Carcinoid tumors of appendix: treatment and outcome

Apandiks'in karsinoid tümörü: Tedavisi ve sonuçları

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BACKGROUND

The aim of this study is to evaluate the clinical and histopathological features and the treatment of carcinoid tumors of the appendix.

METHODS

A retrospective review of medical records and pathology specimens of patients with carcinoid tumor of the appendix has been done. The data derived from this study has been evaluated by descriptive statistical methods (mean, SD, frequency).

RESULTS

The histopathological examination of the appendices revealed carcinoid tumor in 11 out of 6777 (0.16%) patients operated for acute appendicitis. Six (54.54%) patients were male, 5 (45.45%) were female and the mean age was 20.2±6.7 years (13-35). The tumor was localized in the distal 1/3 region in 10 patients and in the proximal 1/3 region in 1 patient. The mean tumor diameter was 0.73±0.36 cm (0.3-1.5). Ten patients had classical type carcinoid tumor whereas goblet cell carcinoid tumor was only seen in one patient. None of the patients underwent an expanded resection. The mean follow up of the patients is 28.5±15.2 months (6-48), and no recurrences were seen.

CONCLUSION

In tumors with a diameter of 1 to 2 cm, appendectomy is the treatment of choice. No recurrence was detected with tumors smaller than 2 cm with simple appendectomy.

Key Words: Adenocarcinoma/diagnosis; appendiceal neoplasms/diagnosis; carcinoid tumor/diagnosis.

AMAÇ

Bu çalışmada apendiksin karsinoid tümörlerinin klinik ve histopatolojik özellikleri ve tedavi yöntemleri değerlendirildi.

GEREÇ VE YÖNTEM

Apendiksin karsinoid tümörü olan hastaların tıbbi kayıtları ve patoloji piyesleri retrospektif olarak incelendi. Çalışma verileri tanımlayıcı istatistiksel metodlar (ortalama, SD, frekans) kullanılarak değerlendirildi.

BULGULAR

Akut apandisit tanısıyla ameliyat edilen 6777 hastanın 11'inde (%0.16) histopatolojik incelemede karsinoid tümör saptandı. Altı hasta (%54.54) erkek, 5 hasta (%45.45) kadındı; hastaların yaş ortalaması 20.2±6.7 (13-35) idi. Tümör 10 hastada 1/3 distal bölgede, 1 hastada ise 1/3 proksimalde yerleşimliydi. Ortalama tümör çapı 0.73±0.36 cm (0.3-1.5) idi. On hastada klasik tip karsinoid tümör saptanırken, bir hastada goblet hücreli karsinoid tümör görüldü. Hastaların hiçbirinde genişletilmiş rezeksiyon yapılmadı. Hastaların ortalama takip süresi 28.5±15.2 (6-48) ay olup hiçbir hastada nüks görülmedi.

SONUÇ

Tümör çapı 1-2 cm olan olgularda uygun tedavi yöntemi apandektomidir. Basit apandektomi ile 2 cm'nin altındaki tümörlerde kısa sürede nüks saptanmamaktadır.

Anahtar Sözcükler: Adenokarsinom/tanı; apendis neoplazi/tanı; karsinoid tümör/tanı.

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Primary appendix neoplasm is a rare pathology found in 0.5-1% of all surgically removed appendices.[1-3] Carcinoid tumors represent more than 50% of appendix neoplasms, and they are seen mostly in children and young adults.[4-7] The recent studies, which use the surveillance, epidemiology and end-results (SEER) programme of the National Cancer Institute, reported 324 malignant carcinoids (19.7%) and 227 goblet carcinoids (13.8%) among 1645 appendiceal neoplasms.[8] Clinical presentation of the carcinoid tumor of the appendix usually resembles that of acute appendicitis and the diagnosis is often incidental.[9]

In this study, we reviewed the 10 year experience of our surgical unit in carcinoid tumors of the appendix, by analysing the clinical presentation, the histopathological diagnosis and the treatment of the disease.

MATERIALS AND METHODS

Patients who had undergone appendectomy for acute appendicitis at the Department of Surgery, Şişli Etfal Training and Research Hospital, between February 1993 and March 2003 were reviewed retrospectively. Patients with a diagnosis of carcinoid tumor had been analysed. Age and gender 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 and histopathological cell type of the tumor were defined. The appendectomy specimens were examined by two senior pathologists. Postoperatively, all patients were reevaluated with an abdominal tomography and 24-hours urinary excretion of 5-hydroxy-indoleacetic acid (5-HIAA) was measured.

The data derived from this study has been evaluated by descriptive statistical methods (mean, standard deviation, frequency).

RESULTS

The histopathological examination of the appendices revealed carcinoid tumor in 11 out of 6777 (0.16%) patients operated for acute appendicitis. Six patients (54.54%) were male, 5 (45.45%) were female and the mean age was 20.2±6.7 years (13-35). When reevaluated retrospectively, all patients were clinically diagnosed as acute appendicitis and none of them had a history of flushing, diarrhea, Cushing's or carcinoid syndrome and none were preoperatively diagnosed with carcinoid tumor. The appendices were inflamed in all cases but none of the patients had appendiceal perforation or any other pathology. The tumor was localized in the distal 1/3 site in 10 patients and in the proximal 1/3 site in 1 patient. The mean tumor diameter was 0.73±0.36 cm (0.3-1.5). Histopathological examination revealed goblet cell carcinoid tumor in one case and classical type carcinoid tumor in 10 cases. The goblet cell carcinoid tumor was localized distally and the tumor diameter was 0.5 cm. Two patients had subserosal invasion, two patients had serosal invasion, one had invasion of the muscularis propria and in 6 patients the tumor was localized in

Table 1. Carcinoid tumor of appendix: clinical data

No	Age (year)	Sex	Size (cm)	Localization	Pathology	Treatment	Follow up (months)	Parietal spread	Invasion of mesoappendix
1	35	F	0.5	Distal	Classic	SA	11	Subserosa	–
2	18	F	1.2	Distal	Classic	SA	46	Submucosa	–
3	18	M	0.5	Distal	Classic	SA	13	Serosa	+
4	26	F	1	Distal	Classic	SA	36	M. propria	–
5	17	F	0.3	Distal	Classic	SA	26	Submucosa	–
6	14	F	0.5	Proximal	Classic	SA	24	Submucosa	–
7	13	M	0.8	Distal	Classic	SA	38	Submucosa	–
8	25	M	1.5	Distal	Classic	SA	19	Serosa	–
9	25	M	0.5	Distal	Classic	SA	6	Submucosa	–
10	14	M	0.5	Distal	Goblet	SA	48	Submucosa	–
11	18	M	0.8	Distal	Classic	SA	46	Subseroza	–

SA: Simple appandectomy; F: Female; M: Male.

the submucosa (Table 1). In a distally localized classical type carcinoid tumor measuring 0.5 cm in diameter, the mesoappendix and fatty tissue were infiltrated (Fig. 1, 2). No mitotic cells were found.

Postoperative abdominal tomographies were not remarkable and none of the patients underwent an expanded resection. In the postoperative follow up 24-hours urinary excretion of 5-HIAA was normal in all patients. The mean follow up of the patients is 28.5±15.2 months (6-48), and no recurrences are seen.

DISCUSSION

Carcinoid tumor of the appendix is a rare incident, seen mostly in children and adolescents.[10] It is the most frequent tumor of the gastrointestinal system in young patients.[5-7] Histopathological evaluation of the appendix specimens in children reveal carcinoid tumor in 0.085-0.169%, and the frequency decreases in adults.[11] Our clinical series is mostly composed of young adults, and the incidence of carcinoid tumors was 0.16%.

There are no specific symptoms or signs to identify carcinoids preoperatively.[4] Appendix carcinoids present mostly with signs and symptoms of acute appendicitis, and are diagnosed incidentally. In our patients, diagnosis was performed after appendectomy and pathological examination. History of chronic abdominal pain and presence of neuroendocrine symtoms may help diagnosis. Very

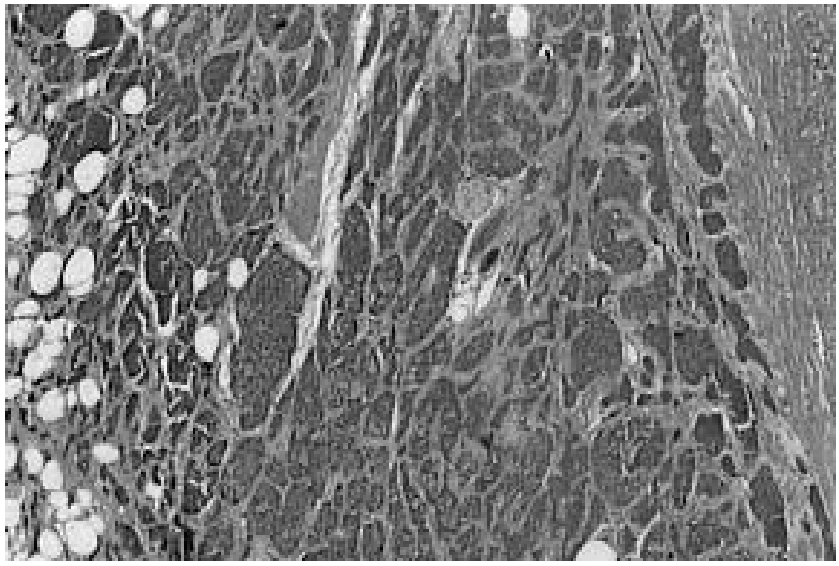

Fig. 1. Carcinoid tumor invasion of periappendicular fatty tissue (H-E x 40).

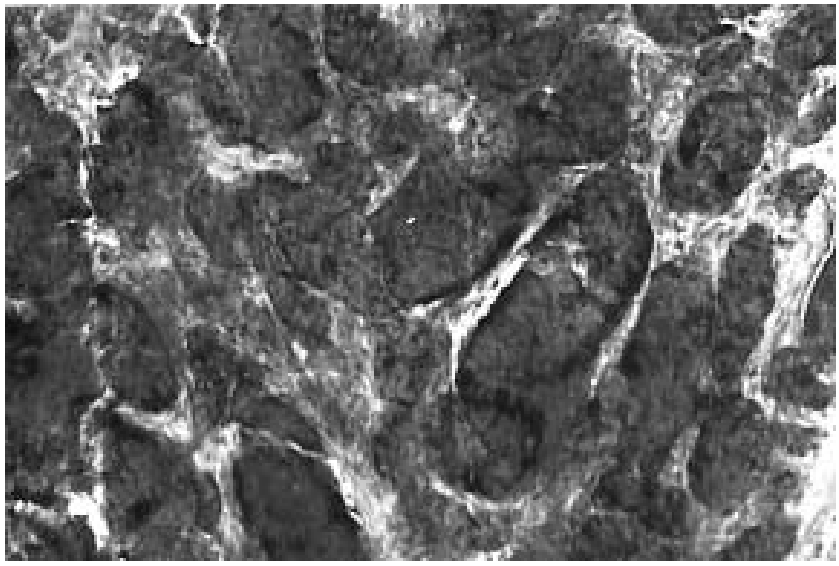

Fig. 2. Chromogranin staining of carcinoid tumor cells (Chr x 100).

rarely, carcinoid syndrome may be seen with retroperitoneal or hepatic metastasis.[12]

Classical type carcinoid tumors are the most frequently seen.[5] They are derived from the subepithelial neuroendocrine cells of the appendix and represent 80% of all appendiceal neoplasms.[2-6] Five year survival in classic carcinoid tumor is over 90%.[5] A small portion of the carcinoids of appendix shows glandular differentiation, which consists of 3 types of tumor: Tubular carcinoid tumor, goblet cell carcinoid tumor, and mixed carcinoid-adenocarcinoma.[13] Tubular carcinoid tumors are a rare variant of classic carcinoid tumors. The two types can only be distinguished histopathologically.[14] Their clinical courses and survival rates are similar. Most goblet cell carcinoids contain intracytoplasmic mucin and small numbers of endocrine cells can be demonstrated with immunoexpression of neuroendocrine markers.[15] These tumors are also called adenocarcinoid tumors or mucinous carcinoids. Carcinoembryonic antigen and cytokeratin immunereactivity are frequently seen.[13] Goblet cell carcinoid tumors are infiltrative and typically involve the entire appendix circumferentially. They are mostly localized proximally in the appendix. Their biological activity is more malignant than other type carcinoid tumors, but less malignant than adenocarcinomas, with 5 year survival of 80%.[15,16]

Mixed type carcinoid-adenocarcinoma is a very rare tumor of the appendix and shows histological features of both adenocarcinoma and carcinoid tumor.[17] Infiltration of the appendiceal wall is frequent, cecal or lymph node involvement may be present. They are rather malignant tumors with a high incidence of metastasis and a survival rate of 20%.[13] High-quality histopathological examination is essential if a sensible decision on further intervention is to be achieved.[18]

In literature, some authors recommend right hemicolectomy or ileocecal resection for goblet cell carcinoid tumors.[19] In our series one patient revealed goblet cell carcinoid tumor, located distally in the appendix, measuring 0.5 cm in diameter. After getting the pathology reports the patient was recommended to undergo a right hemicolectomy operation, however he refused the procedure and joined the follow up program. During the 48 months follow up of the patient revealed no problems. Tumor size is the most approved prognostic indicator of metastatic potential. In most of the cases appendectomy is the first and the only choice of treatment. However, in tumors measuring 2 cm or more, right hemicolectomy is recommended because of the potential to metastase.[19] In recent years, there are studies suggesting ileocecal resection as an alternative procedure to right hemicolectomy in tumors larger than 2 cm.[20-21] The need for ileocecal resection or right hemicolectomy for tumors sized 1-2 cm is still under debate as their frequency of metastasis is not exactly known. Thirlby et al.[22] in their study, had identified 46 cases of metastatic appendix carcinoids, where in only 5 cases the tumor diameter was 1-2 cm, but larger in all the rest. In our series 3 out of 11 carcinoid cases had a tumor diameter of 1-2 cm and these patients underwent simple appendectomy. The mean follow up of the patients is 32.5 months (19-46) and no metastases were seen.

Besides the tumor diameter and cell type, tumor localization, degree of invasion, mesoappendicular invasion and mitotic cells are other important prognostic factors.[23,24] Mitotic cells are not frequently observed. In most cases, mitotic cells are seen at less than 1 per 10 high-powered magnification fields. If more than 2 or 3 were to be found per 10 high-powered magnification fields, then the prognosis would be very poor.[17,18] In the all cases presented, no mitotic cells were found. The tumor is usually limited in the submucosa and muscular layer. Serosal invasion is seen in 20% of cases whereas invasion of the mesoappendix is more frequent in large tumors.[25] Ileocecal resection or right hemicolectomy is recommended when the tumor is located at the base of the appendix or when the mucin secreting cells are seen.[23] In a study, Prommegger et al.[19] had defined two cases with tumors located at the base of the appendix. In one case, ileocecal resection was done two weeks after the first operation, and the other had undergone appendectomy only. On follow up of the second patient, no metastasis was seen. We performed appendectomy only on one of our patients although the tumor was located at the base. The tumor was a 0.5 cm, classical type carcinoid, resected with a 5 mm tumor free margin.

Carcinoid tumor of the appendix is a rare pathology, diagnosed usually after histopathological examination of the appendectomy specimen. In

tumors with a diameter of 1 to 2 cm, appendectomy is the treatment of choice. No recurrence was detected in tumors smaller than 2 cm with simple appendectomy.

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