

ORIGINAL RESEARCH



Incidental appendiceal neoplasias: ten years' experience with 1,642 patients

Server Sezgin Uludag^{1,*}, Nazim Gures², Abdullah Kagan Zengin¹

¹Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of General Surgery, İstanbul, Turkey

²Balikesir Atatürk City Hospital, Department of General Surgery, İstanbul, Turkey

***Correspondence**

sszgn.uludag@gmail.com

(Server Sezgin Uludag)

Abstract

Background: Acute appendicitis is the most common surgical emergency. In this study, we investigated the rate of neoplasia among patients who underwent an appendectomy in our center, a large Tertiary Care Teaching Hospital. **Methods:** We retrospectively reviewed 1,642 cases of appendectomies performed between 2007 and 2017. In this study, the data included demographic data, operative and pathological findings, and additional procedures following the appendectomy. **Results:** Of the 1,642 appendectomies, 1,294 were laparoscopic, and 348 were open procedures. Appendiceal neoplasia was encountered in the examination of appendix specimens taken from 20 patients. Sessile serrated adenoma (SSRA) was found in seven patients, neuroendocrine tumor (NET) in six patients, low-grade mucinous neoplasia (LGMN) in four patients, mucinous cystadenoma (MCA) in two patients, and diffuse adenoma (DA) in one patient. Two patients underwent right hemicolectomy due to positive surgical margins from previous surgeries. Colonoscopy and computed tomography (CT) control were performed on all neoplasia patients during the postoperative period, and no additional pathology was seen. **Conclusions:** Although the probability of neoplasia after appendectomy is low, it should be considered. Adenomas and neuroendocrine tumors seem to be the most common neoplasias that are incidentally encountered in appendectomy specimens.

Keywords

Acute appendicitis; Appendiceal neoplasia; Sessile serrated adenoma; Neuroendocrine tumor

1. Introduction

Acute appendicitis is the inflammation of the appendix, and the appendix is an essential organ since it is considered the most common emergency surgical pathology worldwide [1]. The pathogenesis of appendicitis is still not fully understood. Multiple factors, such as mechanical, infectious and genetic issues, may cause inflammation of the appendix [2]. Appendicitis may be simple or complicated. The simple form does not cause inflammation to surrounding tissues, while in complex appendicitis, inflammation may lead to gangrene or perforation, with or without the development of an abscess. Perforation occurs in 13-20% of patients presenting with acute appendicitis [3]. Apart from open and standard laparoscopic approaches, single-incision laparoscopic surgery and the natural orifice transluminal endoscopic surgery (NOTES) procedures are the surgical techniques used in the treatment of acute appendicitis [4].

Appendiceal neoplasias, classified as mucinous and non-mucinous, are found in appendix specimens with rates of 0.9-1.4%, and the incidence rates are increasing [5]. Thus, in this 1,642-case series, we sought to determine the rate of

appendiceal neoplasia and the types of neoplasia that were seen in appendectomy specimens.

2. Methods

We retrospectively reviewed 1,642 cases of appendectomies performed between 2007 and 2017. The present study included patients over 18 years of age who underwent appendectomy with a preliminary diagnosis of appendicitis. Patients with incidental appendix neoplasias were studied. The male/female ratios and open-laparoscopic procedure rates were determined. The demographic characteristics and pathological findings of 20 cases of appendiceal neoplasia were revealed. Additional follow-up and interventions were also reviewed for these 20 patients.

3. Results

Of the 1,642 reviewed patients, 553 were women and 1,089 were men. Moreover, 1,294 of the cases were performed laparoscopically and 348 cases of appendectomy were performed using open surgery (Table 1).

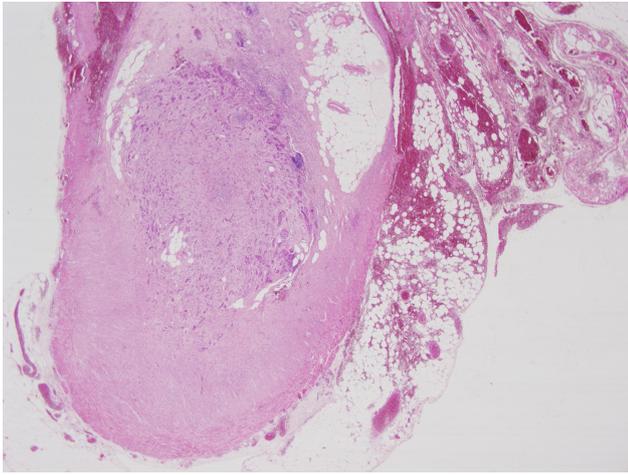


FIGURE 1. X20, hematoxylin-eosin staining, neuroendocrine tumor.



FIGURE 2. Operative image of appendiceal mucinous cystadenoma (MCA).

TABLE 1. Demographics and Operation Types of the Appendectomies (All Series)

	Female	Male
Patient Age (Years; Mean \pm SD)	23.1 \pm 18.2	25.8 \pm 7.6
LA (%)	52.1	70.18
OA (%)	47.9	29.82
Total (%)	100	100

LA: Laparoscopic appendectomy; OA: open appendectomy.

All 20 patients with appendiceal neoplasia were diagnosed using ultrasound and clinical examination, and all cases were diagnosed preoperatively as acute appendicitis. There was

TABLE 2. Demographics of Neoplasia-Detected Patients, Patients' Previous Histories, and Pathology Results of the Specimens

Patient Age	M/F	Previous History	Pathology Result
40	F	None	SSRA
53	M	RA, DUC	LGMN
57	M	None	SSRA
33	M	ARF	SSRA
44	F	ITP	LGMN
59	F	UC	SSRA
44	F	EC	NET (WHO Grade 1)
22	F	None	NET (WHO Grade 1)
32	M	None	DA (Traditional)
25	F	None	NET (WHO Grade 1)
62	M	HT	SSRA
25	F	None	NET (WHO Grade 1)
63	M	None	MCA
62	F	HT	MCA
60	F	DM, HT	LGMN
21	F	Allergy	NET (WHO Grade 1)
71	M	AS, AF, BPH	SSRA
69	M	CAD	SSRA
48	M	None	LGMN
37	M	None	NET (WHO Grade 1)

SSRA: Sessile serrated adenoma; LGMN: low-grade mucinous neoplasia; NET: neuroendocrine tumor; MCA: mucinous cystadenoma; DA: diffuse adenoma; RA: rheumatoid arthritis; DUC: drug-induced colitis; ARF: acute rheumatoid fever; ITP: idiopathic thrombocytopenic purpura; UC: ulcerative colitis; EC: endometrial carcinoma; DM: diabetes mellitus; HT: hypertension; AS: ankylosing spondylitis; AF: atrial fibrillation; BPH: benign prostatic hyperplasia; CAD: coronary artery diseases.

no preoperative evidence that the patients had appendiceal neoplasia. An appendectomy was performed for all cases. Seventeen patients underwent laparoscopic surgery, while three patients underwent open surgery. The distribution of intraoperative staging was 40% catarrhal, 50% phlegmonous, and 10% gangrenous stages and perforation two patients with sessile serrated adenoma (SSRA).

In the pathological examinations performed after the appendectomies, appendiceal neoplasia was found in 20 patients. Their mean age was 45.65 years; 10 (50%) of the patients were women, and 10 (50%) were men. SSRA was found in seven patients (35%), neuroendocrine tumor (NET) in six patients (30%) (Fig. 1), low-grade mucinous neoplasia (LGMN) in four patients (20%), mucinous cystadenoma (MCA) in two patients (10%), and diffuse adenoma (DA) in one patient (5%; Table 2). Tumors were located in the distal part of the appendix in 80% of cases, at the proximal end in 5% of cases, and in the middle part in 15% of cases. Tumors were smaller than 1 cm in 75% of cases, between 1 and 2 cm in 20% of cases, and larger than 2 cm in 5% of cases. The tumor penetration depth was in the submucosa or muscular layer in 60% of cases, in the serosa in 25% of cases, and in the mesoappendix in 15% of cases. Detailed analysis of appendix NET patients is also shown in Table 3, and an operational image of a patient with appendiceal MCA is shown in Fig. 2.

TABLE 3. Detailed Analysis of Appendiceal Neuroendocrine Tumor (NET) Patients

Age	Gender	Diagnosis	Diameter	Therapy	Involvement	Surgical border	Mesoappendiceal invasion	Lymphovascular invasion	Follow up (months)
44	F	NET (WHO Grade 1)	1	Appendectomy	Serosa	Negative	None	None	32
22	F	NET (WHO Grade 1)	1.1	Appendectomy–right hemicolectomy	Subserosa	Positive	None	None	21
25	F	NET (WHO Grade 1)	0.4	Appendectomy	Subserosa	Negative	None	None	96
25	F	NET (WHO Grade 1)	0.6	Appendectomy	Serosa	Negative	Positive	None	86
21	F	NET (WHO Grade 1)	0.3	Appendectomy	M. propria	Negative	None	None	14
37	M	NET (WHO Grade 1)	0.7	Appendectomy	M. propria	Negative	None	None	18

In 18 patients, neoplasia was limited to the appendix, and no additional surgical intervention was required. Two patients (10%; one patient with MCA and one patient with NET) underwent right hemicolectomy due to positive surgical margins from previous surgery. Colonoscopy, abdominal, and chest computed tomography (CT) controls were performed on all patients during the postoperative period. Chromogranin A (NET) and tumor marker levels (epithelial tumors) were measured. All the patients were included in a routine follow-up program. The patients were followed up for a mean period of three years (0.6-5 years) with abdominal ultrasonography and gallium 68 positron emission tomography (PET)-CT in terms of recurrences. Recurrences were not detected in any of the patients.

4. Discussion

Acute appendicitis, which causes the most frequent surgical emergency operation, has been treated with the open operation until Karl Semm performed the first laparoscopic appendectomy in 1980. Nowadays, laparoscopic appendectomy is the preferred method of treating acute appendicitis due to advantages, such as less pain, shorter hospitalization time, and a quick return to work [1, 4, 6].

There are approximately 300,000 appendectomies performed annually in the United States. The rate of neoplasia, which is showing an increasing trend, is 0.9-1.4% [5, 7]. The 1.12% rate in our series is consistent with this. The appendix may be epithelial-derived adenoma and adenocarcinoma, as well as non-epithelial NET and lymphoma. Epithelial tumors are also classified as mucinous and non-mucinous, and LGMN, also seen in our series, is more common [5, 7].

NET, formerly called carcinoid tumor, is the most common neoplasia of the appendix. However, there has been a tendency toward epithelial neoplasia in recent years [5, 7, 8]. Similar to the 0.33% rate of Eğin *et al.*'s [8] large appendectomy series, NET was observed in our series at a rate of 0.36%. Senel *et al.* [9] studied 13,863 appendectomy specimens, and they also observed NET, with a 0.20% ratio (29 patients). While appendectomy is curative for small appendiceal NET (< 2 cm) with an excellent prognosis [10], six patients underwent right hemicolectomy due to the large tumor size or surgical margin positivity in Şenel *et al.*'s [9] study. In addition, it was noticed in our study that NET was seen at a younger age than epithelial

neoplasias.

Large intestine polyps showing a serrated morphology are divided into three groups as follows: hyperplastic polyps, SSRAs and traditional adenomas. SSRAs are mostly seen in the colon and rectum, but they are also observed in the appendix [11, 12]. There have been studies stating that SSRAs may cause acute appendicitis, especially in patients over 30 years of age. In our series, SSRA was observed in seven patients older than 30 years, with the eldest being 71 years old [7, 13]. Only one patient had traditional adenoma, which also had the malign potential [11–13].

Based on the work of Misdraji *et al.* [14] in 2003, as outlined in the World Health Organization (WHO) Classification of Digestive System Tumors (2019), malignant mucinous neoplasms of the appendix can be divided into two categories as follows: LGMN (characterized by a low-grade neoplastic mucinous epithelium with extracellular mucin and thrusting tumor margins) and mucinous adenocarcinoma (characterized by infiltrative invasion). LGMNs are commonly incidental in the appendix. Additional interventions (e.g., cytoreductive surgery) may be required according to the histological grade and degree of dissemination in the case of perforation and peritoneal dissemination (pseudomyxoma peritonei) [15]. In addition, radical appendectomy instead of right hemicolectomy is recommended for all high-stage epithelial neoplasias of the appendix in the literature [16].

Appendiceal MCAs are a type of appendix mucocoeles; pathological distinctions from cystadenocarcinomas may be challenging [17]. Although appendiceal MCAs are rare neoplasms, they are reported at relatively high rates in some appendectomy series [18, 19]. Since appendectomy is curative, right hemicolectomy should be performed when there is suspicion of cystadenocarcinoma or the presence of free perforation [17, 19]. In the present series, when there were a proximal adenoma placement and surgical margin positivity, as well as a suspected case of MCA for malignancy, right hemicolectomy was performed.

5. Conclusions

Since appendectomy is one of the most common emergency procedures performed worldwide, the number of appendectomy pathologic specimens increases accordingly. As a result, pathologists are faced with an increased number of specimen

observations. These specimens should be carefully studied by the pathologists since rare neoplasias of the appendix may be present. This is important for the prognosis of the patient and may require additional treatment modalities. Any delay in treatment modality may directly affect the outcome of the patient since the prognosis of the patient depends on whether a tumor is present.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethics approval was not required for this study.

AUTHOR CONTRIBUTIONS

S.S.U., N.G. and A.K.Z. actively involved in the compilation of the data and drafting of this article. All authors read and approved the final manuscript.

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CONFLICT OF INTEREST

All authors declare no conflict of interest and financial relationships.

CONSENT STATEMENT

Written informed consent was not necessary because no patient data have been included in the manuscript.

HUMAN RIGHTS STATEMENT

This study was conducted according to the World Medical Association Declaration of Helsinki.

AVAILABILITY OF DATA AND MATERIALS

The materials described in the manuscript will be freely available to any scientist wishing to use them for non-commercial purposes without breaching participant confidentiality.

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