

Aim of the study: Acute appendicitis is one of the most common causes of emergency surgical intervention. Most commonly it concerns children and young adults. Beside the inflammatory process there may also be neoplastic lesions in the appendix.

The purpose of this work was to describe two cases of patients treated in our facilities in the emergency duty department due to acute appendicitis in the course of mucin-secreting carcinoma of this organ.

Case description: We present the case of a 41-year-old woman and a 70-year-old man operated on due to acute appendicitis, in whom mucin-secreting carcinoma was histologically diagnosed. The patients underwent a planned right hemicolectomy with removal of the major omentum. After receiving the final histopathological examination results the patients were referred to a regional oncological facility with recommendations of further treatment

Conclusions:

1. Acute appendicitis may co-exist with other diseases of this organ.
2. Adenocarcinoma of the appendix is a rare neoplasm of epithelial origin in the gastrointestinal tract.

Key words: appendicitis, adenocarcinoma.

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Acute appendicitis as a manifestation of adenocarcinoma

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Introduction

When taking the diseases of appendix into consideration we usually think about acute appendicitis. It is one of the most common causes of urgent surgical interventions. It is estimated that about 40% of urgent surgeries performed in Poland is due to acute appendicitis. Most commonly this disease occurs in young adults (second or third decade of life).

The aetiology of acute appendicitis is not entirely known. Generally it is believed that in older patients the inflammatory process is preceded by occlusion of the appendix by a faecal stone with secondary increase in pressure, ischaemia and bacterial infection. In children the cause is said to be oedema of lymphatic nodules, which initiates a cascade of events leading to acute appendicitis.

Diseases of the appendix, besides acute appendicitis, also include neoplastic diseases. There may be either benign or malignant neoplasms in the appendix, which are the following: lipoma, adenoma, carcinoid, lymphoma and adenocarcinoma. Malignant neoplasms of the appendix, especially adenocarcinoma, are rare tumours of the gastrointestinal system, and they occur with a frequency between 0.1 and 0.2 per 100 000 per year. Estimated data indicate that these are about 0.01–0.5% of gastrointestinal neoplasms [1] and about 1% of all epithelial gastrointestinal tumours [2, 3]. The most common tumour in the appendix is carcinoid – a neuroendocrine lesion. This group of tumours is not homogeneous and it contains the following histological forms: carcinoid, highly differentiated neuroendocrine tumour, tubular carcinoid, goblet-cell carcinoid, mixed tumour carcinoid-adenocarcinoma, atypical carcinoid and highly differentiated neuroendocrine carcinoma. The assessment of the clinical course of different cases led to the identification of factors indicating the aggressiveness of these neoplasms, which are as follows: the size of the tumour – the main criterion; histological type – tubular carcinoids have better prognosis, especially compared to goblet-cell carcinoids. In patients with advanced tumours (metastases in imaging examinations) the concentration of chromogranin A is a prognostic factor. Adenocarcinoma of the appendix is mentioned among the rarest neoplastic diseases of this organ [2, 3]. Neoplasms of low differentiation in the appendix are thought to be precursors of lesions like pseudomyxoma peritonei (PMP) and with sub-optimal surgical treatment may lead to the spread of the disease throughout the whole peritoneal cavity. Among the histological forms of adenocarcinoma of the appendix there are: non-infiltrative adenocarcinoma, adenocarcinoma,

medullary cancer, mucin-secreting cancer, mucocellulare carcinoma, planoepitheliale carcinoma, adenoplanoepitheliale carcinoma, small cell carcinoma, undifferentiated carcinoma and not otherwise specified carcinoma. The most frequent form of adenocarcinoma is mucin-secreting carcinoma. The characteristic features of this tumour are metastases limited to the peritoneal cavity, often without metastases in lymph nodes and liver. These neoplasms have better prognosis than those not producing mucus.

Aim of the study

The purpose of this work is to describe two cases of patients treated in our hospitals in an emergency duty due to acute appendicitis in the course of mucin-secreting adenocarcinoma of this organ.

Case description

Pre-operative assessment (interview and physical examination)

A female patient aged 41 years, body mass 62 kg, height 1.65 m, body mass index (BMI) 22.7 and a male patient aged 70, body mass 82 kg, height 1.76 m, BMI 26.4 were admitted to the ward on emergency duty due to acute appendicitis. The patients gave typical interviews for the disease. In the case of the female patient, the interview revealed that her mother was operated on due to adenocarcinoma G3 of sigmoid eight years previously. On admission the patients were in generally good condition, conscious, orientated, cardiovascular and respiratory stability, body temperature in the first case was 37.8°C and in the second case 37.6°C. Blood pressure was within normal range, and heart rate was 110/min and 100/min, respectively. Oral cavity mucous dry, tongue dry and coated. Chest physical examination was within normal range. The stomach was a bit flatulent, and painful in the right iliac fossa. Blumberg's symptom was positive in the above-mentioned region in both cases. Moreover, in the operated female patient, peritoneal signs were noticed also in the lower abdomen, and peristalsis was not heard, while in the male patient peristalsis was lazy. The patients were qualified to operation in the emergency room.

Preparation and operation

Preparation for the operations were as follows: infusion fluids (Ringer's solution, 10% glucose with potassium chloride solution), anticoagulant prevention (LMWH s.c.), acute ulcer prevention (pantoprazole IV), antibiotic therapy ciprofloxacin, metronidazole IV in the first case, and ceftriaxone and metronidazole in the second.

Surgical procedure

The surgical procedure in both cases was typical. Intraoperative assessment confirmed acute appendicitis in both cases, with perforation in the female patient. The intraoperative assessment in the female patient, beside the features of advanced appendicitis, revealed that the length of the preparation was 16 cm and that at the base of the organ there was a significant thickening, but that

did not make appendectomy and caecum debridement more difficult.

Histopathological examination results

The first case – adenocarcinoma mucin-secreting G3 partly signet ring cell carcinoma. It developed on the base of adenoma tubulo-villosum. The tumour infiltrated all layers of the appendix walls and crossed the serous membrane. The rest of the appendix beside the tumour showed gangrenous inflammation and perforation T4aNxMx. The second case – adenocarcinoma G2. The tumour crossed the muscular layer, the base of the appendix, without neoplastic infiltration T3NxMx. The appendix changed in an inflammatory–phlegmonous way.

The patients were qualified to operative treatment. We performed right hemicolectomy with adequate lymphadenectomy and removal of the major omentum. Intraoperative assessment of abdominal organs and peritoneal cavity did not reveal any features of neoplastic spread.

Post-operative treatment and course

Infusion fluids (crystalloid solutions and glucose), antibiotic therapy (ciprofloxacin and metronidazole IV), acute ulcer prevention, anticoagulant prevention, prokinetic treatment and non-steroidal anti-inflammatory medicines.

Postoperative course in both cases was without significant complications apart from a postoperative wound infection in the female patient on the sixth day after the procedure. The wound was healed by granulation after suture removal. Histological assessment of the preparations after radicalisation of the surgical procedure in both cases confirmed adenocarcinoma.

Histopathological assessment after radicalisation of the surgical procedure

The first case. There was no neoplastic tissue in the intestinal wall. In the caecum, in the region of the appendix orifice, there was granulation surrounding surgical sutures with polynuclear cells. In the intestinal wall there were numerous reactively enlarged lymphoid nodules. Moreover, there were features of melanosis in the mucous membrane. In two out of twelve lymph nodes there were metastases of mucin-secreting adenocarcinoma. The major omentum was without neoplastic lesions. On the basis of the described picture, it should be assumed that the primary lesion (mucin-secreting adenocarcinoma, partly signet-cell) localised in the appendix was removed during the previous procedure. Tumour staging T4aN1bMx.

The second case. There was no neoplastic tissue in the small or large intestine walls. In fourteen lymph nodes present in the preparation there were no metastases. Reactive enlargement of lymphoid nodules was seen. The major omentum was without metastases. The preparation assessment allowed diagnosis of adenocarcinoma T3N0M0 stage IIa.

The patients were discharged in generally good condition and with recommendations of control and further treatment in the Regional Oncological Facility. The male patient died four years after the procedure in the course

of a pulmonary embolism on the fifth day after right pneumonectomy, due to planoepithelial carcinoma of the right lung. The female patient was further twice operated on due to neoplasm recurrence in the ovaries. The first procedure (left ovary removal) was performed in our facility in the month following intestine resection, and the second, including uterus removal, was performed in the gynaecological clinic two months after our operation on the left ovary. The short time in which the above-mentioned recurrences were discovered in follow-up imaging examinations is significant. It should be highlighted that during every surgical procedure we assessed all abdominal and pelvic organs, and due to the lack of additional neoplastic lesions besides those diagnosed in imaging examinations (CT) the procedure was planned on the basis of CT examination. In both cases we confirmed the metastatic character of ovarian tumours. Histopathological assessment: mucin-secreting adenocarcinoma of the ovary G3, partly signet-cell (CK7-, CDX-2+, CK20+). In the appendix, as well as in the ovaries, there were morphologically similar neoplasms of identical immunohistochemical profile. This indicates metastases of appendix carcinoma to the ovaries. Until now the patient remains in the care of the Regional Oncological Facility.

Discussion

Symptoms of acute appendicitis presented by patients are frequently untypical, which is the cause of misdiagnosis in many cases. Attempts are being made to create an algorithm or scale to make the diagnostics easier. All methods thus far, e.g. the Alvarado scale, are unsatisfactory. That is why clinical assessment is still of fundamental significance (assessment of peritonitis) in connection with analysis of additional examinations assessing inflammatory reaction. The common phenomenon of so-called “unnecessary” appendectomies when inflammatory lesions of appendix are not confirmed intraoperatively or histologically is highlighted due to a high number of complications such as infection, adhesive obstruction of the digestive tract or infertility in women. It is commonly believed that observation for a few hours in situations when physical and additional examinations are not unambiguous is not dangerous for the patients and may be of benefit in lowering the number of unnecessary operations to about 10–15% [4]. Data from the literature indicate that in about 25–30% of cases, during observation and repeated assessment by the same team, the symptoms diminish. According to the observations of some authors, the risk of perforation is different in different age groups. This index is highest in the case of infants and patients over 60 years of age (50% vs. 30%). In patients among whom acute appendicitis is the most common this index is lowest (10%) [5]. The factor of significant value for the risk of perforation is the time from the first symptoms of acute appendicitis to admission to hospital [6]. Also the percentage of appendectomies performed in condition of diffuse peritonitis should not be larger than 10–15%, which could indicate prolonged observation, delayed surgical intervention or late patient's reporting to the hospital.

Neoplasms of the appendix, in particular adenocarcinoma, are rare tumours of the gastrointestinal system [3]. This was also confirmed by our observations. In facilities where the authors have worked during the last five years 364 patients were operated on due to acute appendicitis and only in three cases, on the basis of histopathological examination, was adenocarcinoma of the appendix diagnosed, which amounts to 0.82%. The small number of cases does not allow us to propose an unambiguous thesis but confirms the general tendency of the occurrence of rare neoplastic lesions of epithelial origin in the appendix. In some of the tumours there is a discrepancy between the benign character in morphological assessment and the aggressiveness of the biological potential connected with bad prognosis and mortality. The course of the disease is usually asymptomatic or mildly symptomatic, particularly in the early phase. In most cases it manifests as acute appendicitis, a tumour in the ileocecal region or pain in the right iliac fossa [7–9]. The diagnostics of the disease are difficult and diagnostic examination results are not characteristic [9]. Among the symptoms, those causing initiation of diagnostics are as follows: abdominal pain, tumour in the right lower quarter of the abdomen or anaemia in control examinations performed due to other causes [8, 10]. In both of the presented cases the cause of reporting to hospital and operative treatment was acute appendicitis. In the interview, besides pain in the lower abdomen, in particular on the right for about 5–6 months in the operated female patient, and constipation in the male patient, there were no other symptoms. This confirms the uncharacteristic course of the disease. After we received the histopathological examination results, the patients were reoperated. The operation was right hemicolectomy with adequate lymphadenectomy and removal of the major omentum. A similar range of operations is recommended in the literature [7, 11]. In publications from the last year, the range of intervention is discussed. Foster *et al.* tried to answer the question whether routine right hemicolectomy has more advantages than appendectomy when comparing the time of survival and the risk of recurrence. They analysed and statistically worked out 120 cases of mucin-secreting carcinoma of the appendix, in which 48 patients had appendectomy performed and the rest 72 had right hemicolectomy performed. Statistical analysis revealed that the kind of operation did not have any influence on survival time. The general condition and completeness of cytoreduction were the only factors having an influence on the patients' survival time. The authors confirmed that the frequency of metastases to lymph nodes was low and the procedure of right hemicolectomy in the case of pseudomyxoma peritonei as well as mucin-secreting neoplasms of the appendix is a safe one [12]. An important factor in patients treated due to malignant neoplasms of the appendix is the histological type of the tumour. This was confirmed in the publication of Turag *et al.*, in which the authors proved in a large group of patients (more than 5000) that the best prognosis measured in a 5-year survival was for malignant carcinoid – 93%, while for goblet-cell carcinoid this index was 81%. The data for mucin-secreting adenocarcinoma and signet ring-cell tumours are less optimistic – 58 vs. 27% [13].

The most frequent histological form of adenocarcinoma is mucin-secreting carcinoma. This was confirmed in the presented material; in both described cases there was mucin-secreting carcinoma. In the female patient it was grade III T4aN1b (metastases in 2 out of 12 lymph nodes) M0 (no features of spread either intraoperatively or in diagnostic imaging), and in the operated male patient it was grade II T3N0M0. The operated female patient had a negative prognostic factor – appendix perforation diagnosed during the first surgical procedure (appendectomy). According to the available literature, it may be connected with higher risk of neoplastic cell implantation to the peritoneum or ovary [14], which was present in this case. Moreover, the tumour may spread in the extra-peritoneal space. Other authors report that the disease being limited to the light of the appendix has a significant influence on the risk of recurrence (group I) as well as, besides the mentioned perforation, the tumour exceeding the borders of the organ and the related peri-appendicular structures (group II). This has significant clinical implications. In the first group the authors of the quoted work propose watch-and-wait surveillance, which includes repeated assessment of tumour markers and abdominal CT examinations. In the second group they performed cytoreductive procedures with intra-peritoneal chemotherapy. Within the observation (median 40 months) the authors did not observe any progress of the disease in either group [8]. Mucin-secreting carcinoma spreads mainly locally; a small percentage of tumours (about 2%) are metastatic in the lymph nodes and, in another 2% of patients, in the liver [15]. Intra-peritoneal chemotherapy is performed in the case of patients with appendix perforation in the course of mucin-secreting carcinoma. Hyperthermic intra-peritoneal chemotherapy involves giving medicines (cytostatics) to a perfusion fluid heated to 42°C. A thesis about the synergic activity of medicines and high temperature is the basis of this procedure. Its effectiveness is greatest when the primary tumour is removed entirely and in the surgeon's assessment there are no other lesions in the peritoneum. In situations when the advancement of the process in the peritoneum is high, the effect of such chemotherapy is improved by maximum available radical removal of the peritoneal lesions. It is recommended that this procedure be performed intra-operatively and in the first week after surgery (before any adhesions develop) [16]. The results of work in which the authors state that application of pre-operative chemotherapy significantly increases the histological response and allows reduction of the area of predicted intervention in comparison with a group in which such treatment was not applied, are encouraging. They observed lengthening of survival time in the group with significant histological response [17]. Application of intravenous chemotherapy is indicated in case of spread to the peritoneum and/or in case of metastases. In the case of further recurrences, cytoreductive procedures are performed (including peritoneal removal) with the above-mentioned preoperative chemotherapy.

In conclusion:

1. Acute appendicitis may co-exist with other diseases of this organ.

2. Adenocarcinoma of the appendix is a rare neoplasm of epithelial origin in the gastrointestinal tract.

The authors declare no conflict of interest.

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