

Problems in the management of the appendiceal carcinoid tumors.

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Abstract

Background: Carcinoid tumor is the most common type of neuroendocrine tumor. Appendix is one of the most common sites of gastrointestinal carcinoid tumors. Appendectomy may be performed without mesoappendix excision by some surgeons in general practice. In that case, what happens, if a carcinoid tumor turns out to be responsible for the symptoms? In our series, this practice and carcinoid cases were discussed.

Methods and Findings: Carcinoid tumor cases that were operated on between the years 2002-2010 were examined retrospectively. Average age, female-male ratio, location of the tumor, invasion to the mesoappendix, inflammatory changes, and management of the cases were discussed.

The number of carcinoid cases was 6 (0,29%). Average tumor size was (0,2-1,4)cm. None of the cases had clinical signs of carcinoid syndrome. In one case, microinvasion was detected in periappendiceal fatty tissue at the mesoappendicular side. But mesoappendix had not been removed in the operation, therefore, lymphadenopathy could not be evaluated by the pathologist.

Conclusions: The carcinoid syndrome is diagnosed by biochemical tests. If the tumor is greater than 1cm in diameter or is in the base of the appendix, or if there is evidence of nodal metastases, a right hemicolectomy is recommended. In five cases, appendectomy alone was thought to be enough, however, the case that was shown to have mesomicroinvasion was evaluated by MRI, colonoscopy, octreotide scintigraphy and biochemical tests. Extended resection was not performed and the case was followed more than a year. To date nothing suggestive of residual tumor or the like was detected.

Key words: acute abdomen, appendicitis, carcinoid syndrome, carcinoid tumors, neuroendocrine tumor



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Introduction

Appendectomy is performed frequently in surgical practice. Etiology of the acute appendicitis is variable. Some of the causes can be listed as fecaliths, lymphoid hyperplasia, parasites, undigested plant residuals, fruit seeds, foreign bodies and appendiceal tumors etc. Appendiceal tumors may be

prognostically the most important etiologic factor. Because, while appendectomy alone is curative for benign diseases, it is not sufficient for appendiceal tumors. Sometimes, during emergency operations, mesoappendix excision is not performed along with appendectomy. In those situations, oncologic grading is not possible. Whether or not an extended resection is needed remains unanswered, which may jeopardize the well being of patient.

The aim of this article is to define the frequency of the carcinoid tumors of the appendix, management of these cases, and to do a review of the literature.

Methods

Prevalence of the carcinoid tumor in urgently performed appendectomy cases was investigated between years 2002-2010. Average age, female-male ratio, location of the tumor, invasion of the mesoappendix, and inflammatory changes were investigated and management of the cases were discussed.

Results

Carcinoid tumor cases in our study were operated on at Buca Seyfi Demirsoy, a large state hospital in Izmir, Turkey between 2002-2010. The total number of cases which underwent appendectomy was 2076. Number of cases which were found to have carcinoid tumor was 6 (0,29%).

In the carcinoid tumor arm, average age was 30,1 (16-49) and male/female ratio was 1/5. In two cases, tumor's location was the corpus of the appendix, whereas in four cases, tumor's location was fundus. Average tumor size was 0,6 (0,2-1,4) cm. None of the cases showed clinical signs of carcinoid syndrome.

In the case in which tumor location was in corpus, tumor size was found to be 1,4 cm and purulent material was detected in the appendicular lumen, because the lumen was obstructed by the tumor. In the other two cases, fecalith was detected in the lumen, while in the remaining cases only the tumor was seen.

In one case, the tumor was in the fundus and microinvasion was seen in periappendiceal fatty tissue at the mesoappendicular side. But mesoappendix had not been removed in the operation, so, lymphadenopathy could not be evaluated by the pathologist. Therefore, the case was further evaluated by magnetic resonance imaging (MRI), colonoscopy, and octreotid scintigraphy.

No sign of residual tumor was found. The case was followed without any further operation. After a year of follow-up, still no clinical or radiologic signs of residual or recurrent tumor was evident.

As for TNM classifications of the subjects; 5 cases were T1N0M0, and one case was T1NxM0 (1).

Discussion

Appendix is one of the most common places for carcinoid tumors (2). Carcinoid tumors originate from neural crest cells. They are generally located in gastrointestinal system (3). Carcinoid tumors are the most common type of neuroendocrine tumor. Carcinoid syndrome is encountered only in less than 10% of the cases (4). Generally, the tumor is found incidentally after appendectomy (0,3-0,9%). It is more frequently seen in females than males (5,6). Malignancy potential (tendency to metastasize) is related to the localization and size of the tumor, invasion depth and growth pattern. Tumors smaller than 1 cm in diameter metastasized in 2% of cases. Metastasis ratio of tumors measured 1-2 cm is 50%. If the tumor is greater than 2 cm, metastasis ratio is 80-90% (7). In management of the patients, lymphatic drainage is important. Lymphoid drainage of the appendix is to the lymph nodes in the mesoappendix and to the paracolic nodes that lie along the ileocolic artery (8).

The liver metabolizes serotonin released into the portal venous circulation, thus, carcinoid syndrome rarely occurs in the absence of metastatic liver deposits. But carcinoid tumors may release hormones into the systemic circulation (e.g. bronchial carcinoids) in the absence of hepatic metastases. The most commonly seen clinical features of the syndrome are flushing (15%), diarrhea (20%), hepatomegaly (15%), sweating, hemoptysis, wheeze and hypotension. Serotonin directly causes endocardial fibrosis, right-sided valvular lesions, such as pulmonary stenosis and tricuspid incompetence (4,9).

The carcinoid syndrome is diagnosed biochemically. A high concentration of urinary 5-HIAA in 24- hour urine sample or an elevated serotonin level in plasma helps to establish the diagnosis of gastrointestinal carcinoid tumor. Radiologic imaging techniques can also be used. Computed tomography (CT) scan and MRI are better diagnostic tools for the detection of metastasis. Positron emission tomography (PET) using ¹¹C-5-hydroxytryptophan (a serotonin precursor), is a recently developed alternative technique to localize these tumors (4,9,10). Spread of the disease can be better detected and delineated with somatostatin receptor scintigraphy (11).

The patients with carcinoid lesions have a notable risk of developing a synchronous or metachronous colorectal neoplasm up to 33%. Follow-up by colonoscopy should be recommended (10,12).

Therapies for carcinoid tumors/syndrome are: surgery, somatostatin analogs, interferon-alpha, radiotherapy, liver dearterialization, liver (chemo, or radio)-embolization, alcohol sclerotherapy of liver metastases, radiofrequency ablation and cryosurgery of liver metastases, liver transplanta-

tion, radiotherapy-coupled somatostatin analogs, ^{131}I -MIBG and chemotherapy (9). Curative therapy is surgery. Surgical therapy varies according to the site of the tumor, size and metastases. For the tumors of the appendiceal origin, appendectomy is generally enough. If the tumor size is larger than 2 cm, right hemicolectomy is indicated. Some investigators think; if intramural lymphatic invasion, or serosal invasion or microscopic mesoappendiceal invasion is found, extended resection should be performed even if tumor is smaller than 2 cm (3).

Others, on the other hand, believe that if carcinoid tumor is in the mid- or distal appendix and is smaller than 1cm in diameter, simple appendectomy is adequate. If the tumor is greater than 1cm in diameter or located in the base of the appendix or if there is evidence of nodal metastases, a right hemicolectomy is recommended (13,14). Surgical treatment of large hepatic metastases by wedge resection may relieve symptoms (4). Re-intervention is advised in high-grade malignant carcinoids and goblet cell adenocarcinoids. Goblet-cell carcinoids have a worse outcome than the other types of carcinoid tumors and frequently present with metastatic disease (12). In postoperative period, the patients must be followed for early diagnosis of recurrence (15).

In one case in our series, microinvasion was seen in the peri-appendicular fatty tissue in the mesoappendicular side, but the mesoappendix had not been removed totally. The sur-

geon performing the appendectomy did not notice lymphadenopathy in the mesoappendix. In postoperative period, microinvasion was major problem for us. It could not be decided whether or not an extended surgical excision should be performed. The case was 17 years old female patient. Extended resection was a major procedure for her. She had not had symptoms of the carcinoid syndrome. Colonoscopy and abdominal magnetic resonance imaging were normal. Biochemical and urine tests were normal. Finally, octreotide scintigraphy was performed to detect metastasis and the test results were normal. So, she was followed for one year. To date, no pathologic finding was found.

Appendiceal tumors are generally diagnosed in postoperative period (16). By some surgeons and sometimes even by us, appendectomy is performed without mesoappendectomy. But if a tumor is diagnosed in the appendix, the mesoappendix becomes a very important tissue for prognosis. In our opinion, mesoappendix must be removed routinely with appendix during appendectomy. If any suspicious tumoral mass is found in appendix intraoperatively, frozen-section may be done.

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