Case Report

More than an Appendicitis: A Case of an Appendiceal Neuroendocrine Tumor

Mais que uma Apendicite: Um Caso de Tumor Neuroendócrino Apendicular

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ABSTRACT

Appendiceal neuroendocrine tumors are the most common neoplasms of the appendix, often diagnosed incidentally during appendectomy in cases of acute appendicitis. Their estimated prevalence ranges from 0.16%-2.3%, with a higher incidence among women in their second to fifth decades of life. While most tumors exhibit an indolent course with a favorable prognosis, more aggressive histological subtypes may metastasize, most commonly to the liver.

We report a clinical case of a 12-year-old female presenting with a case of acute appendicitis for which she underwent an urgent laparoscopic appendectomy. Histopathological examination identified a well-differentiated 15 mm neuroendocrine tumor, with serosal invasion and perineural involvement, without lymphovascular or mesoappendiceal invasion. Following a multidisciplinary discussion, the patient was placed under surveillance with annual ultrasound monitoring.

Appendiceal neuroendocrine tumors are rare but represent the most common neoplasms of the appendix, and they are often detected incidentally. Proper histopathological evaluation is essential for determining optimal management.

Keywords: Appendectomy; Appendiceal Neoplasms; Appendicitis; Neuroendocrine Tumors

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RESUMO

Os tumores neuroendócrinos do apêndice são o tipo mais frequente de neoplasia apendicular, frequentemente diagnosticadas acidentalmente aquando apendicectomia por apendicite aguda. A sua prevalência é estimada em 0,16%-2,3%, com uma maior incidência em doentes do sexo feminino entre a segunda e quinta décadas de vida. A maioria dos tumores tem um curso indolente e um prognóstico favorável, no entanto subtipos histológicos mais agressivos tendem a metastizar, especialmente para o fígado.
Apresentamos um caso de uma criança de 12 anos do sexo feminino com um quadro de apendicite aguda, submetida a apendicectomia via laparoscópica. O exame histopatológico revelou um tumor neuroendócrino de 15 mm, bem diferenciado, com invasão da serosa e perineural, sem envolvimento linfovascular ou mesoapendicular. Após discussão multidisciplinar, a doente permaneceu em vigilância.
Os tumores neuroendócrinos do apêndice são tumores raros, no entanto representam a maioria das neoplasias apendiculares, sendo frequentemente diagnosticados de forma incidental. A avaliação histopatológica é essencial para otimizar a abordagem terapêutica.

Palavras-chave: Apendicectomia; Apendicite; Neoplasias do Apêndice; Tumores Neuroendócrinos

INTRODUCTION

Appendiceal neuroendocrine tumors (NETs) are the most common neoplasms of the appendix. The diagnosis is typically incidental, often discovered upon an urgent appendicectomy performed for acute appendicitis, with an estimated prevalence of 0.16%-2.3% among all cases of acute appendicitis.[1] These tumors predominantly affect women, with the highest incidence observed between the second and fifth decades of life.[2,3] Although appendiceal neuroendocrine tumors generally exhibit a favorable prognosis, more aggressive histological subtypes are frequently associated with liver metastasis.[1] Preoperative diagnosis is uncommon; however, chromogranin A can serve as a tumor marker, potentially aiding in diagnosis.

Local disease control is primarily achieved through surgery, which may involve either appendicectomy or right hemicolectomy. In some cases, chemotherapy or targeted therapies are recommended as adjunctive treatment.[1-13]

Known prognostic factors include tumor size, histological grading, tumor staging, the presence of high-risk features and evidence of distant disease. Despite these variables, most cases of appendiceal neuroendocrine tumors are associated with a favorable prognosis.[1,12]

CASE REPORT

A 12-year-old female patient presented to the emergency room with a two-day history of abdominal pain, nausea and vomiting. Laboratory results indicated elevated acute-phase reactants, with a leukocytosis of 17 000 cells/uL and a C-reactive protein higher than 15 mg/dL. An ultrasound imaging revealed findings consistent with uncomplicated appendicitis. The patient underwent a consented laparoscopic appendicectomy. Intraoperatively, a necrotic appendix was identified, but no evidence of peritonitis was observed. The patient was discharged the following day without any complications.

Histopathological examination of the appendix revealed a well-differentiated neuroendocrine tumor measuring 15 mm, serosal invasion (pT4) and a 3 mm surgical margin. The tumor demonstrated perineural invasion, but no evidence of lymphovascular or mesoappendiceal invasion. Immunohistochemical staining showed positive results for CAM5.2, synaptophysin and chromogranin, with a Ki67 proliferation index of less than 3%.

Following a multidisciplinary review, it was determined that no adjuvant therapy was necessary. The patient was placed under surveillance with annual ultrasound examinations.

DISCUSSION

Neuroendocrine tumors originate from neuroendocrine cells, including enterochromaffin cell, L-cells and tubular cells. They represent a rare pathology and their exact pathogenesis remains incompletely understood.[3]

The classification of neuroendocrine tumors has been the topic of ongoing debate. Current guidelines recommend classification based in tumors' proliferation rate, categorizing them as follows: G1 tumors, which are indolent with low proliferation rate (Ki67<3%), G2 tumors, which exhibit a moderate proliferation rate (Ki67 3%-20%) and G3 tumors, which are aggressive tumors with a high proliferation rate (Ki67>20%).[1,7,10] An alternative classification system is based

on cellular origin, distinguishing between enterochromaffin cell or serotonin-producing neuroendocrine tumors, goblet cell carcinoid tumors, L-cell or glucagon-like-peptide-producing tumors and tubular carcinoid neuroendocrine tumors.[2,4] Among these, enterochromaffin cell tumors are typically associated with more aggressive behavior.

Appendiceal neuroendocrine tumors are rare and frequently discovered incidentally.[1] The appendix is the third most common site for neuroendocrine tumors.[2] A study involving 8304 patients who underwent appendectomy for acute appendicitis revealed a prevalence rate of neuroendocrine tumors of the appendix of 0.4%,[12] while a Portuguese study of 74 patients reported a rate of 0.47% per appendectomy, with two age peaks at 17 and 55 years old.[9] In children, appendiceal neoplasms are extremely rare but remain the most common site for neuroendocrine tumors.

The majority of appendiceal neuroendocrine tumors are incidental findings in patients undergoing appendectomy for acute appendicitis.[12] These tumors are most commonly located at the tip of the appendix, but may also occur in the body or base of the appendix.[2] Tumors located at the base of the appendix are frequently associated with poorer outcomes, as they are more often linked to incomplete resection during the initial surgery. In extremely rare cases, patients may present with carcinoid syndrome, manifesting as facial plethora, diarrhea and wheezing.[1,8,13] Although the majority of appendiceal neuroendocrine tumors are small and indolent, cases with lymphatic and hepatic metastatic disease can occur, particularly in tumors with high-risk features, such as those larger than 2 cm, or those with lymphovascular or perineural invasion.[1,3]

The European neuroendocrine tumor society classifies appendiceal neuroendocrine tumors based on their extent of invasion. The pT1a tumors are less than 1 cm in size and involve only the submucosa or muscularis. pT2 tumors are less than 2 cm in size with submucosal or muscularis invasion or mesoappendix invasion less than 3 mm. pT3 tumors exceed more than 2 cm in size and/or demonstrate mesoappendix or subserosa invasion greater than 3 mm. pT4 tumors involve serosal perforation or extension into neighboring organs. Mesoappendix invasion has been associated with a higher risk for disseminated disease.[2] Further classification includes lymph node metastasis and distant metastasis, particularly to the liver, bone and lungs.

For appendiceal neuroendocrine tumors smaller than 2 cm, the preferred surgical approach is appendectomy. For tumors larger than 2 cm, as well as those demonstrating lymphovascular or perineural invasion or located at the appendiceal base, right hemicolectomy is recommended.[11] Complete surgical resection is associated with improved outcomes, even in high-grade tumors. In cases of hepatic metastasis, local treatment such as transarterial chemoembolization or ablative techniques may be considered. For other cases, systemic treatment with somatostatin analogues (for tumors expressing somatostatin receptors), mTOR inhibitors or angiogenesis inhibitors is necessary.[1] Although mTOR inhibitors and angiogenesis inhibitors have demonstrated the ability to reduce cell growth, their results are not consistently reproducible across various study series. Chemotherapy plays a limited role and it is typically reserved for patients with distant disease, with regimens such as capecitabin, temozolomide and oxaliplatin; however, the outcomes remain suboptimal.[1]

In most cases, surgery is considered curative. Surveillance is recommended particularly for patients with high-risk features, including tumors between 1 and 2 cm that are not fully resected, tumors greater than 2 cm, lymph node involvement or G2/G3 tumors.

This case presents a G1 pT4 tumor; however, it did not exhibit lymphovascular or mesoappendix involvement, therefore suggesting an indolent tumor with a favorable prognosis. Although the diagnosis was incidental, appendectomy alone was sufficient, and no further interventions were required. The patient continues to undergo surveillance.

CONCLUSION

Appendiceal neuroendocrine tumors are exceedingly rare. This case report highlights the incidental diagnosis of such tumors and emphasizes the significance of the histopathological evaluation and subsequent follow up after an appendectomy, even in cases of acute appendicitis.

ETHICAL DISCLOSURES

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MP: Data interpretation and writing.

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MP: Interpretação de dados e redação.

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