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Case Report

# Neuroendocrine Tumor of the Appendix: Case Report and Literature Review

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## Abstract

Appendix neuroendocrine tumors are rare and frequently incidentally found in the histopathological examination of the surgically removed appendices. Symptoms are unspecific and very similar to those presented in acute apendicitis.

Tumor size is the most important the most important prognosis factor and the principal parameter for surgery decision-making. However, other criteria should be taken in consideration when deciding the extent of the surgery, such as mesoappendix invasion, tumor location among others.

We present the case of a 14-year-old male with neuroendocrine tumor of the appendix.

***Keywords:*** *Neuroendocrine Tumors; Appendix; Carcinoid Tumor*

## Introduction

Appendix neuroendocrine tumors are rare with an approximate incidence rate of 0.15 - 0.6/100,000/year and with a slight female preponderance [1-3]. The majority of cases are incidentally diagnosed in the histopathological examination of the appendectomy specimen, most commonly after surgical treatment for acute appendicitis [4,5]. Symptoms are generally unspecific and the clinical presentation mimes an acute appendicitis, making the preoperative diagnosis extremely difficult [5,6].

These tumors have an overall excellent prognosis and tumor size is currently the most important predictor of potential metastatic disease [1,7]. Surgical management with appendicectomy is curative in the majority of cases but wider excisions for disease control may be necessary. Right hemicolectomy is the standard surgery for tumors that present high risk of local or distant recurrence and is indicated in tumors ≥ 2 cm or with mesoappendix invasion [1,5,8].

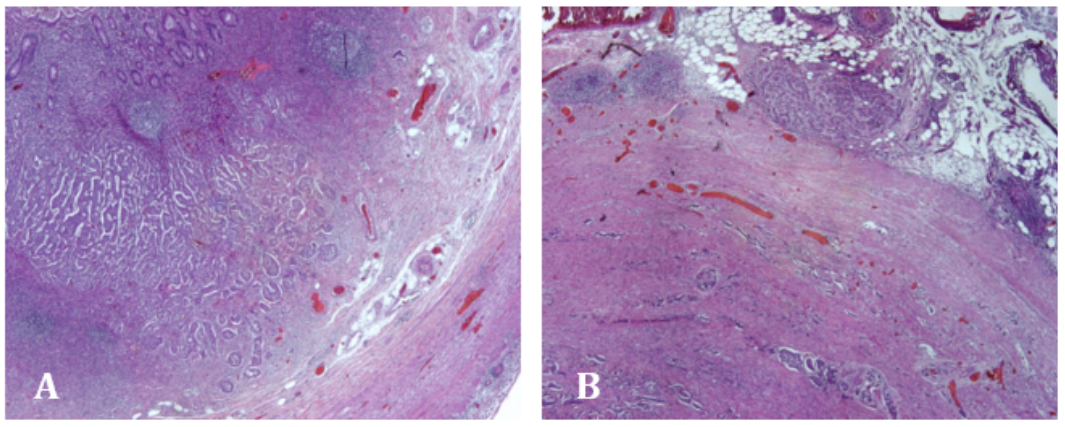
## Case Report

A 14-year-old healthy male patient present to our emergency department with a history of 12 hours of lower abdominal pain, that shifted from the umbilical region to the right iliac fossa, associated with nausea and vomiting. On examination the abdomen was soft, although positive rebound tenderness was observed in the right iliac fossa. White blood count was 13,760/μL. with 89.9% neutrophils and PCR 1.5mg/dL, with all the other laboratory values within normal range.

Abdominal ultrasound was suggestive of acute appendicitis with periappendiceal fluid and many locoregional reactive lymph nodes. The patient underwent an emergency laparoscopic appendectomy. Postoperative course was uneventful and the patient was discharged at the second day.

Gross pathological examination showed a yellowish tumor in the middle portion of the appendix with 14mm of diameter (Figure 1). The submucosa and the muscularis propria were infiltrated by tumor cells with little pleomorphism, arranged in rounded solid nests, in palisading at the periphery. The nuclei were round to oval and the chromatin finely granular "salt-and-pepper" type. A 1.3mm discontinuous foci of implantation in the mesoappendix was present (Figure 2). Immunohistochemical staining for chromogranin A, synaptophysin, CD56 and CDX-2 were positive (Figure 2E) and negative for Keratins 7 and 20 and TTF1. The proliferative index with Ki67 was low (< 1%). Lymphatic and peri-neural invasion were not observed.


***Figure 1:*** *Macroscopic section of appendix.*
*A solid, well circumscribed and non-capsuled nodule in the appendix wall, with 14 mm diameter and a yellow coloration.*



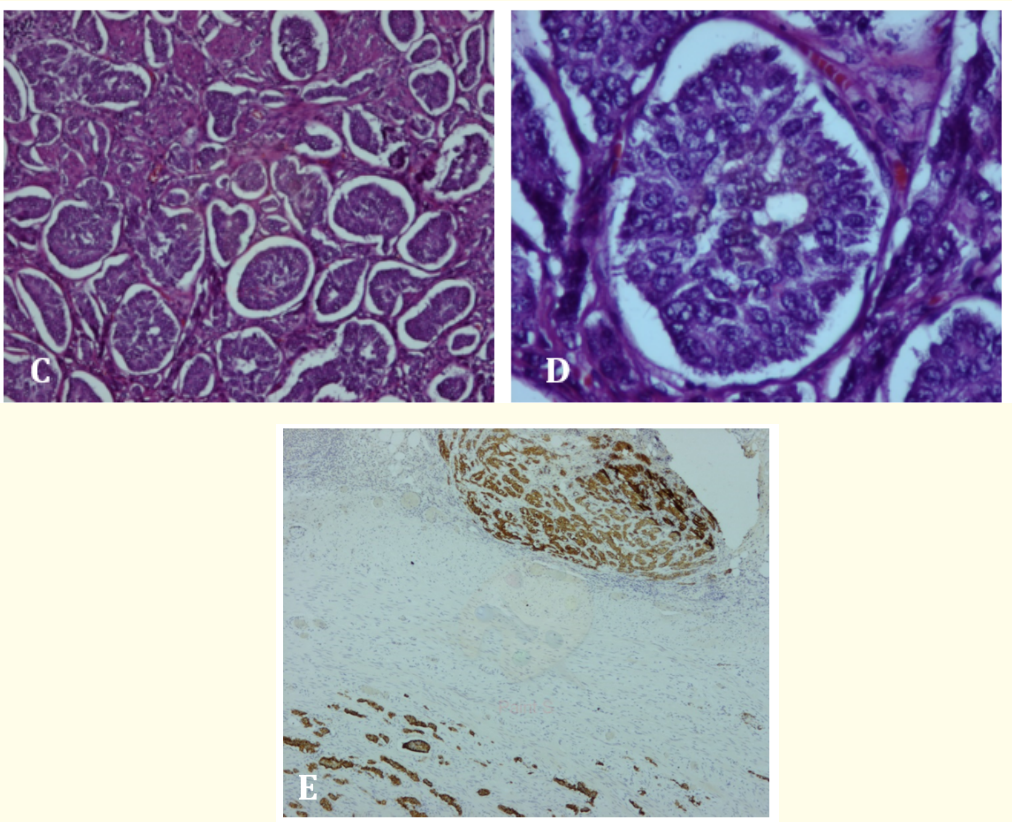



***Figure 2:*** *Microscopic pictures of appendix neuroendocrine tumor.*
*A: The tumor infiltrates submucosa and muscular propria layers; B: Discontinuous mesoappendix foci implant with 1.3 mm; C and D: Tumor cells arranged in round nests, with little pleomorphism and the typical coarsely granular, salt-and-pepper pattern of the chromatin; E: Citoplasmatic Chromogranin A immuno-expression.*

A complete workup study with a thoraco-abdominal CT-scan, a Gallium-Dota-Noc PET and a complete endoscopic study were made and no signs of active, residual or metastatic disease were found. Tumor marker Cromogranin A was within the normal range.

A multidisciplinary team with radiology, oncology, pediatrics and general surgery reviewed the case and decided for further treatment. Therefore, the patient was submitted to a laparoscopic right hemicolectomy. Postoperative course was uneventful and the patient was discharged 7 days after the procedure. Histopathology examination showed no evidence of disease in the specimen or in the 70 lymph nodes that were removed.

## Discussion

Appendix neuroendocrine tumors are rare and mostly incidentally found in the histopathological examination of 0.3 - 0.9% of all the surgically removed appendices [4,5]. They represent around 32 and 57% of all appendix tumors with a mean age at diagnosis between 38 and 51 years and they are also reported in pediatric patients between 4.5 and 19.5 years of age [1,9].

Since clinical presentation is similar to acute appendicitis, preoperative diagnosis of appendicular neuroendocrine tumor is challenging, unless they present with features of carcinoid syndrome. Due to their small size, ultrasonography and CT scan are also unlikely to identify this type of tumor preoperatively [6,11].

Surgery is the only curative treatment for neuroendocrine tumors, and an accurate examination and classification of the tumor is important to define the extension of the surgery, the need of other complementary treatments and to define the follow-up plan and to determine the prognosis [1].

The overall prognosis of the majority of appendix neuroendocrine tumor is excellent with series reporting 5-year survival rates between 85 - 100% on lower tumor stages [1,2,10]. Tumor size is the most important prognostic factor being the principal parameter for surgery decision-making and defining the main criteria for the elaboration of the two current classifications (Table 1): one from the European Neuroendocrine Tumor Society (ENETS) and one from the American Joint Committee on Cancer (AJCC). Mesoappendix invasion is also considered in ENETS classification. Apart from this two validated parameters, other factors such as lymph node and vascular invasion, ki67, mitotic index and tumor location should be considered [1,5,13].

| | ENETS guidelines | AJCC classification |
|---|---|---|
| T0 | No evidence of primary tumor | |
| T1 | Tumor ≤ 1 cm with submucosa and muscularis propria infiltration | |
| T1a | | Tumor ≤ 1cm |
| T1b | | Tumor >1 cm but ≤ 2cm |
| T2 | Tumor ≤ 2 cm with infiltration of the submucosa, muscularis propria and/or minimal (≤ 3 mm) infiltration of the subserosa and/or mesoappendix | Tumor > 2 cm but ≤ 4cm or with extension into the cecum |
| T3 | Tumor > 2 cm and/or extensive (> 3 mm) infiltration of the subserosa and/or mesoappendix | Tumor > 4 cm or with extension into the ileum |
| T4 | Tumor with infiltration of the peritoneum and/or other neighboring organs | Tumor with perforation of the peritoneum or invasion of other adjacent structures |
| N0 | No regional lymph node metastasis | |
| N1 | Locoregional lymph node metastasis | |
| M0 | No distant metastasis | |
| | Distant metastasis | |

***Table 1:*** *TMN staging for appendix neuroendocrine tumor according to ENETS guidelines and AJCC classification.*

There are two main surgical procedures that should be applied while treating local or locoregional neuroendocrine tumors of the appendix: appendectomy and right-sided hemicolectomy. For tumors < 1 cm (T1 by ENETS or T1a by AJCC) appendectomy alone is a sufficient treatment, with a 100% 5 years-survival. Tumors measuring between 1 - 2 cm (T2 by ENETS and T1b by AJCC) are a group where the decision of surgical extent is more challenging, therefore other criteria should be taken into consideration. For tumor with deep or discontinue mesoappendix invasion or lymph node invasion, tumors of the base of the appendix, positive resection margins or high-grade tumors (Ki67 > 3%) a right hemicolectomy should be performed. Similarly, for tumors ≥ 2 cm a right hemicolectomy is required since these tumor harbours the potential for metastasis [1,5,10-13].

Tumors < 1 cm require no postoperative follow-up. For tumors measuring between 1 - 2 cm the available data is still insufficient for a clear-cut decision. Nevertheless, in cases with deep or discontinue infiltration of the mesoappendix or with vascular invasion, imaging

should be performed to rule out any residual disease. In patients with tumors > 2 cm, with local or distant metastases or R1 resection, the postoperative follow-up includes CT-scan or MRI 6 months after surgery. If negative, it should be repeated after another 6 months, and then with 1-year intervals. A Gallium-Dota-Noc PET should be done after surgery and then with intervals of 2 years. Chromogranin A levels should also be controlled [1,5,14].

## Conclusion

The case described highlights the importance of maintaining an adequate follow-up of patients undergoing 'simple' appendectomies. It also emphasizes the value of a complete en bloc resection of the mesoappendix with the appendix in routine appendicectomies, since it has the advantage of providing more complete staging of any incidental tumor, and in some cases reduce the need for unnecessary further surgery [15].

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