Case report

Neuroendocrine Tumor of the Small Intestine in a Patient from the Northern Fluminense Region of the Province of Rio de Janeiro, Brazil

ABSTRACT

Neuroendocrine tumors are a rare class of malignant epithelial neoplasms characterized by prominent neuroendocrine differentiation. Cells within these tumor types display a unique blend of neuronal and endocrine capacities, enabling them to secrete both hormones and neurotransmitters. The distribution of these tumors is most frequently observed in the stomach, colon, rectum, appendix, pancreas, and bronchopulmonary complex.The primary objective of this article is to present a case report of a patient diagnosed with an ileal neuroendocrine tumor that initially manifested as intestinal subocclusion. A 54-year-old Afro-Brazilian male presented clinical signs of intestinal subocclusion. Diagnostic imaging revealed bilateral pleural effusion, marked small bowel dilation, and a narrowed ileal loop, suggestive of mechanical obstruction. Surgical intervention included segmental enterectomy and ileal anastomosis, with pathological analysis indicating a neuroendocrine tumor with potential confirmation through immunohistochemistry. The patient is currently under oncology department care for ongoing monitoring. The present investigation delineates a quintessential case, emblematic of the prevailing diagnostic and therapeutic norms prevalent in the northern reaches of Rio de Janeiro. It meticulously elucidates the diverse determinants that underpin the diagnostic journey and therapeutic stratagem instrumental in the successful eradication of an ileal neuroendocrine tumor. The clinical strategies adopted in this endeavor concur with established European and North American guidelines governing the resection of neuroendocrine tumors of the small intestine.

Keywords: Neuroendocrine Tumor,Small Intestine, Surgical Intervention, Cancer.

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1. INTRODUCTION

Neuroendocrine tumors are a class of malignant epithelial neoplasms characterized by prominent neuroendocrine differentiation. Cells within these tumor types display a unique blend of neuronal and endocrine capacities, enabling them to secrete both hormones and neurotransmitters. The distribution of these tumors is most frequently observed in the stomach, colon, rectum, appendix, pancreas, and bronchopulmonary complex. This diverse range of anatomical sites gives rise to a wide spectrum of clinical presentations and disease progression patterns. The variability in the development and growth of these tumors is closely tied to the affected organ, specific tumor location, and the stage and extent of cellular differentiation [1,2].

Despite their rarity [1,2,3,4,5,6,7], neuroendocrine tumors hold particular significance when arising in the small intestine, where they represent the predominant form of primary malignancy within this gastrointestinal segment [8,9].

Neuroendocrine tumors of the small intestine are an infrequent neoplastic entity. The yearly incidence rate for this condition, within a population of 100,000 individuals in the United States, is estimated to range between 0.67 and 1.20 [3,10,11,12,13]. In the United States of America, these tumors now account for a noteworthy 37% of small intestine tumor cases, surpassing the previously more prevalent adenocarcinomas[14]. A study by Kaçmaz et al. [15] projected an incidence of 0.52 to 0.81 cases per 100,000 individuals annually in France between 2005 and 2015. In the Queensland region of Australia, the estimated incidence stands at 1.42 cases per 100,000 individuals [16]. In Norway, for the period spanning 2010 to 2017, the estimated incidence rate was 2.27 cases per 100,000 individuals [6]. Notably, epidemiological investigations consistently reveal a significant rise in the occurrence of neuroendocrine tumors over recent years [1,2,3,4,5,6,7,8,9,15,16]. Some studies even point to an astounding over 300% increase in small intestine neuroendocrine tumor incidence rates over recent decades [8,9,16,17]. This prominent surge prompts further investigation, with advancements in diagnostic technology being a remarkable factor contributing to the heightened frequency of diagnoses [17,18].

Early detection is infrequent. These neoplasms manifest sluggish growth patterns and tend to disseminate via the bloodstream, primarily targeting mesenteric lymph nodes, liver, and lungs. The management challenge at this juncture substantially contributes to the heightened mortality rate [2,3,4].

The occurrence of neuroendocrine tumors within the small intestine is largely attributed to genetic factors [19,20,21,22]. However, Bogaards et al. [23] propose that lifestyle-related hazards, such as alcohol consumption and smoking, may play a role in the genesis of these tumors. The condition affects both genders with statistically insignificant variations [3] or a slight male predominance [4,5,8]. Most diagnoses arise during advanced stages due to the well-differentiated and indolent clinical presentation, characterized by late-onset symptoms and potentially unfavorable prognosis. Surgical intervention, involving extensive tumor resection, is the preferred treatment approach. Nevertheless, patients in advanced stages face a considerable risk of recurrence. Timely diagnoses correlate with improved treatment prognoses [2,4,7,9,24,25].

While the etiology of small intestine tumors' rarity remains incompletely elucidated, studies have linked neoplastic occurrences to genetic syndromes like familial adenomatous polyposis, Peutz-Jeghers syndrome, and Gardner syndrome. Chronic inflammatory conditions such as Crohn's disease and celiac disease have also been implicated. Increased IgA secretion has been suggested as a protective factor [26].

Neuroendocrine tumors constitute a subset of neoplasms arising from small cell clusters dispersed throughout the body, collectively termed the diffuse neuroendocrine system. These clusters primarily reside in gastrointestinal and pancreatic tissues, respiratory tissue, the thymus, urogenital tissue, and the skin. Within the gastrointestinal tract, the small intestine, cecal appendix, and rectum are the principal sites of affliction. Neuroendocrine tumors of the small intestine, although less common than those in the lung and rectum, hold the third most frequent position in this spectrum [14,27,28]. Despite their rarity, comprising around 3% of all primary duodenal tumors, these small intestine tumors are noteworthy for being the most prevalent site for distant metastasis formation [14]. The peak incidence of this condition occurs between the sixth and seventh decades of life. Approximately 80% of cases display somatostatin receptors, and about 10% of these tumors secrete bioactive agents leading to carcinoid syndrome, a manifestation observed in around 5% of small intestine neuroendocrine tumor cases [26].

Characterized by an indolent course, neuroendocrine tumors of the small intestine progress insidiously, leading to significant diagnostic challenges based on clinical presentation. The distal ileum is the most commonly affected site, often exhibiting a multicentric pattern likely originating from intraepithelial endocrine cells producing serotonin [2,3,9,18]. Symptomatology encompasses intermittent abdominal discomfort, subocclusive symptoms, and potential non-secretory diarrhea [14,26,27,28,29].

Patients with this condition often present complaints of abdominal pain, intestinal obstruction, and hydronephrosis [26]. These phenomena can be explained physiologically by mesenteric desmoplastic formations that cause peritoneal fixation, triggering obstructive and/or renal symptoms [28]. Both alterations are evident in the clinical case presented in this article.

Another manifestation involves intermittent abdominal pain, diarrhea, flushing, facial flushing, bronchospasm, cyanosis, and fluctuating blood pressure, collectively constituting the carcinoid syndrome [14,26,27,28,29]. Typically, over 10% of patients with this clinical syndrome, accompanied by obstructive symptoms and hematochezia, exhibit distant metastases [27,28], primarily in the liver and typically in an advanced stage of dissemination [28]. This reflects impaired liver function in inactivating hormone-related mediators via the portal circulation. The pathophysiology of this syndrome is rooted in the secretory nature of hormones like serotonin, neurokinin A, and histamine, which, when overactive, give rise to these symptoms, affecting approximately 5 to 7% of patients. Conversely, tumors that don't secrete these substances, or secrete them in an inactive form, contribute to the syndrome through mass effect [27,28].

Generally, neuroendocrine tumors of the small intestine manifest as diminutive growths with a propensity to induce mesenteric fibrosis, causing chronic peritoneal fixation. In most cases, as exemplified by the clinical case described herein, lymph node involvement accompanies these tumors. Fibrotic areas, besides leading to intestinal obstruction - the most common complication - can exacerbate the situation by instigating ischemia. Intestinal subocclusion results in colicky abdominal pain, while complete obstruction necessitates emergency surgery, a juncture at which a majority of diagnoses are made, often with approximately 30% of cases already featuring disseminated metastases [14].

The primary objective of this article is to present a case report of a patient diagnosed with an ileal neuroendocrine tumor that initially manifested as intestinal subocclusion.

2. CASE PRESENTATION

A 54-year-old male of Afro-Brazilian ethnicity presented to the Medical Clinic department of the General Hospital of Guarus in Campos dos Goytacazes, a city situated in the Northern Fluminense region of the Rio de Janeiro province, Brazil. His clinical presentation raised suspicion of intestinal subocclusion. Subsequent to his admission, the patient underwent abdominal computed tomography, revealing bilateral laminar pleural effusion. Moreover, there was marked dilation of small bowel loops, along with a noticeable reduction in the caliber of the ileal loop topography, indicative of mechanical obstruction. Notably, small mesenteric lymph nodes were observed on the right flank, adjacent to the point of obstruction. Additionally, moderate fluid distention was noted in colonic segments, devoid of signs of obstruction. Ultrasonography examination of the urinary tract unveiled an enlarged right kidney (13.6 x 7.2 x 7.1 cm) in comparison to the left kidney (13.3 x 5.53 x 5.1 cm).

Following assessment by the General Surgery service, the patient underwent exploratory laparotomy. During the procedure, a segmental enterectomy was conducted, succeeded by an ileal lateral-to-lateral anastomosis approximately 20 cm from the ileocecal valve, without encountering complications. Subsequent pathological analysis demonstrated a proliferation of monotonous regular cells characterized by round or oval nuclei exhibiting "salt and pepper" chromatin patterns. The cells displayed moderate eosinophilic granular cytoplasm, adopting an organoid arrangement and occasionally forming nests within the region of the ileocecal valve. Furthermore, areas indicating transmural hemorrhagic infarction were discernible. The surgical resection margin was devoid of neoplastic growth. The histological features strongly support the preliminary diagnosis of a neuroendocrine tumor, although confirmation and diagnostic supplementation are pending via immunohistochemical investigation.

Following the surgical procedure, the patient was referred to the oncology department for ongoing clinical monitoring.

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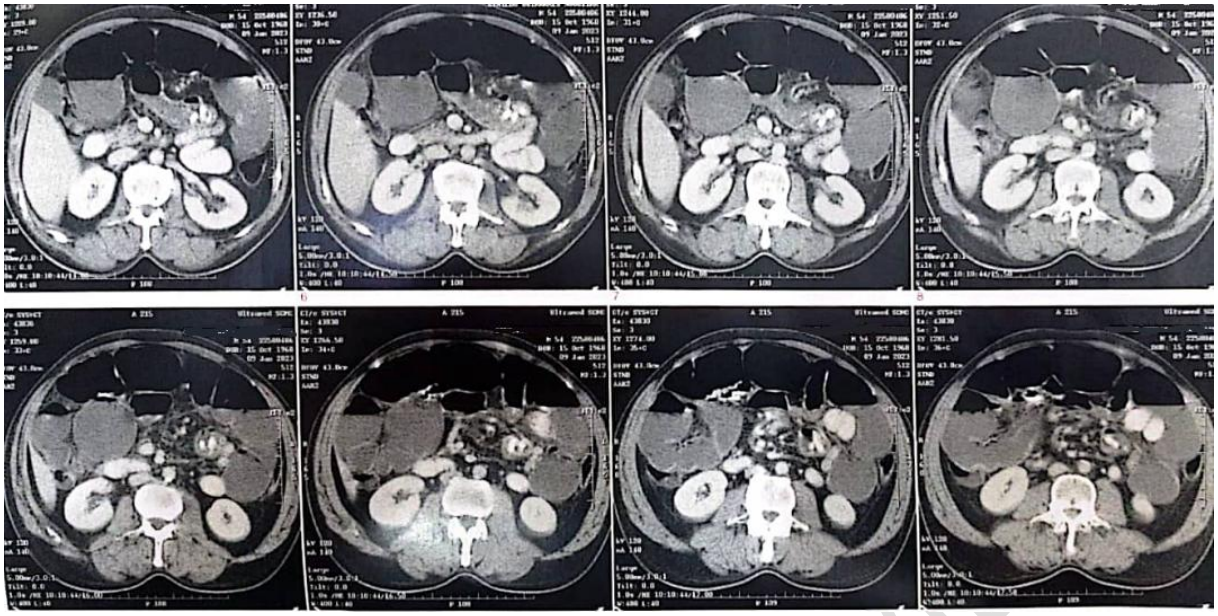

FIG. 1. COMPUTED TOMOGRAPHY OF THE ABDOMEN, REVEALING BILATERAL LAMINAR PLEURAL EFFUSION AND MARKED DILATION OF SMALL BOWEL LOOPS, WITH AN APPARENT AREA OF CALIBER REDUCTION IN THE ILEAL LOOPS' TOPOGRAPHY. SMALL MESENTERIC LYMPH NODES ARE ALSO OBSERVED ON THE RIGHT FLANK, ADJACENT TO THE AREA OF APPARENT OBSTRUCTION, FOLLOWED BY MODERATE LIQUID DISTENSION OF THE COLIC SEGMENTS, WITHOUT SIGNS OF OBSTRUCTION.

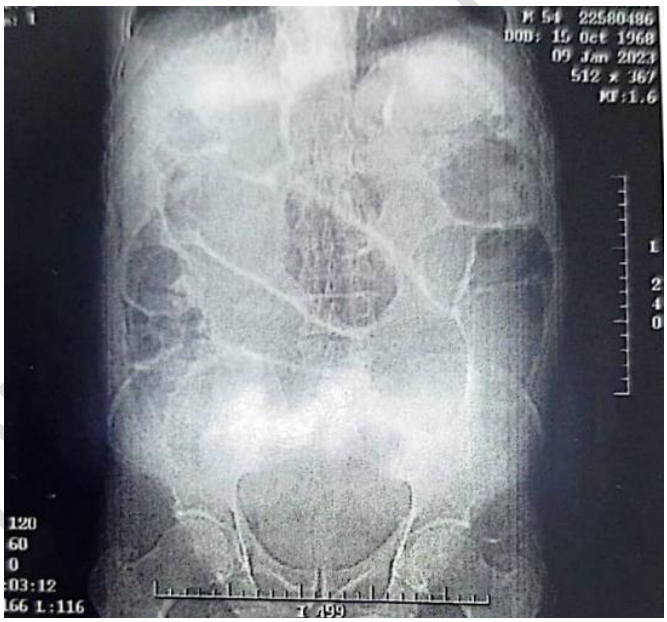

FIG. 2. ULTRASONOGRAPHY OF URINARY TRACT. THE RIGHT KIDNEY DISPLAYED ENLARGED DIMENSIONS (13.6 X 7.2 X 7.10 CM) COMPARED TO THE LEFT KIDNEY (13.3 X 5.53 X 5.10 CM).

3. DISCUSSION

The clinical case description was constructed using patient records and retrospective clinical data from the General Hospital of Guarus. The utilization of data was conducted under explicit consent provided by the patient through the signing of an Informed Consent Form. The publication of findings received ethical approval from the Ethics Committee of the General Hospital of Guarus. The utmost care was taken to preserve patient anonymity, ensuring no information capable of revealing the individual's identity was disclosed. Data for this case report were extracted from archived medical records. All procedures undertaken for the development of this case report rigorously adhered to the principles outlined in the Declaration of Helsinki.

The patient under our evaluation conforms to the prevailing pattern observed in neuroendocrine tumor diagnoses of the small intestine, having been identified with a subocclusive intestinal condition induced by mass effect. This alignment underscores the observations made by various authors regarding the latent progression of the condition until generic clinical manifestations emerge, leading to its

detection [2,3,8,10,11,15,18,23,24]. Remarkably, the patient did not exhibit carcinoid syndrome, a departure from cases with metastatic disease upon diagnosis, often accompanied by obstructive symptoms. The presence of lymph node clusters in the peri-lesional mesentery aligns intrinsically with analogous cases documented in the literature, reinforcing the well-established epidemiological profile. Prominent symptoms manifesting in neuroendocrine tumors are primarily nonspecific, encompassing abdominal pain, weight loss, partial intestinal obstruction, gastrointestinal bleeding, or local ischemia. Symptoms arising from metastasis may include carcinoid syndrome or anemia. The diverse and nonspecific nature of these symptoms may initially lead healthcare professionals to consider alternative diagnoses. More severe instances can involve phenomena such as carcinoid heart disease, characterized by heart valve plaque deposits, and bronchoconstriction [3,7,9,18]. Analogous to the case we examined, incidental diagnoses are commonplace, often based on symptoms attributed to the mass or uncovered during routine examinations, subsequently confirmed through histopathological scrutiny [28]. Consequently, prevalent symptoms encompass pain, nausea, vomiting, diarrhea, obstruction, jaundice, active bleeding, and/or anemia [14,26,28]. The typical lesion findings involve a size exceeding two centimeters, invading the proper muscle layer, and disseminating to regional lymph nodes [14].

The use of diverse imaging techniques, such as computed tomography, nuclear magnetic resonance, or ultrasound, plays a pivotal role in the diagnosis of gastrointestinal neuroendocrine tumors. By harnessing the complementary advantages of each modality, the precision in locating and staging the neoplasm is enhanced, offering valuable support for more effective surgical intervention that mitigates the risk of residual foci reemerging as localized tumors or spreading via metastatic routes [7,30,31,32,33,34]. The selection of imaging modalities hinges upon the tumor's location and necessitates supplementation with other diagnostic methodologies, including histopathological analysis and biomarker-specific biochemical assays [7,30,34]. Early-stage tumors are often diminutive and asymptomatic, which poses a challenge for early imaging-based diagnosis. At present, the foremost biochemical marker in the diagnostic exploration for patient surveillance in confirmed diagnoses or suspected cases is chromogranin A (CgA), displaying elevated levels in 60 to 100% of patients and offering sensitivity and specificity ranging from 70 to 100% [14,35]. Other biomarkers exhibit limited sensitivity and specificity, often producing pseudo-alterations in patients with chronic kidney disease or those utilizing medications like proton pump inhibitors [14]. The patient featured in the clinical case did not benefit from these alternatives, as the presentation aligned with a classical, previously asymptomatic scenario that progressed into a subocclusive intestinal condition necessitating urgent surgical intervention, a diagnosis confirmed through preoperative abdominal computed tomography scanning.

The preferred treatment is surgical resection with extensive tumor removal. However, for tumors smaller than one centimetre, local endoscopic resection is an option. Surgical resection should extensively cover primary tumors, regional lymph nodes, and, if possible, mesenteric fibrosis, in order to reduce the chances of recurrence. A thorough inventory of the pelvic cavity, sigmoid colon, mesentery, and diaphragm is necessary, as peritoneal metastases can be detected in up to 20% of cases, and the hepatic surface should be examined for metastases evaluation [14,35].

European and North American guidelines define open resection as more successful than laparoscopy due to its better accuracy in evaluating lesions in other parts of the intestine [7,14,30]. Thus, the patient in question underwent right ileocolectomy with ileotransverse anastomosis after ileocecal intussusception, revealing a nodule suggestive of a neuroendocrine tumor through histopathological examination, confirmed by immunohistochemistry. Subsequently, two one-year follow-up visits are recommended, followed by annual surveillance for ten years with clinical, biochemical, and radiological examinations [14,35].

4. CONCLUSION

Neuroendocrine tumors of the small intestine represent an infrequent neoplastic occurrence characterized by a subdued clinical trajectory and gradual onset of symptoms. This indolent course often culminates in delayed diagnoses, significantly compromising prognosis. Consequently, a considerable proportion of patients receive diagnostic confirmation in the advanced stages of the ailment, often necessitating prompt surgical interventions, yielding favorable outcomes upon histopathological and immunohistochemical evaluations. Surgical intervention remains the cornerstone of therapeutic intervention, demonstrating commendable efficacy in terms of survival benefits. This holds true not only for tumors in their early developmental stages but also for select cases exhibiting metastatic spread. Simultaneously, ongoing research endeavors in the realm of medical therapy continue to explore novel drug combinations, seeking to arrest tumor growth and alleviate symptomatic distress. The present investigation delineates a quintessential case, emblematic of the prevailing diagnostic and therapeutic norms prevalent in the northern reaches of Rio de Janeiro. It meticulously elucidates the diverse determinants that underpin the diagnostic journey and therapeutic stratagem instrumental in the successful eradication of an ileal neuroendocrine tumor. The clinical strategies adopted in this endeavor concur with established European and North American guidelines governing the resection of neuroendocrine tumors of the small intestine.

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