CASE REPORT

EXPERIMENTAL ONCOLOGY

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APPENDICULAR MUCINOUS CYSTADENOMA AND CYSTOADENOSARCOMA IN GYNECOLOGICAL PRACTICE. CLINICAL CASES AND LITERATURE REVIEW

Tumors of the right uterine appendages cannot always be distinguished from mucous neoplasms of the appendix (MA) at the preoperative stage. According to the literature, MA is traditionally considered more common in women than in men at the age of 50 years, with a ratio of 4:1. We have identified 2 cases of surgical treatment of MA in gynecological practice, one of mucinous cystadenoma and the other of mucinous cystadenocarcinoma. We present the visual intraoperative assessment of the appendix condition in cystadenoma and cystadenocarcinoma, clinical manifestations, diagnostic discrepancies, and operative tactics. The literature on the detection of appendicular mucocele that mimics ovarian tumor formations in women has been reviewed. The features of diagnostics and possible diagnostic errors were summarized. Diagnostic laparoscopy, visual and operative clinical experience of the surgeon, and cytological and histological examinations of intra- and postoperative results allow for an adequate treatment. It is advisable that the stages and course of appendectomy be reviewed by operating gynecologists and, if necessary, general surgeons.

Keywords: right uterine appendage, mucocele, appendix, appendicular mucinous cystadenoma, cystadenocarcinoma.

The differential diagnosis of non-urgent tumors of the uterine appendages — ovaries and fallopian tubes — during a routine examination by an obstetrician-gynecologist requires additional investigations to determine gynecological, gastrointestinal, or urinary tract metastasis [1, 2]. In this case, the state of clinical manifestations, bimanual examination, ultrasound, MRI, CT, tumor markers, colonoscopy, and fibrogastroscopy are always used. Unfortunately, in the case of pathologies of

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the right ovary and fallopian tube, it is not possible to make a clear diagnosis of appendicular mucoceles (MA) — mucinous cystadenoma and mucinous cystadenocarcinoma in the preoperative stage, even when all the examination methods are used [3]. This is an obstructive dilatation of the appendix lumen due to mucus hyperproduction (0.2%—0.3% of all appendectomies), but it can also occur in the practical surgical work of operating gynecologists [4, 5].

According to the literature, MA is traditionally thought to be more common in women than in men at a ratio of 4:1 after the age of 50, but this pattern is not always observed. Its clinical manifestations are not specific and often mimic acute appendicitis. Currently, there are 4 histological types of MA: 1) simple mucocele or retention cyst (18%); 2) limited or diffuse hyperplasia (20%); 3) mucinous cystadenoma (52%—84%), and 4) mucinous cystadenocarcinoma (10%—20%) [6]. MA was first described by Rokitansky in 1842 and characterized in 1973 by Aho et al. [7]. In 2010, Professor N. Carr and colleagues from the Basingstoke Medical Centre (UK) finally proposed a binary classification system for such tumors based on morphological studies — low-grade and high-grade (including an intermediate type) of peritoneal pseudomyxoma [8]. The most aggressive is mucinous cystadenocarcinoma, the spread of which during surgery may lead to pseudomixed peritoneum in the form of multiple mucinous deposits [9, 10]. The peculiarity of MA is that it is difficult to diagnose via ultrasound and MRI, which show tumor formation in the right uterine appendages [11—13].

We report 2 cases of discrepancy between the preoperative preliminary diagnosis (pathology of right ovary or tube) and the intraoperative/postoperative conclusion (tumors of appendicular origin — appendicular mucinous cystadenoma or cystadenocarcinoma) in women operated by gynecologists. Case 1 was partly described in our previous work [14], and case 2 is presented for comparison between different types of pathological tumors of the appendix. As appendicular and adnexal masses mimic each other, we also use a literature review to describe similar cases. We report this case according to the updated Consensus-Based Surgical Case Report (SCARE) guidelines [15].

Case presentation

Case 1. A 50-year-old woman from the Lviv region of Ukraine presented to the gynecological clinic of the Yu. Lypa Lviv Regional Hospital of War Veterans and Repressed. The patient, who had been using the Mirena IUD for 3 years for the treatment of uterine fibroids and abnormal uterine bleeding, developed pain in the right iliac region, and a slight increase in temperature to 37—37.5 °C for the past 10 days. The patient had no gastrointestinal problems.

The patient had been undergoing regular gynecological examinations for 3 years while using the Mirena IUD for the treatment of uterine fibroids; before the Mirena IUD was inserted, she had puterine bleeding, and during the treatment, her menstrual flow became shorter and lighter. On the protrusion of the right adnexa, a 7 × 4 cm mass, tender to palpation, uterine fibroids, and unremarkable processes were found on the left side. The cervix was clean, and the Pap test was normal. Pelvic ultrasound showed a right uterine adnexal volume of 67 × 25 × 31 mm, no vascular invasion on Doppler, an intrauterine device in the uterine cavity, and 3 subserosal lymph nodes measuring 10 × 13 mm along the anterior uterine wall.

The tumor morphology on dynamic and lymph node examination had not changed in the past 2 years. MRI showed a cystic lesion in the right adnexa (72 × 40 × 35 mm) with thin septa, and no signal intensity, but there were 3 small myometrial lesions (10—15 mm) with a low T2 signal. The ureter was unremarkable.

The patient was diagnosed with a right fallopian tube tumor or pyosalpinx based on ultrasound and MRI, and the rest of the physical examination was unremarkable.

Antibiotic therapy for 10 days was recommended for the treatment of right pyosalpinx: intravenously Ceftriaxone 1.0 g twice daily, Metronidazole 100 mL twice daily, Levofloxacin 500 mg twice daily, Diclofenac 100 mg rectally for 10 days. On admission, her vital signs were normal. Tumor markers showed normal HE 4 and CA 125, and blood cell counts and metabolic panel were within normal limits, not consistent with a diagnosis of pyosalpinx. On the last day of antibiotic therapy, an endometrial punch biopsy was performed on ultrasound to reveal a 2.4 mm endometrium.

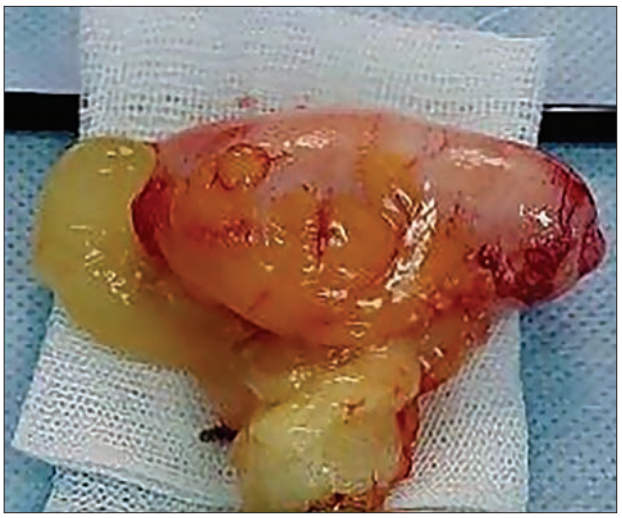

Fig. 1. Appendicular mucocele

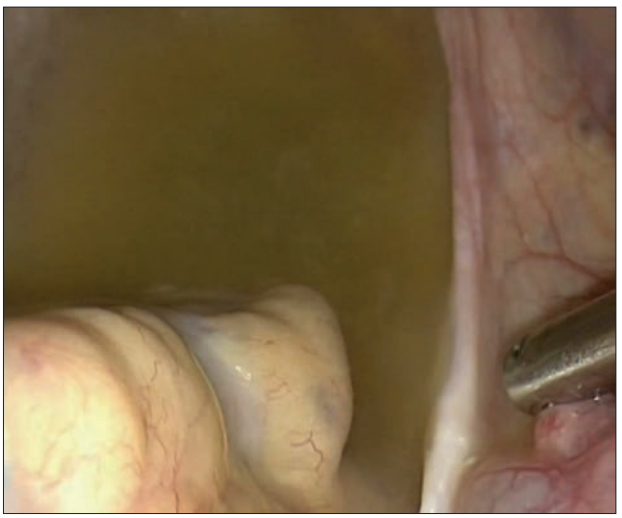

Fig. 2. Mucinous content found in the Douglas space

After a benign histology report, endometrial biopsy, and follow-up ultrasound, she was determined to undergo surgery.

At a conference examination of the patient in the surgical department, we performed laparoscopic bilateral salpingo-oophorectomy and myomectomy because this 50-year-old patient insisted on retaining the uterus and ovaries and not removing the Mirena IUD. Taking into account the history of cesarean section and the expectation of postoperative adhesions, a surgical team consisting of a gynecologist and a general surgeon was formed.

The patient was admitted to the hospital for diagnostic laparoscopic surgery, bilateral salpingectomy, and myomectomy with preservation of uterine fibroids.

After an abdominal pelvic examination, the appendix tumor was isolated from the ovary without mucus leakage. No mucus was found in the abdominal cavity. The liver, spleen, and kidneys were normal, and there were no peritoneal lymph nodes affected. First, the gynecologist performed bilateral salpingectomy and myomectomy with preservation of 3 subserosal lymph nodes. The appendectomy was performed by an experienced surgeon.

Cytology during the appendectomy showed no neoplastic process. The postoperative course was uneventful, and the patient was discharged on the second postoperative day without any complaints.

The histopathology revealed a mucinous appendiceal tumor (6 × 2.5 × 3 cm): a cystic mass lined by mucus-producing intestinal epithelium with numerous papillae and formed from fibrous tissue with lymphocytic infiltration, lymph nodes, and uterine tube — without features (Fig. 1). The diagnosis was appendiceal mucocele — Low-Grade Appendiceal Mucinous Neoplasm LAMN (pT4aNxMx).

Case 2. A 38-year-old woman presented for examination and treatment with complaints of pain in the right pelvic region without fever and visited the gynecological clinic of the Second Lviv Territorial Medical Association. The patient did not complain of dyspeptic disorders and occasional watery stools. The patient had a history of 2 deliveries and a recurrent pelvic inflammatory disease. Her social, environmental, family, and occupational history was unremarkable. She had never smoked, was a moderate drinker, and was not on any long-term medication. Examination revealed a 5 × 4 cm tumor on the right side which was tender to palpation. Physical examination and laboratory tests were unremarkable, there was no leukocytosis, and CA 125, CEA, and HE4 were normal. Transvaginal ultrasound showed a periovarian cystic mass in the right lower quadrant of the abdomen with a diameter of 4 × 5 cm. MRI showed a 5 × 4 cm right ovarian mass.

The patient was diagnosed with a right tubo-ovarian tumor according to ultrasound and MRI, and the rest of the physical examination was unremarkable. Intraoperatively, up to 30 ml of mucus was found in the Douglas space, 2 fallopian tubes were found to be intact, and a 4.5 cm appendicular tumor without adhesions was found. Intraoperative cytology of the appendix was not performed.

The liver, spleen, and kidneys were normal on palpation, and the peritoneal nodes were not affected. A laparoscopic appendectomy without hemi-

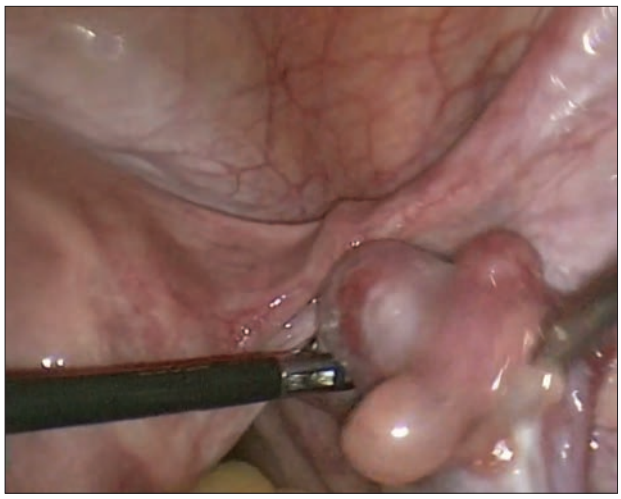

Fig. 3. Intact right uterine appendages: ovary and fallopian tube

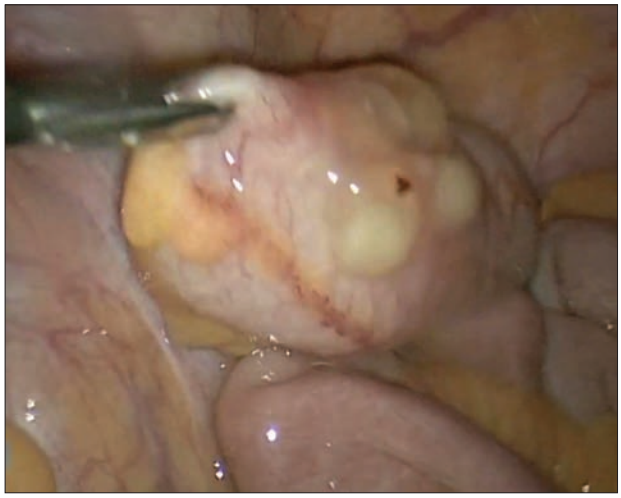

Fig. 4. Appendicular formation from which mucin was released

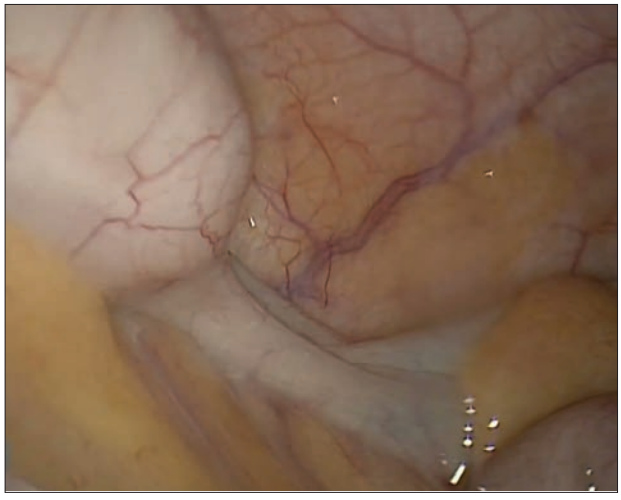

Fig. 5. The appendix base and cecal dome were not involved in the pathological process

colectomy was performed (Figs. 2—5). The postoperative period was uneventful, and the patient was discharged on postoperative day 2 without any complaints.

Histopathological examination revealed a high-grade mucinous cystadenocarcinoma of the appendix pT4NxMxG3, and the patient was referred to an oncology clinic for the next stage of hemicolectomy. After a laparoscopic operation in Germany, there were no recurrences during the two-year follow-up.

Discussion. MA belongs to the category of rare gastrointestinal tumors and is more common in postmenopausal women [16, 17]. However, in recent years, there has been an increasing number of publications on the detection of appendiceal tumors in women of reproductive age [18—20]. In terms of clinical manifestations, MA is often nonspecific. This rare pathology may never be encountered by obstetricians and gynecologists in practice, especially in the outpatient setting. The situation is similar for ultrasound and MRI physicians. In the preoperative period, less than 30% of general surgeons can diagnose appendicular mucinous cystadenomas before surgery using transvaginal/transabdominal ultrasound, MRI, CT, and positron emission tomography (PET) [21, 22].

Toffaha et al. [23] described a case of MA in a 58-year-old woman with fibroids and a tumor of the right ovary, with a worm-like process adjacent to the ovary, discharging mucus through its tip. Hysterectomy, bilateral salpingo-oophorectomy, and appendectomy were performed. Histopathology showed a mucinous neoplasm of the right ovary, but the origin was a low-grade mucinous neoplasm of the appendix (pT4aNxMx). The patient had no recurrence during the 3-year follow-up.

Aleter and El Ansari [24] presented the case of a 61-year-old woman who was diagnosed with a large mass of the right appendix during a control ultrasound examination. The patient refused further imaging examination, and based on laparotomy, she was diagnosed with an appendicular mucocele with normal left and right ovaries. An appendectomy was performed, and the final pathology was a mucinous neoplasm of the appendix. Her postoperative course and 3-year follow-up were uneventful.

Alghamdi et al. [25] published the case of a 41-year-old woman who was diagnosed with an

appendiceal tumor incidentally discovered on MRI, which showed a large cyst measuring 7 × 4 × 3 cm in the right iliac fossa with high suspicion of MA. The patient underwent an open right-side limited hemicolectomy in the surgical department. She was diagnosed with a well-differentiated low-grade MA neoplasm of stage 0 (pTis, pN0, M0) according to the 8th edition of the American Joint Committee on Cancer (AJCC) staging system. The patient recovered without complications and was recommended for regular follow-up for at least 5 years.

Lomei et al. [26] published the case of a 51-year-old woman who was admitted for suspected appendicitis. She underwent an open appendectomy in the surgical department and was diagnosed with mucinous cystadenocarcinoma of the appendix pT4NxMxG3. The patient recovered without complications, and CT and ultrasound of the abdominal cavity for 5 years showed no pathological changes and no pseudomyxoma peritonei.

Gortchev [27] reported the case of a 68-year-old postmenopausal woman with hypertension and diabetes mellitus. A transvaginal ultrasound revealed a cystic mass in the right lower quadrant of the abdomen with a diameter of 3.9 cm. Diagnostic laparoscopy revealed bilateral atrophic ovaries, a normal-size uterus, a small bowel, and the liver with a normal appearance. There was a 3—4 cm mass from the cervix apex adjacent to the right ovary. A laparoscopic appendectomy was performed, and there was no tumor rupture at the time of surgery. Histological examination of the surgical specimen revealed an appendicular mucocele.

Guio et al. [28] described a 43-year-old patient after 38.1 weeks of her first pregnancy. She had a history of gestational diabetes and morbid obesity. She was admitted to the hospital for an emergency caesarean section, indicated because of intrauterine growth retardation, with no possibility of waiting for treatment. A prenatal ultrasound scan in the first trimester showed a cystic mass, septal, measuring approximately 12 × 12 cm. Abdominal MRI showed a cystic lesion on the right flank, probably caused by a right appendage, measuring 12 × 9 cm. Histopathological examination revealed a poorly differentiated mucinous neoplasm associated with mucin extravasation from the celiac process and a peritoneal pseudomyxoma.

The best surgical management of these patients remains controversial. There is no consensus on either the optimal surgical procedure, which may be a right hemicolectomy or simple appendectomy, or the optimal surgical technique, i.e. laparoscopy versus laparotomy. While a right hemicolectomy has been associated with a survival benefit in the treatment of mucinous cystadenocarcinoma, recent prospective data show no benefit with respect to potential peritoneal pseudomyxoma or mucinous carcinomatosis. Nevertheless, precautions should be taken to prevent the spread of mucus, such as careful handling of the appendix. In the absence of local invasion, appendectomy with mesoappendectomy is the optimal treatment approach. However, if the cecum or colon is involved, a right hemicolectomy is mandatory. Regarding the surgical technique, some authors argue that laparotomy allows better visualization of the abdominal cavity and detection of potential pseudomyxomas compared to the laparoscopic approach. Conversely, laparoscopy has been associated with a higher incidence of peritoneal implants and inadvertently missed lesions [29].

Therefore, MA should be considered in the differential diagnosis of women with ultrasound neoplasms while selecting the optimal surgical approach. A gynecologist can perform a diagnostic laparoscopy if a general surgeon is available in the medical facility when a neoplasm of appendicular origin is detected. Thorough preoperative preparation is recommended. Discussion of such cases can help minimize the possibility of intraoperative surprises for both patient and surgeon.

A thorough preoperative diagnosis is necessary in the examination of right uterine appendages, which does not always provide a definitive answer to the clinical diagnosis. CT is preferable to MRI for better diagnosis. Diagnostic laparoscopy, visual and operative clinical experience of the surgeon, and cytological and histological examination of intra- and postoperative results allow for an adequate treatment. The stages and course of appendectomy should be reviewed by operating gynecologists and, if necessary, general surgeons. Patients should be counseled about doubts concerning the outpatient diagnosis, the appropriate diagnosis after abdominal and pelvic examination, and possible changes in the intraoperative plan. Emergency care should be provided in facilities with appropriate teams and equipment. The presentation of atrial fibrillation is usually non-specific due to its anatomical location.

Physicians should consider this in the differential diagnosis of an ever-expanding ovarian cyst or epididymal growth.

Declaration of Competing Interests

There are no competing interests to declare.

Consent

Written informed consent was obtained from the patients for the publication of this case report and accompanying images. A copy of the written consent is available for review by the editor-in-chief of this journal upon request.

Authors' contribution

SV: data collection, research concept, clinical case; MV: research concept, interpretation, article writing; CR: research concept, article writing; NO: studying the concept; RT: interpreting the data, writing an article; MY: data collection, clinical case; CV: study of literature data.

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АПЕНДИКУЛЯРНА МУЦИНОЗНА ЦИСТАДЕНОМА І ЦИСТОАДЕНОСАРКОМА В ГІНЕКОЛОГІЧНІЙ ПРАКТИЦІ. КЛІНІЧНІ ВИПАДКИ ТА ОГЛЯД ЛІТЕРАТУРИ

Пухлини правих придатків матки не завжди можна відрізнити від пухлини апендикса мукоцеле червоподібного відростка (МА) до операції. За даними літератури, МА традиційно зустрічається частіше в жінок, ніж у чоловіків. У 50 років це співвідношення становить 4:1. Нами оцінено два випадки хірургічного лікування МА в гінекологічній практиці (муцинозна цистаденома та муцинозна цистаденокарцинома). Описано етапи інтраопераційної візуальної оцінки стану червоподібного відростка при цистаденомі та цистаденокарциномі, клінічні прояви, діагностичні розбіжності на дооопераційному етапі та хірургічну тактику. Наведено огляд літератури стосовно ідентифікації апендикулярних муцинозних кіст у жінок, що імітують пухлини яєчників і маткових труб. Визначено особливості діагностики на амбулаторному етапі та узагальнено можливі діагностичні помилки. Діагностична лапароскопія, візуальний та операційний клінічний досвід хірурга, цитологічне та гістологічне дослідження інтраопераційних та післяопераційних результатів дозволяють призначити адекватне лікування. Ми рекомендуємо узгоджувати питання розширення хірургічної тактики щодо видалення апендикса з гінекологами та хірургами на етапі дооопераційного консультування пацієнтів.

Ключові слова: праві придатки матки, муцинозна кіста, апендикс, муцинозна цистаденома апендикса, цистаденокарцинома.