CASE STUDY

MALIGNANT TUMORS OF THE APPENDIX: CLINICAL AND MORPHOLOGICAL ANALYSIS OF CASES FROM THE PRACTICE

DOI: 10.36740/WLek202105143

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ABSTRACT

The authors have analyzed medical histories of two patients, treated in health care facilities of Kharkiv region from 2008 to 2020. These patients underwent urgent appendectomy, given the existing clinic of acute appendicitis. Morphological examination of the surgical material allowed us to diagnose adenocarcinoma in one case, and neuroendocrine tumor in combination with endometriosis in the other case.

Morphological examination of the surgical material in the first case revealed a moderately differentiated adenocarcinoma and diffuse neutrophilic infiltration in all layers of the appendix, and in the second case – a well-differentiated neuroendocrine tumor (G3), combined with the signs of phlegmonous-ulcerative appendicitis and loci of endometriosis. In both cases, there were no specific for the oncological process anamnestic and clinical-instrumental data, and these tumors were manifested by the clinic of acute appendicitis. Only morphological examination of the surgical material allowed identifying the pathological process.

Clinical and morphological analysis of cases from the practice of malignant tumors of the appendix (neuroendocrine tumor and adenocarcinoma) will be useful and interesting for the medical community and should stimulate cancer vigilance in physicians.

KEY WORDS: neuroendocrine tumor, adenocarcinoma, appendix, clinical and morphological analysis

Wiad Lek. 2021;74(5):1277-1280

INTRODUCTION

Malignant tumors of the appendix are a rare pathology, accounting for 0.4% to 1.0% of cases among all malignant neoplasms of the gastrointestinal tract. The incidence of the appendix malignant tumors, according to world statistics, is 0.12 per 1.000.000 people per year [1].

According to most scientists, its true incidence is unknown. This figure is usually calculated based on morphological examination of surgical material (surgically removed appendicitis) and does not take into account the results of autopsy [2]. As a rule, the appendix is studied macroscopically, and it is not subject to microscopic examination. As a result, the existing tumor process is skipped and not diagnosed by the pathologist.

Benign and malignant tumors of different histogenesis may develop in the appendix. Its epithelial layer is characterized by the presence of enterocytes, goblet cells, enterochromaffin cells, which can be a source of epithelial, goblet and neuroendocrine tumors development. Lymphoid tissue of the mucous and submucosal of the appendix can be a source of lymphoma. Tumors of mesenchymal origin can also develop in the appendix [3].

The most common among all malignant tumors of the appendix are neuroendocrine tumors (65-90% of cases) and tumors of epithelial origin, represented by adenocarcinomas (up to 20% of cases) [4].

Neuroendocrine tumors of the appendix are 1.7 times more often diagnosed in women than in men, mostly between the ages of 20 and 40 years. There have been also cases of neuroendocrine tumor of the appendix in children. Adenocarcinoma of the appendix develops more often in men than in women aged 45 to 70 years [1, 5].

Malignant tumors of the appendix in the initial stages are characterized by asymptomatic course or manifest in the clinic of acute appendicitis. The expressed clinical manifestation of malignant process, as a rule, occurs at its progression and distribution on adjacent organs, development of metastasises, accession of purulent-septic complications in the form of periapendicular abscesses, intestinal fistulas, etc. [6]. Neuroendocrine tumors may

also manifest by carcinoid syndrome due to the production of serotonin, bradykinin, histamine, prostaglandins by tumor cells. The most characteristic manifestations of this syndrome are seizures, lasting from a few seconds to 10 minutes, characterized by sudden and short-term red face skin and upper torso, attacks of bronchospasm, weakness, fever, tachycardia, hypotension, convulsions and nausea [7, 8].

Methods of medical imaging in the diagnosis of malignant neoplasms of the appendix have a very limited application. Radiography of the abdominal cavity only allows us to diagnose intestinal obstruction, possibly caused by a tumor process in the appendix. Ultrasound, computed tomography and magnetic resonance imaging also do not provide reliable signs that would allow a correct diagnosis. Only morphological examination of the surgical material, i.e. the removed appendix, allows us to diagnose a malignant tumor of the appendix [9].

THE AIM

The aim is to analyze clinical and morphological features of two cases from the practice of adenocarcinoma and neuroendocrine tumor of the appendix.

MATERIALS AND METHODS

The authors have analyzed medical histories of two patients, treated in health care facilities of Kharkiv region from 2008 to 2020. These patients underwent urgent appendectomy, given the existing clinic of acute appendicitis. Morphological examination of the surgical material (removed appendix) allowed us to diagnose adenocarcinoma in one case, and neuroendocrine tumor in combination with endometriosis in the other case. Microspecimens stained with hematoxylin and eosin were studied using an Olympus BX-41 microscope (Japan).

CLINICAL CASES AND DISCUSSION

Up to 650 appendixes, removed due to acute appendicitis, are examined annually in the pathology department of the Public Nonprofit Organization of the Kharkiv District Council «Regional Clinical Hospital». A morphological examination of the removed appendages has revealed two cases of malignant tumors of the appendix over the past 13 years.

The rare development of tumors in the appendix may be due, firstly, to the fact that it does not actively participate in digestive processes and performs mainly an immunogenic function. Secondly, its proliferative activity of the mucous membrane epithelium is less pronounced, compared with other parts of the gastrointestinal tract [10]. Third, there is a significant amount of immune infiltration in the wall of the appendage, suppressing and inhibiting the development of the neoplastic process [11].

Here is a clinical and morphological analysis of the two cases from our practice.

In the first case, patient P, 68 years old, was urgently hospitalized with complaints of intense pain in the right iliac region, vomiting, nausea, dry mouth, weakness and fever up to 38°C. An objective examination revealed muscle tension of the anterior abdominal wall, pain on palpation, positive symptoms of Rovsing, Shchotkin-Blumberg, Voskresensky. The general blood test revealed leukocytosis, acceleration of erythrocyte sedimentation rate. Biochemical blood test and clinical analysis of urine were normal. Ultrasound examination of the abdominal organs revealed no pathology. The patient was diagnosed with acute appendicitis. She was performed a laparotomy with Volkovich-Dyakonov access in the right iliac area and had the appendix removed.

On macroscopic examination, the appendix was 9.5 cm long, characterized by uneven thickness (its diameter ranged from 0.5 cm to 1.4 cm) and dense consistency. The serous membrane was dull and whitish-gray in color. The appendix was cut with some difficulty. Fecal masses were noted in the section in the appendix cavity. In places, the cavity in the appendix was not visualized. A moderately differentiated adenocarcinoma, germinated in all its layers, was found in the appendix under the microscope (fig. 1), as well as diffuse neutrophilic infiltration in all layers.

The postoperative period in the patient proceeded without deviations. Taking into account the results of the morphological examination of the surgical material, the patient was sent to a specialized oncological institution for further treatment.

Microscopically, appendix adenocarcinomas are characterized by significant fluctuations in mucus production, which is why they are divided into mucinous and non-mucinous ones. In practice, as a rule, there is approximately the same number of the mentioned adenocarcinoma variants [6]. In our case, we analyzed mucinous adenocarcinoma.

Mucinous adenocarcinoma of the appendix may be the cause of pseudomyxoma peritonei. In this case, mucous jelly-like masses accumulate in the abdominal cavity and retroperitoneal space. We can see tumor epithelial cells, producing mucus in them, under the microscope. Angiomatosis fields form around the mucous masses, a cellular reaction develops with a predominance of lymphocytes and plasma cells. Death from pseudomyxoma occurs as a result of mechanical compression of vital organs [1].

Appendix adenocarcinomas are characterized by implantation and lymphogenic metastases to the pelvic organs [12].

In the second case, patient D, 47 years old, was hospitalized with a clinical picture of acute appendicitis. The patient had an acute onset of pain, and the pain was localized first in the epigastrium, and then moved to the right iliac region. This patient also had dyspeptic and intoxication syndromes, and on palpation – classic appendicular symptoms. Neutrophilic leukocytosis was found in a clinical blood test. No pathological changes were found in the clinical test of urine and biochemical blood test. Ultrasound examination of the abdominal organs revealed signs of liver adiposity and chronic cholecystitis. The patient underwent urgent appendectomy.

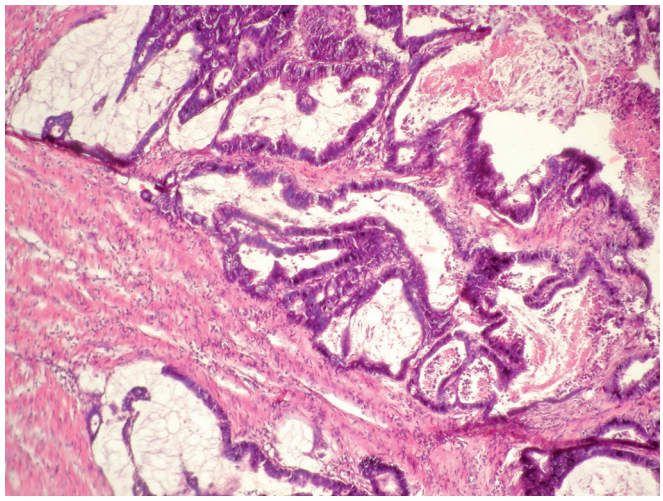

Fig. 1. Moderately differentiated adenocarcinoma of the appendix. Hematoxylin and eosin staining, × 100.

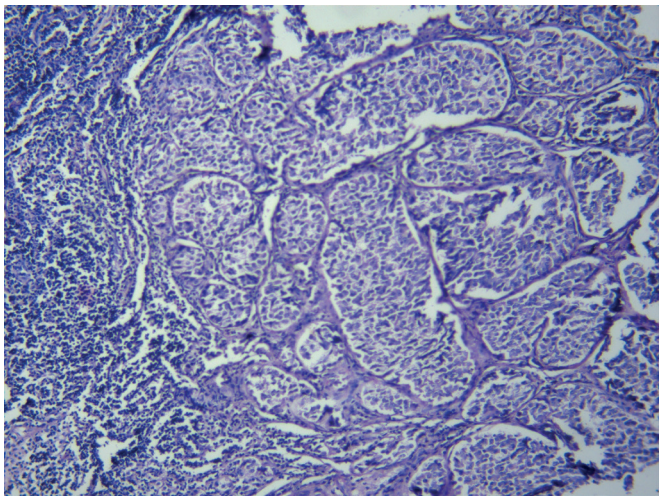

Fig. 2. Microscopic structure of well-differentiated neuroendocrine tumor (G3) of the apex of the appendix. Hematoxylin and eosin staining, × 100.

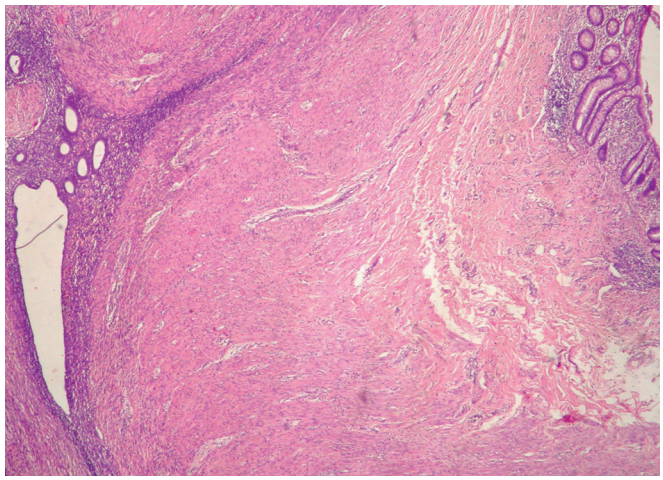

Fig. 3. Loci of endometriosis in the muscular layer of the appendix. Hematoxylin and eosin staining, × 40.

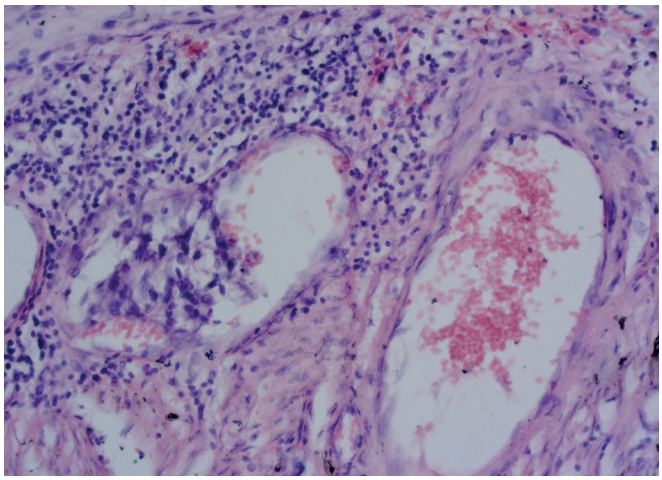

Fig. 4. Complexes of neuroendocrine tumor cells in the vessels of the muscular and serous membranes of the appendix. Hematoxylin and eosin staining, × 200.

On macroscopic examination, the appendix was 11 cm long, sharply thickened at the apex. The diameter of the appendix ranged from 0.5 cm to 0.8 cm, and at the site of thickening – from 1.2 cm to 1.6 cm. The serous membrane of the appendix was dull with dark red areas. Fecal masses were found in the section in the appendix cavity. Histological examination revealed a neuroendocrine tumor in all layers of the appendage wall.

According to the modern classification of neuroendocrine tumors of the appendix, developed by experts of the World Health Organization, there are well-differentiated neuroendocrine tumors (G1, G2, G3), poorly differentiated neuroendocrine carcinomas (large-cell and small-cell types), as well as well or poorly differentiated mixed neuroendocrine/nonneuroendocrine neoplasm. Mixed tumors are usually characterized by a combination of neuroendocrine carcinoma and adenocarcinoma [13].

A prerequisite for the morphological diagnosis of neuroendocrine tumors of the appendix is immunohistochemical study with chromogranin A, synaptophysin, CD 56, as well as determination of the proliferation index and mitotic index, using marker Ki-67 [8].

Immunohistochemical examination, as well as determination of mitotic and proliferative activity of tumor cells, revealed a well-differentiated neuroendocrine tumor (G3) of the appendix apex in patient D. (fig. 2). The latter combined with the signs of phlegmonous-ulcerative appendicitis and loci of endometriosis, localized in the muscular layer (fig. 3). Tumor cell complexes were found in part of the visual fields in the vessels localized in the muscular and serous membranes of the appendix (fig. 4).

The postoperative period in the patient proceeded without deviation. The patient was discharged from the hospital and, taking into account the results of morphological examination of the surgical material, was sent to a specialized oncological institution to resolve the issue of further treatment tactics.

Neuroendocrine tumors of the appendix, according to most scientists, are more often (in 60-75% of cases) localized at its apex [14], which we also noted while analyzing our own case from practice. This is due to the fact that the largest number of neuroendocrine cells from which this group of tumors develops, is localized at the apex of the appendix [15].

In our second case, an interesting histological finding was the combination of neuroendocrine tumor of the appendix with endometriosis. The latter is a very rare phenomenon. Among all cases of endometriosis, it accounts for about 1%. It has been proven that endometriosis is a precancerous condition for ovarian tumors [16].

CONCLUSIONS

Malignant tumors of the appendix are a very rare pathology, mainly represented by neuroendocrine tumors and adenocarcinomas. The analysis of our cases from practice show that in patients with neuroendocrine tumor and adenocarcinoma of the appendix, manifested in the clinic of acute appendicitis, there were no anamnestic and clinical-instrumental data, specific for the oncological process. Their absence does not allow the doctor to diagnose the tumor process, leading to diagnostic errors. Morphological examination of the surgical material (removed appendix) is the only method verifying the pathological process. Doctors should always be vigilant about the presence of a tumor in the appendix.

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Conflict of interests:

The Authors declare no conflict of interest.

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Received: 21.12.2020
Accepted: 05.04.2021

A – Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article