ARTÍCULO ORIGINAL

Gac Méd Caracas 2022;130(Supl 1):S64-S67
DOI: 10.47307/GMC.2022.130.s1.13

Well-Differentiated Neuroendocrine Tumor of the Appendix

Tumor neuroendocrino bien diferenciado del apéndice

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SUMMARY

Appendiceal Neuroendocrine Tumors (NET) comprise rare tumors of the appendix, mainly affecting young populations and characterized by a rather favorable prognosis. Appendiceal NET is either asymptomatic or present as acute appendicitis, which is then diagnosed incidentally during surgery. We reported the case of a 9-year-old girl presenting with the common appendicitis symptoms of fever and abdominal pain. The preoperative diagnosis was peritonitis due to suspicion of perforated appendicitis. The surgical procedure was performed for the treatment of appendicitis, and the neuroendocrine tumor was identified incidentally during the histological examination of the excised surgical specimen. A well-differentiated neuroendocrine tumor was diagnosed by histopathological examination.

Keywords: *Appendix, human and health, neuroendocrine tumor.*

RESUMEN

Los tumores neuroendocrinos apendiculares (NET) comprenden tumores raros del apéndice, que afectan principalmente a poblaciones jóvenes y se caracterizan por un pronóstico bastante favorable. Los TNE apendiculares son asintomáticos o se presentan como apendicitis aguda, que luego se diagnostica incidentalmente durante la cirugía. Presentamos el caso de una niña de 9 años que presenta los síntomas comunes de apendicitis de fiebre y dolor abdominal. El diagnóstico preoperatorio fue peritonitis por sospecha de apendicitis perforada. El procedimiento quirúrgico se realizó para el tratamiento de una apendicitis, y el tumor neuroendocrino se identificó incidentalmente durante el examen histológico de la pieza quirúrgica extirpada. Un tumor neuroendocrino bien diferenciado fue diagnosticado por examen histopatológico.

Palabras clave: *Apéndice, humano y salud, tumor neuroendocrino.*

DOI: https://doi.org/10.47307/GMC.2022.130.s1.13

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Recibido: 1 de mayo 2022
Aceptado: 5 demayo 2022

INTRODUCTION

Appendiceal NETs are rare tumors in young populations. They originate from the neuroendocrine cells of the gastrointestinal tract and are the most common type of appendiceal

tumor, occurring in 0.226 % of appendectomies in all ages but diagnosed at lower ages compared to other appendiceal tumors (1-3).

The majority of the appendiceal NETs cannot be diagnosed preoperatively and are incidentally found in post appendectomy specimens from patients with acute appendicitis symptoms. There are no tumor characteristic symptoms for appendiceal NETs (4-6).

NETs are usually easy to diagnose due to their distinctive histologic appearance of solid, insular, trabecular patterns of uniform tumor cells. The tumor cells usually have a little pleomorphism and sparse mitosis (3,5,7). The present case highlights the importance of histopathologic examination in every appendectomy specimen.

CASE DESCRIPTION

A 9-year-old girl was admitted to the hospital complaining of abdominal pain and fever. Physical examination revealed the signs of peritonitis. The preoperative diagnosis was peritonitis due to suspected perforated appendicitis. The laboratory result revealed the elevation of leukocytes. There is no family history of cancer. An appendectomy was performed, and the appendix was examined.

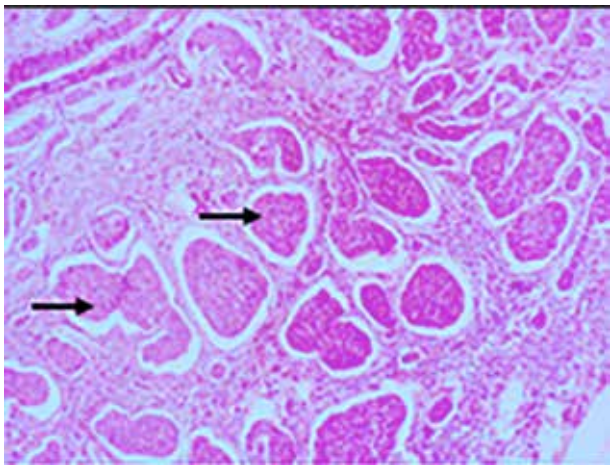

Figure 1. Tumor cells are arranged in a solid nest (H&E Stain, x100).

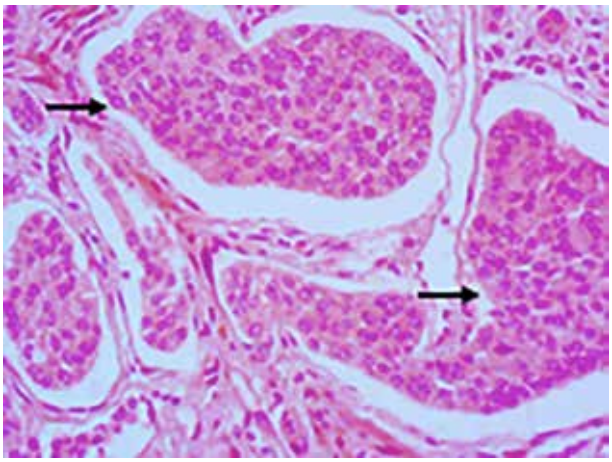

Figure 2. Uniform tumour cells (H&E stain, x400).

Macroscopically the appendix tissue measured 10x1.5x1.5cm and was edematous in appearance. Histological examination revealed the solid nests (Figure 1) and clusters of uniform tumor cells with rare mitosis (Figure 2). The tumor arose in the mucosal layer and extended to the superficial muscular layer of the appendix. From the histopathological findings, we conclude, that it was a well-differentiated neuroendocrine tumor of the appendix.

DISCUSSION

Neuroendocrine tumors of the appendix are relatively uncommon neoplasms. Although they are rare tumors, they are the most frequent tumors of the appendix occurring in 0.226 % of appendectomies in all ages but diagnosed at lower ages compared to other appendiceal tumors (1,2). The other studies in Qatar found this tumor in 0.230 % of all appendectomies, consistent with 0.400 % in Belgium, 0.620 % in the United Kingdom, and 0.930 % in the United Arab Emirates (2). These tumors are also the most common tumors of the gastrointestinal tracts in childhood and adolescence (7). Females are affected more often than males (2,8,9).

Clinically, the preoperative diagnosis is difficult because it has an indolent course, appears asymptomatic, or presents as acute appendicitis.

Most of these tumors are incidentally found during histopathological examination of specimens from appendectomy for acute appendicitis (1,2,10,11). The carcinoid syndrome rarely occurs in association with appendiceal lesions (5).

The cell origin of appendiceal NET is the subepithelial Kultschitzky cell which has both endocrine and neural features. The majority of the cases of these tumors arise at the tip of the appendix. The size of the tumor is commonly smaller than 1 cm. This tumor usually spreads by extending into the serosa or by permeating serosal lymphatics and veins but metastases are rare (1,5,12).

The risk factors for the development of sporadic NETs are still unknown. The risk factor shown to be most significantly associated is the parental history of a carcinoid tumor in an extrapulmonary site. A similar pattern was seen with a history of carcinoid tumors in a sibling (13). Five to ten percent of GI NETs are linked to hereditary syndromes MEN1, NF1, Von Hipple-Lindau Syndrome, and Tuberous Sclerosis Complex (3).

Histologically, the tumor cells are uniform and arranged in solid and rounded nests. NETs are usually easy to diagnose because of their distinctive histologic appearance. The classic histologic appearance of the tumors includes trabecular, insular, or ribbon-like cell clusters with little pleomorphism and scant mitosis. Immunohistochemical analyses to confirm the diagnoses are Chromogranin A and synaptophysin antibody (5,12,14,15). The microscopic appearance of the appendix in the present case has an insular (solid nest) pattern of uniform cells in the mucosal and muscular layer of the appendix. According to the WHO classification, appendix NETs are defined as (1) well-differentiated neuroendocrine tumor (carcinoid) with benign behavior, confined to the appendiceal walls, diameters $\leq$ 2 cm and without angioinvasion or uncertain malignant potential, invading the mesoappendix, angioinvasive and $>$ 2 cm in diameters; (2) well-differentiated neuroendocrine carcinoma (malignant carcinoid); (3) goblet cell carcinoma (5,12,16). According to a retrospective study from Onimoe et al. (2017), the majority of their patients had low-grade tumors with a tumor size of less than 2 cm. As in this patient, the tumor was less than 2 cm in size, only arising in the mucosa and muscular layer of the appendix without any angioinvasion; thus, it was concluded as a well-differentiated neuroendocrine tumor of the appendix (4).

The prognosis for this tumor is favorable. The important criteria include the size of the tumor and depth of invasion. Tumors smaller than 2 cm and limited to the appendiceal wall are cured with complete local excision by appendectomy (5,7,17,18). The patient, in this case, had an appendiceal NET with a size of less than 1 cm confined only to the appendiceal mucosal layer, hence the simple appendectomy was adequate treatment for this patient.

CONCLUSION

Appendiceal NETs in children are rare and usually discovered incidentally post appendectomy due to acute appendicitis. The diagnosis of this patient was concluded by histopathologic examination of the tumor's distinctive appearance. Therefore, a routine histopathological examination of the removed appendix from acute appendicitis is important for identifying the unsuspected conditions.

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