Open Access Library Journal
2022, Volume 9, e8902
ISSN Online: 2333-9721
ISSN Print: 2333-9705

Neuroendocrine Carcinoma of the Cecum

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How to cite this paper: Krimou, H., Errabi, N., Cisse, M., El Kaoukabi, A., Boudhas, A., Said, B., Menfaa, M., Hasbi, S., Sakit, F. and Choho, A. (2022) Neuroendocrine Carcinoma of the Cecum. *Open Access Library Journal*, **9**: e8902.
https://doi.org/10.4236/oalib.1108902

Received: May 19, 2022
Accepted: June 26, 2022
Published: June 29, 2022

Abstract

Neuroendocrine carcinoma (NEC) is a malignant tumor with a poor prognosis and can grow at many different sites in the body, but the colon is a very rare site. **Clinical Case:** We report a case of a 62-year-old man operated on for a tumor of the cecum, which was diagnosed as a high-grade neuroendocrine carcinoma. An immunohistochemical study showed positive marking with synaptophysin. No cancer metastasis was found. Postoperative chemotherapy was applied but the patient died after 8 months of disease progression. **Results:** The diagnosis of neuroendocrine tumors is often late at the metastasis stage. Colonoscopy identifies most colonic NECs. An abdominal scanner can detect a colonic exophytic mass which is strongly enhanced after the injection of contrast product. The histological appearance is identical to that described in the lung and must be supplemented by an immunohistochemical study. **Treatment:** No consensus regarding the treatment of colorectal NEC. For localized tumors, surgery associated or not with adjuvant treatment is proposed while chemotherapy is associated or not with radiotherapy. **Conclusion:** Tumors with locoregional involvement have the best results with resection whenever possible. Optimal management requires a multidisciplinary and systemic approach, and the therapy is limited.

Subject Areas

Oncology, Surgery & Surgical Specialties

Keywords

Neuroendocrine Carcinoma, Cecum, Synaptophysin

1. Introduction

Neuroendocrine carcinomas are malignant tumors that show histopathological

and immunohistochemical evidence of neuroendocrine differentiation. Neuroendocrine tumors can grow at many different sites in the body, but the colon is a very rare site. Most neuroendocrine tumors are carcinoids and they have a better prognosis than conventional adenocarcinomas. The original term "carcinoid" is equivalent to grade 1 and 2 neuroendocrine tumors (well-differentiated), but grade 3 neuroendocrine tumors are mainly small cell neuroendocrine carcinomas (SCNEC) of which a minor component is of the large cell type (poorly differentiated).

Cell neoplasia most often arises from the lung but also from other sites such as the skin, thymus, kidney, breast, ovaries, uterus, hepatobiliary tree, pancreas and salivary glands. Specifically, colorectal SCNEC accounts for 0.2% - 1.5% of all colon cancers and is considered an aggressive, fast-growing, early-spreading neoplasm with a poor prognosis [1].

The objective of this article is to present and compare the clinical, radiological and histological aspects of colonic neuroendocrine tumors with other digestive localizations as well as their prognosis and therapeutic attitude.

2. Observation

A 62-year-old man, with no significant pathological history, who presented with diffuse paroxysmal abdominal pain with bloating and chronic constipation without signs of gastrointestinal bleeding evolving in a context of conservation of general condition and unquantified weight loss. Abdominal examination was unremarkable, in particular no palpable mass.

Biology report found iron deficiency anemia at 9.8 Hg (ferritin 3.88 ng/ml) with no abnormalities in liver function or renal function.

Colonoscopy has objective ulcero-budding process of the cecum, semi-circumferential, with a sessile polyp of the ascending colon measuring 2 cm, this tumor was limited to the cecum without extension to the valve of Bauhin and to the last small loop.

The anatomopathological study of the biopsies was in favor of a poorly differentiated and infiltrating carcinoma latero-caecal thickening with no sign of local invasion or secondary localization.

A right hemicolectomy was performed in this patient. The postoperative follow-up was marked by an anastomotic fistula directed at low flow which dried up spontaneously after 45 days of evolution.

The anatomopathological study of the operating specimen showed a tumoral proliferation made up of wide cords and masses rarely hollowed out with pseudo glandular lights. Its structure is lined with polyhedral cells with acidophilic cytoplasm and large hyperchromatic and anisokaryotic nuclei showing numerous atypical mitotic figures with the presence of numerous foci of tumor necrosis, which suggests colonic localization of a high-grade neuroendocrine carcinoma with tumor necrosis and lymph node metastasis (T3N1).

Immunohistochemistry confirmed the neuroendocrine nature, with moderate

and granular cytoplasmic marking greater than 50% for anti-synaptophysin antibodies.

The absence of CK20 marking as well as the absence of mucus secretion eliminated an associated adenocarcinomatous component.

The patient received adjuvant chemotherapy based on etoposide and cisplastin the evolution was marked by the appearance of peritoneal carcinomatosis 6 months after chemotherapy the general condition deteriorated rapidly and the patient died eight months after the diagnostic.

3. Discussion

Neuroendocrine tumors (NET) of the digestive tract are rare tumors, the frequency of which is estimated at less than 5% of tumors of the digestive tract [2], they are most often described in the rectum and since the first localization described in 1950 by Dukes, their frequency in the colon is estimated at 0.2% of small cell carcinoma (SCC), with a predilection for the right colon [3]. They constitute approximately 1.5% of colon cancers [4]. They are observed at any age, gladly in the elderly, more often in men.

The diagnosis of digestive NETs is often delayed because most of them are small and initially asymptomatic. This is why the discovery is fortuitous.

Symptoms related to primary tumors depend on their location and are often non-specific such as abdominal pain, transit disorders or nausea, which explains why there is often a significant delay in diagnosis.

NETs in the colon are often associated with metastases at the time of diagnosis compared to other locations in the digestive tract. Carcinoid syndrome is not observed.

They show significant heterogeneity in terms of prognosis and treatment. Most gastric, appendicular, colonic, or rectal NETs are small NETs that are usually cured by resection.

On the other hand, the well or poorly differentiated character of the tumors as well as the measurement of the proliferation index has a major influence on their prognosis and their management.

Colonoscopy can identify most colonic NETs. The abdominal CT scan can detect a colonic exophytic mass which is strongly enhanced after injection of iodinated contrast product in the arterial phase, and their density gradually decreases in the portal phase. It must be completed by a chest CT scan, looking for localizations mediastino-pulmonary.

SCCs may present as a large polyp, a tumor infiltrating the colonic wall, an obstructive annular lesion, or diffuse infiltration of the colonic wall, suggestive of linitis plastica.

The diagnosis, histological, is rarely made on biopsies performed during endoscopy, as in our observation, but more regularly on surgical specimens.

The histological appearance is identical to that described in the lung, most often marked by the proliferation in sheets of small cells with scarce cytoplasm and

a high nucleocytoplasmic ratio, with significant cytonuclear atypia and very high mitotic activity, within a richly vascularized and necrotic stroma. The morphological aspect, even if it is evocative, must be supplemented by an immunohistochemical study highlighting the expression of neuroendocrine epithelial markers (synaptophysin and chromogranin).

K-ras gene mutation was found in extra-pulmonary (EP) SCCs unlike their pulmonary equivalent, and even if the morphological aspects are comparable, there seem to be several complex genotypic anomalies in cascade in the tumorigenesis of SCCs,but different according to their site [5].

Microsatellite instability in colorectal SCCs has even been observed, as described for adenocarcinomas of the same location [6].

Even if partial responses are observed under chemotherapy combining cisplatin and etoposide, the prognosis for these forms remains appalling, with a median survival after diagnosis of six to nine months. Perhaps, like their pulmonary equivalent, abnormalities of the c-Kit gene could have an important role in the biology of extrapulmonary poorly differentiated endocrine carcinomas, with the consequent possibility of targeted therapy [7]. Progress is to be expected from a better molecular understanding of the mechanisms of oncogenesis in order to implement a better strategy combining targeted therapy and cytotoxics.

The evaluation of the prognosis of NETs of the digestive tract is based first on their histoprognostic classification according to their degree of differentiation and their proliferation index, since these elements are major independent prognostic factors [8].

The main prognostic factor for digestive NETs is the tumor stage according to the TNM classification (**Table 1**). Median survival for each location of digestive NET is determined according to stage.

The presence of peritoneal carcinomatosis is a poor prognostic factor and a source of excess morbidity [9]. It is observed mainly in the NETs of the small intestine, the appendix and the colon. In metastatic forms, tumor volume is a prognostic factor [8].

4. Therapeutic Modalities

Currently, there is no consensus regarding the treatment of colorectal NET. For localized tumors, surgery associated or not with adjuvant treatment is proposed,

Table 1. Classification of colorectal neuroendocrine tumors (NETs) according to the 8th classification of the International Union against Cancer (UICC) [8].

T1	T invades the mucosa or the submucosa T1a: <1 cm T1b: 1 - 2 cm
T2	T invades the muscular or T > 2 cm with invasion of the mucosa or submucosa
T3	T invades the subserosa
T4	T invades the peritoneum or adjacent organs

while chemotherapy associated or not with radiotherapy is proposed as first line for stage IV tumors [10]. In case of disseminated metastases, the role of surgery and radiotherapy is palliative. The poor prognosis and the high risk of recurrence are at the origin of heavy chemotherapy associated or not with radiotherapy.

The chemotherapy proposed for colorectal NEC is generally based on the protocols used for pulmonary NET [11] [12]. Combinations of cisplatin, etoposide, cyclophosphamide and doxorubicin are often proposed [13].

5. Conclusion

Neuroendocrine tumors of the colon are rare. They present with various symptoms depending on the stage and location of the tumor. Tumors with locoregional involvement have the best outcome with resection whenever possible. Optimal management requires a multidisciplinary and systemic approach, and the therapy is limited.

Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] Kitada, M., Yasuda, S., Abe, M., Takahashi, N., Okazaki, S., Ishibashi, K. and Hayashi, S. (2017) Clinicopathologic Study of Neuroendocrine Carcinoma of the Breast. *Journal of Cancer Therapy*, **8**, 793-799. https://doi.org/10.4236/jct.2017.88069

[2] Williams, G.T. (2007) Endocrine Tumors of the Gastrointestinal Tract-Selected Topics. *Histopathology*, **50**, 30-41. https://doi.org/10.1111/j.1365-2559.2006.02570.x

[3] Yasui, O., Tsukamoto, F. and Kudo, K. (2006) Small Cell Undifferentiated Carcinoma of the Ascending Colon with Rapid Enlargement after Resection: Report of a Case and Review of the Literature. *The Tohoku Journal of Experimental Medicine*, **209**, 361-367. https://doi.org/10.1620/tjem.209.361

[4] Kim, H.C., Park, S.I., Park, S.J., Shin, H.C., Oh, M.H., Kim, H.H., *et al.* (2005) Small Cell Carcinoma of the Colon: Barium Study and CT Findings. *The British Journal of Radiology*, **78**, 255-256. https://doi.org/10.1259/bjr/36083619

[5] Dacic, S., Finkelstein, S.D., Baksh, F.K., Swalsky, P.A., Barnes, L.E. and Yousem, S.A. (2002) Small-Cell Neuroendocrine Carcinoma Displays Unique Profiles of Tumor-Suppressor Gene Loss in Relationship to the Primary Site of Formation. *Human Pathology*, **33**, 927-932. https://doi.org/10.1053/hupa.2002.126875

[6] Stelow, E.B., Moskaluk, C.A. and Mills, S.E. (2006) The Mismatch Repair Protein Status of Colorectal Small Cell Neuroendocrine Carcinomas. *The American Journal of Surgical Pathology*, **30**, 1401-1404. https://doi.org/10.1097/01.pas.0000213272.15221.38

[7] Naeem, M., Dahiya, M., Clarc, J.I., Creech, S.D. and Alkan, S. (2002) Analysis of c-Kit Protein Expression in Small-Cell Lung Carcinoma and Its Implication for Prognosis. *Human Pathology*, **33**, 1182-1187. https://doi.org/10.1053/hupa.2002.129199

[8] Hentic, O., Couvelard, A., Rebours, V., Zappa, M., Dokmak, S., Hammel, P., *et al.* (2011) Ki-67 Index, Tumor Differentiation, and Extent of Liver Involvement Are

Independent Prognostic Factors in Patients with Liver Metastases of Digestive Endocrine Carcinomas. *Endocrine-Related Cancer*, **18**, 51-59. https://doi.org/10.1677/ERC-09-0319

[9] Bierley, J., Gospodarowicz, M.K. and Wittekind, C. (2017) TNM Classification of Malignant Tumors. Wiley-Blackwell, Oxford, UK; Hoboken, NJ.

[10] Smith, J. and Reidy-Lagunes, D. (2013) The Management of Extrapulmonarypoorly Differentiated (High-Grade) Neuroendocrine Carcinomas. *Seminars in Oncology*, **40**, 100-108. https://doi.org/10.1053/j.seminoncol.2012.11.011

[11] Klimstra, D.S., Modlin, I.R., Coppola, D., Lloyd, R.V. and Suster, S. (2010) Thepathologic Classification of Neuroendocrine Tumors: A Review of Nomenclature, Grading, and Staging Systems. *Pancreas*, **39**, 707-712. https://doi.org/10.1097/MPA.0b013e3181ec124e

[12] Anthony, L.B., Strosberg, J.R., Klimstra, D.S., Maples, W.J., *et al.* (2010) The NANETS Consensus Guidelines for the Diagnosis and Management of Gastrointestinal Neuroendocrine Tumors (NETs): Well-Differentiated Nets of the Distal Colon and Rectum. *Pancreas*, **39**, 767-774. https://doi.org/10.1097/MPA.0b013e3181ec1261

[13] Gaffey, M.J., Mills, S.E. and Lack, E.E. (1990) Neuroendocrine Carcinoma of the Colon and Rectum. A Clinicopathologic, Ultrastructural, and Immunohistochemical Study of 24 Cases. *The American Journal of Surgical Pathology*, **14**, 1010-1023. https://doi.org/10.1097/00000478-199011000-00003