ORIGINAL ARTICLE

Carcinoid tumors of appendix presenting as acute appendicitis

Bora Barut, M.D., Fatih Gönültaş, M.D.

Department of General Surgery, İnönü University Faculty of Medicine, Malatya-*Turkey*

ABSTRACT

BACKGROUND: We aim to present the data of patients who underwent appendectomy due to acute appendicitis, and incidental carcinoid tumor was detected on pathology.

METHODS: Retrospective analysis of the patient charts between January 1999 and September 2018 were performed.

RESULTS: 2778 appendectomy was performed due to acute appendicitis. Appendiceal carcinoid tumor was detected in 12 (0.43%) patients. Eight patients were (66.7%) female. Median age 37.5 years (range: 21–60). The median tumor size was 0.7 cm (range: 0.1–2.5). No perforation was detected. Eleven patients underwent appendectomy, and one patient had right hemicolectomy. The median follow-up period was 41.5 months (range: 22–49). There were no recurrences.

CONCLUSION: Appendix carcinoid tumors are quite rare, usually asymptomatic and diagnosed incidentally on histopathological examination after appendectomy. The treatment of carcinoid tumors of the appendix is directly related to the tumor size, localization, presence of lymphovascular and mesoappendix invasion, mitotic activation rate and level of Ki67. Thus, it is important to follow the histopathological results after appendectomy. The prognosis of appendix carcinoid tumors is very good if the appendix is non-perforated.

Keywords: Acute appendicitis; appendectomy; carcinoid tumor.

INTRODUCTION

Primary appendix neoplasm is a rare pathology found in 0.5-1% of all appendectomy specimens. Carcinoid tumors represent more than 50% of appendix neoplasms that demonstrate no specific clinical presentation and present as acute appendicitis. They are usually diagnosed incidentally after appendectomy. Most carcinoid tumors are located at the tip of the appendix, and they are usually less than1 cm but rarely larger than 2 cm in diameter.[1,2] In the present study, we reported a series of 12 appendiceal carcinoid tumors detected after emergency appendectomy at our clinic.

MATERIALS AND METHODS

Patients who had undergone appendectomy for acute appendicitis at Inonu University, Department of General Surgery between January 1999 and September 2018 were reviewed retrospectively. Patients with a diagnosis of carcinoid tumor were analysed. Age, gender, symptoms, physical examination findings, follow-up times of the patients, preoperative abdominal ultrasonography findings, the indication for operation and the type of the operation were evaluated. Location of the tumor, tumor diameter, depth of invasion, histopathological cell type, mitotic activation rate and level of Ki67 of the tumor were defined.

Statistical Analysis

For statistical evaluation, descriptive analysis was used. For homogenous distributions, we used mean and standard deviation, and for heterogeneous distributions we preferred median and range.

RESULTS

During the study period, a total of 2778 patients underwent an emergency appendectomy. The patients who underwent

Cite this article as: Barut B, Gönültaş F. Carcinoid tumors of appendix presenting as acute appendicitis. Ulus Travma Acil Cerrahi Derg 2019;25:510-513.

Address for correspondence: Bora Barut, M.D.
İnönü Üniversitesi Tıp Fakültesi, Genel Cerrahi Anabilim Dalı, Malatya, Turkey
Tel: +90 422 - 341 06 60 / 6402 E-mail: borabarut@mynet.com

Ulus Travma Acil Cerrahi Derg 2019;25(5):510-513 DOI: 10.5505/tjtes.2018.99569 Submitted: 19.11.2018 Accepted: 27.12.2018 Online: 22.08.2019

appendectomy in addition to other operations were excluded from this study. Twelve of which (0.43%) were found to have histological evidence of carcinoid tumor of the appendix. These 12 patients comprised 4 (33.3%) males and 8 (66.7%) females, with a median age of 37.5 years (range, 21–60 years). All patients presented with clinical and radiological appendicitis. Ten patients had localized (right lower quadrant) pain, and the other two patients had generalized pain. Tenderness and rebound were detected in the right lower quadrant in all patients. Ultrasonography (USG) was used as radiological imaging. Demographic data, symptoms, physical examination findings, follow-up time of patients, and preoperative abdominal ultrasonography findings and the indication for operation are summarized in Table 1.

Histologically, in 10 (83.4%) patients tumors were located at the tip of the appendix, in one patient it was in the middle, and the other one was at the base of the appendix, with a median diameter of 0.7 cm (range: 0.1–2.5 cm). While in 4 (33.3%) patients, the mesoappendix was invaded. Submucosal involvement was demonstrated histologically in six (50%) patients and the invasion of muscularis propria was detected in the other two (16.7%) patients. Mitotic index and Ki67 levels were <2 in all patients.

Open appendectomy was performed in all patients. In one patient, who had a diameter of 2.5 cm tumor and mesoappendix invasion, right hemicolectomy was performed in the second operation. In this patient, cecal tumor infiltration was detected on histopathological examination. The other two patients with a tumor diameter of 1.2 and 1 cm who had mesoappendix invasion did not accept right hemicolectomy. In these two patients, the follow-up time without recurrences or metastasis was 22 and 42 months, respectively. The median follow-up period was 41.5 months (range: 22–49). The histopathologic results and operation types of patients were summarized in Table 2.

DISCUSSION

Appendiceal tumors are rare clinical condition and rarely associated with the manifestation of clinical symptomatology. Thus, they are detected incidentally either during surgery or generally after pathological examination of a resected appendix specimen. The most often type of appendiceal malignancy is a carcinoid tumor that accounts for about 60% of all appendiceal tumors. The incidence of appendiceal carcinoid tumor is 0.30%–2.27% in patients undergoing an appendectomy.[3] In this study, none of the patients had a suspicion of appendix carcinoid tumor preoperatively and the incidence of appendiceal carcinoid tumor was 0.43% in patients who underwent an emergency appendectomy.

Table 1. Demographic, clinical, radiological findings and follow-up time of patients

No	Age	Gender	Symptoms	Preoperative diagnosis	Preoperative radiology (USG)	Follow-up time (month)
1	37	Female	Localized pain, anorexia, nausea and vomoting	Accute appendicitis	Accute appendicitis	46
2	23	Female	Localized pain, anorexia	Accute appendicitis	Accute appendicitis	48
3	38	Male	Localized pain, anorexia, nausea and vomoting	Accute appendicitis	Accute appendicitis	34
4	56	Female	Localized pain, anorexia, nausea and vomoting	Accute appendicitis	Accute appendicitis	42
5	33	Male	Localized pain, anorexia	Accute appendicitis	Accute appendicitis	38
6	40	Male	Genaralized, anorexia, nausea and vomoting	Accute appendicitis	Accute appendicitis	33
7	41	Female	Genaralized, anorexia, nausea and vomoting	Accute appendicitis	Accute appendicitis	36
8	28	Female	Localized pain, anorexia	Accute appendicitis	Accute appendicitis	49
9	28	Female	Localized pain, anorexia	Accute appendicitis	Accute appendicitis	44
10	60	Female	Localized pain, anorexia, nausea and vomoting	Accute appendicitis	Accute appendicitis	22
11	21	Male	Localized pain, anorexia	Accute appendicitis	Accute appendicitis	42
12	52	Female	Localized pain, anorexia, nausea and vomoting	Accute appendicitis	Accute appendicitis	41

USG: Ultrasonography.

Table 2. The histopathologic results and operation types of patients

No	Pathology	Tumor localizations	Depth of invasion	Tumor size (cm)	Mitosis	Ki67	Operation type
1	Classical carcinoid tumor	Tip	Submucosa	1.3	<2	<2	Open appendectomy
2	Classical carcinoid tumor	Tip	Muscularis propria	0.2	<2	<2	Open appendectomy
3	Classical carcinoid tumor	Middle	Submucosa	0.5	<2	<2	Open appendectomy
4	Classical carcinoid tumor	Tip	Submucosa	0.4	<2	<2	Open appendectomy
5	Classical carcinoid tumor	Tip	Submucosa	0.1	<2	<2	Open appendectomy
6	Classical carcinoid tumor	Tip	Submucosa	0.7	<2	<2	Open appendectomy
7	Classical carcinoid tumor	Base	Mesoappendix	2.5	<2	<2	Right hemicolectomy
8	Classical carcinoid tumor	Tip	Submucosa	0.5	<2	<2	Open appendectomy
9	Classical carcinoid tumor	Tip	Mesoappendix	0.8	<2	<2	Open appendectomy
10	Classical carcinoid tumor	Tip	Mesoappendix	1.0	<2	<2	Open appendectomy
11	Classical carcinoid tumor	Tip	Mesoappendix	1.2	<2	<2	Open appendectomy
12	Classical carcinoid tumor	Tip	Muscularis propria	1.3	<2	<2	Open appendectomy

The median age (37.5 years) of the patient in our study is in agreement with a report of a consecutive series of 1570 appendectomies, where the mean age of appendiceal carcinoid tumor patients was 42.2 years.[4] Appendiceal carcinoid tumors are generally diagnosed more often among female than in male patients.[5–7] Similar to these studies, our study showed that the female to male ratio was 2:1.

Most of the appendiceal carcinoid tumor is located at the tip of the appendix, and majority of the cases are smaller than 1 cm. The malign potential of carcinoid tumors is directly related to tumors size, and metastasis is very rare for the tumors smaller than 1 cm.[8] In the present study, the tumors were localized at the tip of the appendix at a rate of 83.4% with a median diameter of 0.7 cm (range: 0.1–2.5).

Generally, appendiceal carcinoid tumors are asymptomatic, difficult to diagnose because of no classic symptoms specifically attributed to a tumor, presented as acute appendicitis and incidentally found on histopathological examination.[9,10] In our study, also all patients were diagnosed with acute appendicitis preoperatively, however, appendiceal carcinoid tumor was detected on histopathological examination.

The prognosis and treatment of appendiceal carcinoid tumors are associated with tumor size and location, depth of invasion, mitotic and Ki67 index, presence of perineural and lymphovascular invasion. The tumor with a diameter >2 cm is rare (<10%), but has up to 40% risk for systematic dissemination. In these tumors, right hemicolectomy should be performed.[11] Because of the long-term risk of recurrence, right hemicolectomy should also be considered in carcinoids 1–2 cm in size, if the following factors are present: involvement of the mesoappendix, demonstrable angioinvasion, apparent high proliferative index and Ki67 level, tumor located at the base of the appendix with positive margins, and in younger patients with positive lymph nodes. If tumor size <1 cm, appendectomy is enough for a cure.[12,13] In the present study, in seven patients who had <1 cm tumor size and in 2 patients had >1 cm tumor size without mesoappendix invasion. Thus, appendectomy was performed. In one patient with 2.5 cm tumor and mesoappendix invasion, right hemicolectomy was performed, but two patients with >1 cm tumor and mesoappendix invasion did not accept right hemicolectomy. However, in these two patients, no recurrence or metastasis was not detected during follow-up of 22 and 42 months, respectively.

In conclusion, this study reports the frequency and outcomes of incidentally detected appendiceal carcinoid tumors in patients who underwent appendectomy for clinically suspected acute appendicitis. Appendiceal carcinoid tumor is a rare clinical entity and usually presented as acute appendicitis and generally diagnosed incidentally on histopathological examination. Small appendiceal carcinoid tumors (<1 cm) have an excellent prognosis after an appendectomy, while those >2 cm require hemicolectomy. Hemicolectomy should be considered in carcinoid tumors 1–2 cm in size if the mesoappendix is involved, angioinvasion is demonstrable, a high proliferative index and Ki67 level is apparent, and tumors are located at the base of the appendix with positive margins. Thus, the results of the histopathological examination are so important for deciding on additional surgical treatment and providing curative resection. Our results represent incidental carcinoid tumors, therefore; the stage of the disease was rather early, and the results were good without a major operation. Therefore, early diagnosis and low threshold for appendectomy in any individual from any age group are essential to obtain a cure.

Conflict of interest: None declared.

REFERENCES

1. Coşkun H, Bostanci O, Dilege ME, Mihmanli M, Yilmaz B, Akgün I, et al. Carcinoid tumors of appendix: treatment and outcome. Ulus Travma Acil Cerrahi Derg 2006;12:150–4.
2. Abdelaal A, El Ansari W, Al-Bozom I, Khawar M, Shahid F, Aleter A, et al. Frequency, characteristics and outcomes of appendicular neuroendocrinetumors: A cross-sectional study from an academic tertiary care hospital. Ann Med Surg (Lond) 2017;21:20–4. [CrossRef]
3. Yilmaz M, Akbulut S, Kutluturk K, Sahin N, Arabaci E, Ara C, et al. Unusual histopathological findings in appendectomy specimens from patients with suspected acute appendicitis. World J Gastroenterol 2013;19:4015–22. [CrossRef]
4. Sandor A, Modlin IM. A retrospective analysis of 1570 appendiceal carcinoids. Am J Gastroenterol 1998;93:422–8. [CrossRef]
5. Yao JC, Hassan M, Phan A, Dagohoy C, Leary C, Mares JE, et al. One hundred years after "carcinoid": epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. J Clin Oncol 2008;26:3063–72. [CrossRef]
6. Pape UF, Perren A, Niederle B, Gross D, Gress T, Costa F, et al; Barcelona Consensus Conference participants. ENETS Consensus Guidelines for the management of patients with neuroendocrine neoplasms from the jejuno-ileum and the appendix including goblet cell carcinomas. Neuroendocrinology 2012;95:135–56. [CrossRef]
7. Saylam B, Küçük ÖK, Düzgün AP, Özer MV, Coşkun F. Carcinoid tumor of the appendix: report on ten cases. Eur J Trauma Emerg Surg 2011;37:491–3. [CrossRef]
8. Cakar E, Bayrak S, Bektaş H, Colak Ş, Guneyi A, Sevinc MM, et al. Carcinoid tumor of the cecum presenting with acute appendicitis: a case report. Chirurgia (Bucur) 2015;110:171-4.
9. Alemayehu H, Snyder CL, St Peter SD, Ostlie DJ. Incidence and outcomes of unexpected pathology findings after appendectomy. J Pediatr Surg 2014;49:1390–3. [CrossRef]
10. Akbulut S, Tas M, Sogutcu N, Arikanoglu Z, Basbug M, Ulku A, et al. Unusual histopathological findings in appendectomy specimens: a retrospective analysis and literature review. World J Gastroenterol 2011;17:1961–70. [CrossRef]
11. Moris D, Tsilimigras DI, Vagios S, Ntanasis-Stathopoulos I, Karachaliou GS, et al. Neuroendocrine Neoplasms of the Appendix: A Review of the Literature. Anticancer Res 2018;38:601–11. [CrossRef]
12. Parkes SE, Muir KR, al Sheyyab M, Cameron AH, Pincott JR, Raafat F, et al. Carcinoid tumours of the appendix in children 1957-1986: incidence, treatment and outcome. Br J Surg 1993;80:502–4. [CrossRef]
13. Stinner B, Rothmund M. Neuroendocrine tumours (carcinoids) of the appendix. Best Pract Res Clin Gastroenterol 2005;19:729–38. [CrossRef]

ORİJİNAL ÇALIŞMA - *ÖZET*

Akut apandisit gibi bulgu veren apendiks karsinoid tümörleri

Dr. Bora Barut, Dr. Fatih Gönültaş

İnönü Üniversitesi Tıp Fakültesi, Genel Cerrahi Anabilim Dalı, Malatya

AMAÇ: Bu çalışmanın amacı, kliniğimizde akut apandisit tanısıyla apendektomi yapılan ve histopatolojik inceleme sonucunda apendiks karsinoid tümörü tespit edilen hastalara ait verilerimizi sunmaktır.

GEREÇ VE YÖNTEM: Ocak 1999–Eylül 2018 tarihleri arasında akut apandisit ön tanısı ile apendektomi yapılan hastalar içinden histopatolojik olarak apendiks karsinoid tümörü tespit edilen hastaların sonuçları geriye dönük olarak incelendi.

BULGULAR: Bu tarihler arasında toplam 2778 hastaya akut apandisit tanısı ile apendektomi yapıldı. On iki (%0.43) hastada apendiks karsinoid tümörü tespit edildi. Dört (%33.3) hasta erkek, sekiz (%66.7) hasta ise kadındı. Medyan yaş 37.5 yıl (21–60) idi. Medyan tümör çapı 0.7 cm (0.1–2.5) idi. Hiçbir hastada perfore apandisit gözlenmedi. On bir (%91.7) hastaya sadece apendektomi yapılırken, bir (%8.3) hastaya sağ hemikolektomi yapıldı. Medyan takip süresi 41.5 ay (22–49) olup hiçbir hastada nüks izlenmedi.

TARTIŞMA: Apendiks karsinoid tümörleri oldukça nadir görülürler. Genellikle semptomsuz seyreder. Tanı çoğunlukla akut apandisit nedeniyle apendektomi yapıldıktan sonra histopatolojik incelenme sonucu, insidental olarak konulur. Apendiks karsinoid tümörlerinin tedavisi tümör boyutu, yerleşim yeri, lenfovasküler ve mezoapendiks invasyon varlığı, mitotik aktivasyon oranı ve Ki67 seviyesi ile doğrudan ilişkili olduğundan patoloji sonuçlarının takip edilmesi son derece önemlidir.

Anahtar sözcükler: Akut apandisit; apendektomi; karsinoid tümör.

Ulus Travma Acil Cerrahi Derg 2019;25(5):510-513 doi: 10.5505/tjtes.2018.99569