

Incidental Finding of Appendiceal Neuroendocrine Tumor during Laparoscopic Exploration for Deep Endometriosis: Case Report

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Achado Incidental de Tumor Neuroendócrino de Apêndice durante Exploração Laparoscópica para Endometriose Profunda: Relato de Caso

Hallazgo Incidental de Tumor Neuroendocrino en Apéndice durante Exploración Laparoscópica por Endometriosis Profunda: Informe de Caso

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ABSTRACT

Introduction: Endometriosis is one of the most prevalent gynecological diseases, affecting 7 to 10% of women at a reproductive age. It consists of endometrial glands and stroma growing outside the uterine cavity, the deepest is the most harmful. Gastrointestinal neuroendocrine tumors are rare, but they are one of the most common neoplasms of the cecal appendix, being more common in women. The objective of this article is to describe a rare case in which, during a videolaparoscopy for deep endometriosis, an incidental appendiceal neuroendocrine tumor was found. **Case report:** A 44-year-old female patient underwent a videolaparoscopy to control deep endometriosis. It was decided to perform a resection of endometriosis foci associated with appendectomy due to the finding during intestinal exploration. The patient was stable postoperatively with no complications. The anatomopathological examination (cecal appendix) revealed a well-differentiated neuroendocrine tumor (grade 1), pT1, measuring 0.5 cm in its largest diameter, with free margins, without lymphovascular invasion. **Conclusion:** This case reinforces the importance of a complete evaluation of the peritoneal cavity, including the appendix, during laparoscopy for patients with endometriosis.

Key words: Neuroendocrine Tumors/surgery; Endometriosis; Laparoscopy; Appendectomy.

RESUMO

Introdução: A endometriose é uma das doenças ginecológicas mais prevalentes, afetando de 7% a 10% das mulheres em idade reprodutiva. Consiste na presença de glândulas endometriais e estroma fora da cavidade uterina, e a forma profunda é a mais grave. Os tumores neuroendócrinos gastrointestinais são raros, mas estão entre as neoplasias mais comuns do apêndice cecal, sendo mais comuns em mulheres. O objetivo deste artigo é descrever um caso raro no qual, com base na videolaparoscopia para endometriose profunda, foi feito o diagnóstico incidental de um tumor neuroendócrino no apêndice. **Relato do caso:** Paciente do sexo feminino, 44 anos, submetida à videolaparoscopia para controle de endometriose profunda. Optou-se pela ressecção dos focos de endometriose associados à apendicectomia em razão de um achado durante a exploração intestinal. O paciente apresentou-se estável no pós-operatório, sem complicações. No exame anatomopatológico (apêndice cecal), foi constatado um tumor neuroendócrino bem diferenciado (grau 1), pT1, medindo 0,5 cm em seu maior diâmetro, com margens livres, sem invasão linfovascular. **Conclusão:** Este caso reforça a importância de uma avaliação completa da cavidade peritoneal, incluindo o apêndice, durante a laparoscopia em pacientes com endometriose.

Palavras-chave: Tumores Neuroendócrinos/cirurgia; Endometriose; Laparoscopia; Apendicectomia.

RESUMEN

Introducción: La endometriosis es una de las enfermedades ginecológicas más prevalentes, afectando del 7 al 10% de las mujeres en edad reproductiva. Consiste en la presencia de glándulas endometriales y estroma fuera de la cavidad uterina, y la forma profunda es la más grave. Los tumores neuroendócrinos gastrointestinales son raros, pero se encuentran entre las neoplasias más comunes del apéndice cecal y siendo más frecuentes en mujeres. El objetivo de este artículo es describir un caso raro en el que, durante una videolaparoscopia por endometriosis profunda, se realizó un diagnóstico incidental de un tumor neuroendocrino en el apéndice. **Informe del caso:** Paciente femenina de 44 años, sometida a videolaparoscopia para el control de endometriosis profunda. Se decidió resear los focos de endometriosis, junto con una apendicectomía, debido a un hallazgo intraoperatorio durante la exploración intestinal. La paciente ha estado estable en el posoperatorio, sin complicaciones. En el examen anatomopatológico del apéndice cecal, se identificó un tumor neuroendocrino bien diferenciado (grado 1), pT1, de 0,5 cm en su diámetro mayor, con márgenes libres y sin invasión linfovascular. **Conclusión:** Este caso refuerza la importancia de una evaluación completa de la cavidad peritoneal, incluyendo el apéndice, durante la laparoscopia en pacientes con endometriosis.

Palabras clave: Tumores Neuroendócrinos/cirugía; Endometriosis; Laparoscopia; Apendicectomía.

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INTRODUCTION

Endometriosis is defined by the presence of endometrial glands and stroma out of the uterine cavity. It is a chronic inflammatory disease causing pain and infertility in 10-15% of women in reproductive age in addition to other symptoms as dysmenorrhea, abnormal uterine bleeding, dyspareunia, post-coital bleeding, irritable bowel syndrome and pelvic inflammatory disease¹.

There are three types of endometriosis: peritoneal endometriosis, ovarian endometriotic cysts (endometrioma) and deep endometriosis (DE). DE is defined by infiltrative peritoneum lesions >5 mm. Surgery is indicated in three conditions: medication refractory pain, ileal involvement (risk of bowel obstruction) and appendiceal involvement (risk of neoplasm)^{2,3}.

Neuroendocrine tumors (NETs) may develop almost in any organ in wide clinical, morphological, genomic presentations and prognosis. Typically, NETs appear at the tip, most of them found incidentally during surgical procedures. Macroscopically, these neoplasms are yellowish well-demarcated nodules and historically, are considered indolent tumors; NETs on gastrointestinal tract (GIT) are usually named carcinoids⁴.

Although NETs are considered rare with good prognosis, they are the second most common type of GIT tumor with an increase of incidence of appendiceal NETs of 70-133% in the last ten years. The diagnosis of appendiceal NETs is generally determined histologically and occurs in 0.16-2.3% of appendectomies^{5,6}.

Usually, appendiceal NETs affect women between 15 and 19 years of age and men between 20 and 29 years of age according to some studies. The prognosis depends on the stage, grade, primary site and mitotic activity. The grade is determined by Ki67 index and/or mitosis/High Power Field⁶. In addition, only seven articles addressing the rarity of the association have been found at PubMed utilizing the terms “Neuroendocrine tumor”, “Appendix” and “Endometriosis” in any year.

The Ethics Committee approved the article, report number 7,130,629 (CAAE (submission for ethical review): 81074124.0.0000.5047) in compliance with Directive 466/2012⁷ of the National Health Council.

CASE REPORT

Women, 44 years of age referred for specialized follow-up because of DE and infertility. Presented deep dyspareunia, dysmenorrhea, abnormal uterine bleeding, chronic pelvic pain (CPP), and changes of bowel habits. At physical examination, complained of pain during cervix manipulation and palpation of rectovaginal septum.

The patient had no surgical history, alcohol or smoking consumption but had family history of many neoplasms as multiple myeloma, hepatocarcinoma, melanoma, bowel and central nervous system cancers.

Transvaginal ultrasound after bowel preparation revealed foci suggestive of endometriosis, lateral displacement of the right ovary due to approximately 3 cm adnexal cyst and normal ovaries and foci affecting the anterior wall of the rectum, vagina and uterine serosa in addition to pelvic adhesions. The patient was submitted to videolaparoscopy in May 2022 for DE control and during the procedure, invasive, 1-15 mm purple-like endometrial foci were found in large quantity in tubes, uterosacral ligaments, ureters, bladder, rectovaginal septum, right diaphragm and appendix, in addition to endometrioma at the right ovary. It was decided to resect the foci and during the exploration, a hard, yellowish nodule was found at the tip of the appendix (Figure 1), which led to the appendectomy (Figure 2). Postoperatively, her evolution was satisfactory for two days without complications.



Figure 1. Yellowish nodule at the tip of the cecal appendix

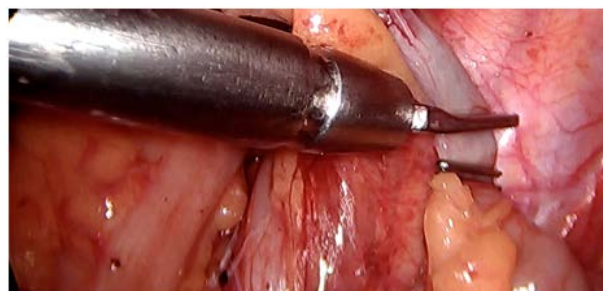


Figure 2. Placement of clips for further laparoscopic appendectomy

The anatomopathological analysis of the nodule revealed a well-differentiated NET (grade 1), according to the WHO (World Health Organization) classification confirmed by immunohistochemistry (positive synaptophysin, positive chromogranin, positive CD56 and positive Ki-67 in 1% of the cells) (Figure 3), pT1, measuring 0.5 cm in its largest diameter located at the

submucosa layer and free surgical margins with no lymphovascular invasion. Thus, adjuvant therapy or other surgical approach was not required.

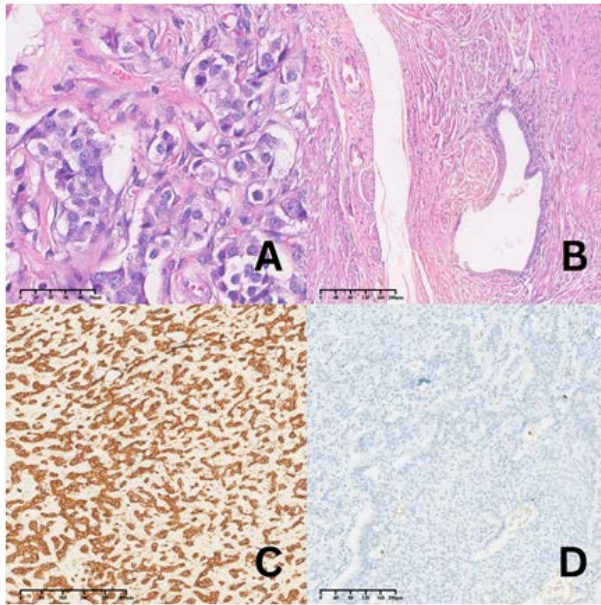


Figure 3. Neoplastic cells of neuroendocrine phenotype with rounded nuclei and speckled chromatin (A), adjacent endometriosis implants to the neoplasm (B), diffuse marking for synaptophysin (C), low Ki-67 proliferative index (D)

Later, the patient was submitted to mammotomy of a hyalinized fibroadenoma at the left breast in September 2022 and total thyroidectomy in November 2022 due to a follicular papillary carcinoma on the medium third measuring 0.8 x 0.5 x 0.4 cm and stage pT1a.

Currently, the patient is clinically stable three years after the diagnosis of NET in annual follow-up in two tertiary hospitals with no signs of relapse according to upper digestive endoscopy, colonoscopy and computed tomography performed at six months and one year after the surgery.

DISCUSSION

The present case presented a classic condition of signs and symptoms of DE of the gastrointestinal tract referred for surgical treatment when an appendiceal lesion was found. Three techniques described in the literature are adopted for surgical approach of DE: shaving, disk excision and segmental resection of the bowel, with major risk of rectovaginal fistula for the last two¹.

Presurgical evaluation utilizing several imaging techniques (3D vaginal ultrasound, double contrast opaque enema and magnetic resonance) is essential to determine the surgical conduct. The consensus, however,

is a full evaluation of the peritoneal cavity including the appendix during DE laparoscopy. Whether suspicious lesions occur, appendectomy is indicated. For the case in question, surgery was based on ultrasound findings, clinical status and extent of the endometriosis, not being required additional confirmatory exams⁸.

For this purpose, a study standardized a technique called “running peritoneal organs in endometriosis” (COPE) to evaluate and correlate gastrointestinal and gynecological signs and symptoms of endometriosis and location of the lesions of each segment of the GIT. It is a systematic investigation of the abdominal organs following a pattern: 1) monitor placed close to the feet; 2) 5 mm puncture of the right hypochondrium; 3) 30-degree laparoscope; 4) position of Trendelenburg with gynecological stirrups; 5) initiate analysis of the small intestine through the terminal ileum towards the duodenojejunal angle⁹.

According to the study describing the technique COPE with women diagnosed with endometriosis, it was noticed that 70% of the 40 cases of the sample were affected by the disease. It has been shown a clear relation among signs and symptoms at the GTI and lesions on the rectosigmoid and ileum. Appendiceal lesions are detected only if COPE is applied correctly because there was no difference between patients with and without signs and symptoms at the GIT in NETs. COPE was utilized in the present case⁹.

Based on a study utilizing pathology files of an Israeli institution, it was noticed that of the 8,162 appendectomies, the histopathologic diagnosis was performed in 153 tumors, of which 57 (37.3%) were NETs, 35 (22.9%) were mucinous cystadenomas and 34 (22.2%), metastasis of ovarian cancer¹⁰. NETs are the most common appendiceal tumors encompassing nearly 32% to 57% of the cases, but, overall, do not present specific symptoms. The literature reports variations of the annual incidence around 0.4-0.6/100,000 individuals¹¹. In addition, the appendix is the third most common site (16.7%) of the NETs, behind small intestine and rectum, respectively¹².

A series of five cases with pre-operative diagnosis of CPP described appendiceal NETs found in patients during gynecological surgical procedures. Four patients had endometriosis post histological revision and a mature cystic teratoma was found in one patient, reinforcing the importance of the investigation of CPP and the possibility of incidental findings during gynecological procedures¹³. Despite the presence of similar cases found in the literature, a systematic review identified that NETs rates are identical in individuals with endometriosis and in the general population¹⁴.

The prognosis of appendiceal NET is usually favorable depending on the tumor size. Ki-67 value is also relevant, many studies have shown that high expression of Ki-67 is associated with lower survival¹⁵. A meta-analysis revealed that the 5-year survival for patients with gastroenteropancreatic NETs was 89% for grade 1 (Ki-67 \leq 2%) and 70% for grade 2 (Ki-67 3-20%). Given a cutoff of 5%, survival was 89% for Ki-67 \leq 5% and 51% for Ki-67 between 5-20%. So far, the clinical evolution of the patient can be considered favorable with Ki-67 of 1%¹⁶.

The guidelines of the North-American Neuroendocrine Tumor Society (NANETS) recommend right hemicolectomy for appendiceal tumors located at the base or larger than more than 2 cm, or in case of lymphovascular invasion or meso-appendiceal adipose tissue, lymph node metastasis or intermediate or high grade tumors. For 1-2 cm tumors, there is no consensus about the treatment due to the paucity of studies. Tumors smaller than 1 cm require close monitoring with 3-6 months visits after curative resection followed by annual visits for the upcoming seven years. For tumors \leq 1 cm as the present case (0.5 cm, non-invasive, well-differentiated,) single appendectomy is sufficient. The follow-up of the present case was annual without relapse in three years and the management followed NANETS guidelines with satisfactory monitoring and favorable outcome¹⁶.

CONCLUSION

This case reinforces the importance of full evaluation of the peritoneal cavity including the appendix during the laparoscopy for patients with DE. Careful and individualized approach to NETs is necessary and strengthens the indication of appendectomy when there is appendiceal compromise in the context of DE. In addition, it highlights the importance of more studies that are able to systematize the evaluation and tracking of these lesions for digestive surgery, coloproctology and gynecology.

CONTRIBUTIONS

All the authors contributed substantially to the study design, acquisition, analysis and interpretation of the data, writing and critical review. They approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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