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Ovarian tumor as an early recurrence of mucinosecretans appendix adenocarcinoma

Guz jajnika jako wczesna wznowa raka gruczołowego śluzotwórczego wyrostka robaczkowego

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Słowa kluczowe
zapalenie wyrostka robaczkowego, rak gruczołowy śluzotwórczy, guz jajnika

Summary

The aim of this work is to describe a case of a patient treated in our facility due to acute appendicitis in the course of mucinosecretans adenocarcinoma. The patient was re-operated on – she had a right hemicolectomy performed. In 3 months the patient was operated twice more due to recurrence of the process in the ovaries.

A 41-year-old woman operated on due to acute appendicitis had mucinosecretans appendix adenocarcinoma diagnosed in the post-operative histopathological examination. The patient underwent planned right hemicolectomy with major omentum removal. In a month from operative treatment radicalization the patient was re-operated on due to neoplasm recurrence in the form of cystic left ovarian tumor and next, after 5 weeks, again due to right ovary tumor.

Conclusions. 1. Acute appendicitis does not exclude other diseases of this organ including neoplastic lesions. 2. Appendix adenocarcinoma is a rare neoplasm of epithelial origin in gastrointestinal tract. 3. Patients with mucinosecretans appendix adenocarcinoma should be included to follow-up program of the local recurrences diagnostics.

Streszczenie

Cel pracy. Celem pracy jest opis przypadku chorej leczonej w naszym ośrodku z powodu ostrego zapalenia wyrostka robaczkowego w przebiegu raka gruczołowego śluzotwórczego. Z tego powodu chorą reoperowano – wykonano prawostronną hemikolektomię. Chora operowana jeszcze dwukrotnie z powodu wznowy procesu w jajnikach.

Opis przypadku. W pracy przedstawiamy przypadek 41-letniej kobiety operowanej z powodu ostrego zapalenia wyrostka robaczkowego, u której na podstawie badania histopatologicznego materiału pooperacyjnego stwierdzono gruczolakoraka śluzotwórczego wyrostka robaczkowego. Pacjentkę poddano planowej hemikolektomii prawostronnej z wycięciem sieci większej. W miesiąc po radykalizacji leczenia operacyjnego chora reoperowana z powodu wznowy nowotworu pod postacią torbielowatego guza jajnika lewego, a następnie po kolejnych 5 tygodniach z powodu guza jajnika prawego.

Wnioski. 1. Ostre zapalenie wyrostka robaczkowego nie wyklucza innych chorób tego narządu ze zmianami o charakterze nowotworowym włącznie. 2. Gruczolakorak wyrostka robaczkowego jest rzadkim nowotworem przewodu pokarmowego pochodzenia nabłonkowego. 3. Chorzy z rakiem śluzotwórczym wyrostka robaczkowego powinni zostać włączeni do programu follow up diagnostyki ewentualnych wznów miejscowych.

Conflict of interest
Konflikt interesów
None
Brak konfliktu interesów

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INTRODUCTION

Appendix neoplasms are rare tumors of the gastrointestinal tract (1). The appendix may be the place of either malignant or benign neoplasms' development. The first group among others includes: lipoma and adenoma. The second one: carcinoid, lymphoma and adeno-

carcinoma. Over the years appendix adenocarcinoma surgically and oncologically was treated like colon adenocarcinoma. The standard of surgical treatment was right hemicolectomy with adequate lymphadenectomy. Clinical observations prove that appendix neoplasms, neuroendocrine as well as adenocarcinoma differ from colon adenocarcinomas in their clinical course, metastatic activity and local recurrences and that is why they are classified according to separate criteria. The frequency of appendix occurrence is estimated on 0.1 up to 0.2 cases in 100 000 a year. It is 0.01-0.5% of gastrointestinal neoplasms and about 1% of all epithelial gastrointestinal tumors (1-3). The most frequently diagnosed tumor in the appendix is carcinoid, which is an endocrine neoplasm. There are different histopathological forms of this neoplasm: carcinoid, highly differentiated neuroendocrine tumor, tubular carcinoid and goblet cell carcinoid, mixed tumor – carcinoid – adenocarcinoma, atypical carcinoid and highly differentiated neuroendocrine tumor. Among main criteria of neoplastic aggressiveness there are: tumor's size, the presence of metastases (patients without metastatic lymph nodes and distant metastases have better prognosis). Tubular carcinoids have better prognosis than other histopathological forms, especially in comparison with goblet cell carcinoid. Goblet cell carcinoids are classified according to rules concerning adenocarcinomas because their clinical course seems to be similar. Moreover, goblet cell carcinoids probably tend to produce metastases in ovaries. Also a high plasma concentration of chromogranin A is a prognostic factor in patients who have metastases diagnosed.

Appendix adenocarcinoma is even rarer disease (1, 3). Among its histopathological types there are: non-infiltrative adenocarcinoma, adenocarcinoma, medullary cancer, mucinosecretans cancer, mucocellulare carcinoma, planoepithelial carcinoma, adenoplanoepithelial carcinoma, small cell carcinoma, undifferentiated carcinoma and not otherwise specified carcinoma. The most frequent form is mucinosecretans adenocarcinoma. Mucinosecretans adenocarcinoma and cystadenocarcinoma make about 50% of appendix neoplasms. Their characteristic feature is local spread of the process and metastases limited to peritoneal cavity, often without metastases in lymph nodes and liver. They have better prognosis than those not producing mucous. With distant metastases the 5-year survival is 40-50% (compared to 10% in other appendix cancers). This fact justifies division into mucinosecretans and not-mucinosecretans adenocarcinomas. Clinically significant prognostic factors are: concentration of carcino-embryonic antygen CEA, concentration of Ca – 19.9 (before treatment), the number of neoplastic cells' deposits in the mesentery and data about microsatellite instability an loss of heterozygosity 18q.

The aim of this work is to present a case of a patient treated in our facility on an emergency duty due to acute appendicitis in the course of mucinosecretans adenocarcinoma of this organ.

CASE DESCRIPTION

Pre-operative assessment (patient's history and physical examination)

A patient, aged 41, with body mass 62 kg and height 165 cm, BMI 22.7 kg/m^2 was admitted to the ward on an emergency duty due to acute appendicitis. The patient had typical history of the disease. Family history revealed that her mother was operated on 8 years earlier due to caecum mucinosecretans adenocarcinoma (adenocarcinoma G3 – oral information gained during history taking, no documentation). The patient was qualified to urgent surgery.

Surgery

The surgery went in a typical way. Intraoperative assessment confirmed acute appendicitis with perforation. In an operated patient, beside the length of the preparation – 16 cm, there was a significant thickening of the organ on its basis which, however, did not make appendectomy and caecum debridement difficult. We analyzed the material and made the preparation; the diagnosis was established in ZOZ Olympus Consilio. After two weeks we got the following histopathological examination result: mucinosecretans adenocarcinoma G3, partly goblet cell. The neoplasm developed on the basis of tubulovillous adenocarcinoma with infiltration of all appendix layers and extension into serous membrane. Appendix beyond the tumor with necrotic inflammation and perforation T4aNxMx.

The patient was again qualified to surgery. Before the surgery we performed colonoscopy, due to exclude any synchronic lesions, and abdominal ultrasound examination. Examination results: colonoscopy: per rectum examination without resistance. Colonoscope entered caecum. Bauhin valve identified. In the bottom there is an intussuscepted appendix stump. The whole mucous with melanosis. Hemorrhoids in the rectal canal. Ultrasound examination: liver, spleen, pancreas without focal lesions, of typical size. Gallbladder with thin walls, without stones. Bile ducts not dilated. Retroperitoneal space without signs of lymphadenopathy. Urinary bladder moderately filled. We performed right hemicolectomy with adequate lymphadenectomy and major omentum removal. Locally, apart from caecum walls thickening (the infiltration was about 2 cm in diameter) in a place of intussuscepted appendix stump the colon and the rest of abdominal organs within normal range. Intraoperative assessment of peritoneal organs in pelvis did not reveal features of neoplastic spread.

Postoperative course without significant complications apart from postoperative wound infection on the sixth day after the surgery, which required partial removal of sutures and healing the wound by granulation (a smear was taken to bacteriological examination).

Histological assessment of preparation after treatment radicalization revealed no neoplastic tissue in the intestinal wall. In the caecum, in the region of appendix mouth there was granulation with multinucleated cells

surrounding suture. There are numerous reactively enlarged lymphoid nodules in the intestinal walls. Moreover, there is melanosis in the mucous membrane. In two out of twelve lymph nodes there are metastases of mucinosecretans adenocarcinoma. Major omentum without metastatic lesions. On the basis of the described picture it should be assumed that the primary lesion (mucinosecretans adenocarcinoma, partly goblet cell) localized in the appendix was removed during the previous surgery. Neoplastic severity T4aN1bMx. Preparations from appendix showing different stages of neoplastic growth – from tubulovillous adenoma to adenocarcinoma are presented on figures 1-6.

After having the patient signed off, she was directed to the cancer center with the view of further treatment. One month after radicalization of treatment the patient had follow-up imaging examinations performed. Chest X-ray, abdominal ultrasound and abdominal CT. Chest X-ray results: lung fields without focal lesions and parenchymal densities. Abdominal ultrasound: Right ovary 28 x 18 mm with correct follicular structure. The whole left ovary occupied by simple cyst 51 x 37 mm compressed by large cystic lesion 105 x 57 mm with thick-walled partitions. In the partitions there is a low resistance flow. Sonographical picture may be an equivalent of mucous lesion. In the Douglas recess there is free fluid 12 mm thick. Abdominal CT: liver, pancreas, spleen homogeneous, without focal lesions. Kidneys of typical size without focal lesions. Pelvicalyceal systems without stones. Urine excretion efficient. Signs of stasis in the right kidney. Right ureter dilated to 9 mm. Adrenal glands homogeneous, not enlarged. Above the urinary bladder, to the front and over the uterus there is a pathological encapsulated mass with two chambers, 115 x 66 x 95 mm, with density of 26 HU and little contrast enhancement (up to 37 HU in the parenchymal phase). In the lesion there are blood vessels. The lesion compresses right ureter which causes stasis in the pelvicalyceal system. Intra and retro peritoneal spaces without signs of lymphadenopathy (fig. 7-10). On the basis of the previous course of the disease and imaging studies (the lack of clear connection between the lesions described and the reproductive organ), the patient was qualified to the next surgical treatment and directed to our centre as the place where the surgical treatment of the patient has been carried out so far. Intraoperatively, apart from planar adhesions there was a cystic lesions attached to peritoneum which originated from the left ovary. The patient had left uterine adnexa with the described lesion and left iliac fossa peritoneum removed. Right ovary with correct structure The course of hospitalization without complications. The histopathological examination result confirmed recurrence of mucinosecretans adenocarcinoma in the researched material. Histopathological assessment: ovarian mucinosecretans adenocarcinoma G3 partly goblet cell (CK7-, CDX-2+, CK20+) (fig. 11). In the appendix as well as in the ovaries there are morphologically similar neoplasms with identical immunohistochemical profiles. It indicates the presence of metastases of appendix carcinoma into the ovary. One and a half months after left ovary removal there was a follow-up ultrasound

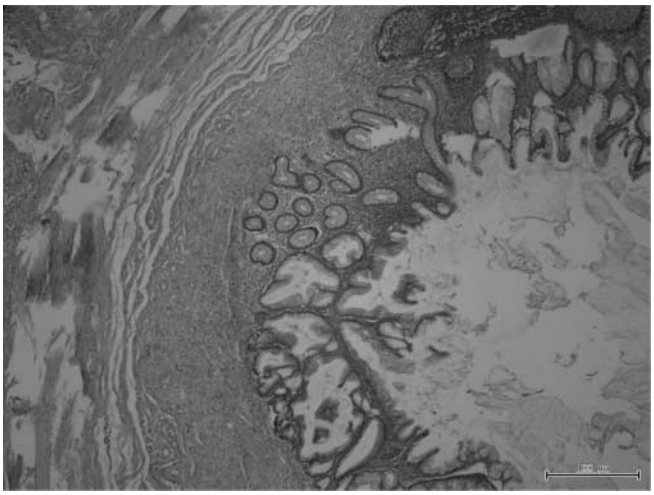

Fig. 1. The appendix wall with tubulovillous adenoma tissue and a small degree dysplasia and fragments of “still correct” mucous of appendix

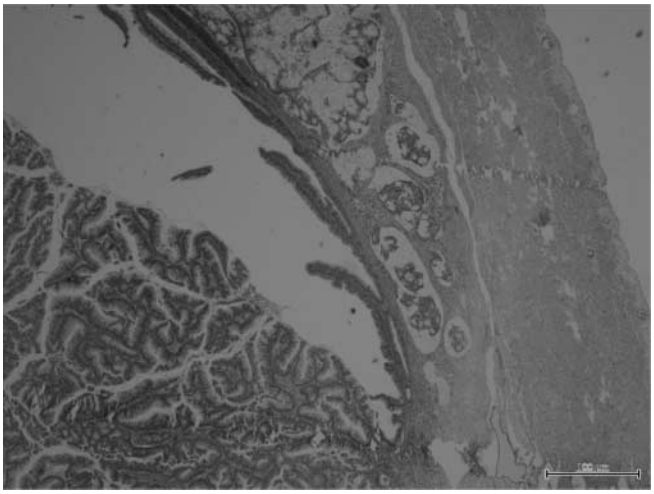

Fig. 2. The appendix wall with tubulovillous adenoma tissue and a large degree dysplasia and adenocarcinoma on its basis. Cancer tissue is visible deep in the muscle tissue of appendix with vessel obstruction. Some tissue is mucinously differentiated

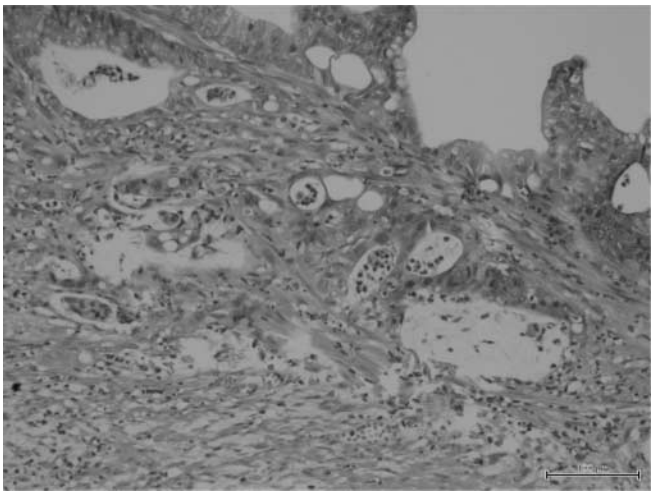

Fig. 3. The appendix wall with typical adenocarcinoma infiltration

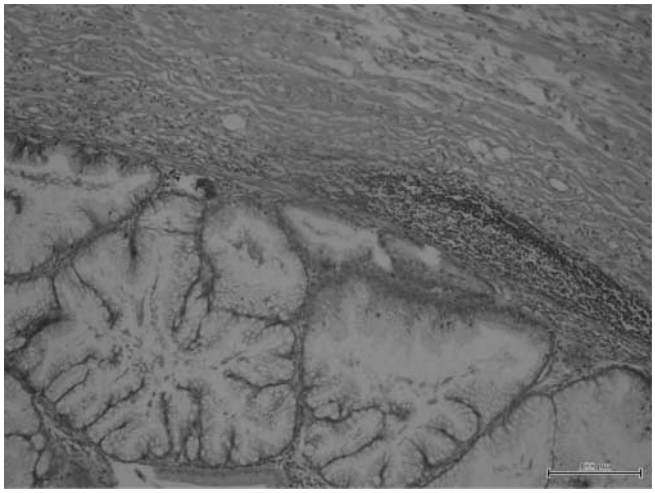

Fig. 4. The appendix wall with tubulovillous adenoma tissue and a small degree dysplasia

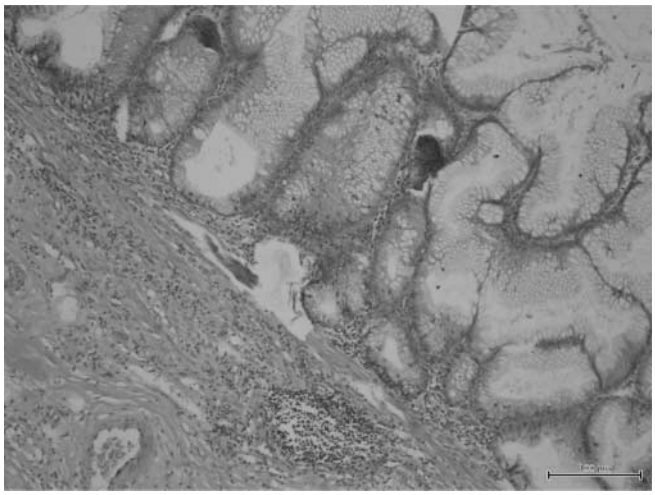

Fig. 5. Tubulovillous adenoma tissue and a small degree dysplasia

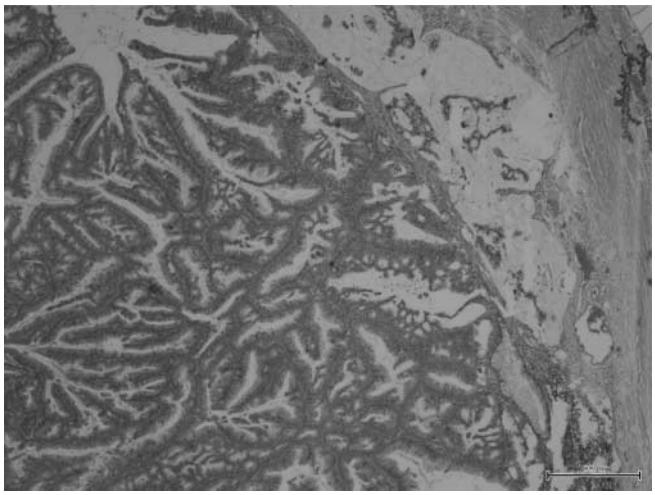

Fig. 6. Tubulovillous adenoma tissue and a large degree dysplasia and adenocarcinoma on its basis

examination which revealed a right ovary tumor. Ultrasound examination result: liver, spleen, pancreas not enlarged, without focal lesions. Gall bladder without stones. Bile ducts not dilated. Kidneys of typical size,

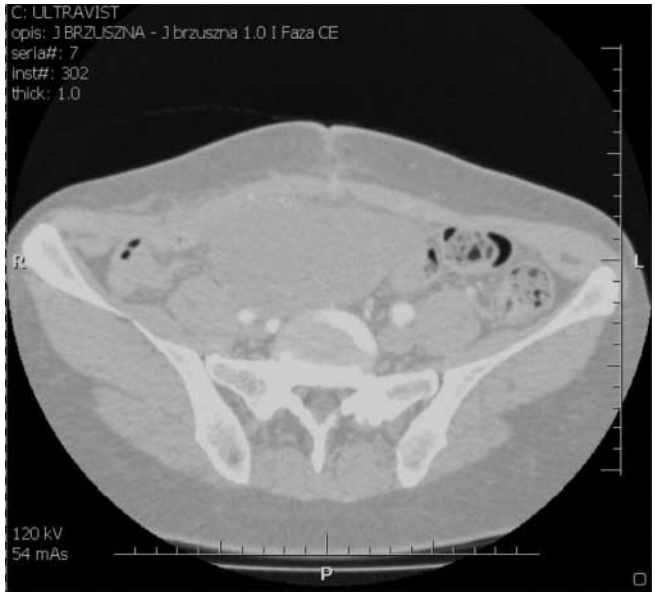

Fig. 7. Abdominal CT, the first phase of examination

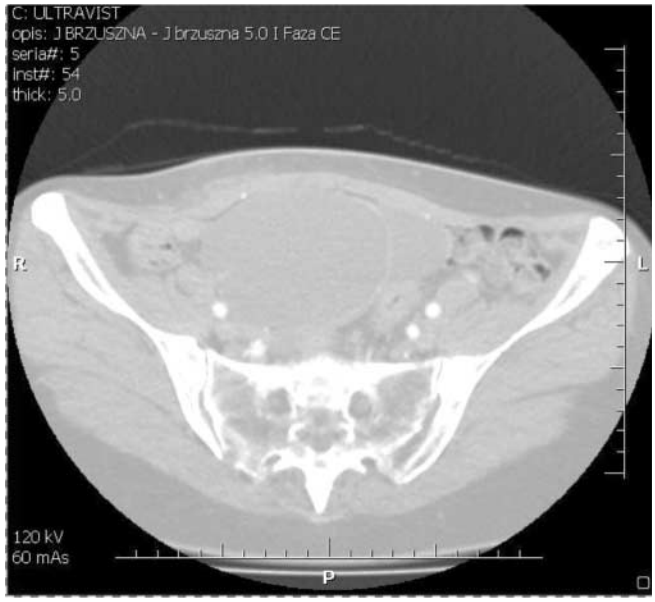

Fig. 8. Abdominal CT, the first phase of examination

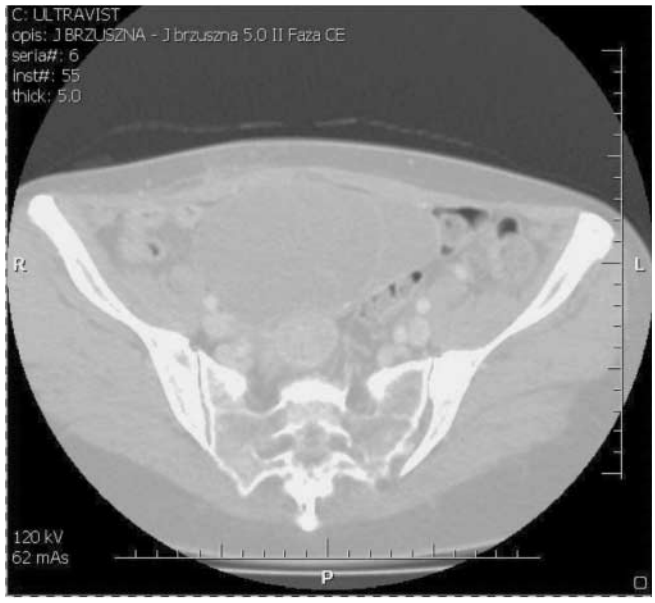

Fig. 9. Abdominal CT, the second phase of examination

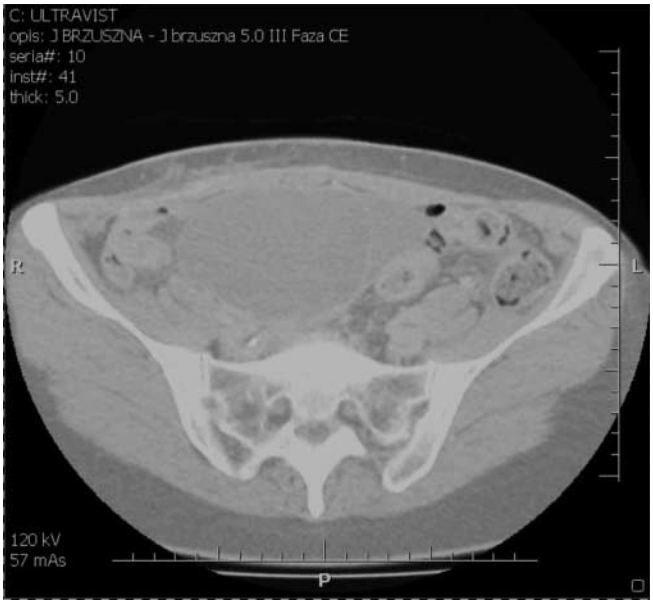

Fig. 10. Abdominal CT, the third phase of examination

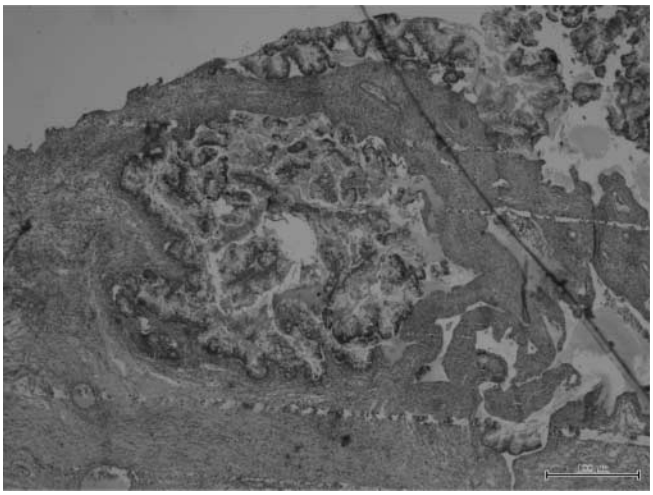

Fig. 11. A fragment of an ovary with infiltrating adenocarcinoma, its tissue responds to metastases form the primary adenocarcinoma of appendix

without focal lesions, without stasis and stones. Retroperitoneal space without signs of lymphadenopathy. Urinary bladder poorly filled. In the right adnexa there is a solid-cystic lesion 85 x 71 x 56 mm. It the solid part there is vascularisation. Corpus uterus translocated to the left. Peritoneal cavity without free fluid. The patient was qualified to operative treatment. Removal of uterus and right adnexa was performed in the Gynecology Clinic. The histopathological examination result: *adenocarcionoma mucinosum typus intestinalis ovaria dextri metastaticum. Oviductus deuter normalis. Mucosa portionis vaginalis coli uteri normalis. Hyperplasia glandularum endocervicis. Endometrium menopausale atrophicum. Polypus fibro-glandularis endometria lis. Leiomyomata corporis uteri.* Until now (a year after the last surgery) the patient remains under care of local oncological facility. The patient's medical record was sent to one of the British facilities that specialize in treatment patients with appendix neoplasms.

DISCUSSION

Appendix neoplasms, particularly adenocarcinoma, are rare tumors of gastrointestinal tract (1). We confirmed it in our observations. In facilities where authors work, in the past 5 years 364 patients were operated on due to acute appendicitis, only 3 patients had, on the basis of histopathological examination, adenocarcinoma diagnosed, which in percentage makes 0.82%. The disease is asymptomatic or with a few symptoms especially in the early stages. The symptoms may be different and depend on the severity of the disease, infiltration of other organs and complications. The most frequent manifestation of the disease is an acute appendicitis or a tumor in the ileocecal region (4). The diagnostics is difficult which results from the above mentioned mildly symptomatic course of the disease in its early stage, the lack of disturbing symptoms which make the patient report to the doctor or to the hospital. In this phase imaging examinations are also uncharacteristic (4). The disturbing symptoms that incline to start the diagnostics occur later and include abdominal pain, tumor in the lower right abdominal quadrant or anemia diagnosed in the laboratory tests performer form another reason (5).

In the presented case the cause of surgical intervention was acute appendicitis which is confirmed in the available literature (4). On the basis of patient's history there were no other symptoms apart from lower abdominal pain for about 5 months before the surgery, which confirms mildly symptomatic course of the disease. Radicalization of surgical treatment involved right hemicolectomy with adequate lymphadenectomy and removal of major omentum. Similar range of operation is recommended in the literature (6, 7). Presented cases as well as other authors' observations confirm the basic surgical rule that all surgical preparations must be examined histopathologically (6). Differences in the course of the disease caused isolation of these neoplasms and creating a separate classification. Nowadays appendix adenocarcinoma is divided into mucinosecretans and non-mucinosecretans. Mucinosecretans neoplasms occur more often. It is confirmed in our material; beside the described patient we had two more cases of mucinosecretans appendix adenocarcinoma in the last five years. Indeed small number of cases does not allow making a straightforward thesis. However, our material confirms the general tendency of mucinosecretans neoplasms occurring more often. Mucinosecretans cancers are also less malignant in comparison to those non-mucinosecretans. Histopathological assessment revealed IIIB grading T4N1 (metastases in 2 out of 12 removed lymph nodes) M0 (no signs of neoplastic spread in imaging examinations). Perforation of the appendix during the first intervention is an unfavorable prognostic factor. Unfortunately our patient had this negative factor. According to other authors' observations it may be connected to higher risk of metastatic implants in the peritoneum (hernial peritoneum) or the ovary (8).

Reoperation in the patient due to cystic ovarian tumors and confirmed in histopathology metastatic character of these tumors corroborate appendix perforation to be a factor of recurrences in case of patients with appendix carcinoma. Mucinosecretans carcinoma spreads mainly locally (including retroperitoneal space), only in about 2% of cases there are metastases in lymph nodes and in another 2% in the liver (9). In case of patients with appendix perforation in the course of mucinosecretans adenocarcinoma some authors propose application of intraperitoneal chemotherapy. It may be applied intraoperatively and in one week after the surgery (until adhesions occur) (10). With peritoneal spread and/or in case of metastases it is recommended to apply intravenous chemotherapy (11). In case of other recurrences cytoreductive procedures including peritoneal removal are performed.

CONCLUSIONS

1. Acute appendicitis does not exclude other diseases of this organ including neoplastic lesions.
2. Appendix adenocarcinoma is a rare neoplasm of epithelial origin in gastrointestinal tract.
3. Patients with mucinosecretans appendix adenocarcinoma should be included into a follow-up program of local recurrences diagnostics.

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