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Carcinoid tumor of appendix: Review of consecutive 5131 appendectomy

Apendiksin karsinoid tümörü: Ardışık 5131 apendektominin incelemesi

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Abstract

Aim: Appendiceal carcinoid tumor (neuroendocrine tumor) is rarely seen, and it is frequently found incidentally after evaluation of appendectomy specimen. Histopathologically, the appendiceal carcinoid tumor is usually the type of enterochromafine cell and stems from a sub-epithelial cell population that differs from the neuroendocrine tumor in other regions. Although it is often detected in appendectomy, appendiceal one is the most common type of primary malignant lesion and is detected in 0.3-0.9% of patients with appendectomy. In this study, it is intended to present an appendix carcinoid tumor series that is diagnosed incidentally after appendectomy.

Methods: 5131 appendectomy that was performed between years of 2009 and 2017 constituted the study universe. 35 (0.68%) patients diagnosed with carcinoid tumors were evaluated in the histopathological examination. The patients were recorded in terms of demographic data, clinical status, histopathology and surgical reports. Additional operations and follow-up data were noted.

Results: 21 of the 35 patients with appendiceal carcinoid tumors were males, and 14 were women. Male/Female ratio was 1.5. The mean age of the patients was 27.3±11.0. There was no difference in terms of gender and age with other appendectomy patients who diagnosed non-tumor (p=0.476 and p=0.413, respectively). The clinical presentation of the patients with all carcinoid tumors was in favor of acute appendicitis. Histopathological examination revealed simultaneous acute appendicitis in 25 (71.4%) patients.

Conclusion: The treatment of the appendiceal carcinoid tumor is controversial, but tumor size, tumor localization, surgical margin and lympho-vascular invasion are the main determining factors. The evaluation of pathological examination and the necessary additional therapies should be planned due to the fact that it is often diagnosed with incidental and is unlikely to be noticeable during surgery.

Keywords: Appendectomy, Carcinoid tumor, Right hemicolectomy

Öz

Amaç: Apendikste karsinoid tümör (nöroendokrin tümör) nadir olarak görülmekle birlikte, apendiks karsinoid tümörün sık olarak bulunduğu bir alandır. Histopatolojik olarak apendiks karsinoid tümör çoğunlukla enterokromaffin hücre tipindedir ve diğer bölgelerdeki nöroendokrin tümörden farklı olan bir subepitelyal hücre popülasyonundan kaynaklanmaktadır. Genellikle tesadüfen apendektomide tespit edilse de, apendiks primer malign lezyonunun en sık rastlanan türüdür ve apendektomi yapılan hastaların %0,3-0,9'unda saptanmaktadır. Bu çalışmada apendektomi sonrası insidental tespit edilen apendiks karsinoid tümör serisini sunmak amaçlanmıştır.

Yöntemler: Çalışma evrenini 2009-2017 yılları arasında gerçekleştirilen 5131 apendektomi olgusu oluşturdu. İncelemede karsinoid tümör saptanan 35 (%0,68) hasta değerlendirildi. Hastalar demografik veriler, klinik durum, histopatoloji, ameliyat raporları ve takipler açısından kayıt edildi.

Bulgular: Apendiks karsinoid tümör saptanan 35 hastanın 21'i erkek, 14'ü kadın olmak üzere Erkek/Kadın oranı 1,5 olarak bulundu. Hastaların yaş ortalamasının 27,3±11,0 olduğu görüldü. Tümör dışı tanı alan diğer apendektomi yapılan hastalar ile cinsiyet ve yaş açısından fark saptanmadı (sırasıyla p=0,476 ve p=0,413). Tüm karsinoid tümör saptanan hastalar için klinik tablo akut apandisit lehinde idi.

Sonuç: Apendiks karsinoid tümörün tedavisi tartışmalı olmakla birlikte tümör boyutu, tümör lokalizayonu, cerrahi sınır ve lenfovasküler invazyon ana belirleyici faktörlerdir. Sıklıkla insidental saptanan ve ameliyat esnasında fark edilme ihtimali düşük olması nedeniyle patolojik inceleme ile değerlendirme ve gerekli ek tedaviler planlanmalıdır.

Anahtar kelimeler: Apendektomi, Karsinoid tümör, Sağ hemikolektomi

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Introduction

It is considered carcinoid tumors is derived from the enterocromaffin cells (EC), which can be seen everywhere in the body, but formed as a primer in the gastrointestinal tract and the main bronchus submucosa. According to the origin of carcinoid tumors; it can be called as carcinoids of foregut, midgut and hindgut. Appendicular carcinoids are found in the group of carcinoids of the midgut. Differences of carcinoids of midgut compared to carcinoids of other origins; they are histologically different staining features, have higher serotonin content, more often cause metastases to carcinoid syndrome and less bone metastases than others [1]. Carcinoid tumors are the most common tumor of the appendix, accounting for 0.5% of the appendectomy materials. In this study, we aimed to present our experience of appendiceal carcinoid tumors under review of literature.

Materials and methods

We designed an observational study to evaluate the patients with carcinoid tumors. Records of patients who underwent appendectomy between January 1, 2009 and December 31, 2017 were retrospectively investigated. Patients with histopathological records of carcinoid tumors constituted the study group. Detailed surgery and pathological reports were recorded. Further surgery and treatment if any was also recorded. Follow-up data is investigated.

Statistical analysis

The frequency and percentage is used to present the data with categorical variables, mean ± standard deviation is used for parametric data that match the normal distribution, median and interquartile range is used for parametric data that does not conform to the normal distribution. In comparison, the t-test for parametric data, Fisher's exact test was used for categorical data. If the value of p is lower than 0.05 in the confidence range of 95%, the differences were considered statistically significant.

Results

During the study period, 5131 appendectomy was performed. 35 (0.68%) of them was diagnosed with carcinoid tumors in histopathological examination. 21 of the 35 patients with appendiceal carcinoid tumors were males, and 14 were women. Male/Female ratio was 1.5. The mean age of the patients was 27.3±11.0. There was no difference in terms of gender and age with other appendectomy patients who diagnosed non-tumor (p=0.476 and p=0.413, respectively). The clinical presentation of the patients with all carcinoid tumors was in favor of acute appendicitis. Histopathological examination revealed simultaneous acute appendicitis in 25 (71.4%) patients.

The histologically distribution of tumors is examined; Grade 1 carcinoid in 32 patients, grade 2 carcinoid in 1 patient, multifocal carcinoid in 1 patient, grade 2 carcinoid and adenocarcinoma in 1 patient. The tumor placement in the appendix is examined; Tip of the appendix in 26 (74%) patients, body in 7 (20%) patients and tip and body in 1 patient who had multifocal tumor. Median tumor diameter was found as 6 mm (4-10, 5mm) (range: 1-24 mm). Tumor size was 15 mm and more in 6 (17%) patients, 20mm in 3 (9%) patients. In all patients, the surgical margin was negative, and lympho-vascular invasion was positively identified in 3 (9%) patients. After pathological examination, 3 patients underwent to right hemicolectomy and 1 patient to total colectomy.

Discussion

Appendiceal carcinoid tumor (neuroendocrine tumor) is rarely seen, but it is an area where carcinoid tumor is frequently found. They form 80% of all appendicitis masses [2]. Appendix is most common localization of carcinoid tumors in the gastrointestinal tract with a rate of 40-50% [3,4]. Modlin and Sandar, however, present the largest epidemiological series with 8305 cases on carcinoid tumors; reported that carcinoid tumors were located in the bronchopulmonary system with a rate of 73.1% in the gastrointestinal tract and 25.9% in the gastrointestinal tract and 18.9% in the gastrointestinal tract with a maximum of 28.7% in the gastrointestinal tract [5-8]. The main reason for changing these rates is the clinical examination of carcinoid tumors in jejunoileum are found at a much higher rate than the tumors in the surgical series and it is suggested that many small intestinal carcinoid tumors cannot be clinically detected [9]. 80% of the carcinoid tumors localized to the appendix are smaller than 1 cm, 15% and 5% are tumors larger than 2 cm. While ¾ of these tumors are located proximal to the appendix, only about 10% of them are localized [10].

Carcinoid tumors can be seen in all ages, but in adults and women they are more frequently detected [2]. Diagnose is usually revealed in appendectomies with acute appendicitis. However, clinical findings of carcinoid syndrome, especially in the presence of metastases, are of importance in terms of preoperative diagnosis. It is known that these tumors secrete many gastrointestinal peptides and hormones, especially 5-hydroxytryptamine (serotonin). Depending on their release, especially carcinomatous syndrome leading to clinical findings such as flushing, diarrhea, asthma or wheezing, valvuler heart diseases and fascial telangiectasia may occur in the skin localized on the head and neck and upper body [1]. In the diagnosis of carcinoid tumors leading to carcinoid syndrome, serotonin and 5-HIAA 5-hydroxy indole acetic acid) levels are important. Ultrasonography and computed tomography can determine the localization and size of the tumor. In addition, I-131 iodobenzylguanidine scintigraphy is particularly useful in the detection of metastatic carcinoid tumors [1,11]. Appendices have a close association with tumor size and metastases, as in other localizations of localized carcinoid tumors. About 90% of carcinoid tumors are benign, and the vast majority of cases are less than 1 cm. The prognosis deteriorates if the size of the tumor is greater than 2 cm. The risk of metastasis in tumors smaller than 1 cm is 2%, while in lesions greater than 2 cm this rate reaches 80%. A 5-year surveillance of appendiceal carcinoid tumors is accepted above 90% [2,10,12,13].

In the treatment of appendicitis carcinoid tumors; Appendectomy is indicated as adequate treatment. The recurrence rate in all cases is 2%. Appendectomy is adequate in the treatment of cases with a diameter less than 1 cm and appendicitis limited, but the treatment of tumors between 1 and 2 cm in diameter is controversial. Right hemicolectomy is

performed in the treatment of tumors larger than 2 cm. In terms of right hemicolectomy treatment, not only tumor size but also many other factors play a role. Lesions larger than 2 cm, localized tumors at the base of the appendix, invasion of lymphatic ducts, serosa and mesoapendix, presence of regional lymph node metastasis, mucin production (mucinous carcinoid tumors), high mitotic fast cellular pleomorphism and childhood carcinoid tumors are defined as the indications for right hemicolectomy in the treatment of carcinoid tumors of appendix [13-16]. In our study, we performed additional right hemicolectomy in patients requiring further treatment according to these guidelines. Total colectomy was performed in one patient because of synchronous involvement of other colon segments.

Hepatic resection in patients with carcinoid syndrome and metastatic liver involvement may be performed if possible; both in terms of loss of symptoms and cure if necessary. Hepatic artery embolization and interferon treatment have been reported to be highly successful in cases where resection is not possible. For patients with disseminated carcinoid tumors, a multidisciplinary approach including chemotherapy regimen is recommended [15,16].

This study has some limitations. First retrospective design of the study lowers the quality of assumptions. Second limitation is that follow-up data couldn't be reported with detail. The study patients represent one hospital in Turkey. These findings suggest that instruction to attend to specific features can enhance the accuracy, but feature selection is crucial and generalization across the world may be limited.

In conclusion, carcinoid tumors of appendix are rarely seen, and mostly incidental after appendectomy. Routine pathological examination of appendectomy specimen is offered to reveal the condition, and to choose necessity of additional therapies.

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