

ORIGINAL ARTICLE

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Histopathological examination after appendectomy: Neoplastic lesions** Mehmet Sabri Ciftci¹,  Burak Ucaner²**¹Sincan Training and Research Hospital, General Surgery Clinic, Ankara, Türkiye²University of Health Sciences Gulhane Training and Research Hospital, General Surgery Clinic, Ankara, Türkiye

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**Abstract**

Appendiceal neoplasms include rare tumor formations, whose treatment ranges from an appendectomy, hemicolectomy, and chemotherapeutic agents for benign or malignant lesions. In this study, we aimed to evaluate appendiceal neoplastic lesions according to the literature on histological subgroups. A review was performed on 2.124 patients who had undergone appendectomy between January 2017 and December 2021. Patients were evaluated retrospectively according to their demographic, clinical, radiological, and histopathological characteristics. In the histopathological evaluation of the 23 (1.06%) patients, who were included in the study upon the detection of the appendiceal neoplastic lesion, sessile serrated adenoma was observed in 7 patients, low-grade appendiceal mucinous neoplasm (LAMN) in 6 patients, mucinous adenocarcinoma in 4 patients, signet ring cell mucinous adenocarcinoma in 1 patient, neuroendocrine tumor (NET) in 4 patients, and tubulovillous adenoma in 1 patient. Appendiceal neoplasms are generally asymptomatic; therefore, pathological examination results should be carefully evaluated after appendectomy, and it should be remembered that appendectomy is not always sufficient alone.

Keywords: Appendix, mucinous neoplasia, appendectomy, neuroendocrine tumor**Introduction**

Tumor formations of the appendix constitute a highly heterogeneous group of lesions and are a clinical entity rarely encountered by clinicians and surgeons. In the literature, the incidence of tumor lesions detected after appendectomy varies between 0.78-2.3% [1-3]. Appendiceal neoplastic lesions are encountered in a wide range, including adenomatous lesions such as sessile serrated, villous, and tubulovillous, adenocarcinomas, low and high-grade mucinous neoplasms, lesions formerly known as carcinoids and expressed as neuroendocrine tumors in current terminology. Patients usually present with the clinical characteristics and symptoms of acute appendicitis and are rarely detected during increased health screenings and random imaging.

In general, appendiceal neoplasms can be broadly defined as epithelial lesions such as adenomas and adenocarcinomas and non-epithelial lesions such as neuroendocrine tumors and lymphomas. Mucinous tumors have different biological behaviors and oncological results from non-mucinous neoplasms; therefore, epithelial neoplasms are divided into subgroups according to mucin production. The World Health Organization classifies most noninvasive epithelial lesions as low-grade appendiceal mucinous neoplasias (LAMNs), and LAMNs include lesions formerly defined as mucosal or mucinous cystadenomas [4]. Mucinous appendiceal neoplasms usually have a good prognosis; however, they may lead to the clinical characteristics of pseudomyxoma peritonei, which refers to the peritoneal scattering of the mucinous component, albeit

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low-grade, and the treatment may have a wider spectrum [5]. Appendectomy is usually sufficient; nevertheless, the treatment options may vary from right hemicolectomy to cytoreductive surgery.

In this study, we aimed to present our clinical experience related to the histopathological subtypes, surgical treatment, and treatment outcomes of appendiceal neoplastic lesions.

Material and Methods

Population and study design

The study included 23 patients who were reported to have appendiceal adenocarcinoma, low and high-grade mucinous appendiceal neoplasms, neuroendocrine tumors, and adenomatous lesions in the histopathological examination performed by scanning 2.124 patients who underwent elective appendectomy after an emergency or preoperative imaging in the General Surgery Clinic of Gulhane Training and Research Hospital of the University of Health Sciences between January 2017 and December 2021. Information about age, gender, symptoms for presentation, the clinical, radiological, and intraoperative results, and complementary surgical procedures were recorded retrospectively according to the patient files. The subtype, diameter, localization, differentiation, and grades of the tumors, rate of mitosis and Ki-67 index in neuroendocrine tumors, and degrees of dysplasia in adenomatous lesions were determined.

The study was conducted in accordance with the Declaration of Helsinki and this study was approwed by University of Health Sciences Gülhane Training and Research Hospital Clinical Research Ethics Committee (Date: June 07, 2023, Decision No:2023/127).

Statistical analysis

The statistical analysis was performed on the SPSS v22.0 software package. Descriptive statistics were expressed as number, percentage, and mean with standard deviation, and median (min-max). The conformity of the variables to the normal distribution was examined using visual (histograms and probability graphs) and analytical methods (“Kolmogorov–Smirnov” and “Shapiro-Wilk”).

Results

The mean age of 23 patients included in the study was 57.9±16.2 years (24-84 years). Of the patients, 15 (65.3%) were female and 8 (34.7%) were male. The main symptom at admission was abdominal pain and the median symptom duration was 2 (1-10) days. Comorbidity was observed in 7 (30.4%) patients. Of the patients, 15 (65.3%) had been evaluated by computed tomography (CT) and 8 (34.7%) by ultrasonography (USG) (Table 1).

The preferred operative methods were open appendectomy (n=13),

laparoscopic appendectomy (n=7), and right hemicolectomy (n=3). According to the intraoperative examinations, acute phlegmonous appendicitis was observed in 14 (60.9%) patients, acute perforated appendicitis in 5 (21.8%) patients, palpable mass in 2 (8.7%) patients, plastron appendicitis in 1 (4.3%) patient, and diffuse mucinous acid and pseudomyxoma peritonei in 1 (4.3%) patient. Complementary surgery was performed on five patients (Table 2).

In the histopathological evaluation, sessile serrated adenoma was observed in 7 patients, low-grade appendiceal mucinous neoplasm (LAMN) in 6 patients, mucinous adenocarcinoma in 4 patients, neuroendocrine tumor (NET) in 4 patients, tubulovillous adenoma in 1 patient, and signet ring cell mucinous adenocarcinoma in 1 patient. All patients with neuroendocrine tumors were classified as ‘NET,G1’, their Ki-67 proliferation index was <3%, and their mitosis rate was <2 (mitosis/2 mm²). The median tumor diameter was 28 mm (5-55 mm). Tumors were localized at the distal to the appendix in 9 patients, proximal in 8 patients, and median in 6 patients (Table 3).

The demographic, clinical, and histopathological characteristics of all patients are presented in Table 4.

Table 1. Descriptive characteristics of patients

Characteristic	Number (percentage)
Age*	57.9±16.2
Gender	
Female	15 (65.2)
Male	8 (34.8)
BMI (kg/m ²)	25.5±3.6
ASA	
I	6 (26.1)
II	10 (43.5)
III	7 (30.4)
Comorbidity	7 (30.4)
Hypertension	7 (30.4)
CAD/CHF	3 (13.0)
Diabetes mellitus	2 (8.7)
Abdominal pain symptom duration (days)**	2 (1-10)
Imaging	
Computed tomography	15 (65.2)
Ultrasonography	8 (34.8)

*Mean±SD, **Median (min-max)
†CAD: coronary artery disease, CHF: congestive heart failure, ASA: American Society of Anesthesiologists, BMI: body mass index

Table 2. Characteristics of patients related to surgery

Characteristic	N=23	Number (percentage)
Surgery		
Open appendectomy		13 (56.5)
Laparoscopic appendectomy		7 (30.4)
Right hemicolectomy		3 (13.0)
Intraoperative finding		
Acute phlegmonous appendicitis		14 (60.9)
Acute perforated appendicitis		5 (21.8)
Palpable mass		2 (8.7)
Plastrone appendicitis		1 (4.3)
Mucinous acid/pseudomyxoma peritonei		1 (4.3)
Complementary surgery		5 (21.7)
Right hemicolectomy+cytoreductive surgery+HIPEC		3 (13.0)
Right Hemicolectomy		1 (4.3)
Cytoreductive surgery+HIPEC		1 (4.3)

Table 3. Characteristics of patients related to the tumors

Characteristic	N	Number (Percentage)
Histopathology		
Sessile serrated adenoma	23	7 (30.4)
LAMN		6 (26.1)
Mucinous adenocarcinoma		4 (17.4)
NET		4 (17.4)
Tubulovillous adenoma		1 (4.3)
Signet ring cell mucinous adenocarcinoma		1 (4.3)
Tumor diameter (mm)	23	28 (5-55)
Tumor localization		
Distal	23	9 (39.1)
Proximal		8 (34.8)
Median		6 (26.1)
Degree of adenoma dysplasia		
Low	8	8 (100)
Grade		
Low	15	11 (73.3)
Moderate		1 (6.7)
High		3 (20.0)
Differentiation		
Good	9	5 (55.6)
Moderate		1 (11.1)
Poor		3 (33.3)

LAMN: low-grade appendiceal mucinous neoplasm, NET: neuroendocrine tumor

Table 4. Demographic, clinical, and histopathological characteristics of all patients

No	Gender	Age	Symptom duration (days)	Imaging	ASA	Surgery	Histopathology	Tumor diameter (mm)	Tumor localization
1	Female	65	2	USG	II	O	SSA	25	Median
2	Female	72	3	CT	III	O	SSA	28	Proximal
3	Female	68	2	CT	III	O	SSA	30	Proximal
4	Female	46	3	CT	II	O	SSA	18	Distal
5	Female	77	4	USG	III	LA	SSA	35	Proximal
6	Male	39	2	CT	I	O	SSA	20	Proximal
7	Male	44	2	CT	II	LA	SSA	26	Median
8	Male	48	3	USG	I	O	TVA	34	Median
9	Female	68	1	USG	II	RH	LAMN	42	Distal
10	Male	53	2	USG	I	LA	LAMN	30	Median
11	Male	77	4	CT	III	RH	LAMN	45	Distal
12	Female	84	10	CT	III	LA	LAMN	20	Proximal
13	Female	71	2	CT	II	LA	LAMN	36	Distal
14	Male	54	2	USG	I	RH	LAMN	25	Distal
15	Female	60	5	CT	II	O	MA	33	Proximal
16	Female	78	7	CT	II	O	MA	16	Distal
17	Female	74	3	CT	III	LA	SRMA	44	Proximal
18	Male	46	2	CT	II	O	MA	55	Median
19	Female	61	3	CT	III	O	MA	38	Proximal
20	Male	24	2	USG	I	LA	NET	5	Median
21	Female	33	1	USG	I	O	NET	11	Distal
22	Female	41	3	CT	II	O	NET	8	Distal
23	Female	50	2	CT	II	O	NET	17	Distal

*USG: ultrasonography, CT: computed tomography, O: open appendectomy, LA: laparoscopic appendectomy, RH: right hemicolectomy, SSA: sessile serrated adenoma, LAMN: low-grade appendiceal mucinous neoplasm, TVA: tubulovillous adenoma, MA: mucinous adenocarcinoma, SRMA: signet ring cell mucinous adenocarcinoma, NET: neuroendocrine tumor

Discussion

Appendectomy surgeries performed due to the preliminary diagnosis of acute appendicitis are among the most common procedures in emergency abdominal surgery. Appendiceal neoplasms usually do not show signs before surgery and are detected in histopathological examination. They are rarely defined intraoperatively in 0.7 to 5% of patients [6,7]. They often present with the clinical characteristics of acute appendicitis; however, they may also develop as intestinal obstruction or pelvic mass, and non-specific symptoms such as fatigue, chronic abdominal pain, and early saturation may be symptoms of advanced disease [8].

The incidence of appendiceal neoplastic lesions has been reported at variable rates in different studies. The incidence was found as 1.06% in the study of Yildirim et. al on 2.821 patients

[1] and 0.74% in the study of Lee et al. on 3.744 patients [7]. Contrary to the studies reporting that neuroendocrine tumors are the most common lesions among appendix neoplasms [9,10], the literature also contains studies reporting that appendiceal mucinous neoplasms are more common [3,11]. In our study, 23 (1.08%) of the 2,124 patients screened had appendiceal tumors, and 11 (47.8%) patients were diagnosed with appendiceal mucinous neoplasm (LAMN, mucinous adenocarcinoma).

The term mucocoele, which means the cystic dilatation of the appendix with mucinous material, is currently referred to as appendiceal mucinous neoplasm. Appendiceal mucinous neoplasms (AMNs) include a heterogeneous group of diseases that constitute less than 1% of all cancers and have variable malignant potential [12]. The World Health Organization (WHO) classifies most noninvasive epithelial lesions as low-grade appendiceal mucinous neoplasms (LAMNs), and

LAMNs are histopathologically expressed as well-differentiated adenomas with the potential to spread outside the appendix. High-grade appendiceal mucinous neoplasms (HAMN) share some histological features with LAMN; however, they exhibit more aggressive biological behaviors.⁴ The Peritoneal Surface Oncology Group International (PSOGI) has also classified mucinous neoplasms as serrated polyps, LAMNs, HAMNs, and mucinous adenocarcinoma (with or without signet ring cells) [13]. Perforation of the appendiceal mucinous neoplasms and the development of diffuse mucinous acid throughout the peritoneal cavity are referred to as pseudomyxoma peritonei (PMP). PMP has a clinical characteristic with high recurrence after treatment, and the 10-year overall survival (OS) rate after surgery has been reported as 63% [14]. In the treatment approach, appendectomy, including mesoappendix for LAMN without perforation or peritoneal mucinous spread, has been proven to provide low recurrence rates [15,16]. Even if appendectomy alone is sufficient for HAMN, which lacks infiltrative invasion similar to adenocarcinoma but exhibits high-grade cytology, it is recommended to perform the histological analysis of the entire material and consider right hemicolectomy in the presence of possible invasive adenocarcinoma [4]. Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) provide survival advantages in selected patients with diffuse peritoneal involvement. In our study, CRS and HIPEC options were preferred in patients with LAMN and pseudomyxoma peritonei findings and patients with mucinous adenocarcinoma and diffuse peritoneal carcinomatosis.

Appendectomy is sufficient in neuroendocrine tumors with a diameter of less than 1 cm (NET) that are proximal to the appendix and not distant metastatic, including the mesoappendix, and long-term disease-free survival has been reported to be almost 100% in these patients [17]. Formal right hemicolectomy is recommended for tumors larger than 2 cm in diameter [18]. In addition to size, the mitotic index and Ki-67 index are among the histological parameters to be considered in the surgical decision. Appendiceal NETs are usually localized at the distal end of the appendix; however, the scope of surgery may need to be expanded in patients with localization in the base and positivity at the surgical margin after appendectomy [19]. All patients with NET included in our study had a tumor diameter of less than 2 cm, complied with the differentiated 'NET, G1' terminology in the 2019 WHO classification, and had been treated with appendectomy alone.

Appendiceal sessile serrated polyps are precursor adenomatous lesions proximal to the muscularis mucosa and lamina propria with malignant potential, have different histopathological features compared to colorectal serrated polyps, and undergo malignant transformation through different pathways with the conventional 'adenoma-carcinoma sequence' [20]. In addition, colonoscopic examination is recommended in patients with appendix sessile serrated lesions since the incidence of synchronous colorectal lesions is approximately four times higher compared to the overall

population [21]. In our study, appendectomy was curatively sufficient in patients who had undergone appendectomy due to the preliminary diagnosis of acute appendicitis and reported as sessile serrated adenoma with low dysplasia in histopathology; however, no colonoscopic examination data about the patients were available.

The retrospective design of the study, relatively small patient population, and heterogeneous population due to the fact that the patients had not been operated by a single surgeon could be considered among the main limitations.

Conclusion

Appendiceal neoplastic lesions constitute a highly heterogeneous group, which usually present the clinical characteristics of acute appendicitis secondary to luminal obstruction and are diagnosed in the postoperative process unless they form a massive mass lesion. Appendectomy is sufficient in many patients; however, it should be remembered that the surgical procedures can vary according to the histological subgroup.

Conflict of Interests

The authors declare that there is no conflict of interest in the study.

Financial Disclosure

The authors declare that they have received no financial support for the study.

Ethical Approval

This study was approved by University of Health Sciences Gülhane Training and Research Hospital Clinical Research Ethics Committee (Date: June 07, 2023, Decision No:2023/127).

References

1. Yıldırım E, Kegin M, Özdemir M, et al. Neoplasms of the appendix: Single institution and ten-year experiences results. *Ulus Travma Acil Cerrahi Derg.* 2022;28:352-60.
2. Hancerliogullari O, Kahraman SD, Peker YS, et al. Our three year clinical experience at appendiceal incidental neoplasms and management of appendiceal tumors. *J Clin Exp Pathol.* 2016;5:260.
3. Tajima T, Tajiri T, Mukai M, et al. Single-center analysis of appendiceal neoplasms. *Oncol Lett.* 2018;15:6393-9.
4. Glasgow SC, Gaertner W, Stewart D, et al. The American Society of Colon and Rectal Surgeons, clinical practice guidelines for the management of appendiceal neoplasms. *Dis Colon Rectum.* 2019;62:1425-38.
5. Young S, Sueda SK, Hotta M, et al. Surgical management of appendiceal mucinous neoplasm: Is appendectomy sufficient?. *J Surg Oncol.* 2020;122:1173-8.
6. Deans GT, Spence RA. Neoplastic lesions of the appendix. *Br J Surg.* 1995;82:299-306.
7. Lee WS, Choi ST, Lee JN, et al. A retrospective clinicopathological analysis of appendiceal tumors from 3,744 appendectomies: a single-institution study. *Int J Colorectal Dis.* 2011;26:617-21.
8. Moris D, Tsimigras DI, Vagios S, et al. Neuroendocrine neoplasms of the appendix: a review of the literature. *Anticancer Res.* 2018;38:601-11.
9. Connor SJ, Hanna GB, Frizelle FA. Appendiceal tumors: retrospective clinicopathologic analysis of appendiceal tumors from 7,970 appendectomies. *Dis Colon Rectum.* 1998;41:75-80.

10. Raoof M, Dumitra S, O'Leary MP, et al. Mesenteric lymphadenectomy in well differentiated appendiceal neuroendocrine tumors. *Dis Colon Rectum*. 2017;60:674-81.
11. Toprak S, Sönmez RE, Büyük M, et al. Surgical management of appendix tumors: a single-center review of 15 years. *J Ist Faculty Med*. 2022;85:312-20.
12. Shaib WL, Assi R, Shamseddine A, et al. Appendiceal mucinous neoplasms: diagnosis and management. *Oncologist*. 2017;22:1107-16. Erratum in: *Oncologist*. 2018;23:137.
13. Fish R, Renehan AG, Punnett G, et al. Referral and treatment pathways for pseudomyxoma peritonei of appendiceal origin within a national treatment programme. *Colorectal Dis*. 2018;20:888-96.
14. Carr NJ, Cecil TD, Mohamed F, et al.; Peritoneal surface oncology group international. A consensus for classification and pathologic reporting of pseudomyxoma peritonei and associated appendiceal neoplasia: the results of the Peritoneal Surface Oncology Group International (PSOGI) modified delphi process. *Am J Surg Pathol*. 2016;40:14-26.
15. Fournier K, Rafeeq S, Taggart M, et al. Low-grade appendiceal mucinous neoplasm of uncertain malignant potential (LAMN-UMP): prognostic factors and implications for treatment and follow-up. *Ann Surg Oncol*. 2017;24:187-93.
16. Morano WF, Gleeson EM, Sullivan SH, et al. Clinicopathological features and management of appendiceal mucocoeles: a systematic review. *Am Surg*. 2018;84:273-81.
17. Mullen JT, Savarese DM. Carcinoid tumors of the appendix: a population-based study. *J Surg Oncol*. 2011;104:41-4.
18. Pape UF, Niederle B, Costa F, et al.; Vienna Consensus Conference participants. ENETS consensus guidelines for neuroendocrine neoplasms of the appendix (excluding goblet cell carcinomas). *Neuroendocrinology*. 2016;103:144-52.
19. Moertel CG, Weiland LH, Nagorney DM, Dockerty MB. Carcinoid tumor of the appendix: treatment and prognosis. *N Engl J Med*. 1987;317:1699-701.
20. Rossi A, Maloney Patel N. Appendiceal neoplasms-a practical guide. *J Surg Oncol*. 2023;127:1300-5.
21. van Herwaarden YJ, Madani A, van der Post RS, et al. Incidental diagnosis of serrated polyp in the appendix warrants colonoscopy to screen for colorectal neoplasia. *Br J Surg*. 2021;108:e373-e374.