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Case Report

# A Rare Case of Poorly Differentiated Neuroendocrine Carcinoma of the Descending Colon with Regional Lymph Node Involvement Presenting in a Young Adult Nigerian Male: A Case Report.

***John IfeanyiNwadiokwu[1], *Victor Chimezie Okebalama[1], Rukayat Abiodun Olayemi[2], Olutomiwa Ayoola Omokore[3], Belusochi Blessing Joe-Ikechebelu [4], Harrison Onyekachi Duru[5], Uchechukwu Nwudele[6], Andrew Isimenmen Okoawoh[7], Ogheneovo Sunday[8], Andleeb Manzoor[9].**

[1]Department of Anatomic Pathology and Forensic Medicine, Babcock University Teaching Hospital, Ilishan-Remo, Ogun State, Nigeria, [2]Crescent University, Abeokuta, Ogun State, Nigeria, [3]Department of Surgery, Babcock University Teaching Hospital, Ilishan-Remo, Ogun State, Nigeria, [4]Department of Surgery, Chukwuemeka Odumegwu Ojukwu University Teaching Hospital, Amaku, Awka., Anambra State, Nigeria, [5]Department of Anaesthesia, Federal Medical Centre Birnin Kebbi, Kebbi State, Nigeria, [6]Department of Emergency Medicine, Doncaster and Bassetlaw Teaching Hospital NHS Foundation Trust, England, United Kingdom, [7]St Peters Hospital, Ashford and St Peters NHS Foundation Trust, Chertsey, Surrey, England, United Kingdom, [8]Department of Family Medicine, University of Benin Teaching Hospital, Benin City, Nigeria, [9]Department of Haematology, University of Sussex Hospital NHS Foundation Trust, United Kingdom

## Abstract

Malignant colonic neuroendocrine tumours are rare. Even more uncommon is their occurrence in the left colon. They also infrequently occur in males and young adults. We describe a rare case of poorly differentiated neuroendocrine carcinoma of the descending colon in a 32-year-old male who presented with signs of intestinal obstruction. He later had exploratory laparotomy and tumour resection with 5 cm gross tumour margins and Hartman-type colostomy and completed six cycles of Etoposide and Carboplatin combination. He has been tumour- and symptom-free for 36 months. Even though rare, neuroendocrine tumours should be an important differential of all colonic tumours, irrespective of the patient's age and sex, and surgeons should have a high index of suspicion for them. Although they most commonly occur in the right colon (cecum), they can also be found in the descending colon, where they can present with intestinal obstruction. Tumour resection with 5 cm gross tumour margins and Hartman-type colostomy can be handy. Etoposide and Carboplatin combination can improve overall survival in complicated World Health Organization (WHO) stage 3 neuroendocrine carcinoma with regional lymph node involvement, and generally poor prognosis, but without evidence of distant metastasis, and relatively fair performance index. Younger patients with neuroendocrine carcinomas may benefit better from platinum-based chemotherapy.

**Keywords:** *Poorly Differentiated Neuroendocrine Carcinoma; Descending Colon; Intestinal Obstruction; Colostomy; Etoposide; Carboplatin.*

***Correspondence:** Okebalama Victor Chimezie, Babcock University Teaching Hospital, Ilishan-Remo, Ogun State, Nigeria
**Email**: okebalsvictor@gmail.com

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## Introduction:

Neuroendocrine neoplasms (NENs) are diverse arrays of uncommon tumours that originate from neuroendocrine cells found all over the body and synthesize peptide hormones together with/or biogenic amines. [1] They can be benign or malignant. On the other hand, Neuroendocrine carcinoma (NEC) is a poorly differentiated neuroendocrine malignancy with mitotic figures of >10 per 2 $mm^2$ and/or a Ki-67 proliferation index >20%. [2]

NETs originate out of the dispersed neuroendocrine cell's structure that is cells with characteristics encompassing the pair of neurons (with the potential to pick up messages from the neural network) and endocrinal cells (which can synthesize and secrete monoamines, peptides, and hormones). [3] The nervous impulses deriving from the systema nervosum can be transformed into endocrinal signals by producing hormonal substances, oligopeptides, and amines. NETS are a heterogeneous group of benign and cancerous tumours with diversified morphologies and functions. Because cells of the neuroendocrine variety are all over the human body, neuroendocrine tumours can manifest in several body parts but most predominantly in the gastrointestinal tract (55%) followed by the respiratory tract (25%). [4] NETs, however, account for just 0.5% of the entire malignant pathologies of the gastrointestinal tract, even as colorectal NETS constitute <1% of all colonic malignant neoplasms. [3, 5] Gastrointestinal NETS (GI-NETS) most commonly involve the small intestine (45%), rectum (20%), and appendix (16%). [6] The colon proper is the least involved area for intestinal neuroendocrine neoplasms as only about 7.5% of the entire neuroendocrine tumours originate from this site. [7] Furthermore, the colonic NETs are more common in the cecum (69.6%) with the other involved sites being the sigmoid (13.0%), ascending (13.0%), and transverse (4.3%) colons. [5]

Indeed, the cases of descending colonic NETs are very sparse in the literature. NETs grow slowly, and as previously stated have both endocrinal and neuronal features. The cytoplasmic serried cores of these neoplasms can produce and discharge several materials having physiological functions such as monoamines, oligopeptides, and endocrine substances even as they also subsume chromogranin A (CgA), synaptophysin, and Neuron-specific enolase (NSE). Chromogranin A and synaptophysin are required for confirmatory diagnosis of NETS even though the rate of mitosis and Ki-67 proliferative index are essential for proper prognostication of the tumours. [8]

Although a Japanese study showed a male preponderance for NETS (especially in upper G.I cases) with an overall incidence of 2.09 per 100,000 population and 1.39 per 100,000 population in males and females respectively, the reverse was the case in Africa as the majority (60%) of the digestive tract NETS occur in females as against the minority (40%) of the cases seen in females. [9, 10] Indeed, NETs have a 2.5:1 female-to-male ratio as they are commoner in the former with more than 65% of the gastrointestinal NETS occurring in those between 60-70 years. [3, 10]

More specifically, colonic NETS are more common in females than males with a ratio of 2:1. [11] Bronchopulmonary tract neuroendocrine tumours have a predilection for Caucasians while those of gastrointestinal origin are more predominantly seen in people from Africa. [1]

NETs can form in different parts of the GI, stomach, duodenum, pancreas, ileum and jejunum, appendix, colon, and rectum. Colonic NETs are rare with the majority occurring in the right colon, particularly in the cecum. [12, 13]

Furthermore, Aldera and colleagues, in their 13-year retrospective South African study, demonstrated that gastrointestinal neuroendocrine carcinoma (GI-NEC) is the least common of the entire gastrointestinal NETS. It constituted only 8.6% of their evaluated cases, even as the colon was one of the least involved sites of the whole gastrointestinal tract. [9]

There have been very few reports of neuroendocrine tumours in Nigeria, the majority of which occurred outside the gastrointestinal system. [14-17] In a study that evaluated the clinicopathological characteristics of lower gastrointestinal tract endoscopic biopsies involving 249 specimens in Benin City, Nigeria, only two cases of NETS (both of rectal origin) representing just 2.9% of the entire malignant lesions were found even as Uchendu et al. in their scientific exploration of the epidemiology and histopathology of primary gastrointestinal malignancies in Delta State Nigeria only found a case of GI-NET (from the colorectum) constituting just 0.9% of the entire 180 primary GI cancers studied [18, 19] further demonstrating the rarity of GI-NETS. In some Western countries, however, there has been a rising prevalence of NETs recently due to extensive endoscopic and imaging investigations applications in gastrointestinal pathologies, increased recognition, and early-stage diagnosis. [11] To the best of our knowledge, our case nonetheless represents the first incidence of poorly differentiated neuroendocrine tumour of the descending colon to have been reported in Nigeria.

NETs grow slowly, and as previously stated have both endocrinal and neuronal features. The cytoplasmic serried cores of these neoplasms can produce and discharge several materials having physiological functions such as monoamines, oligopeptides, and endocrine substances even as they also subsume chromogranin A (CgA), synaptophysin, and Neuron-specific enolase (NSE). Chromogranin A and synaptophysin are required for confirmatory diagnosis of NETS even though the rate of mitosis and Ki-67 proliferative index are essential for proper prognostication of the tumours. [1, 8]

Although some neuroendocrine tumours of the digestive system discharge biologically active amines together with hormones, and exhibit endocrine-related syndromes, most of these tumours are not functional and have no symptoms. Also, affected individuals can have clinical features from mechanical compression as the neoplasm grows or results in fibrosis with gastrointestinal bleeding, [1] pain, and changes in bowel habits. [12]

Endoscopy in addition to biopsy, endoscopic ultrasound, biomarkers serology, imaging investigations, and functional somatostatin scans are employed in diagnosing and staging GI-NETS. [11, 20] According to the 9$^{th}$ version of the American Joint Committee on Cancer (AJCC), the staging of colorectal neuroendocrine tumours using the TNM staging system is as follows:

**Primary tumour (pT)**

**TX**: primary tumour cannot be assessed; **T0**: no evidence of primary tumour

**T1**: tumour invades the mucosa or submucosa and is ≤ 2 cm in greatest dimension

**T1a**: tumour ≤ 1 cm in greatest dimension; **T1b**: tumour > 1 cm but ≤ 2 cm in greatest dimension

**T2**: tumour invades the muscularis propria or is > 2 cm with invasion of the mucosa or submucosa

**T3**: tumour invades through the muscularis propria into subserosal tissue without penetration of overlying serosa

**T4**: tumour invades the visceral peritoneum (serosa) or other organs or adjacent structures

**Regional lymph nodes (pN)**

**NX**: regional lymph nodes cannot be assessed; **N0**: no tumour involvement of regional lymph node(s); **N1**: tumour involvement of regional lymph node(s)

**Distant metastasis (pM)**

**cM0**: no distant metastasis; **cM1**: distant metastasis; **cM1a**: metastasis confined to the liver

**cM1b**: metastasis in at least 1 extrahepatic site (e.g., lung, ovary, nonregional lymph node, peritoneum, bone); **cM1c**: both hepatic and extrahepatic metastases

**pM1**: microscopic confirmation of distant metastasis; **pM1a**: microscopic confirmation of metastasis confined to liver

**pM1b**: microscopic confirmation of metastasis in at least 1 extrahepatic site (e.g., lung, ovary, nonregional lymph node, peritoneum, bone); **pM1c**: microscopic confirmation of both hepatic and extrahepatic metastasis.[21]

Surgical resection is usually curative in localized NETS. [20] Systemic therapies (such as cytotoxic chemotherapies, and peptide receptor-targeted therapy), interferons, targeted therapies, radiofrequency ablation, trans arterial embolization, and radioembolization can be of use in managing advanced (metastatic) NETS even as platinum-based chemotherapy is the treatment of choice for poorly differentiated NETS. [20]

Factors such as the tumour size, grade, stage, morphological differentiation, vascular invasion, location, histological type, surgical approach, and the patient's age can be used to evaluate the prognosis of colonic NETS. [1, 22-24]

## Case Report

A 32-year-old man presented with constipation and abdominal pain for 2 months and a 2-week history of abdominal distension and intermittent vomiting. He had been otherwise healthy before then and had no co-morbid illness. He had previous inguinal herniorrhaphy 5 years ago. Physical examination showed a dehydrated man with gross abdominal distension and hyperactive bowel sounds. The respiratory rate was 20 cycles per minute, the pulse rate was 90 beats per minute, the blood pressure was 76/122 mm/Hg, and the random plasma glucose level was 90 mg/dL. Also, his urinary output over 6 hours was 29 mL/hour while his temperature was 36.8°C. Abdominal examination showed a well-healed surgical scar on the left iliac region while a rectal examination revealed an empty rectum. Other systemic examinations showed no significant abnormal findings. A clinical diagnosis of intestinal obstruction complicated by acute renal failure in the oliguric phase from a colonic tumour to rule out abdominal adhesion was made. A performance status (PS) assessment that was done using the Eastern Cooperative Oncology Group (ECOG) scale [25] was 1 meaning that he had a relatively fair prognosis. The measured serum urea and creatinine levels were remarkably elevated with the former showing a disproportionate increment against the later. Plain abdominal radiographs showed grossly dilated small and large bowel loops.
However, the serum sodium and chloride were mildly reduced while the serum potassium, calcium, and phosphate were within normal limits. Apart from lactate dehydrogenase which showed an independent increment, all other liver enzymes were within normal values. The full blood count (FBC), chest x-ray, and tumour markers checked all showed no abnormal findings. (Table 1)

On the day of presentation, He had urinary catheterization and a nasogastric tube inserted and was commenced initially on I Liter (L) of normal saline (N/S) over I hour, then 1L of N/S to be alternated with I Liter of 5% dextrose saline (5% D/S) 6 hourly over 24 hours but was changed to I L N/S start, followed by 60mg of intravenous frusemide administration. Then subsequently, I L of N/S to be alternated with 1 L of D/S 4 hourly over 24 hours when he was observed not to be making adequate urine. He was also placed on nil per oral (NPO) with an hourly urine monitoring chat opened.

**Table 1: Investigation Results of patient at presentation**

| Laboratory Investigation | Result | Reference Range |
|---|---|---|
| Serum urea | 66 mg/dL | 8-24 mg/dL |
| Serum creatinine | 3.7 mmol/L | 0.7-1.3 mg/dL |
| Serum potassium | 3.7 mmol/L | 3.5-5.5 mmol/L |
| Serum calcium | 8.7 mg/dL | 8.5-10.2mg/dL |
| Serum chloride | 94 mmol/L | 96-106 mmol/L |
| Serum phosphate | 2.9 mg/dL | 2.8-4.5 mg/dL |
| Serum sodium | 133 mE/L | 135-145 mE/L |
| Lactate dehydrogenase (LDH) | 228 IU/L | 135-225 IU/L |
| Alanine aminotransferase (ALT) | 8 U/L | 7-56 U/L |
| Alkaline phosphatase (ALP) | 48 IU/L | 44-147 IU/L |
| Aspartate aminotransferase (AST) | 12 U/L | 8-33 U/L |
| Total serum bilirubin | 0.4 mg/dL | 0.1-1.2 mg/dL |
| Gamma-glutamyl transferase (GGT) | 10 U/L | 5-40 U/L |
| Albumin | 3.9 g/dL | 3.4-5.4 g/dL |
| Total protein | 8 g/dL | 6.0-8.3 g/dL |
| Prothrombin time (PT) | 12 seconds | 11-13.5 seconds |
| Serum carcinoembryonic antigen (CEA) | 0.3 ng/mL | 0-2.5 ng/mL |
| CA 125 | 1 U/mL | 0-35 U/mL |
| Serum CA 19-9 | 3,5 U/mL | 0-37 U/Ml |
| Hemoglobin count | 14 g/dL | 14-17 gm/dL |
| White blood cell count | 6.3 x $10^9$L | 4.5-11.0 x $10^9$/L |
| Platelet count | 180,000 | 150,000-450,000 |
| Chest x-ray | Normal findings | |

His urinary output improved to 95 mL/hour within 24 hours, and he subsequently had an emergency laparotomy with findings of a constricting tumour of the descending colon extending to the serosa. There was gross dilation of the proximal colon and the small bowel due to an incompetent ileocaecal valve.
He had tumour resection with 5cm gross tumour margins, and a Hartman-type colostomy was fashioned. A post-operative diagnosis of intestinal obstruction secondary to a left colonic tumour was made.
He had an uneventful post-operative (post-op) stay and was discharged 9 days following surgical intervention after being commenced on oral feeding. His urinary output on discharge was 100 mL/hour, and the serum urea and creatinine were 10 mg/dL (normal: 8-24 mg/Dl) and 0.8 mg/dL (normal: 0.7-1.3 mg/dL) respectively. The serum lactate dehydrogenase (measured twice), chloride, and sodium all returned to normal levels before discharge.

Histology revealed a malignant epithelial neoplasm composed of tumours predominantly in nested packets, focal areas of sheets, and poorly formed glandular patterns. The component cells have moderately pleomorphic hyperchromatic to vesicular nuclei, prominent nucleoli, moderate eosinophilic cytoplasm, and atypical mitosis. Some of the cells have stippled chromatin patterns resembling salt and pepper appearance (Figure 1). These tumour cells have invaded the serosa and involved all six regional lymph nodes (with associated tumour necrosis) (Figure 2). The margins of resection are free of tumour cells. The accompanying skin tie is unremarkable and free of the tumour. The stage of this tumour is $pT_4N_1M_0$

An initial assessment of poorly differentiated neuroendocrine carcinoma with metastasis to all the submitted lymph nodes was made. The overall prognosis based on this was poor.

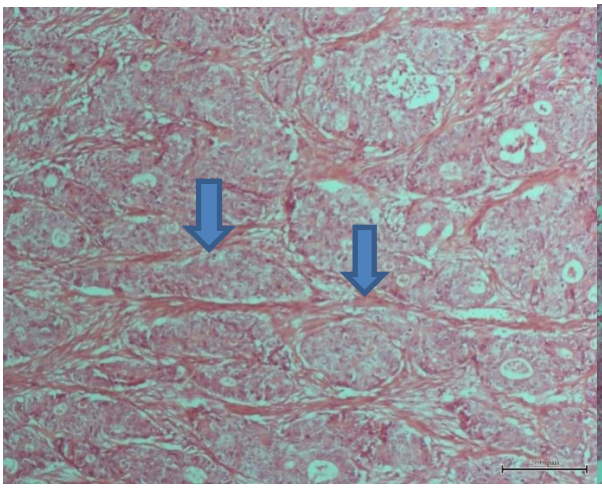

**Figure 1**: (H and E x 100) shows nested packets of moderately to markedly pleomorphic tumour cells (arrows) having predominantly stippled chromatin pattern resembling salt and pepper appearance consistent with neuroendocrine carcinoma.

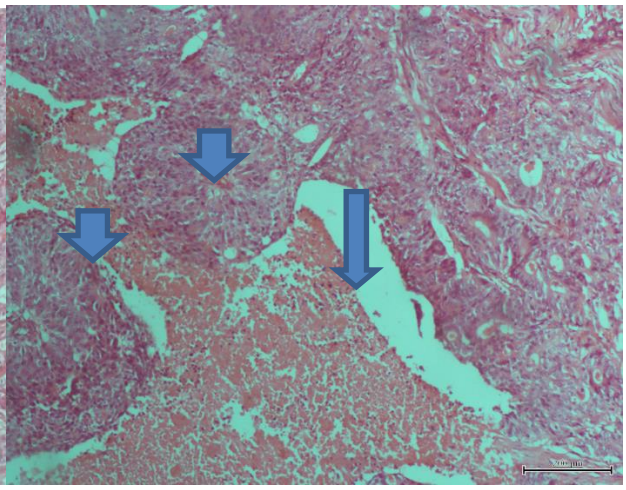

**Figure 2:**(H and E x 100) shows neuroendocrine tumour cells invading the serosal layer (short arrow) with associated tumour necrosis (long arrow)

Immunohistochemistry showed positivity for chromogranin, epithelial membrane antigen, and anticytokeratin monoclonal antibodies 1 and 3 and was negative for CD 117 and CD 45 (Figure 3). K167 was not available in our setting so it was not done. A final assessment of poorly differentiated neuroendocrine carcinoma of the descending colon with metastasis to all the submitted lymph nodes was made.

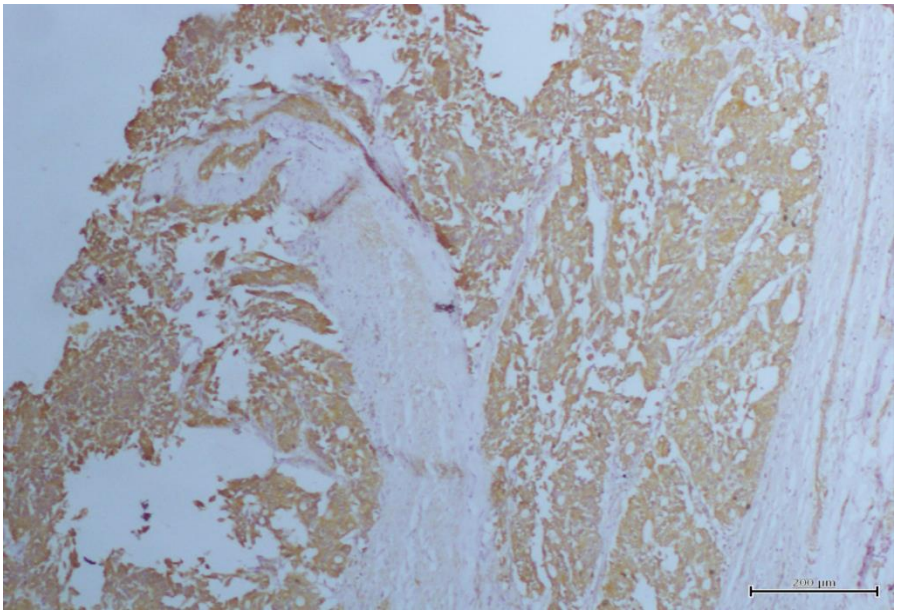

**Figure 3:** (Chromogranin Immunohistochemical stain x 100) shows strong 3+ immunopositivity (brown staining) in more than 80% of the tumour cells consistent with neuroendocrine carcinoma.

He later commenced (7 months after the surgery) and completed six cycles of adjuvant chemotherapy with Etoposide (100mg/$m^3$) (on day one) followed by Carboplatin (100 mg/$m^3$) (on days one to three) 21 days apart. Our Patient has been stable for 36 months following the completion of treatment.

## Discussion

NETs of the gastrointestinal tract and pancreas include a range of rare and diverse neoplasms with unique tumour biology, natural history, and clinical management. [26]

Gastrointestinal NETs are rare, commoner in females, and the malignant subtype only accounts for 2% of all GI malignancies, [3] with only 11% of all GI NETs occurring in the colon with a predilection for the right side, particularly the cecum [12] unlike our patient who is a male and had a tumour on the left side (the descending colon). The mean age of presentation is in the seventh decade. [12, 20] Globally, there has been a rising prevalence of NETs owing to extensive endoscopic and imaging investigations applications in gastrointestinal pathologies, increased recognition, and early-stage diagnosis. [11] In our case, our ability to recognize the tumour cells with histology and immunohistochemistry studies was instrumental in making a prompt and accurate diagnosis. Nonetheless, only a handful of neuroendocrine tumours have been reported in Nigeria with most of them occurring outside the GI, having about an equal gender distribution in males and females with an age range of 45-68 years. [14-19] Of the very scarce GI-NETS reported in Nigeria, they mostly tend to prefer either the cecum or the rectum with the patient in the former presenting with right-sided lower abdominal fullness, audible bowel sounds, occasional diarrhoea, nausea, vomiting, and epigastric pain. [17, 18] In a more elaborate retrospective African study of GI-NETS, most of the involved patients (60%) were females and had a mean age of 56 years at presentation with the small intestine being the most involved area [9] Additionally, colonic NETs can clinically show up with pain in the abdomen, as a result of the pushing or displacement of surrounding tissues by the growing neoplasm or desmoplastic changes, weight loss, and rectal bleeding but less commonly with intestinal obstruction. [3] In our case, the patient was a male, young adult (32 years), who had a tumour on the descending colon and presented with constipation, vomiting, dehydration, and signs of acute renal failure.

Less commonly, they could be an incidental finding on colonoscopy. [3] Also because most NETs are not functional (not hormone-secreting) they lack specific biomarkers that cause the spectrum of symptoms that allow quick diagnosis; consequently, patients don't present until metastasis has ensued (12-22% of all cases). [27] In our case, however, our patient had no evidence of metastasis at presentation.

As outlined by the World Health Organization [28], NET is classified into three grades: The neuroendocrine tumour (NET; G1) have a mitotic count of <2/10 high-power fields (HPF) and/or a Ki67 index of ≤2%; NET grade 2 has a mitotic count of 2–10 per 10 HPF and/or a Ki67 index between 3% and 20% and the NEC which is grade 3 has a mitotic count of more than 20/10 HPF and/or a Ki67 index >20%. The grade 3 NEC represents a poorly differentiated neoplasm previously classified as small cell carcinoma or poorly differentiated NEC (PDNEC).

Accordingly, the tumour in our patient was diagnosed as a poorly differentiated colonic neuroendocrine carcinoma which can be categorized as a WHO grade 3 neuroendocrine tumour with the following criteria: a high mitotic count of >20 per 10hpf, pleomorphism, diffuse sheets in areas, necrosis, tumour invasion through the colonic serosa layer and histological evidence of metastases to all the 6 harvested lymph nodes. Poorly differentiated neuroendocrine carcinomas (NECs) are rare and aggressive neoplasms with poor prognosis that can originate anywhere along the GI and other parts of the body. [15, 29]

The gastrointestinal poorly differentiated neuroendocrine carcinomas (GI-NECs) are uncommon and have a very high malignant potential with a poor prognosis. These malignancies are identified at around a rate of 1,000 cases annually, and hence nothing is known regarding their tumour biology or cytogenetics. Although they can develop in almost any part of the GI tract, including the biliary system, only 11% of poorly differentiated NECs occur in the GI. More significantly, at the time of diagnosis, over half of the patients have metastatic disease. This indicates a bad prognosis for these individuals because, in the absence of intervention, their median overall survival (MOS) is only 5 months; however, if some treatment is given, this can increase to 8–20 months. [29] In contrast, our patient has been alive and well for 36 months following medical intervention. This could be because even though the neoplasm he had involved the regional lymph nodes and he had a complicated NEC, there was no evidence of distant metastasis, and his performance status index was fair. Also, his young age could have helped him combat the disease and survive this long.

In addition to these tumours lacking systemic indicators, tissue diagnosis is crucial for their identification because the differentiation grade has prognostic implications. [29] Microscopically, gastrointestinal neuroendocrine tumours exhibit typical morphologic features: a well-circumscribed lesion composed of monomorphic neoplastic cells having round nuclei with "salt and pepper" (stippled) chromatin. Tumour nests are arranged in trabecular, glandular, acinar, and solid patterns. In the index case, the histology consistent with the histological feature of NETS showed a malignant epithelial neoplasm composed of tumour cells disposed in nests, sheets, and poorly formed glandular patterns. The component cells have moderately pleomorphic hyperchromatic to vesicular nuclei, prominent nucleoli, moderate eosinophilic cytoplasm, and atypical mitosis. Some of the cells have stippled chromatin pattern resembling salt and pepper appearance. Immunohistochemically, chromogranin and synaptophysin are strongly associated with the tumour. [30] In the immunohistochemistry evaluation of our case, the tumour cells showed positivity for chromogranin, epithelial membrane antigen, and anticytokeratin monoclonal antibodies 1 and 3. (Figure 3)

Usually, colonic NETs are treated with segmental colectomy and extensive regional clearance with a 5-year survival of 32 to 44%. Due to the heterogeneity of NETs, their prognosis remains unclear. [20] However, Chen et Al found that there is a strong correlation between prognosis and these variables: lymphatic metastasis, international standardized ratio, prothrombin time, tumour differentiation, and number of tumour metastatic sites. [31] Other factors that can be used for prognostication are the rate of mitosis (mitosis count), Ki-67 proliferative index, tumour size, stage, grade, vascular permeation, location, histological type, surgical type, serum creatinine, carcinoembryonic and aspartate transaminase levels, and the age of the patient can be useful in the prognostication of NETS [1, 8, 22-24, 31]
Research has indicated that the Ki-67 level for grade 3 NEC is clinically significant since tumours with a Ki-67 level below 60% respond less well to standard chemotherapy treatments for NECs that are poorly differentiated. [29] In our case, we could not measure Ki-67 and it is not available in our setting.

Furthermore, serum lactate dehydrogenase (LDH) showed an isolated elevation in the index case. This is due Warburg effect (commonly seen in NETS and other malignancies), which is the term for the dependence of cancer cells on enhanced glycolysis that leads to elevated lactate synthesis rather than aerobic respiration in the mitochondria. [32] Elevated LDH is associated with poor prognosis in NEC with an OS of 9 months [33] However, our patient has been tumour- and disease-free for 36 months following surgical intervention and the completion of his prescribed platinum-based chemotherapy.

Although poorly differentiated NEC, higher tumour grade, males with abnormal serum creatinine level, and lymphatic metastasis are associated with poor prognosis in NETs [31], normal prothrombin time, normal total serum bilirubin, normal aspartate transaminase, and absence of distant metastasis favour better prognosis [31]. These could have helped with the longer survival rate observed in our patient.

Also, the etoposide and carboplatin or cisplatin combination for 4–6 cycles is the recommended therapy for limited or widespread poorly differentiated NECs and has been shown to improve overall outcomes in poorly differentiated neuroendocrine tumours of intestinal origin with an overall survival period of 11.5 months. [29, 34] In our case, despite having regional lymph node metastasis as was histologically confirmed, our patient has been tumour and symptom-free for 36 months following surgical intervention and the completion of the chemotherapeutic combination.

In conclusion, malignant NETs however rare should be an important differential of all colonic tumours irrespective of patient's age, and sex and surgeons should have a high index of suspicion for it. Although they most commonly occur in the right colon (caecum), they can also be found in the descending colon where they can present with clinical features of intestinal obstruction. Tumour resection with 5cm gross tumour margins and Hartman-type colostomy can be handy. Etoposide and Carboplatin combination improves overall survival especially in cases with only limited regional involvement. Platinum-based chemotherapy can also improve outcome in complicated NEC cases in the young.

## References


1. Ciobanu OA, Martin S, Fica S. Perspectives on the diagnostic, predictive, and prognostic markers of neuroendocrine neoplasms. Experimental and Therapeutic Medicine. 2021 Dec 1;22(6):1-4.
2. Israel AK, Cracolici V, Griffith CC. Challenging differential diagnoses in small biopsies from the sinonasal tract. InSeminars in Diagnostic Pathology 2023 Sep 1 (Vol. 40, No. 5, pp. 321-332). WB Saunders.
3. Ahmed M. Gastrointestinal neuroendocrine tumours in 2020. World J Gastrointest Oncol 2020; 12(8): 791-807
4. Waisberg DR, Fava AS, Martins LC, Matos LL, Franco MI, Waisberg J. Colonic carcinoid tumours: a clinicopathologic study of 23 patients from a single institution. Arquivos de Gastroenterologia. 2009;46:288-93.
5. Maggard MA, O'Connell JB, Ko CY. Updated population-based review of carcinoid tumours. Annals of surgery. 2004 Jul 1;240(1):117-22.
6. Hrabe J. Neuroendocrine tumours of the appendix, colon, and rectum. Surgical Oncology Clinics. 2020 Apr 1;29(2):267-79.
7. Maggard MA, O'Connell JB, Ko CY. Updated population-based review of carcinoid tumours. Ann Surg 2004; 240: 117-122
8. Capdevila J, Meeker A, García-Carbonero R, Pietras K, Astudillo A, Casanovas O, Scarpa A. Molecular biology of neuroendocrine tumours: from pathways to biomarkers and targets. Cancer Metastasis Rev 2014; 33: 345-351
9. Aldera AP, Govender D, Locketz ML. Neuroendocrine neoplasms of the digestive tract: incorporating the 2019 WHO grading schema in the South African context. South African Journal of Surgery. 2021;59(1):27a-e.
10. Masui T, Ito T, Komoto I, Uemoto S, JNETS Project Study Group. Recent epidemiology of patients with gastro-entero-pancreatic neuroendocrine neoplasms (GEP-NEN) in Japan: a population-based study. BMC cancer. 2020 Dec;20:1-7.
11. Ahmed M. Gastrointestinal neuroendocrine tumours in 2020. World journal of gastrointestinal oncology. 2020 Aug 8;12(8):791.
12. Anthony LB, Strosberg JR, Klimstra DS, Maples WJ, O'Dorisio TM, Warner RR, Wiseman GA, Benson AB 3rd, Pommier RF; North American Neuroendocrine Tumour Society (NANETS). The NANETS consensus guidelines for the diagnosis and management of gastrointestinal neuroendocrine tumours (nets): well-differentiated nets of the distal colon and rectum. Pancreas 2010; 39: 767-774

13. Jiang M, Tan Y, Li X, Fu J, Hu H, Ye X, et al. Clinicopathological Features and Prognostic Factors of Colorectal Neuroendocrine Neoplasms. Gastroenterol Res Pract. 2017;2017:4206172
14. Agada H, Grimah V, Emmanuel O. Skin Involvement of Metastatic Neuroendocrine Tumour in a Black African: A Rare Occurrence. Nigerian Journal Of Dermatology. 2023;13(1).
15. Okebalama VC, Nwadiokwu JI, Osaze E, Ayodeji AA, Chinatu-Nwankwo OM. Poorly differentiated carcinoma with neuroendocrine features in two patients with sinonasal tumours: a report of two cases. Pan African Medical Journal. 2022 May 16;42(1).
16. Kumar K, Tariq H, Ahmed R, Chukwunonso C, Niazi M, Ihimoyan A. Small-Cell Type, Poorly Differentiated Neuroendocrine Carcinoma of the Gallbladder: A Case Report and Review of the Literature. Case Reports in Oncological Medicine. 2019;2019(1):8968034.
17. Obateru OA, Taiwo JA, Oladejo S, Awelimobor DA, Fadaunsi OO, Olokoba AB. Cecal carcinoid tumour in a Nigerian man: a case report and review of literature. Nigerian Journal of Clinical Practice. 2017 May 24;20(5):634-6.
18. Umana IO, Obaseki DE, Ekanem VJ. The clinicopathological features of lower gastrointestinal tract endoscopic biopsies in Benin City, Nigeria. Saudi Surgical Journal. 2017 Jan 1;5(1):9-20.
19. Uchendu OJ, Akpo EE. Primary gastrointestinal tract cancers in Nigeria, epidemiological and histopathological study. Asian Pacific Journal of Cancer Care. 2021 Mar 26;6(1):3-7.
20. Kapoor R, Bhattacharyya T, Gupta R, Mitta BR, Kalra N. A systematic review of management of neuroendocrine tumours: An experience from a tertiary care centre from India. Clin Cancer Investig J. 2014;3:363–72
21. Gonzalez RS. Staging-neuroendocrine. PathologyOutlines.com website. https://www.pathologyoutlines.com/topic/colontumourstagingneuroendocrine.html. Accessed November 21st, 2024.
22. Yu YJ, Li YW, Shi Y, Zhang Z, Zheng MY, Zhang SW. Clinical and pathological characteristics and prognosis of 132 cases of rectal neuroendocrine tumours. World journal of gastrointestinal oncology. 2020 Aug 8;12(8):893.
23. Chi Y, Du F, Zhao H, Wang JW, Cai JQ. Characteristics and long-term prognosis of patients with rectal neuroendocrine tumours. World Journal of Gastroenterology: WJG. 2014 Nov 11;20(43):16252
24. Shen C, Yin Y, Chen H, Tang S, Yin X, Zhou Z, Zhang B, Chen Z. Neuroendocrine tumours of colon and rectum: validation of clinical and prognostic values of the World Health Organization 2010 grading classifications and European Neuroendocrine Tumour Society staging systems. Oncotarget. 2017 Mar 3;8(13):22123.
25. Azam F, Latif MF, Farooq A, Tirmazy SH, AlShahrani S, Bashir S, Bukhari N. Performance status assessment by using ECOG (Eastern Cooperative Oncology Group) score for cancer patients by oncology healthcare professionals. Case reports in oncology. 2020 Sep 25;12(3):728-36.
26. Neychev V, Steinberg SM, Cottle-Delisle C, Merkel R, Nilubol N, Yao J, et al. Mutation-targeted therapy with sunitinib or everolimus in patients with advanced low-grade or intermediate-grade neuroendocrine tumours of the gastrointestinal tract and pancreas with or without cytoreductive surgery: protocol for a phase II clinical trial. BMJ Open 2015;5:e008248.
27. Komarnicki P, Musiałkiewicz J, Stańska A, Maciejewski A, Gut P, Mastorakos G, Ruchała M. Circulating Neuroendocrine Tumour Biomarkers: Past, Present and Future. J Clin Med. 2022 Sep 21;11(19):5542. doi: 10.3390/jcm11195542.
28. Cavalcanti MS, Gönen M, Klimstra DS. The ENETS/WHO grading system for neuroendocrine neoplasms of the gastroenteropancreatic system: a review of the current state, limitations and proposals for modifications. International journal of endocrine oncology. 2016 Aug 1;3(3):203-19.

29. Mertz AT, Ojemuyiwa MA. A case of poorly differentiated large-cell neuroendocrine carcinoma of the cecum: a rare malignancy, with review of the literature. Case Reports in Oncology. 2017 Jan 6;9(3):847-53.
30. Lakhe, R. R., Swami, R. M., Kulkarni, P., Doshi, P. R., & Mani, N. S. (2020). Immunophenotyping in incidental gastrointestinal neuroendocrine tumours: study at tertiary care centre. Journal of Pathology of Nepal, 10(2), 1751–1755.
31. Chen JX, Lin Y, Meng YL, Zhao AX, Huang XJ, Liang R, Li YQ, Liu ZH. Predicting the Survival Probability of Neuroendocrine Tumour Populations: Developing and Evaluating a New Predictive Nomogram. Biomed Res Int. 2021 Jan 28;2021:9126351
32. Freis P, Graillot E, Rousset P, Hervieu V, Chardon L, Lombard-Bohas C, Walter T. Prognostic factors in neuroendocrine carcinoma: biological markers are more useful than histomorphological markers. Scientific Reports. 2017 Jan 11;7(1):40609.
33. Freis P, Graillot E, Rousset P, Hervieu V, Chardon L, Lombard-Bohas C, Walter T. Prognostic factors in neuroendocrine carcinoma: biological markers are more useful than histomorphological markers. Scientific Reports. 2017 Jan 11;7(1):40609.
34. Frizziero M, Spada F, Lamarca A, Kordatou Z, Barriuso J, Nuttall C, McNamara MG, Hubner RA, Mansoor W, Manoharan P, Fazio N. Carboplatin in combination with oral or intravenous etoposide for extra-pulmonary, poorly-differentiated neuroendocrine carcinomas. Neuroendocrinology. 2019 Jan 21;109(2):100-12.