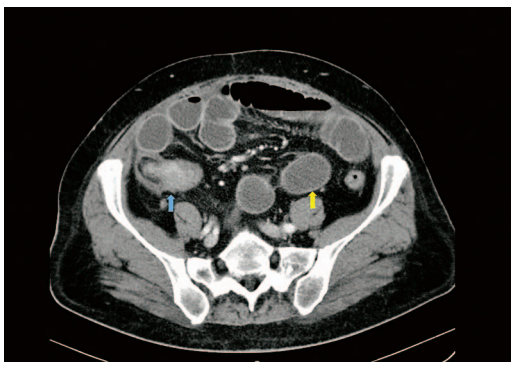

Figure 4. CT of the abdomen and pelvis, performed with contrast

visible, which was post-contrast opacified, about 2.5 cm in size, along which the surrounding adipose tissue is inhomogeneously altered, and several round lymph nodes size up to about 1 cm. The lesion described was a tumor or inflammatory etiology that obstructs the intestinal lumen of the ileum – see blue arrows in Fig. 3 and Fig. 4. As a result of obstruction, the ileus of the small intestine was visible, the curves of which are dilated to about 4.5 cm and thickened walls – yellow arrows in Fig. 3 and Fig. 4.

CT findings did not indicate a neuroendocrine tumor. An ultrasound of the abdomen could not provide enough information about the tumor itself. The patient went through the standard procedure and preparation for emergency operations; there was no need for urgent additional optimization of the patient. The patient received preoperative parenteral antibiotics according to a standard protocol by national and local guidelines.

The patient underwent surgery by an experienced abdominal surgeon, with a medial laparotomy performed. Intraoperatively, there was a pronounced distended small intestine in the form of obstructive ileus and a palpable tumor mass in the area of the caecum and Bauchini valve. Due to marked distention and edema of the small intestine and the presence of a tumor, a right hemicolectomy was performed with the formation of a double-barreled ileocolostomy. Abdominal drainage was placed. The laparotomy wound was closed with a continuous uninterrupted PDS suture. On the sixth postoperative day, the patient had short-term transient chest pain; she was examined by an internal medicine specialist who suspected the development of pulmonary embolism, which was ruled out by CT angiography of the pulmonary arteries.

The rest of the postoperative course was without complications. The drain was removed three postoperative days per inactivity. The laparotomy wound healed *per primam*, and the stoma and peristomal skin were neat, and the stoma was active without peristomal complications. Good stoma function was established, and the patient tolerated food intake *per os* well. The patient was discharged for home treatment 10 days after surgery. The pathologist's findings revealed that the mass was a neuroendocrine tumor.

Pathological findings

Gross examination of the right hemicolectomy specimen revealed an elevated, smooth surface, firm nodular, exophytic mass measuring 4 × 2.5 cm, localized at the ileocecal valve, narrowing the lumen of the bowel. Histological examination of the tumor showed nests of atypical cells with slightly polymorphic oval to round nuclei and a notable salt and pepper chromatin pattern. Immunohistochemically, tumor cells were positive for synaptophysin and chromogranin A. The proliferation index was done, and Ki-67 was 6% (1 mitosis per 10 high-power fields was counted). The tumor widely infiltrates the mucosa, muscle layer, pericolic fat tissue, and the serosa, and the mucosal surface was partially ulcerated. Lymphovascular and perineural invasion was also noted within

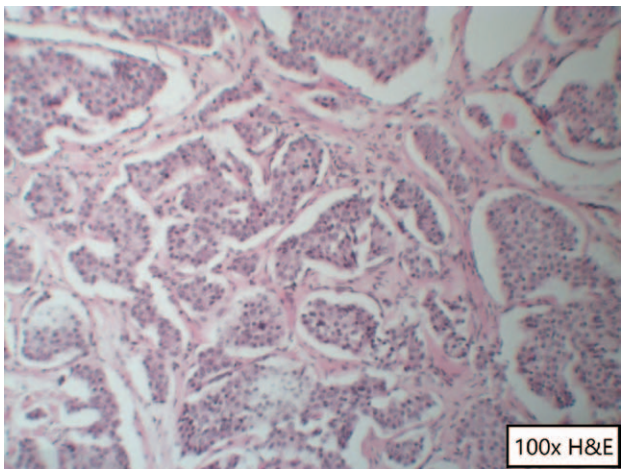

Figure 5. Well-differentiated neuroendocrine tumor (WD-NET, G2) of the ileocecal valve. Nests and islands of uniform cells (H&E stain, 100x). Proof of authenticity of Figure 5. The photo was taken on an Optika B-600Ti microscope SN:254548 with Optikam PRO 5 Digital Camera SN:252224.

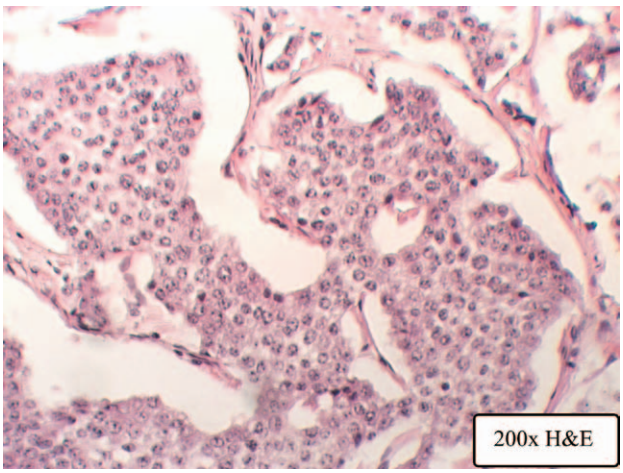

Figure 6. Well-differentiated neuroendocrine tumor (WD-NET, G2) of the ileocecal valve. Nests and islands of uniform cells (H&E stain, 200x). Proof of authenticity of Figure 6. The photo was taken on an Optika B-600Ti microscope SN:254548 with Optikam PRO 5 Digital Camera SN:252224.

the tumor, and 4 out of 17 lymph nodes were positive for metastatic disease (Figs. 5,6,7).

FOLLOW UP AND OUTCOME

The patient has been monitored for almost 2 years since the operation, through the surgeon in a secondary health care hospital, and also through other specialists such as a nephrologist, oncologist, diabetologist, gastroenterologist, and urologist. During the follow-up, the patients underwent regular clinical examinations, laboratory tests, and imaging, which included ultrasound of the abdomen and CT of the abdomen and pelvis. During the early postoperative follow-up, it was noted that the patient poorly tolerated the ileostomy and, due to deterioration in the form of acute exacerbation of chronic renal insufficiency of the prerenal type, required treatment by a nephrologist. Adequate fluid intake resolved the issues mentioned. At the same time, the patient was monitored by an oncologist, and adjuvant oncological therapy was not considered due to the intermediate tumor grade (G2). Further control by a nephrologist raises the suspicion of a kidney stone or tumor and the question of recurrence of the primary disease, which was ruled out by further diagnostic workup.

During further follow-up, almost a year after the surgery, in agreement with the oncologist and

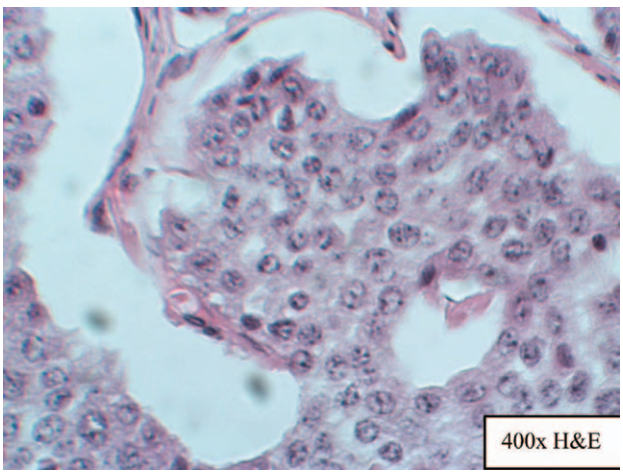

Figure 7. Well-differentiated neuroendocrine tumor (WD-NET, G2) of the ileocecal valve. Neuroendocrine tumor cells showing finely granular chromatin ("salt and pepper" pattern) with no evident nucleoli. (H&E Stain, 400x) Proof of authenticity of Figure 7. The photo was taken on an Optika B-600Ti microscope SN:254548 with Optikam PRO 5 Digital Camera SN:252224.

the surgeon, the patient was prepared for an operation to establish the continuity of the intestine. Considering that the patient was not undergoing active oncological treatment, she consented to the establishment of bowel continuity, which was performed 13 months after the primary surgery. The postoperative stay in the surgical department for

the establishment of bowel continuity went smoothly and without complications. Four months after the establishment of intestinal continuity, a colonoscopy was performed, and biopsies were taken in the area of the intestinal anastomosis between the small intestine and the colon due to suspicion of recurrence. The pathohistological findings of the biopsy that followed did not confirm a neuroendocrine tumor, but instead of inflammatory changes. Further controls that followed, according to the diabetologist, indicate that the patient has well-regulated diabetes (type 2) and a mild form of chronic renal insufficiency, and the ultrasound findings of the thyroid gland were also normal. During the further stay, control CT of the abdomen was without recurrence of the primary disease, and the control colonoscopy 3 months after the initial colonoscopy showed a complete regression of the inflammatory changes with regular findings of the anastomosed ileum, where recurrence was initially suspected, and the rest of the colon without any pathology.

During further follow-up, the oncologist noticed an increase in chromogranin A. Chromogranin A (CgA) is part of the neuroendocrine secretory protein group, and it is the most useful tumor biomarker used in NETs because of its secretion by neuroendocrine cells persisting after their malignant transformation(11). CgA levels are a reliable indicator of recurrence and tumor predictor when there is a 40% or greater increase in their levels(12). Bearing in mind the advantages given by CgA findings, there are also some limitations. Elevated CgA is associated with multiple causes, such as several diseases, but can also be elevated due to pharmacological therapy, including proton pump inhibitors, even after less than one week of use; a similar period is sufficient for cessation of CgA levels after therapy discontinuation(13).

As our patient had chronic gastritis, which was treated with a proton pump inhibitor, CgA levels were falsely positive due to the medication and not as a result of new pathological processes or neuroendocrine tumor relapses.

DISCUSSION

This case was about a 66-year-old woman with multiple comorbidities, such as diabetes mellitus, chronic renal failure, and previous cholecystectomy, who presented with an ileocecal region obstruction due to a neuroendocrine tumor. These comorbidities warranted emergency reaction and treatment measures—in the form of emergency surgical intervention—right hemicolectomy and ileocolostomy. The postoperative course turned out to be more or less smooth, and at the end of it, a diagnosis was confirmed to be that of a neuroendocrine tumor.

Most neuroendocrine tumors arise in the terminal ileum and are quite rare(14). As such, these tumors often present symptomatically only with nonspecific abdominal pain, obstruction, or, much less commonly, carcinoid syndrome(15). Given the nonspecific nature and indolence of most NETs, diagnosis is often delayed; some patients may not even be present until years after having very nonspecific symptoms(16). As happened in this case, obstruction of the small bowel is an infrequent yet serious complication that might even involve surgical intervention. This complies with current management for similar cases in the literature(17).

This example underlines the need for consideration of NETs in treating patients who present with apparent small intestine obstruction, especially when there has been a history of vague abdominal pains. Early detection, facilitated by modern imaging methods such as CT scans, is of great help in making early intervention possible. While NETs are on the rise, with advances in imaging studies and a rise in clinical awareness, the outcomes of patients could be improved as their conditions become identified at earlier stages. Moreover, surgery continues to be the principal treatment, while the possibility of long-term follow-up for metastasis or recurrence is considered open for additional treatment. Adjuvant oncological therapy was not considered in our case because of a well-differentiated intermediate-grade neuroendocrine tumor (grade 2), while only patients with poorly differentiated tumors may benefit from adjuvant oncological therapy (18).

One limitation in this case was the very nonspecific clinical presentation and absence of carcinoid syndrome, common in some NET cases, that led to a considerably delayed diagnosis of NET. The nature of the tumor could not be established preoperatively by nonspecific imaging, hence the need for an exploratory laparotomy. This limitation showed the need for advanced diagnostic

techniques or biomarkers that would reveal the presence of NET at an early stage and more accurately in an emergency setting.

In this rare case, it is evident that neuroendocrine tumors can be unpredictable and present as a surgical emergency as the first symptom of the disease. This is also evident in other papers describing the rarity of neuroendocrine tumors(1,4,5). According to the Norwegian Cancer Registry, which is robust and reliable, the incidence of neuroendocrine tumors affecting the colon is 0.25 per 100,000 population. By comparison, adenocarcinoma of the colon has a far higher incidence. Age-standardized (world) incidence rates per 100,000 of colorectal carcinoma in both sexes are 19.7, in males are 23.6, and in females are 16.3. While the age-standardized incidence rate among men is 30.1/100,000 in high-HDI (human development index) nations, it is 8.4 in low-HDI nations (the same statistics for women are 20.9 and 5.9, respectively)(19). Patients with neuroendocrine tumors are most often asymptomatic; sometimes they may have nonspecific symptoms such as abdominal pain, changes in bowel habits, and weight loss(20). Therefore, we believe that the diagnosis of neuroendocrine tumors in patients has been delayed in large numbers. We also associate with our case where the patient was presented with an acute abdomen requiring immediate emergency surgical therapy without previous symptoms suggestive of neuroendocrine tumor development. NET tumors are aggressive carcinomas due to lymph node metastases(21).

The key clinical lesson in this case is that even a rare condition like NETs should be part of the differential diagnosis in patients who present with acute abdominal obstruction, especially when the imaging shows signs of bowel obstruction or masses. This case also underlines the importance of prompt surgical management in cases of obstructive ileus due to NETs. In future cases, earlier use of CT may lead to better diagnosis and less time to reach definitive management. This case represents one of the difficult patients with successful management, amalgamating many disciplines: surgery, radiology, oncology, and internal medicine. In conclusion, the prompt surgical intervention had a good outcome and underlined the importance of interdisciplinary collaboration in the management of acute abdominal conditions.

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Sažetak

Neuroendokrini tumor ileocekalne valvule prezentiran kao opstrukcijski ileus – prikaz slučaja i pregled literature

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Neuroendokrini tumori ileocekalnog zaliska su rijetki i često se manifestiraju nespecifičnim simptomima koji otežavaju pravovremenu dijagnozu. Ovaj slučaj prikazuje 66-godišnju bolesnicu sa značajnim komorbiditetima, uključujući dijabetes melitus i kronično zatajenje bubrega, koja se javila u hitnu službu zbog jakih grčevitih bolova u abdomenu, praćenih povraćanjem i blagom temperaturom. Inicijalna slikovna i laboratorijska ispitivanja nisu omogućila postavljanje dijagnoze. Međutim, CT abdomena i zdjelice otkrio je opstrukciju tankog crijeva na ileocekalnoj valvuli, uzrokovanu tumorskom masom. Obzirom na akutnu prirodu simptoma, bolesnica je podvrgnuta hitnoj desnoj hemikolektomiji s ileokolostomijom. Histopatološka analiza potvrdila je prisutnost dobro diferenciranog tumora gradusa 2, veličine 4 cm, s limfovaskularnom invazijom i metastazama u 4 od 17 ispitanih limfnih čvorova. Postoperativni tijek bio je nekompliciran, a bolesnica je deseti dan otpuštena iz bolnice u stabilnom općem stanju. Ovaj slučaj ističe važnost razmatranja neuroendokrinih tumora u diferencijalnoj dijagnostici opstrukcije crijeva, osobito kada slikovne metode pokažu masu u ileocekalnoj regiji. Rano prepoznavanje i pravovremena kirurška intervencija ključni su za postizanje pozitivnih ishoda. Obzirom na rijetkost neuroendokrinih tumora na ovoj anatomskoj lokaciji, ovaj slučaj pruža vrijedan uvid u složenost dijagnostike i liječenja koje ti tumori predstavljaju. Kontinuirano praćenje od strane multidisciplinarnog tima od iznimne je važnosti za rano otkrivanje potencijalnih recidiva ili metastaza.

KLJUČNE RIJEČI: *neuroendokrini tumor, opstrukcijski ileus, kromatogranin A, inhibitori protonske pumpe*