

Appendicular tumor causing appendicitis in a young man: a case report

Tumor apendicular causando apendicite em homem jovem: relato de caso

Tumor apendicular causante de apendicitis en un hombre joven: reporte de un caso

Received: 05/13/2022 | Reviewed: 05/22/2022 | Accept: 05/29/2022 | Published: 06/04/2022

Renata Castilho Sperli

ORCID: <https://orcid.org/0000-0002-1167-7899>
Universidade Federal do Triângulo Mineiro, Brasil
E-mail: renata.sperli@hotmail.com

Natinielle Martins de Souza

ORCID: <https://orcid.org/0000-0003-0631-8514>
Universidade Federal do Triângulo Mineiro, Brasil
E-mail: natiniellemartinsdesouza@gmail.com

Octávio Augusto Rodrigues Lima

ORCID: <https://orcid.org/0000-0003-0277-7887>
Universidade Federal do Triângulo Mineiro, Brasil
E-mail: octaviorodrigues97@gmail.com

João Henrique do Amaral e Silva

ORCID: <https://orcid.org/0000-0002-2563-8225>
Universidade Federal do Triângulo Mineiro, Brasil
E-mail: joapatologista@gmail.com

Geisa Perez Medina Gomide

ORCID: <https://orcid.org/0000-0002-6657-5515>
Universidade Federal do Triângulo Mineiro, Brasil
E-mail: geisa.gomide@uftm.edu.br

Sílvia Maria Perrone Camilo

ORCID: <https://orcid.org/0000-0001-9407-0285>
Universidade Federal do Triângulo Mineiro, Brasil
E-mail: smpcamilo@gmail.com

Abstract

Introduction: The most common pathogenesis of acute appendicitis is luminal obstruction of the appendix by fecaliths. However, any material that can directly or indirectly obliterate the appendicular cavity can cause acute appendicitis. Appendicular tumors are relatively rare, but they can obliterate the lumen of the organ, leading to appendicitis. **Case report:** A 23-year-old patient with an acute inflammatory abdomen was preoperatively diagnosed with acute appendicitis. Intraoperatively, the diagnosis of acute appendicitis with a perforated appendix was confirmed. The anatomopathological diagnosis was colonic adenocarcinoma of the appendix and the patient was summoned to receive appropriate treatment. **Methodology:** In addition to studying the patient's medical records, a bibliographic research was carried out on the topic, which permeated the discussion, including the prevalence, diagnosis and management of appendix tumors. **Conclusion:** The importance of clinical, radiological, and anatomopathological diagnoses in acute appendicitis and surveillance during non-operative management are highlighted in this case. Reports of appendicular tumors are increasing, and this scenario can be avoided if risk factors are identified.

Keywords: Appendicitis; Acute abdomen; Appendiceal neoplasms; Adenocarcinoma; Health teaching.

Resumo

Introdução: A patogênese mais comum da apendicite aguda é a obstrução luminal do apêndice por fecalitos. No entanto, qualquer material que possa obliterar direta ou indiretamente a cavidade apendicular pode causar apendicite aguda. Os tumores apendiculares são relativamente raros, mas podem obliterar o lúmen do órgão, levando à apendicite. **Relato de caso:** Paciente de 23 anos com quadro de abdome inflamatório agudo foi diagnosticado no pré-operatório com apendicite aguda. No intraoperatório, foi confirmado o diagnóstico de apendicite aguda com apêndice perfurado. O diagnóstico anatomopatológico foi de adenocarcinoma colônico de apêndice e o paciente foi convocado para receber o tratamento adequado. **Metodologia:** Além do estudo do prontuário do paciente, foi realizada pesquisa bibliográfica sobre o tema, o que permeou a discussão, incluindo prevalência, diagnóstico e manejo dos tumores de apêndice. **Conclusão:** Ressalta-se neste caso a importância do diagnóstico clínico, radiológico e anatomopatológico da apendicite aguda e da vigilância durante o manejo não operatório. Os relatos de tumores apendiculares estão aumentando, e esse cenário pode ser evitado se os fatores de risco forem identificados.

Palavras-chave: Apendicite; Abdome agudo; Neoplasias do apêndice; Adenocarcinoma; Ensino em saúde.

Resumen

Introducción: La patogenia más frecuente de la apendicitis aguda es la obstrucción luminal del apéndice por fecalitos. Sin embargo, cualquier material que pueda obliterar directa o indirectamente la cavidad apendicular puede causar apendicitis aguda. Los tumores apendiculares son relativamente raros, pero pueden obliterar la luz del órgano y provocar apendicitis. **Caso clínico:** Paciente de 23 años con abdomen agudo inflamatorio diagnosticado preoperatoriamente de apendicitis aguda. Intraoperatoriamente se confirmó el diagnóstico de apendicitis aguda con apéndice perforado. El diagnóstico anatomopatológico fue adenocarcinoma colónico de apéndice y se citó a la paciente para recibir el tratamiento adecuado. **Metodología:** Además del estudio del prontuario del paciente, se realizó una investigación bibliográfica sobre el tema, que permeó la discusión, incluyendo la prevalencia, diagnóstico y manejo de los tumores de apéndice. **Conclusión:** Se destaca en este caso la importancia del diagnóstico clínico, radiológico y anatomopatológico en la apendicitis aguda y la vigilancia durante el manejo no operatorio. Los informes de tumores apendiculares están aumentando y este escenario se puede evitar si se identifican los factores de riesgo.

Palabras clave: Apendicitis; Abdomen agudo; Neoplasias del apéndice; Adenocarcinoma; Enseñanza en salud.

1. Introduction

Acute appendicitis is a commonly encountered surgical emergency at all levels of seniority and across different specialties. First described by Fitz in 1886, it is characterized by inflammation of the vermiform appendix. Treves is credited as the first to treat acute appendicitis in 1902 (Teng et al., 2021).

Several guidelines give advice about the diagnostic work-up for suspected acute appendicitis. The traditional way of setting a diagnosis is based on clinical assessment. History taking and physical examination combined with laboratory findings are still seen as the cornerstone of diagnosing acute appendicitis, but have a high intra-observer variability and a far from perfect accuracy. Laboratory tests such as white blood cell count or C-reactive protein are widely used as a next step in diagnosing acute appendicitis. Individually, these inflammatory markers are weak discriminators, but when combined they achieve a higher discriminatory power in diagnosing acute appendicitis versus no appendicitis (Bom et al., 2021).

Diagnosis of appendicitis is challenging, and some controversies on its management are still present among different settings and practice patterns worldwide. In April 2020, the World Society of Emergency Surgery (WSES) published the first update to the Jerusalem Guidelines on the diagnosis and treatment of acute appendicitis. The final version of the statements on the topic is as follows: “Clinical scores alone, e.g. Alvarado, AIR and the new Adult Appendicitis Score are sufficiently sensitive to exclude acute appendicitis, accurately identifying low risk patients and decreasing the need for imaging and the negative appendectomy rates in such patients. We recommend the use of clinical scores to exclude acute appendicitis and identify intermediate-risk patients needing of imaging diagnostics [QoE: High; Strength of recommendation: Strong; 1A]” (Podda et al., 2021).

Acute appendicitis is an abdominal pathology that most often requires emergency surgery. The approximate lifetime prevalence is 8%. The annual incidence is approximately 0.1% in Western countries. The most common pathogenesis of acute appendicitis is luminal obstruction of the appendix by fecaliths. However, any material that can directly or indirectly obliterate the appendicular cavity can cause acute appendicitis. Despite appendicular tumors being relatively rare, they can obliterate the lumen, leading to appendicitis (Şenol et al., 2019). We report the case of a young patient with an acute inflammatory abdomen, in which acute appendicitis was diagnosed. Intraoperatively, acute appendicitis with a perforated appendix was observed and diagnosed as colonic adenocarcinoma of the appendix. This report aims to draw attention to the importance of anatomopathological evaluation in patients with acute appendicitis.

2. Methodology

In order for the present report/case study to be carried out in accordance with current bioethics standards, a research project was developed which was submitted to the Research Ethics Committee and approved by it (CAAE: 57154922.0.0000.8667; Approval No. 5.348.121). The work is a report/retrospective case study on the medical record of a

patient that seeks to correlate the bibliography of the disease with the patient's condition, through reading articles about it and tabulating the patient's symptoms and found in the descriptions of the disease.

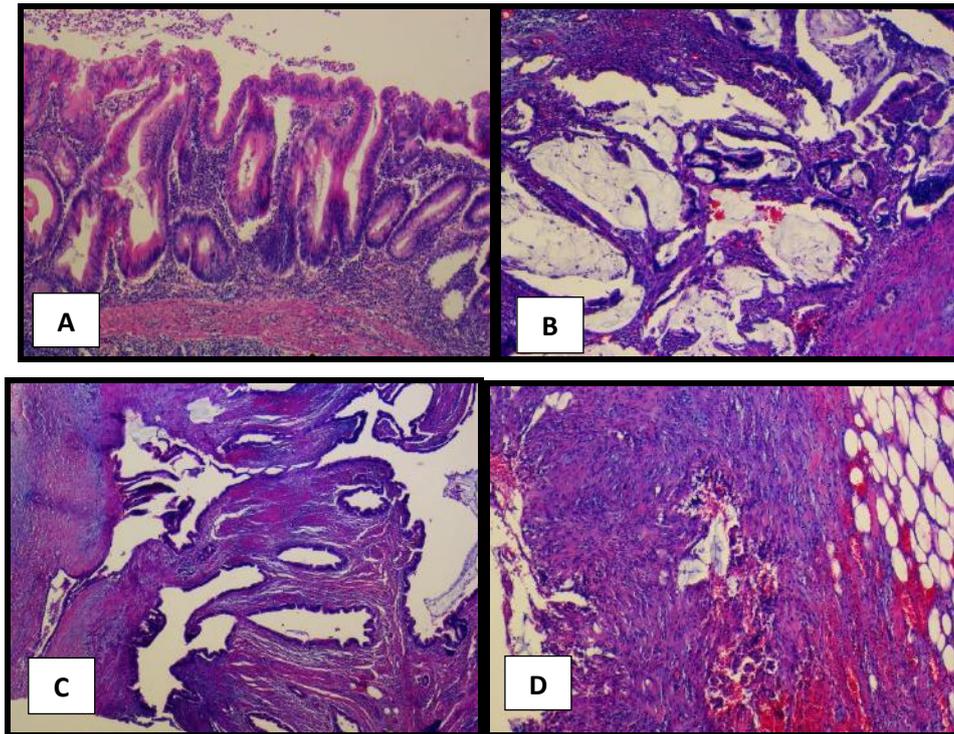
The methodology of the report/case study was, therefore, divided into 3 phases: a) Bibliographic reading and establishment of the main findings described; b) Evaluation of the patient's medical record and survey of the findings found in the case; c) Correlation between what was presented in the patient and what was described in the literature.

That is, after approval by the Ethics Committee, access to the patient's chart was allowed to survey the signs, symptoms and test results. While part of the authors was responsible for collecting data from medical records, another group was directed to establish the main findings described in the literature, in order to avoid possible biases. After the two initial phases, correlations were built between what was seen in the patient and what was presented in the literature review, in order to establish a correspondence.

3. Case Report

A 23-year-old patient presented with severe pain in the right iliac fossa for 3 days. Ultrasonography in the emergency room showed acute appendicitis. He underwent McBurney's appendectomy and, in the inventory of the cavity, a perforated appendix with a preserved appendicular base plugged by the omentum and a small amount of inflammatory fluid in the peritoneal cavity was observed. The patient returned for surgical wound revision and thread removal which were successful. The anatomopathological examination reports, obtained later, revealed invasive adenocarcinoma of the appendix, with less than 50% extracellular mucin (adenocarcinoma non-mucinous, well-differentiated type – G1) with invasion of the serosa and surgical margin at the cecal extremity focally compromised by the adenocarcinoma (Figure 1). The patient was readmitted for oncologic right colectomy, with removal of 18 cm of the colon and 8 cm of the terminal ileum, and retroperitoneal lymphadenectomy. Postoperative anatomopathological examination results revealed two foci of adenocarcinoma in the adipose tissue of the mesocolon. There were 12 lymph nodes and resection margins without evidence of neoplasia. The pathological staging was pT4 pN0 MX. The patient was referred to the oncology department where he underwent adjuvant chemotherapy treatment.

Figure 1: Anatomopathological examination result of the appendix.



Source: Clinical Analysis and Pathological Anatomy Unit. Hospital de Clínicas - UFTM (2022).

In the upper left image (A) it is possible to identify the appendix showing adenocarcinoma in situ (HE 100X). On the right (B) we can see mucus-producing adenocarcinoma, but less than 50% extra-cellular mucin (HE 100X). In the lower left image (C), we can see neoplastic glands invading the muscularis propria (HE 40X). On the right (D), the neoplasm invades the serosa (HE 100X).

4. Discussion

An acute abdomen requires urgent attention and treatment. It can be caused by an infection, inflammation, vascular occlusion, or obstruction. Patients usually present with sudden-onset abdominal pain with associated nausea or vomiting (Patterson et al. 2020). Abdominal pain is a frequent symptom presenting in about 5%–10% of emergency consultations (Abdullah & Firmansyah, 2012). In this case, the patient presented with severe pain in the right iliac fossa but without nausea and vomiting. After a clinical assessment and diagnosis of acute appendicitis, appendectomy was performed.

The lifetime incidence of acute appendicitis is approximately 7.7% in the United States, and appendiceal tumors are found incidentally in appendectomy specimens from patients with acute appendicitis. The incidence of appendicular tumors in appendectomy specimens from patients with acute appendicitis ranges from 0.9% to 1.7% (Loftus et al., 2017). Adenocarcinomas can obstruct the appendicular lumen, often resulting in acute appendicitis (Karande et al., 2019).

Primary cancers of the appendix, including colonic adenocarcinoma, mucinous adenocarcinoma, goblet cell adenocarcinoma, and neuroendocrine carcinoma, are rare, with an incidence of approximately 1.2 cases per 100,000 people per year in the United States. There are no established risk factors for appendiceal cancer development. They may be asymptomatic and detected incidentally as an abnormal-appearing appendicular orifice on colonoscopy, surgery, or imaging for other indications, such as suspected ovarian malignancy. The disease may develop when symptoms are present. For example, many patients present with abdominal distention and pain secondary to the peritoneal spread of appendix cancer (Kelly, 2015).

For the diagnosis of neoplasms, CT has a sensitivity of 95% in symptomatic patients. IV contrast, as well as oral contrast, can be beneficial for the identification and staging of tumors. The diagnostic criterion is an enlarged appendix greater than 15 mm in diameter, characteristics of cystic dilatation, or a soft tissue mass. Magnetic resonance imaging (MRI) has recently increased in use for the pregnant and pediatric populations due to the lack of ionizing radiation. Ultrasound (US) has similar indications to MRI, though it remains useful in children who have thinner musculature and less abdominal fat. It has a sensitivity of 55% and a specificity of 95% for diagnosing acute appendicitis. It is highly operator dependent, however, and therefore an equivocal or negative study cannot rule out appendicitis (Jones et al, 2022). In the patient in question, only ultrasound was performed and the examination concluded that it was acute appendicitis.

The anatomopathological result of the case presented was adenocarcinoma of the appendix, which is considered the most common primary cancer of the appendix, comprising 60% of all cases. However, it constitutes less than 0.5% of all gastrointestinal tract neoplasms. Primary appendiceal adenocarcinomas are classified as "colonic type," which arise from preexisting adenomas similar to colorectal tumors, or "mucinous," which are biologically and histologically distinct from colonic adenocarcinoma. Genetic mutations associated with appendix tumors have already been described, especially in those that produce mucus. KRAS and/or GNAS mutations are commonly found in mucinous subtype while BRAF mutations and microsatellite instability are rarely identified (Assarzadegan & Montgomery, 2021). These data suggest that KRAS mutations are important in tumor initiation but may be less critical for aggressive high grade tumor progression. GNAS mutations, known as essential in abundant mucin production, are also presented in G1 and G2 tumors but less commonly in G3 tumors. The co-mutation of GNAS and KRAS is identified in between 65% to 85% of cases (Kang et al, 2021). However, the case described here presented a non-mucinous adenocarcinoma.

Similar to colon cancer, colonic adenocarcinoma of the appendix presents at an average age of 62–65 years (Kelly, 2015), with a slight male predominance. Appendiceal tumors in young patients harbor a distinct spectrum of somatic cancer gene mutations compared with late-onset cases. Using clinical-grade targeted sequencing data, young patients harbored unique mutation patterns in PIK3CA, GNAS, SMAD3 and TSC2 compared with late-onset cases—providing initial evidence to suggest that early-onset appendix cancer harbors a distinct disease biology (Gibbs et al, 2021)

The management is highly dependent on tumor type, histologic grade, pathologic stage, and resection margin status and may range from radical surgery to systemic chemotherapy or surveillance (Jedrzkiwicz et al., 2019). Thus, complete evaluation of the resected primary tumor and/or biopsy specimens from peritoneal metastatic sites should be performed by an experienced pathologist (Chicago Consensus Working Group, 2020). After histopathological evaluation of the appendectomy product, which showed surgical margin involvement, the patient underwent a right oncological colectomy, following which chemotherapy and the Roswell Park regimen (5-fluorouracil + leucovorin) were initiated.

There are no specific staging systems or guidelines for colonic adenocarcinomas of the appendix. The investigation, staging, and treatment are similar to those for colon cancer. The American Joint Commission on Cancer staging system and colon cancer guidelines of the National Comprehensive Cancer Network and the European Society for Medical Oncology can be used (Van de Moortele et al., 2020).

The molecular profile of appendicular adenocarcinoma has been studied, revealing different molecular characteristics between it and right and left colorectal cancers. In addition, there is molecular heterogeneity between the histopathological subtypes of the neoplasm. Such results may be relevant for an individualized approach to the treatment of appendicular adenocarcinomas (Tokunaga et al., 2019). Therefore, additional researchs are needed to understand appendix cancer carcinogenesis and develop appendix cancer-specific prevention strategies and clinical management guidelines.

5. Conclusion

The importance of clinical, radiological, and anatomopathological diagnoses in acute appendicitis and surveillance during non-operative management requires attention. Contextualizing with the present day, during the COVID-19 pandemic, a decrease in emergency consultations and a change in the treatment of numerous medical conditions was observed (Kohler et al, 2021). Non-surgical management of acute appendicitis in the COVID-19 setting was a safe, long-term alternative to surgery with acceptably low complication rates (Emile et al, 2021). Therefore, the good general condition of young people undergoing appendectomy may lead to underestimation of the importance of postoperative follow-up. Surgeons should provide exhaustive guidance on the need for follow-up until the anatomopathological examination results are available, since the diagnosis is made intraoperatively or during the postoperative period via histologic evaluation (Ruiz et al, 2021). Therefore, the need for additional surgical intervention or medical treatment for patients with tumor, histopathological results must be followed carefully after appendectomy (Yildirim et al, 2022). In the last years, three institutions reported alarming rates of appendicular tumors (12.4%, 27.7%, and 29.4%) found incidentally in appendectomy specimens from patients with acute appendicitis initially treated with non-operative management. This scenario can be avoided if patients at an increased risk of appendix cancer are identified when they experience appendicitis for the first time. The conditions present at admission can accurately predict the presence of an appendicular tumor in patients who present with acute appendicitis. Independent risk factors include advanced age, outpatient use of steroids or immunosuppressants, absence of migrating right lower quadrant pain, and phlegmon appearance on CT (Kelly, 2015). These factors affect decision-making for managing acute appendicitis.

References

- Abdullah, M., & Firmansyah, M. A. (2012). Diagnostic approach and management of acute abdominal pain. *Acta med Indonesiana*, 44 (4), 344-350.
- Assarzagdean, N., & Montgomery, E. (2021). What is New in the 2019 World Health Organization (WHO) Classification of Tumors of the Digestive System Review of Selected Updates on Neuroendocrine Neoplasms, Appendiceal Tumors, and Molecular Testing. *Archives of Pathology & Laboratory Medicine*, 145, 664–677
- Bom, W. J., Scheijmans, J. C., Salminen, P., & Boermeester, M. A. (2021). Diagnosis of uncomplicated and complicated appendicitis in adults. *Scandinavian Journal of Surgery*, 110 (2) 170–179.
- Chicago Consensus Working Group (2020). The Chicago Consensus Guidelines for peritoneal surface malignancies: Introduction. *Cancer*, 126 (11), 2510-2512
- Emile, S. H., Hamid, H. K., Hkan, S. M., & Davis, G. N. (2021). Rate of Application and Outcome of Non-operative Management of Acute Appendicitis in the Setting of COVID-19: Systematic Review and Meta-analysis. *Journal of Gastrointestinal Surgery*, 25 1905–1915
- Gibbs, T., Washington, M. K., Eng, C., Idrees, K., Davis, J., & Holowatyj, A. N. (2021). Histologic and Racial/Ethnic Patterns of Appendiceal Cancer among Young Patients. *Cancer epidemiology, biomarkers & prevention*, 30 (6) 1149–1155.
- Jedrzkiewicz, J., Tateishi, Y., Kirsch, R., Conner, J., Bischof, D., McCart, A., Riddell, R., Pollett, A., Taylor, E. L., & Govindarajan, A. (2019) Impact of referral center pathology review on diagnosis and management of patients with appendiceal neoplasms. *Archives of pathology & laboratory medicine*, 144 (6), 764-768.
- Jones, S., Ranzenberger, L. R. & Carter, K. R. (2022). *Appendix Imaging*. <https://ncbi.nlm.nih.gov/books/NBK549903/>
- Kang, D-W., Kim, B., Kim, J. M., Kim, J., Chang, H. J., Chang, M. S. Sohn, J-H., Cho, M-Y., Jin, S-Y., Chang, H. K., Han, H. S., Kim, J. Y., Kim, H. S., Park, D. Y., Park, H. Y., Lee, S.J., Lee, W., Lee, H. S., Kang, Y.N., Choi, Y., & The Gastrointestinal Pathology Study Group of the Korean Society of Pathologists. (2021). Standardization of the pathologic diagnosis of appendiceal mucinous neoplasms. *Journal of Pathology and Translational Medicine*, 55, 247-264.
- Karande, G. Y., Chua, W. M., Yiin, R., Wong, K. M., Hedgire, S., & Tan, T.J. (2019). Spectrum of computed tomography manifestations of appendiceal neoplasms: acute appendicitis and beyond. *Singapore medical journal*. 60 (4), 173–182.
- Kelly, K. J. (2015). Management of appendix cancer. *Clinics in Colon and Rectal Surgery*, 28 (4), 247–255.
- Kohler, F., Muller, S., Hendricks, A., Kastner, C., Reese, L., Boerner, K., Flemming, S., Lock, J. F., Germer, C-T., & Wiegering, A. (2021) Changes in appendicitis treatment during the COVID-19 pandemic – A systematic review and meta-analysis. *International Journal of Surgery*,. 95 e106148
- Loftus, T. J., Raymond, S. L., Sarosi, G. A., Croft, C. A., Smith, R. S., Efron, P. A., Moore, F. A., Brakenridge, S. C., Mohr, A. M., & Jordan, J. R. (2017). Predicting appendiceal tumors among patients with appendicitis. *The journal of trauma and acute care surgery*, 82 (4), 771-775.

Patterson, J. W., Kashyap, S., & Dominique, E. (2020). *Acute Abdomen*, <https://www.ncbi.nlm.nih.gov/books/NBK459328/>

Podda, M., Pisanu, A., Sartelli, M., Coccolini, F., Damaskos, D., Augustin, G., Khan, M., Pata, F., De Simone, B., Ansaloni, L., Catena, F., & Di Saverio, S. (2021). Diagnosis of acute appendicitis based on clinical scores: is it a myth or reality? *Acta Biomedica*, 92 (4) e2021231.

Ruiz, S. G., Geraghty, F., Padron, D., Chacon, D., & Kahane, G. (2021) The Appendix: A Rare Case of an Appendiceal Collision Tumor. *Cureus Journal of Medical Science*, 13 (8) e17050.

Şenol, K., Ferhatoğlu, M. F., & Tihan, D. (2019). Clinicopathologic and prognostic features in appendiceal malignancies: does tumor invasiveness matter? *Turkish journal of surgery*, 35 (4), 245-251.

Teng, T. Z., Thong, X. R., Lau, K. Y., Balasubramaniam, S., & Shelat, V. G. (2021). Acute appendicitis—advances and controversies. *World Journal of Gastrointestinal Surgery*, 13 (11), 1293-1314

Tokunaga, R., Xiu, J., Johnston, C., Goldberg, R. M., Philip, P. A., Seeber, A., Naseem, M., Lo, J. H., Arai, H., Battaglin, F., Puccini, A., Berger, M. D., Soni, S., Zhang, W., Hwang, J. J., Shields, A. F., Marshall, J. L., Baba, H., Korn, W. M., & Lenz, H. J. (2019). Molecular profiling of appendiceal adenocarcinoma and comparison with right-sided and left-sided colorectal cancer. *Clinical Cancer Research: an official journal of the American Association for Cancer Research*, 25 (10), 3096-3103.

Van de Moortele, M., De Hertogh, G., Sagaert, X., & Van Cutsem, E. (2020). Appendiceal cancer: a review of the literature. *Acta gastro-enterologica Belgica*, 83 (3), 441-448.

Yildirim, E., Kegin, M., Özdemir, M., Bektas, S., Pelen, Z., & Er, M. (2022). Neoplasms of the appendix: Single institution and ten-year experiences results. *Ulus Travma Acil Cerrahi Derg*, 28 (3) 352-360.