

Case Report

Appendiceal Mucinous Incidental Neoplasm a Rare Case Report and Literature Review

Emmanuel Stephano Bracho Ruiz (M.D)^{1*}, Carlos Mata Quintero (M.D)¹, Cuauhtemoc Aguilar Barragan (M.D)¹, Daniela Rodriguez Ramirez (M.D)¹, Sergio Sandoval Tapia (M.D)¹, Esmaragdo Huerta Villeda (M.D)¹, Esteban Jaime Laurean (M.D)¹, Mariano Tovar Ponce (M.D)², Saul Martinez Jimenez (M.D)², Jose David Simonin Lopez (M.D)², Sergio Ignacio Ignacio Ávila Martínez (M.D)², Alejandro Cendrey Santoyo Ortiz (M.D)², Paulina Villegas Ruiz³, María Citlalli Barragán Bernabé³

¹General Surgery Hospital Central Norte Pemex. Mexico City, Mexico

²General Surgery, Hospital Regional Pemex, Minatitlan Veracruz, Mexico

³Antiguo Hospital Civil de Guadalajara "Fray Antonio Alcalde", SSA. Guadalajara, Jalisco

*Corresponding Author: Emmanuel Stephano Bracho Ruiz (M.D)

General Surgery Hospital Central Norte Pemex. Mexico City, Mexico

Article History

Received: 22.10.2023

Accepted: 27.11.2023

Published: 05.12.2023

Abstract: Mucinous appendiceal tumors consist of mucinous adenocarcinoma, low-grade appendiceal mucinous neoplasm, and high-grade appendiceal mucinous neoplasm. The incidence of non-mucinous adenocarcinomas is reduced. The most recent edition of the World Health Organization classification and recent consensus guidelines will enable the consistent application of agreed nomenclature. Not only is precise diagnosis essential for effective patient management, but it also facilitates the comparison of results across centers and tumor registries. The most prevalent benign adenoma in the appendix is serrated. It is imperative to differentiate these conditions from low-grade appendiceal mucinous neoplasms, as the latter can also resemble harmless ailments. Adenocarcinomas of the goblet cells are a rare subtype of appendiceal neoplasm. While appendiceal neoplasms are uncommon, they are not entirely so, and even the most seasoned pathologists may find them difficult to diagnose. In addition, appendiceal neoplasia classification and terminology have been subjects of contention for decades. Nonmucinous appendiceal neoplasms are less prevalent than mucinous tumors, and their association with other appendiceal neoplasm subtypes remains uncertain. A literature review of appendiceal mucinous neoplasms identified during laparoscopic appendectomies is presented here.

Keywords: Appendix, mucocele, Mucinous adenoma, Pseudomyxoma Peritonei, Mucinous Adenocarcinoma.

INTRODUCTION

Primary appendiceal tumors are infrequent occurrences, comprising less than 2% of all appendectomies. Their age-adjusted incidence rate is 0.12 cases per one million individuals per year. A significant proportion of these tumors are not identified prior to surgery; instead, they manifest as acute appendicitis or are discovered by chance during the investigation of another surgical pathology. Endocrine appendiceal tumors comprise 35–85 percent of all appendiceal malignancies. The majority of these tumors, 60–80% of the time, have a maximum diameter of less than 1 cm and are situated at the apex of the appendix. Metastatic disease is uncommon in patients with malignancies less than 2 cm in diameter. Carcinoid tumors are the most prevalent in the appendix, followed by adenocarcinoma, which includes the histologic variants goblet cell and mucinous adenocarcinoid but is also referred to as adenocarcinoid. The appendix may also exhibit benign histology, which encompasses leiomyomas, neuromas, lipomas, and angiomas. The majority of noncarcinoids and carcinoids larger than 2 centimeters should undergo hemicolectomy for definitive resection, according to current recommendations. Appendiceal mucinous lesions are distinguished by the accumulation of gelatinous material, which causes cystic dilatation of the appendix. Appendix low-grade mucinous neoplasms (LAMNs) are uncommon, non-invasive tumors that comprise 0.2–0.7% of all appendix specimens.

Copyright © 2023 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

Citation: Emmanuel Stephano Bracho Ruiz *et al* (2023). Appendiceal Mucinous Incidental Neoplasm a Rare Case Report and Literature Review. *South Asian Res J App Med Sci*, 5(6), 158-162. 158

The differentiation between low-grade and high-grade disease was implemented in the fourth edition of the World Health Organization (WHO) Classification of Tumors of the Digestive System, with the intention of streamlining the diagnostic terminology associated with appendiceal mucinous neoplasms. Metabolic activity, architecture, cytology, and the presence of signet ring cells are morphologic attributes identified by the WHO that can be employed to differentiate between high-grade and low-grade tumors. The Peritoneal Surface Oncology Group International (PSOGI) acknowledged an ongoing dearth of standardized diagnostic terminology in appendiceal mucinous neoplasia, notwithstanding the simplified WHO classification. A consensus on diagnostic terminology for appendiceal mucinous neoplasia was reached by an international working group of surgical pathologists, surgical oncologists, and medical oncologists, which was organized by PSOGI. This consensus builds upon the existing WHO diagnostic terminology. In conclusion, a three-tiered system has been incorporated into the eighth edition of the American Joint Committee on Cancer (AJCC) Staging Manual. Grade G1 designates low-grade tumors, while grades G2 and G3 designate high-grade tumors. The AJCC system employs the descriptive terms "poorly differentiated," "moderately differentiated," and "well-differentiated" in conjunction with the alphanumeric grades (G1, G2, G3, correspondingly). Although these terminologies are commonly employed to categorize various types of gastrointestinal malignancies, they can prove to be especially perplexing and challenging to directly apply to mucinous appendix tumors. Furthermore, substantial modifications were introduced to the staging of appendiceal mucinous neoplasia, specifically for low-grade lesions, with the advent of the AJCC eighth edition.

CASE REPORT

A 24-year-old male patient presents to the emergency room with a 24-hour history of colic-type abdominal pain in the lower right abdomen, accompanied by nausea and minimal vomiting. The patient denies fever and blood tests do not reveal any significant information regarding a systemic inflammatory response. A physical examination does not reveal any indications of acute abdominal pain, as determined by abdominal examination. An abdominal ultrasound reveals a mass with a cystic appearance; therefore, diagnostic laparoscopy is performed; upon locating a cystical mass containing mucinous material, a 2 cm tumor is identified at the end of the appendix with a respected base, and it is a limited availability of mucinose material in the cavity. Diagnostic laparoscopy is performed in the absence of pathological data. As a result, a laparoscopic appendectomy and oncology evaluation with a conclusive pathology report is decided on.

FIGURES

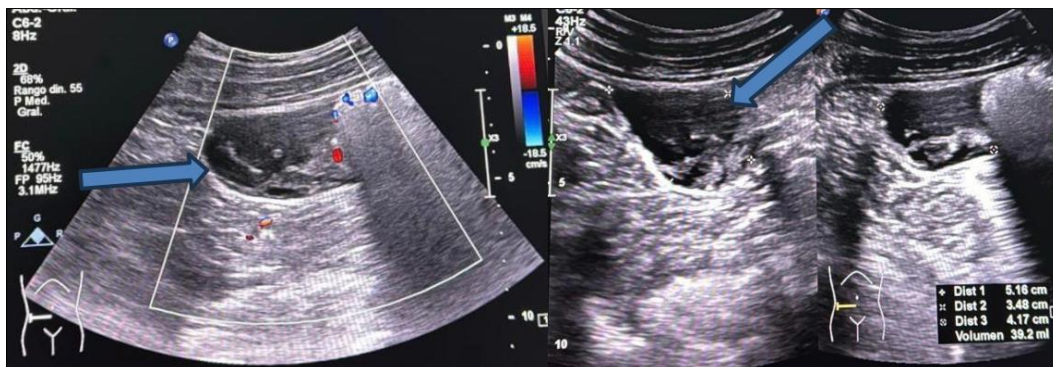


Figure 1: US abdominal, cystic image in the appendix tip, and presence of a cecal appendix body



Figure 2: Appendiceal mucinous neoplasm

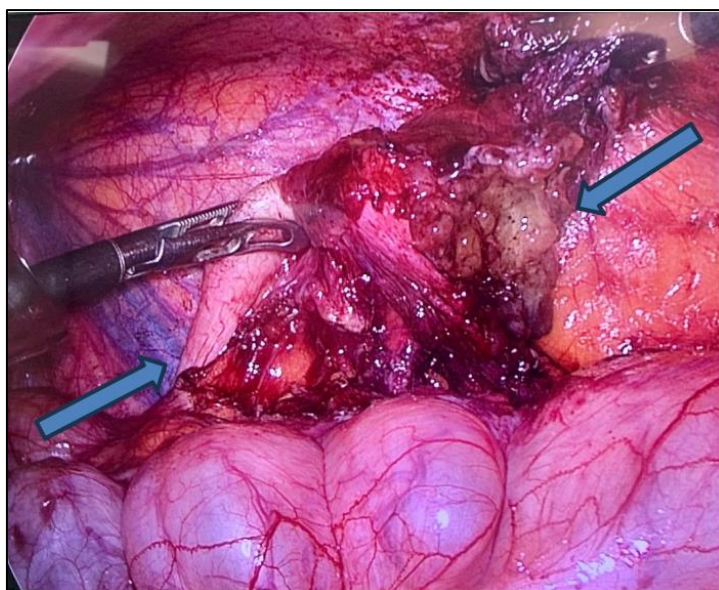


Figure 3: Appendix base respected, and presence of an appendiceal mucinous tumor at the appendix tip

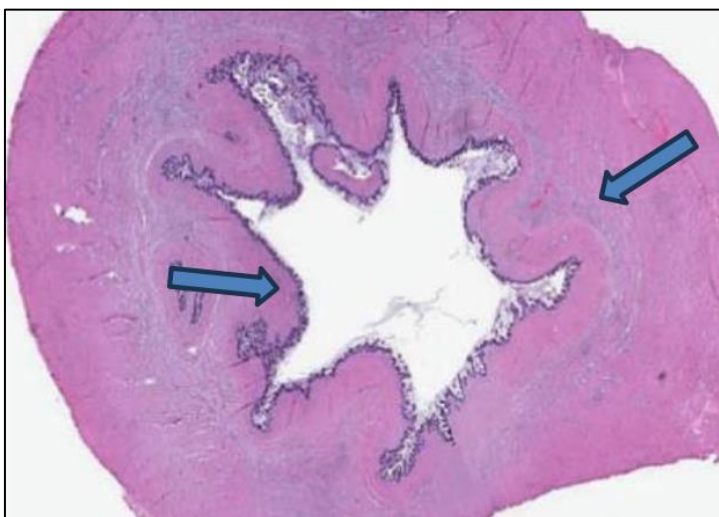


Figure 4: Low-grade appendiceal mucinous neoplasm involvement of the appendix by a mucin-rich epithelium, associated with loss of the lamina propria and muscularis mucosae and fibrosis of the submucosa and muscularis propria.

DISCUSSION

Appendiceal mucinous neoplasms (AMN) are uncommon malignancies of the epithelium; the United States annually diagnoses between one thousand and two thousand cases. These neoplastic epithelial cells are distinguished by the presence of cytoplasmic mucin, which is secreted into the lumen of the appendix in abundance. A propensity for peritoneal metastasis is observed in these individuals, which can arise from transmural invasion of mucin-secreting neoplastic epithelial cells or perforation of the mucin-filled appendix. Peritoneal metastasis originating from AMN is distinguished by the presence of mucinous carcinoma peritonei (MCP) or pseudomyxoma peritonei (PMP), which are peritoneal metastases composed of mucinous ascites and mucinous tumor nodules harboring malignant epithelial cells. Significant prognostic determinants of neoplastic cell characteristics within these mucinous tumors are cytohistologic characteristics, which have been utilized to categorize patients into a number of clinically pertinent classification schemes. The divergent classification systems have generated considerable perplexity and contention. Notwithstanding progressions in our comprehension of appendiceal mucinous neoplasms and their correlation with the pseudomyxoma peritonei syndrome, the categorization of mucinous appendix tumors remains contentious and perplexing. The majority of instances of classic pseudomyxoma peritonei, a clinical condition distinguished by diffuse intra-abdominal mucinous ascites that is readily observable and cytologically inconspicuous or low-grade mucinous tumor implants that affect the peritoneal surfaces, appear to originate from a mucinous neoplasm in the appendix. However, identifying patients with appendiceal mucinous neoplasms who are susceptible to developing the more severe pseudomyxoma peritonei syndrome can be challenging.

The majority of studies have demonstrated that appendix mucosa-confined tumors that are completely resected are benign from a clinical standpoint. On the contrary, tumors that initially present with significant peritoneal involvement put the patient at risk for recurrent pseudomyxoma peritonei. While this condition is inconsequential, it frequently results in fatality for the patient. The precise function, if any, of limited peritoneal involvement during the initial manifestation of these malignancies remains uncertain. It is especially challenging to predict the biologic potential of tumors containing cellular or acellular mucin deposits confined to the right lower quadrant of the abdomen. This is a common occurrence in our consultation practice. Appendiceal tumor patients may exhibit nonspecific clinical manifestations, which may cause a delay in the diagnosis. The predominant clinical manifestation in the early stages of the disease is pain in the right lower quadrant, resembling acute appendicitis, which is caused by distention of the appendix by mucin. Appendicitis or perforation of the appendix may manifest, particularly in cases where the appendiceal orifice is obstructed by the tumor. 32% of patients with appendiceal neoplasms were preoperatively diagnosed with acute appendicitis, according to Carr *et al.*, 23% were diagnosed subsequently. Increasing abdominal circumference is a symptom of advanced-stage disease caused by the accumulation of mucinous ascites in the peritoneum. Additional clinical manifestations associated with this stage comprise persistent abdominal pain, loss of body weight, anemia, infertility, and the emergence of umbilical or inguinal hernias. Despite the prevalence of mucinous peritoneal, serosal, and omental implants among patients, intestinal obstruction is a rare initial manifestation.

Low Grade Appendiceal Mucinous Neoplasm

Acute appendicitis is a rare complication of low grade appendiceal mucinous neoplasm (LAMN) in patients. Appendix cystic dilatation may manifest radiologically. At times, the patient may present with an abdominal or pelvic mass, especially in cases where ovarian spread has transpired. Peritoneal dissemination may result in PMP symptoms. The appendix can exhibit a range of dilation patterns or appear normal at the macroscopic level. Typically, dilated LAMNs have thin fibrous walls, and the wall and/or intraluminal mucin are frequently calcified. Patients with PMP typically exhibit a conspicuous rupture accompanied by the extrusion of mucus. However, the presence of mucin around the appendix may be obscured by a strong inflammatory response to mucus, which can simulate the symptoms of ruptured appendicitis. The neoplastic epithelium in LAMN is histologically low grade by definition. Epithelial cells contain small, darkly stained nuclei that are oriented basally and are relatively uniform in appearance. The nucleoli are dimly lit. Mucin is frequently prevalent in the cytoplasm, which contributes to low nuclear-to-cytoplasmic ratios. The cytological characteristics bear resemblance to typical low-grade dysplasia in the colon, such as slight enlargement of nuclei and increased coloration. However, polarity remains unaltered and there is minimal to negligible mitotic activity. While the epithelium may exhibit architectures such as papillary, villous, undulating, or flat, the typical arrangement of cells is in a monolayer. A mucocoele is an imprecise descriptive term used to refer to an appendix that is cystically dilated and secretes mucus. This is due to the fact that mucocoeles can arise from both neoplastic and non-neoplastic mechanisms. An appendix that is distended, mucin-filled, and marked by extensive epithelial loss and ulceration is a frequent diagnostic issue. Numerous LAMNs exhibit this characteristic. In the absence of a neoplasm upon microscopic examination of the entire appendix, retention cysts or "inflammatory mucocoele" could be speculated upon. However, retention cysts of the appendix are uncommon, and lesions with a diameter greater than 2 cm are considerably more likely to be LAMNs, particularly in the absence of luminal obstruction. LAMNs are distinguished by their propensity for frequent KRAS mutations and, in general, lack microsatellite instability and BRAF mutations. Additionally, they frequently harbor GNAS mutations, which are exceedingly rare in colorectal neoplasms. Diverticulitis of the appendix is a frequent mimicry of LAMN. Cytological atypia, disarray of the crypts, hyperplastic or serrated characteristics, lymphoid atrophy, and mucin extrusion into the appendix wall or beyond the serosa are all possible manifestations of both conditions. Villous architecture, hypermucinous epithelial cells, effacement of lamina propria, congested crypts, and cytological dysplasia are characteristics that favor LAMN. Preservation of essential mucosal architecture, hyperplastic and hypermucinous alterations confined to the luminal portion of the mucosa, and reactive atypia as opposed to dysplasia are characteristics that favor diverticular disease.

High Grade Appendiceal Mucinous Neoplasm

This classification includes mucinous neoplasms that lack infiltrative invasion but possess high-grade dysplasia distinguished by cribriform growth, loss of polarity accompanied by full-thickness nuclear stratification, enlarged nuclei that are conspicuously hyperchromatic or vesicular, prominent nucleoli, and an abundance of atypical mitotic figures. Limited published evidence exists regarding the anticipated behavior of HAMN. Mucinous neoplasms characterized by high-grade cytological features and diverticulum-like growth through the wall may follow a more aggressive course than LAMN, according to scant data; however, the number of cases that have been studied is relatively small. HAMN was more likely to be associated with epithelial cells in extra-appendiceal mucin than LAMN, according to some authors.

Pseudomyxoma Peritonei

Pseudomyxoma peritonei is a clinical condition distinguished by the presence of viscous, gelatinous material accumulated either locally or broadly within the peritoneal cavity of the abdomen and/or pelvis. "Pseudomyxoma peritonei" (akin to "mucocele"), a term that has acquired numerous connotations in the medical literature, is most effectively described clinically, radiologically, or syndromatically rather than histopathologically. Although this term encompasses a wide

variety of entities, the majority of instances of classic pseudomyxoma peritonei seem to originate from a mucinous neoplasm with minimal malignant potential that ruptures spontaneously or intraoperatively from the appendix into the adjacent peritoneum. While the tumor frequently metastasizes via hematogenous or lymphatic systems and affects the ovarian region, invasion into visceral organs is an extremely uncommon occurrence. Metastatic spread via lymphatics or hematogenous means is also non-existent.

CONCLUSION

Appendiceal mucinous neoplasms are an increasing incidence of a heterogeneous group of malignancies. Treatment is determined by histology and stage. Surgical treatment for low-grade tumors consists of resection of the primary site for patients with early-stage disease, or peritoneal debulking and HIPEC for those with advanced-stage disease. Further prospective trials are necessary to determine the most effective treatment for high-grade tumors; alternatives include debulking surgery and HIPEC, with or without preoperative chemotherapy.

Conflicts of Interests: The researchers have disclosed no conflicts of interest.

REFERENCES

- Benedix, F., Reimer, A., Gastinger, I., Mroczkowski, P., Lippert, H., & Kube, R. (2010). Primary appendiceal carcinoma—epidemiology, surgery and survival: results of a German multi-center study. *European Journal of Surgical Oncology (EJSO)*, 36(8), 763-771. <https://doi.org/10.1016/j.ejso.2010.05.025>.
- Carr, N. J., McCarthy, W. F., & Sobin, L. H. (1995). Epithelial noncarcinoid tumors and tumor-like lesions of the appendix. A clinicopathologic study of 184 patients with a multivariate analysis of prognostic factors. *Cancer*, 75(3), 757-768. [https://doi.org/10.1002/1097-0142\(19950201\)75:3%3C757::aid-cnrcr2820750303%3E3.0.co;2-f](https://doi.org/10.1002/1097-0142(19950201)75:3%3C757::aid-cnrcr2820750303%3E3.0.co;2-f).
- Choudry, H. A., Pai, R. K., Parimi, A., Jones, H. L., Pingpank, J. F., Ahrendt, S. S., ... & Bartlett, D. L. (2019). Discordant diagnostic terminology and pathologic grading of primary appendiceal mucinous neoplasms reviewed at a high-volume center. *Annals of Surgical Oncology*, 26, 2607-2614. <https://doi.org/10.1245/s10434-019-07447-z>.
- Kabbani, W., Houlihan, P. S., Luthra, R., Hamilton, S. R., & Rashid, A. (2002). Mucinous and nonmucinous appendiceal adenocarcinomas: different clinicopathological features but similar genetic alterations. *Modern pathology*, 15(6), 599-605. <https://doi.org/10.1038/modpathol.3880572>.
- Leonards, L. M., Pahwa, A., Patel, M. K., Petersen, J., Nguyen, M. J., & Jude, C. M. (2017). Neoplasms of the appendix: pictorial review with clinical and pathologic correlation. *Radiographics*, 37(4), 1059-1083. <https://doi.org/10.1148/rg.2017160150>.
- Madison, B., Ng, J. Y., & Hajir, N. (2022). Delivery of an Incidental Appendiceal Mucinous Neoplasm. *Cureus*, 14(6). <https://doi.org/10.7759/cureus.26214>.
- McCusker, M. E., Coté, T. R., Clegg, L. X., & Sobin, L. H. (2002). Primary malignant neoplasms of the appendix: A population-based study from the surveillance, epidemiology and end-results program, 1973–1998. *Cancer*, 94(12), 3307-3312. <https://doi.org/10.1002/cncr.10589>.
- McGory, M. L., Maggard, M. A., Kang, H., O'Connell, J. B., & Ko, C. Y. (2005). Malignancies of the appendix: beyond case series reports. *Diseases of the colon & rectum*, 48, 2264-2271. <https://doi.org/10.1007/s10350-005-0196-4>.
- Misdraji, J., Yantiss, R. K., Graeme-Cook, F. M., Balis, U. J., & Young, R. H. (2003). Appendiceal mucinous neoplasms: a clinicopathologic analysis of 107 cases. *The American journal of surgical pathology*, 27(8), 1089-1103.
- Pai, R. K., & Longacre, T. A. (2005). Appendiceal mucinous tumors and pseudomyxoma peritonei: histologic features, diagnostic problems, and proposed classification. *Advances in anatomic pathology*, 12(6), 291-311.
- Pai, R. K., Beck, A. H., Norton, J. A., & Longacre, T. A. (2009). Appendiceal mucinous neoplasms: clinicopathologic study of 116 cases with analysis of factors predicting recurrence. *The American journal of surgical pathology*, 33(10), 1425-1439.
- Shaib, W. L., Assi, R., Shamseddine, A., Alese, O. B., Staley III, C., Memis, B., ... & El-Rayes, B. F. (2017). Appendiceal mucinous neoplasms: diagnosis and management. *The oncologist*, 22(9), 1107-1116. <https://doi.org/10.1634/theoncologist.2017-0081>.
- Smeenk, R. M., Van Velthuysen, M. L. F., Verwaal, V. J., & Zoetmulder, F. A. N. (2008). Appendiceal neoplasms and pseudomyxoma peritonei: a population based study. *European Journal of Surgical Oncology (EJSO)*, 34(2), 196-201. <https://doi.org/10.1016/j.ejso.2007.04.002>.
- Turaga, K. K., Pappas, S. G., & Gamblin, T. C. (2012). Importance of histologic subtype in the staging of appendiceal tumors. *Annals of surgical oncology*, 19, 1379-1385. <https://doi.org/10.1245/s10434-012-2238-1>.
- Valasek, M. A., & Pai, R. K. (2018). An update on the diagnosis, grading, and staging of appendiceal mucinous neoplasms. *Advances in anatomic pathology*, 25(1), 38-60. <https://doi.org/10.1097/pap.000000000000178>.