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Original Article

Neuroendocrine tumors of the appendix

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Abstract

Aim: The objective of this study was to evaluate treatment and postoperative recurrence in patients with neuroendocrine tumors of the appendix detected.

Material and Methods: Patients with neuroendocrine tumors of the appendix detected between January 2015 and January 2016 were evaluated retrospectively. Patients who underwent incidental appendectomy due to different malignancies were excluded from the study.

Results: A total of 402 patients who underwent appendectomy were evaluated. Five patients with neuroendocrine tumors detected, were included in the study. The mean age was 30.1 years. There were tumors in the apex, while a second tumor was found in the corpus in one patient. The mean tumor diameter was 0.6 cm. Ki-67 was under 2% in all patients. One patient underwent right hemicolectomy in the postoperative first month due to the infiltration to the periappendiceal tissue. The mean duration of hospitalization was 2 days. The mean duration of follow-up was 38 months (range 12- 54) . Ga 68 PET CT was taken in all patients after the histopathological examination. Control of the patients was performed after the first year with thorax and abdominal CT. None of the patients developed tumor.

Conclusion: In general, clinical course is good and appendectomy is curative. However, right hemicolectomy is needed in patients with poor prognostic factors.

Keywords: Incidental neuroendocrine tumor; appendectomy; general surgery.

INTRODUCTION

Neuroendocrine tumors are rare. These tumors develop from enterochromaffin or Kulchitsky cells of the neuroendocrine system. Appendix is one of the most commonly seen sites (1). Neuroendocrine tumors are mostly asymptomatic. Majority of neuroendocrine tumors of the appendix are incidentally detected during histopathological examination of appendectomy material in patients who underwent appendectomy due to acute appendicitis or recurrent chronic non-specific right lower quadrant pain (2,3).

The rate of neuroendocrine tumor detected in patients who underwent appendectomy is 0.1% to 0.3% (4). According to the World Health Organization, these tumors are divided into three as 1a: well differentiated neuroendocrine tumor with benign biological behavior, 1b: well differentiated neuroendocrine tumor with unclear malignancy potential, 2: well differentiated neuroendocrine carcinoma (low malignant potential) and 3: mixed exocrine-neuroendocrine carcinoma. Carcinoid syndrome is extremely rare (<1%). Carcinoid syndrome is a distinct group of symptoms that patients with NETs may get when tumours in the gastrointestinal system. The main symptoms of this condition include diarrhoea, flushing, stomache, and wheezing.The objective of this study was to evaluate treatment and postoperative recurrence in patients with neuroendocrine tumors of the appendix detected.

MATERIAL and METHODS

Patients with neuroendocrine tumors of the appendix detected between January 2015 and January 2016 were retrospectively evaluated from the hospital registry system. All patients gave written consent. Patients who underwent incidental appendectomy due to different malignancies were excluded from the study. Patients' clinical findings, operation performed, histopathological examination outcomes and rate of recurrence were studied.

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RESULTS

A total of 402 patients who underwent appendectomy were evaluated. Five patients (0.01%) with neuroendocrine tumors detected were included in the study. Of the patients, four were female and one was male. The mean age was 30.1 (range: 18-56) years. Clinical findings of all patients were compatible with acute abdomen. Tumors were not considered in any patient during the operations. There was acute appendicitis in non-neoplastic appendix. All patients underwent laparoscopic appendectomy. There were tumors in the apex, while a second tumor was found in the corpus in one patient. The mean tumor diameter was 0.6 (range: 0.2-1.2) cm. The surgical margins were positive. Ki-67 was under 2% in all patients. One patient underwent right hemicolectomy in the postoperative first month due to the infiltration to the periappendiceal tissue. The mean duration of hospitalization was 2 days (range 1-3). All patients were discharged without complications. The mean duration of follow up was 38 (range: 32-44) months. Ga 68 PET CT was taken in all patients after the histopathological examination. The patients underwent colonoscopy. No additional pathology was observed. Control of the patients was performed after the first year with thorax and abdominal CT. None of the patients developed tumor.

Table 2. Patients data

Patient no	Age	Gender	Tumor diameter	Surgeries	Follow up (Months)
1	22	Female	0.2	Laparoscopic appendectomy	32
2	34	Female	1.2	Right hemicolectomy	44
3	18	Male	0.4	Laparoscopic appendectomy	42
4	56	Female	0.6	Laparoscopic appendectomy	34
5	21	Female	0.7	Laparoscopic appendectomy	38

DISCUSSION

Malignant tumors of the appendix are neuroendocrine tumors, goblet cell carcinoid, lymphoma, mucocele, primary adenocarcinoma, and mucinous cystadenocarcinoma. Primary appendix tumor is detected in less than 3% of patients undergoing appendectomy. The most commonly seen are neuroendocrine tumors. The rate of neuroendocrine tumor detected in patients who underwent appendectomy is 0.1% to 0.3%. In our study, the rate of neuroendocrine tumors was found as 0.01%, which was very low compared to the literature (5). The mean age was found as 30.1 years, consistently with the literature (6). The incidence of neuroendocrine tumors is slightly higher in women compared to men (7,8). In our study, the incidence was higher in the female patients, in parallel with the literature. Appendicular neuroendocrine tumors are rare and usually diagnosed incidentally. Precise examination of routine appendectomy specimen is fundamental in the diagnosis (9).

Evaluating according to the histopathological features, the mean tumor diameter was found as 0.6 cm. This result was consistent with the literature (9,10). Tumor size, presence of lymph node, histologic subtype, tumor positive surgical margins, high mitotic index, cellular pleomorphism and mesoappendiceal invasion are important in determination of tumor behaviour (11,12). Right hemicolectomy was performed in one patient due to the infiltration to the periappendiceal tissue. Mitotic index is usually seen less than 1% at 10 x magnification. The prognosis is very poor if mitotic index is found as two or three at 10 x magnification (11). Ki-67 invasion is helpful in prediction of prognosis, local and distant metastasis (13). Whereas there is no possibility of metastasis in tumors < 1 cm, the incidence of metastasis raises up to 20 in tumors > 2 cm (14). In the present study, none of the patients developed metastasis. Cytoreductive chemotherapy should be considered in patients who develop metastatic or carcinoid syndrome. The rate of response to treatment is under 40% in combined chemotherapy with streptozotocin and 5-fluorouracil or doxorubicin. Octreotide, an analog of somatostatin, is the most potent pharmacological agent. Radiotherapy is also among the treatment options (15). Five-year survival is 90-95% in neuroendocrine tumors localized only in the appendix, 80-85% in cases with local metastasis, and 30-32% in cases with distant metastasis (11). It should be remembered that the risk for development of synchronous or metachronous colorectal neoplasm is over 30% (13,14). In our study, none of the patients developed colorectal neoplasm.

CONCLUSION

These tumors are mostly detected incidentally. In general, clinical course is good and appendectomy is curative. However, right hemicolectomy is needed in patients with poor prognostic factors.

Competing interests: The authors declare that they have no competing interest.

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REFERENCES

1. Tchana-Sato V, Detry O, Polus M, et al. Carcinoid tumor of the appendix: a consecutive series from 1237 appendectomies. World J Gastroenterol 2006;12:6699-701.
2. Gu Y, Wang N, Xu H. Carcinoid tumor of the appendix: a case report. Oncol Lett 2015;9:2401–3.
3. Murray SE, Lloyd RV, Sippel RS, et al. Postoperative surveillance of small appendiceal carcinoid tumors. Am. J.

Surg 2014;207:342–5.

4. Spallitta SI, Termine G, Stella M, et al. Carcinoid of the appendix. A case report. Minerva Chir. 2000;55:77–87.
5. Barretoa SG, Tionga L, Thomasa T, et al. Incidental appendiceal carcinoids: is surgery affecting their incidence? World J Oncol 2012;3:227–30.
6. Tchana-Sato V, Detry O, Polus M, et al. Carcinoid tumor of the appendix: a consecutive series from 1237 appendectomies. World J. Gastroenterol 2006;12:6699–701.
7. Yao JC, Hassan M, Phan A, 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.
8. Hauso O, Gustafsson BI, Kidd M, et al. Neuroendocrine tumor epidemiology: contrasting Norway and North America. Cancer 2008;113:2655–64.
9. Amr B, Froghi F, Edmond M, et al. Management and outcomes of appendicular neuroendocrine tumours: retrospective review with 5-year follow-up. Eur J Surg Oncol 2015;41:1243–6.
10. Anwar K, Desai M, Al-Bloushi N, et al. Prevalence and clinicopathological characteristics of appendiceal carcinoids in Sharjah (United Arab Emirates) World J Gastrointest Oncol 2014;6:253–6.
11. Goede AC, Caplin ME, Winslet MC. Carcinoid tumour of the appendix. Br J Surg 2003;90:317-22.
12. Fornaro R, Frascio M, Sticchi C, et al. Appendectomy or right hemicolectomy in the treatment of appendiceal carcinoid tumors? Tumori 2007;93:587-90.
13. Modlin IM, Lye KD, Kidd M. A 5-decade analysis of 13,715 carcinoid tumors. Cancer 2003;97:934-59.
14. Tchana-Sato V, Detry O, Polus M, et al. Carcinoid tumor of the appendix: a consecutive series from 1237 appendectomies. World J Gastroenterol 2006;12:6699-701.
15. Sweeney JF, Rosemurgy AS. Carcinoid tumors of the gut. Cancer Control 1997;4:18-24.