INTERNATIONAL MULTIDISCIPLINARY WORKSHOP ON APPROACH TO WOMEN WITH PELVIC ORGAN TUMORS

Abstract book

UNIERSITY MEDICAL CENTRE MARIBOR
Department of Gynaecology and Perinatology

January 2018
Maribor, Slovenia

PUBLISHER
University Medical Centre Maribor
Department for Gynaecological and Breast Oncology

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ELECTRONIC ISSUE
Available at:
http://www.ukc-mb.si/

CIP - Kataložni zapis o publikaciji
Univerzitetna knjižnica Maribor

618.1-006(082)(0.034.2)

INTERNATIONAL Multidisciplinary Workshop on Approach to Women with Pelvic Organ Tumors (1 ; 2018 ; Maribor)
Abstract book [Elektronski vir] / 1st International Multidisciplinary Workshop on Approach to Women with Pelvic Organ Tumors, University Medical Centre Maribor, Department of Gynaecologic and Breast Oncology, 12 - 13 January 2018, Maribor ; [editors Maja Pakiž, Nejc Kozar]. - Maribor : University Medical Centre, Department of Gynaecologic and Breast Oncology, 2018

Način dostopa (URL): http://www.ukc-mb.si/

ISBN 978-961-7039-01-6 (pdf)
1. Pakiž, Maja
COBISS.SI-ID 94001153

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UNIVERSITY MEDICAL CENTRE MARIBOR
Department for Gynaecological and Breast Oncology

ABSTRACT BOOK

12 - 13 January 2018

Maribor, Slovenia

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WORKSHOP PROGRAM

Friday, 12. 1. 2018

11.00–12.00
Registration

PART 1
Moderators
(Takač I, Maribor, Slovenia, Verheijen R, Utrecht, The Netherlands)

12.00-12.10
Welcome address
(Takač I, Maribor, Slovenia)

12.10-12.40
What's new in WHO classification of the pelvic organ tumors and how does it influence our clinical approach
(Pakiz M, Kavalar R, Maribor, Slovenia)

12.50-13.20
Ultrasound examination in pelvic tumors – a review
(Knez J, Maribor, Slovenia)

13.30–14.00
Imaging in pelvic tumors – interobserver variability
(Rudolf S, Maribor, Slovenia)

14.10-14.40
What is target therapy? What's new in the field of pelvic organ tumors
(Škof E, Ljubljana, Slovenia)

14.40-15.10 Break

PART 2
Moderators
(Zola P, Turin, Italy, Pakiz M, Maribor, Slovenia)

15.10-15.40
Algorithms and nomograms to direct treatment choices
(Klarić M, Rijeka, Croatia)

15.50-16.20
ESMO-ESGO-ESTRO guidelines for endometrial cancer – a review
(Zola P, Turin, Italy)

16.30-17.00
Early cervical cancer – how radical should we be?
(Dostálek L, Slama J, Prague, Czech Republic)

17.10-17.50
ESGO quality indicators for advanced ovarian cancer treatment – a review. ESGO presentation.
(Verheijen R, Utrecht, The Netherlands)

18.00-18.20
Olaparib in advanced ovarian cancer: rational, data and practice
Sattelite symposium (Astra Zeneca, Erik Škof, Ljubljana, Slovenia)

18.20-18.30
Avastin in the treatment of ovarian cancer in Slovenia
Sattelite symposium (Roche, Maja Ravnik, Maribor, Slovenia)

Saturday, 13. 1. 2018

PART 3

8.30 - 11.30 and 12.00 - 14.00: Real-life case reports;
each will be presented and discussed by:

Coordinator: Maja Pakiž
Moderators: Rene Verheijen, Lukáš Dostálek

1. **Gynecologist** (diagnosis, surgery);
Andraž Dovnik, Jure Knez, Ksenija Rakić, Špela Smrkolj, Sebastjan Merlo
2. **Radiologist** (imaging);
Saša Rudolf, Ksenija Vuković
3. **Pathologist** (definitive diagnosis);
Rajko Kavalar, Tatjana Bujas, Žana Grazio
4. **Oncologist** (oncological treatment and follow up if appropriate);
Maja Ravnik, Matej Horvat, Andrej Žist, Ana Demšar, Erik Škof

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Moderators: Paolo Zola, Iztok Takač

Chiara Macchi, Sebastjan Merlo, Pavo Perković, Urša Lužovec, Rok Šumak, Tamara Serdinšek, Goran Buser

Poster presentations

Gregor Gruškovnjak, Kristina Zadravec, Valentina Trpkovska, Maša Samojlenko, Valentina Trpkovska, Barbara Bonča

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What's new in WHO classification of the pelvic organ tumors and how does it influence our clinical approach

Maja Pakiž (Maribor, Slovenia)

Recent growing body of evidence and scientific research regarding the genetics and histopathology of epithelial ovarian cancer has drastically improved our understanding of ovarian carcinogenesis. The term epithelial ovarian carcinoma has been used to refer to a large group of malignant neoplasms that typically present as ovarian tumors with involvement of the fallopian tube and peritoneum. However, according to the clinical behavior, pathological characteristics, precursor lesions and genetic mutations, there has been proposal to divide all epithelial ovarian tumors to two different types. Type one neoplasms include low-grade serous and low-grade endometrioid cancers, mucinous, clear cell and previous called transitional cell cancers. These are presenting around 25 % of ovarian epithelial cancers, are usually limited to the ovary and have good prognosis. Cystadenomas, endometrioid cysts and cystadenomas as well as borderline tumors are precursor lesions associated with type I cancers. The type I tumors probably originates from Muellerian inclusions in the ovarian cortex, Muellerian epithelial cells are probably transported from the fallopian tubes or endometrium during the reproductive years. The tumors lack p53 mutation and may possess KRAS/BRAF mutation. On the other hand, type II neoplasms account for approximately 75 % of epithelial ovarian cancer, are usually diagnosed at a later stage and have a poor prognosis. Histologically these tumors are high-grade serous and high-grade endometrioid carcinomas, carcinosarcomas and undifferentiated carcinomas. The p53 mutation is prominent. The precursor lesion is probably on the fallopian tubes, called STIC (serous tubal intraepithelial cancer). These tumors (previously called serous adenocarcinoma/papillary surface carcinoma/ adenocarcinofibroma, grade 3) have traditionally been thought to be primary ovarian carcinomas, with a few designated as fallopian tube carcinoma (if the bulk of disease was in fallopian tube) or peritoneal carcinoma (if little or no ovarian or fallopian

tube disease was present). Evidence suggests that many of these neoplasms may originate in the fallopian tube (as STIC). They possess the same clinical behavior, mutation profile and histopathological features, hence there has been a proposal to combine serous high grade adenocarcinomas of fallopian tube, ovary and peritoneum in one disease, called ''extrauterine pelvic serous carcinoma" or ''adenocarcinomas of muellerian origin".
The new WHO classification published in 2014 followed previously mentioned new evidence of pathogenesis and precursor lesions of epithelial ovarian cancers. The old classification focused on the mesothelial surface of the ovary as the point of origin of epithelial ovarian tumors, the new classification eliminates this focus. The earlier transitional cell type of ovarian cancer class has been removed, while seromucinous tumors have been added as a new entity. The role of some borderline tumors as a step in the progression from benign to invasive lesions is incorporated; borderline tumors were renamed to atypical proliferating tumor. The improvement of our understanding of ethiopathogenesis of epithelial ovarian cancers, especially of knowing the STIC to be precursor lesion for the prognostically worst serous high grade carcinoma of ovary, tube and peritoneum has a marked influence on our every day clinical practice and research protocols. Instead of screening to find early stage cancers with ultrasound, cytological evaluation of the fallopian tubes using hysteroscopic approach might be worth to evaluate. The concomitant removal of fallopian tubes while operating for benign gynecological pathology when there is no fertility sparing issues is currently more and more widely used in every day practice, waiting for the long term results in anticipated drop of serous ovarian cancer incidence.

The classical broad classification of endometrial cancer to type I and type II is currently being challenged with emerging evidence

on genetic profile of the tumors. Type I endometrial cancers represent the great majority of endometrial malignant neoplasms, with endometrioid histology, estrogen dependent, presented at early stage, with endometrial hyperplasia as precursor lesion and associated with an excellent prognosis. Whereas type II endometrial cancers are non-endometrioid histological tumors like serous, clear cell, mixed cell and undifferentiated cancers. These are not estrogen dependent, have poor prognosis and are associated with an atrophic endometrium. With emerging new data the new WHO classification introduced some improvements. The category of serous endometrial intraepithelial carcinoma has been included. Formerly it was considered to be a precursor of serous endometrial cancer, however it is now recognized it may be associated with high-stage serous carcinoma, since the cells may spread through the fallopian tube to the peritoneal surface. The categories of squamous cell and transitional cell carcinomas have been deleted, neuroendocrine carcinomas have been incorporated and the category of undifferentiated and dedifferentiated carcinomas has been better defined. However, there are emerging data and publications regarding the new knowledge of genetic characteristics of the endometrial cancers, that are associated with different clinical behavior of the tumors and their susceptibility to systemic treatment, that are becoming more and more clinically relevant. The Cancer Genome Atlas Network (TCGA) performed an integrated genomic, transcriptomic and proteomic characterization of endometrial cancer. They have recognized 4 different groups of endometrial cancer. Group I consisted of endometrioid endometrial cancers with POLE mutations and very high mutation rates. Group II was characterized as endometrioid endometrial cancers with microsatellite instability, MLH-1 promoter hypermethylation and high mutation rate. Group III was defined as endometrioid endometrial cancers with low copy number alterations. And

finally, group 4 showed low mutation rate and frequent TP53 mutations, and was predominantly composed of most serous and grade 3 endometrioid endometrial cancers. The group I showed the most favorable prognosis whereas the group 4 was associated with poorest prognosis. What is interesting from clinical point of view is that most serous and most grade 3 endometrioid (but not all) cancers showed similar genetic profile, meaning that grade 3 tumors might not be classified as type I endometrial cancers. And on the other hand all four genetic groups contained some endometrioid grade1-2 tumors, meaning not every grade1-2 endometrioid cancer is clinically associated with excellent prognosis. And we may have a tool to differentiate those with worse prognosis to tailor treatment and surveillance strategy. There has also been emerging evidence that genetic groups of endometrial cancers shows different immunologic profile and susceptibility to immunologic therapy. However there are still controversities to be solved before fully implementing new knowledge to every day clinical practice.

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Ultrasound examination in pelvic tumors – a review

Jure Knez (Maribor, Slovenia)

Ultrasound is today considered a first line tool in the diagnostics of women with suspected pelvic masses. It is widely accessible, safe and in most cases relatively inexpensive method. Advances in ultrasound technology have been dramatic in the last few decades and especially the introduction of high-resolution transvaginal ultrasound has allowed for detailed diagnostics of pelvic anatomy. A gynaecologist experienced in ultrasound diagnosis using good-quality equipment is usually able to establish with confidence the nature of a pelvic tumour from the ultrasound image. This helps to individualise and optimise the management of women with a palpable pelvic mass.

Pattern recognition for discrimination between benign and malignant tumours can be learned by performing gynaecological ultrasound examinations on a regular basis. However, the diagnostic accuracy of subjective assessment of tumour morphology increases with increasing experience. An experienced ultrasound examiner can distinguish confidently between benign and malignant pelvic tumours using pattern recognition. The reported sensitivity varies from 88-100% and specificity from 62-96%. Although pattern recognition can be superior to all other methods in experienced hands, many diagnostic models have been developed to help standardise and improve diagnostics in general clinical practice. The most widely used and validated are the International Ovarian Tumour Analysis Collaboration (IOTA) models. These are easy to use and can discriminate malignant from benign tumours with high sensitivity and specificity. In cases when these models yield inconclusive results, pattern recognition by an experienced examiner is required.

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Imaging in pelvic tumors – interobserver variability

Saša Rudolf (Maribor, Slovenia)

The most commonly employed imaging modality for pelvic pathologies and adnexal masses is ultrasonography. Ultrasound remains the initial and most important imaging method for ovarian cancer detection. Although increasing evidence shows that ultrasound is an accurate technique to stage and follow up ovarian cancer, it requires an experienced examiner capable of examining both the pelvis and the abdomen. Further imaging is indicated if limitations of ultrasound are found, such as poor image quality or if extra-abdominal spread is expected.

The vast majority of patients presenting with an adnexal mass is referred to the radiologist with a well-defined clinical question: characterisation in a sonographically indeterminate lesion or staging in sonografically and/or clinically obvious ovarian cancer.

Cross-sectional imaging techniques have widely gained acceptance for preoperative tumour assessment of gynaecologic cancers in most countries.

CT has lower soft tissue contrast than MRI and, therefore, is not widely used to differentiate benign from malignant lesions. Early stage ovarian cancer can be missed at CT. In women with adnexal masses of an indeterminate nature on ultrasound, MRI is the diagnostic problem-solving modality of choice.

CT is the most commonly used imaging modality for preoperative staging and follow up and is the standard imaging method for preoperative evaluation of women with ovarian cancer. The limitation of CT is contraindication to contrast agents, ionising radiation exposure, and operator dependence. Inability to use intravenous contrast media adversely affects CT image quality and performance. The radiologist's experience plays a crucial role in the acquisition and interpretation of the images. Intra-

observer agreement is superior to inter-observer agreement for ovarian cancer staging.

Gynaecologic MRI plays an important role in the care of patients with gynaecologic tumours, often contributing to initial diagnosis, determination of disease extent, treatment selection and treatment follow-up. In women with cervical cancer, MRI improves the accuracy of the FIGO clinical stage determination, leading to more precise treatment selection and planning. MRI is crucial for confirming eligibility for fertility-sparing medical or surgical procedures in patients with early-stage endometrial or cervical cancer who desire fertility preservation.

In oncology centres, most of imaging studies obtained elsewhere are often submitted for a second-opinion review and are re-interpreted by sub-specialized radiologists and an official second-opinion report is issued. However, MRI scans are commonly interpreted by general body radiologists, who may have limited subspecialty training in gynaecologic MRI. Interpretation of imaging examinations are subjective and therefore reader dependent, so it is mandatory that every patient is presented and discussed at multi-disciplinary tumour board in tertiary care cancer centre. Multi-disciplinary tumour board should include radiologists with relevant, focused expertise.

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What is target therapy? What's new in the field of pelvic organ tumors

Erik Škof (Ljubljana, Slovenia)

At the present time platinum-based chemotherapy remains standard conventional systemic treatment of patients with gynaecologic cancers. Due to toxicity and lack of specificity of chemotherapy, novel approaches in systemic treatment are being developed – targeted therapy beeing one of the most important.
In recent years many improvements have been made in our knowledge regarding hystopathologic and molecular characteristics of gynaecologic tumors. Terms like »Ovarian carcinoma but also Type I and »Type II ovarian cancer« are outdated. There are at least five patohystologic types of ovarian cancer (high-grade serous -HGS, low-grade serous-LGS, clear cell, endometroid and mucinous)1. Each of these type has its own specific molecular driver alterations – possible tumor targets for therapy. Also in uterine cancer there are many potential molecular targets. »Type I and type II uterine cancer« will be soon outdated2. In cervical cancer screening programmes have shown to be effective reducing the incidence of the disease, whereas only small improvements have been made in systemic treatment3.
Two main types of targeted therapy are monoclonal antibodies and small molecule inhibitors. Both of them are very specific for their target with less sistemic toxicity. Monoclonal antibodies have their targets on the cell surface, whereas targets for small molecules are inside of the cell. With binding to the specific target, signalling pathways in tumors are inhibited, resulting in tumor shrinkage and eventually death4.
There are two targeted drugs that are already part of standard systemic therapy in gynaecologic oncology in Europe – bevacizumab and olaparib.
Bevacizumab is anti-VEGF (vascular epidermal growth factor) monoclonal antibody approved for treatment of advanced ovarian and cervical cancer. Adition of bevacizumab to chemotherapy significantlly prolongs progression-free survival (PFS) for 4 months in first-line ovarian cancer and in relapsed disease, with

no significant benefit on overall survival (OS)5-7.

However in metastatic cervical cancer addition of bevacizumab to chemotherapy significantly prolongs OS for 4 months8. Specific side effects of bevacizumab are arterial hypertension, coagulopathy, proteinuria, arthralgia and fistulae.

Olaparib is a small molecule –inhibitor of PARP (poly-ADP ribose polymerase) that is approved in EU as maintenance treatment of relapsed, platinum sensitive BRCA positive ovarian cancer, after response to platinum based chemotherapy. Therapy with olaparib significantly prolongs PFS for 7 months, compared to placebo. The OS is not significantly improved9. Specific side effects of olaparib are mild nausea, fatigue and anemia.

We should not forget that hormonal treatment of ER/PR positive advanced low grade ovarian or endometrial cancer also represents a treatment option which in fact is targeted therapy10.

There are also targeted drugs that showed activity in prolonging PFS in advanced ovarian cancer, for example inhibitors of angiogenesis (pazopanib, cediranib, nintedanib), but due to additional toxicity and no benefit in OS, they were not approved in EU11-13.

Many other targeted drugs are under clinical evaluation in gynaecologic oncology.

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Algorithms and nomograms to direct treatment choices

Marko Klarić (Rijeka, Croatia)

In recent times with the advancement of medicine, in the treatment of patients with gynecological malignancies there is more and more data that needs to be taken into account to properly diagnose, direct the treatment and prognosis the outcome of the disease.

With the abundance of new options in diagnostic and treatment modalities, a shift in the medical decision process for gynecological cancers has been observed. The emergence of individualized medicine and the increasing complexity of available medical data has lead to the development of new prediction models.
For this purpose algorithms and nomograms are used. A nomogram is a graphic calculating scale designed to provide an approximate computation of a function. In clinical practice, a nomogram is used as an algorithm to predict the probability of a given outcome.

Clinical models (algorithms, nomograms, and risk scoring systems) have been reported, especially for stratifying and subgrouping patients with endometrial cancer, with various unanswered questions regarding such things as the optimal surgical staging for lymph node metastasis as well as the assessment of recurrence and survival outcomes.

Algorithms and nomograms are used to predict ovarian cancer as well as to predict the prognosis of ovarian cancer and direct treatmen of such patients.

In terms of decision making, predictions based on an algorithm or nomograms have been shown to be more accurate than those based on clinical judgment and experience, and superior to risk groups as well.

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ESMO-ESGO-ESTRO guidelines for endometrial cancer - a review

Paolo Zola (Turin, Italy)

Chiara Macchi (Turin, Italy)

(EC) is the most common gynaecological cancer in developed countries. More than 90% of cases of endometrial cancer occur in women > 50 years of age; however, 4% of women are younger than 40 years old and they should preserve their fertility. The majority of endometrial cancers are diagnosed early (80% in stage I), with five-year survival rates of over 95%.

A population based screening is not recommended; otherwise patients with high risk of EC should be monitor and counselled about cancer risk.

Some co morbidity, such diabetes, hypertension and obesity should be considered in order to plan an adequate surgical approach. The patients should be evaluated with pelvic examination, pelvic ultrasound and/or MR to assess the myometrial invasion, cervical extension and the lymph nodes involvement. CT scan or PET/CT is necessary to assess distant metastasis.

Extend of surgery should be adapted to the clinical condition of the patients according to the risk group and the patient's wish to preserve fertility. Total hysterectomy with bilateral salpingo-oophorectomy is the gold standard treatment. This could be done using the open, laparoscopic or vaginal approach. The rationale for the removal of the adnexae is to prevent ovarian cancer and rule out ovarian metastases. Younger patients with endometrial cancer often have early stage and low-grade tumours: in these cases, the ovaries should be maintained, to avoid the consequences of surgical menopause (without statistically significant impact on the overall survival). In case of ovarian preservation, salpingectomy is recommended. However, a careful follow up is necessary to rule out synchronous concomitant ovarian malignancy.

The role of lymphadenectomy in early endometrial cancer is still unclear (it is not recommended in patients with low risk early stage endometrial cancer). In higher stage is better to remove pelvic and para-aortic lymph nodes up to the level of renal veins. Patients with stage IV EC should be treated with combined approach.

In case of stage I intermediate risk of higher adjuvant treatment with RT and/or CT is recommended.

A conservative management approach could be considered in selected patients with a stage I-G1 endometrial cancer and it is based on medical treatment of oral progestins. The women should accept a close follow-up during and after the treatment and they should also be informed of the need for future hysterectomy in case of failure of the treatment and/or after pregnancies.

Early cervical cancer – how radical should we be?

Lukáš Dostálek (Prague, Czech Republic)

Jiří Sláma (Prague, Czech Republic)

Surgery is the dominant treatment modality of the early-stage cervical cancers. The best management comprises only surgery without adjuvat treatment, so the main aim of pre-operative work-up is to avoid necessity of subsequent radiotherapy. There are two separate issues to be addressed - the cervical procedure including extent of parametrectomy and the lymph node staging. Clinical examination must be therefore completed with detailed imaging assessment. Excelent results brings transrectal ultrasound examination.

In terms of local radicality the key parameters are depth of stromal invasion, tumor volume and its topical relation to the pericervical fascia. These factors must be considered in all patients and tailored in three dimensions with effort to reach adequate free margins. Centrally localised, low volume tumors can be safely treated with nerve sparing radical hysterectomy. Less radical fertility sparing procedures (vaginal trachelectomy or conisation) represent recently introduced surgical methods with excellent pregnancy outcomes. Oncological recults are promising, but there are still lack of quality data and possible limitations especially in „pseudo-bulky“ tumors.

The lymphatic staging should include the sentinel lymph node biopsy (SLNB) as a crucial part. Sentinel node biopsy allows per-operative assesment and triage of patiens according to nodal status to surgery or primary radiotherapy, detection of nodes in unusual localisations and subseqent expensive and time-consuming ultrastaging examination. Currently, SLNB alone is acceptable only in stage IA or as a part of clinical trials in stages IB and higher. Several studies showed high sensitinity and low false negativity rates in small IB1s. It is expected that majority of unresolved questions can be answered after completing of our prospectine observational study SENTIX, which is still open for

co-operation. Our another, recently opened trial - ABRAX would answer if it´s reasonable to abandon radical surgery in SLNB positive cases or continue with any type of hysterectomy. Using modified application of detection tracers it´s enable to detect SLNs also in locally advanced cancers. Clinical practice in the management of cervical cancer patiens differs accors the Europe. Recently performed an ESGO survey showed huge variations and significant contrast with published guidelines.

In this oral presentation will be described the new perspectives in the field of the management of the early stage cervical cancer in the context of the trials and analyses performed in our department. It should also clarify how are the early stages of this disease treated in the Czech republic.

ESGO quality indicators for advanced ovarian cancer treatment – a review

René H.M. Verheijen (Utrecht, The Netherlands)

Denis Querleu (Toulouse, France)

Introduction: ESGO has developed clinically relevant and evidence-based criteria for the quality assessment of ovarian cancer surgery throughout Europe. The ultimate goal is to improve the quality of surgery for advanced ovarian cancer and to build a network of European institutions, which meet the standards of proper ovarian cancer surgery and can then be awarded an ESGO recognition for ovarian cancer surgery.

Method: quality indicators for advanced ovarian cancer surgery were developed using a four-step evaluation process inspired by published development processes and earlier initiatives, identified from a systematic literature search carried out in MEDLINE and selected websites. This process development included the nomination of an international Development Group (23 experts), identification of potential quality indicators in the literature, literature search for scientific evidence, evaluation of the potential quality indicators, synthesis of scientific evidence, external evaluation of the retained quality indicators (by 84 independent physicians and 8 ovarian cancer patients).

Result: optimal, minimal and sometimes intermediate targets were defined for 10 quality indicators:

1. Complete surgical resection (optimal: > 65% of cases)
2. Volume (optimal: >100 operations per center, >10 per surgeon per year)
3. Surgery performed by dedicated subspecialist (optimal: >90% of cases)
4. Participation in clinical trials (target: active participation)
5. Involvement of multidisciplinary team (target: >95% of cases)
6. Adequate preoperative work-up (target: >95% of cases)
7. Adequate perioperative management (target: facilities

Pelvic actinomycosis – a malignant appearing mass.

Marija Rebolj Stare (Maribor, Slovenia)

66. years old female patient was treated in outpatient clinic for infectious diseases from beginning of July 2017, for lumbar pain, night fever, weight loss of 12,5 kg within 1,5 months. At the beginning, she was treated for urinal infection, at first with sulfamethoxazole and trimethoprim for a week. Later therapy was changed for cefixime.

Hemo cultures and urinal cultures were sterile. She was referred to abdominal ultrasound examination and chest X-ray. Chest X-ray showed no pathological changes. On abdominal ultrasound examination minor left sided hydronephrosis was presented. Bladder was compressed by enlarged and pathological changed uterus with left adnexal mass. In a beginning of August 2018, she was referred to gynaecological exam.

She was treated for arterial hypertension, had operation of left eardrum. Otherwise was healthy. Had no allergy history.

Her last period was at age 48 years. She had two deliveries, no abortions. For contraception, she had inserted intrauterine contraceptive device. Her last gynaecological check–up was done 30 years ago. She didn't claim any gynaecological problems.

At general examination she had fever, general malaise. At gynaecological examination uterus was in AVF position, enlarged, painless. On a left side in a close connection was a palpable adnexal mass, stretching to a pelvic wall. Intrauterine contraceptive device was removed and PAP cytological smear of cervical channel was made.

On vaginal ultrasound left and posterior uterine wall was irregularly shaped, with non-homogenous change, 54x33 mm in diameter. That could be adnexal tumour ingrowing into uterus

or cystic degenerated uterine wall. For further determination of adnexal pathology, patient was addressed to pelvic and abdominal CT.

At CT minor liquid collection (20x10 mm) in left adnexal region was seen, stretching to left tubal part of uterus. On a level of isthmus uteri inflammation was progressing to the rectum, with small abscess, 13x9 mm. Left ureter was trapped in inflammation or fibrosis. Rectal fistula was in play.

Urologist inserted double J stent into left ureter to prevent further hydronephrosis. Operative therapy was planned. Prior to surgery we received results of cervical channel smear. Acitnomyces were isolated. We resigned surgical procedure, consulted specialists for infectious disease and started with long term antibiotic therapy. Patient was treated with intravenous Penicilline 4x106 U per 6 hours, for 7 weeks. Her general health was improving, malaise vanished. Blood level of leucocytes and tumour marker CA-125, priory elevated, dropped extensively. On vaginal ultrasound left sided adnexal mass shrunk to 35,7x27,1 mm, without liquid collections. Because of an inappropriate visualization of endometrium, diagnostic hysteroscopy with endometrial biopsy was done. There were no pathological findings. On control, pelvic MRI (15.9.2017) uterus and adnexal regions were without pathology. Contours of rectum and sigma were without pathological changes, without thickening of the wall.

Patient was improving, clinical signs were vanishing. With counselling specialist for infectious disease, we changed intravenous therapy into oral. She was prescribed amoxicillin 500 mg per 8 hours and dismissed from hospital. 30 days later she had a control check up.

Blood tests were negative, levels of leucocytes normal. On gynaecological examination uterus was in AVF, normal sized, firm, painless, movable. Left adnexal region was minimally thickened, painless. Vaginal ultrasound was, with an exception of a small right ovarian cyst, without pathology. The same day abdominal ultrasound was without pathology, too.

Patient continued treatment in outpatient clinic for infectious diseases, having controls monthly. Antibiotic therapy with amoxicillin 1g per 8 hours, was to be continued for another 6 months. In December 2017, double J stent was removed.

Actinomycosis

Pelvic actinomycosis is a rare complication of a long-term intrauterine contraceptive device. It can be diagnosed before, during or after surgical treatment of suspected ovarian tumour. It can present as a gynaecological or a lower colonic malignancy, tuberculosis, Crohn's disease or other abdominopelvic inflammatory disease. The most common is pseudotumorous form that can lead to misdiagnosis. Less than 10% are diagnosed preoperatively.

It is a chronic disease, caused by Actinomyces species, gram positive anaerobes. Major human pathogen is Actinomyces israelli. Actinomyces species are opportunistic pathogens. Usually are present in oral cavity, tonsillar crypts, gastrointestinal flora, genital flora of healthy individuals. Incidence of actinomycosis is 1:3000,000. Actinomycosis involves pelvic regions in 3-5% of all cases. Usually is a localized, single organ disease. With the progression of infection granulomatous tissue, reactive fibrosis, necrosis and abscesses are formed.

Diagnosis of actinomycosis is usually made postoperatively (up to 71%), by histological identification of actinomycotic sulphur granules. Sulphur granules represent colonies of Actinomyces. Their characteristic is zone of granulation tissue surrounding one or more oval eosinophilic granules. Beaded or filamentous gram-positive bacilli radiate from these granules.

Definitive diagnosis can also be made by culture of Actinomyces, which is difficult. Actinomyces spp. are oxygene sensitive. Culture should be processed within 15 minutes and placed into anaerobic conditions.

Radiological findings are nonspecific. CT can present infiltrative nature of actinomycosis, with disruption of the tissue planes and demonstrate solid masses with focal low-attenuation areas or cystic masses with thickened walls.

Medical treatment is reasonable for patients, diagnosed with actinomycosis prior to surgery. Penicillin is the choice. For larger lesions with abdominal abscesses, intravenous therapy is required – penicillin G for 4-6 weeks (10-12 x106U per day, divided every 4-6 hours). Than is followed by oral penicillin (2-4g per day) or amoxicillin for 6-12 months. For penicillin, allergic patient's alternative is tetracycline, erythromycin, clindamycin.

Patients who undergo surgical treatment should also be treated with high dose antibiotic therapy.

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Early high grade serous ovarian adenocarcinoma figo IC

Andraž Dovnik, Maja Pakiž (Maribor, Slovenia)

We present a case of a 78-year old patient with early ovarian cancer. She was admitted to our department after being diagnosed with pelvic tumour which was seen on abdominal ultrasound scan performed because of recurrent urinary tract infections at a regional hospital. Preoperative evaluation was performed at our department. Gynaecologic ultrasound revealed a cystic tumour of the right ovary and a solid mass which was seen on the left side of the uterus. The uterine tumour had benign characteristics and the mass of the right ovary had malignant characteristics. Chest X-ray revealed no abnormalities. Abdominal CT scan showed cystic solid masses of both ovaries without evidence of peritoneal metastases, enlarged retroperitoneal lymph nodes or local invasion. Preoperative CA 125 was 66 g/L.

We proceeded with surgery. Lower median laparotomy was performed. Peritoneal washings were obtained. The right ovary with the cystic solid tumour and the right fallopian tube were removed. Intraoperative histologic examination revealed high-grade serous carcinoma of the right ovary. Complete staging including hysterectomy, removal of the left ovary and fallopian tube, pelvic and paraaortic lymphadenectomy, omentectomy and appendectomy was performed. No residual tumour was found in the abdomen. The final histologic examination confirmed high-grade serous carcinoma of the right ovary with malignant cells present in the peritoneal washings. The tumour of the left ovary was a benign fibroma. All other removed tissues were free of disease. The FIGO stage was IC.

The patient was presented at a multidisciplinary tumour board which recommended adjuvant chemotherapy with carboplatin and paclitaxel. Routine follow-up with history and clinical examination every 3-4 months in the first two years and every six months thereafter was recommended.

Discussion

Patients with ovarian cancer which is confined to the ovary may be asymptomatic. Preoperative evaluation consists of a thorough clinical examination and evaluation of serum CA 125. The usefulness of this tumour marker is controversial as it is elevated in only 50% of patients with FIGO stage I disease and 85% of patients with advanced disease. The first imaging investigation performed is usually ultrasound and many morphological characteristisc have been associated with ovarian cancer.1 Irregular solid tumour, ascites, at least four papillary structures, irregular multilocular solid tumour larger than 10 cm and a very strong blood flow are associated with ovarian cancer.2 The risk of malignancy index (RMI) can be calculated from the ultrasound characteristics, clinical factors and CA 125.1 Primary surgery is the preferred approach. The main goal of the surgery is to resect the tumour and to perform adequate staging.1 During the surgery peritoneal washings for cytologic evaluation should be obtained. The staging procedure comprises hysterectomy, bilateral salpingo-oophorectomy, multiple peritoneal biopsies from the paracolic spaces and bilateral subdiaphragmatic spaces, infragastric omentectomy, and pelvic and paraaortic lymphadenectomy.3
Adjuvant chemotherapy can be omitted in patients with stage I grade 1 disease and may be shortened in patients with stage I grade 2 disease. All patients with stage II disease and beyond are recommended at least 6 cycles of adjuvant chemotherapy.3

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Advanced high-grade serous ovarian adenocarcinoma figo IV

Andraž Dovnik, Maja Pakiž (Maribor, Slovenia)

We present a case of a 52-year old patient with advanced stage ovarian cancer. The patient noticed an enlarged lymph node in the left supraclavicular area. Fine needle biopsy showed metastasis of adenocarcinoma. Vaginal ultrasound scan revealed a solid tumour measuring 3 cm with a very strong blood flow. Preoperative evaluation with clinical examination and evaluation of CA 125 was performed. The value of CA 125 was 689,4 IU/L. Thoracic and abdominal CT scan revealed enlarged supraclavicular, paraaortic, right inguinal, and right common iliac lymph nodes. No metastases were seen in the lungs or the liver. PET-CT showed a hypermetabolic lesion in the left ovary and hypermetabolic lymph nodes in the pelvis, abdomen, thorax, the right inguinal area and the left side of the neck. Core needle biopsy of the right inguinal lymph node confirmed metastasis of ovarian adenocarcinoma.

Due to the inoperable nature of the disease she received six cycles of neoadjuvant chemotherapy with carboplatin and paclitaxel. After four cycles of chemotherapy CT scan showed partial regression of the disease.

Interval cytoreduction was performed including hysterectomy and bilateral salpingo-oophorectomy, pelvic and right inguinal lymphadenectomy and infracolic omentectomy. No residual tumour was left in the abdomen.

The patient was presented at a multidisciplinary tumour board which recommended adjuvant chemotherapy with carboplatin and paclitaxel.

Discussion

The most important decision considering the first treatment of patients with ovarian cancer is when to perform surgery. The advantages of primary cytoreduction (when possible) are the ability to establish definitive diagnosis and the removal of symptomatic tumour. However other clinicians prefer neoadjuvant chemotherapy especially if patients are older, have poor performance status or comorbidities.1

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Diagnostic challenges of retroperitoneal malignant tumor: a case report

Ksenija Rakić, Maja Pakiž (Maribor, Slovenia)

A 67-year old woman firstly attended the emergency unit in 31st of May 2016 with prominent pain in the area of left kidney; the pain radiated in labia and left leg. She denied nausea, vomiting, bowel and bladder dysfunction, and gynecological symptoms. The patient had history of hypertension, hyperlipidemia and atrial fibrillation. The patient denied family history of breast, gynecologic and colon cancer.

She was admitted to Department of urology for further diagnostic evaluation and treatment of what it was presumed to be renal colic. A native CT scan was performed on 1st of June; there were no signs of hydronephrosis, ureterolithiasis, or other acute pathology in the abdominal cavity. However, there was a description of edema of perirenal fatty tissue on the left side and there were some lesions in the liver that the radiologist could not interpret without the contrast. She was discharged on 2nd of June with analgesic therapy.

She was referred to abdominal US examination to outpatient clinic on 14th of June. The report described a tumorous formation in left lower abdomen, probably on the bowel, with grade I hydronephrosis on the left side and two lesions in the liver, probably hemangioma. Two days later she was examined by the gynecologist at private outpatient clinic, who did not found gynecologic pathology on examination and pelvic US, and concluded that the patient probably has lumbalgy. An MR of lumbosacral spine was recommended.

Since the pain was more prominent she again attended emergency unite and was admitted to Department for gastroenterology on 17th of June, where colonoscopy was performed, showing some diverticulosis. On 20th of June abdominal US was repeated, describing probably retroperitoneal tumor in left lower abdomen,

up to 9 cm large. On 22nd of June a CT scan with a contrast was performed. A tumor, probably belonging to the left ovary was reported, with signs of left ovarian vein thrombosis and left renal vein thrombosis. Metastasis in the left perirenal fatty tissue were described, with infiltration of left ureter and hydronephrosis. There were small nodular lesions in right lungs, suspected for metastasis, however too small to be precisely defined. Hemangioma and cysts of benign characteristics were seen in the liver. Laboratory results were performed, kidney function was normal, tumor markers were negative.

The patient was examined by gynecologists working at the Department for gynecologic and Breast Oncology. Physical examination showed a large adnexal mass filling the left side of pelvis. Pelvic ultrasound was performed and revealed a large left sided bilocular adnexal complex, predominantly solid, measured 11 x 9 cm with areas of necrosis. The mass seemed to emerge through the left ovary. Uterus appeared normal, hyperechoic multicystic focal mass was noted within the uterine cavity measured 8 x 6 mm, endometrial polip. The right adnexa appeared normal. The ascites was not present.
The finding was highly suspected for malignancy.

The patient was discussed at abdominal tumor board. The percutaneous core needle biopsy of the tumor in perirenal region was recommended and performed on 4th of July. The histological examination showed highly malignant undifferentiated tumor. The patient was again presented at abdominal tumor board, since there were no signs of other lesions in the abdomen and no apparent clear sign of pulmonary metastasis, the decision to operate her was accepted.

During the procedure the mass was excised arising from the left

ovary, growing into the retroperitoneal space. The mass infiltrated the left renal sinus, left ureter and sigmoid mesocolon. Total abdominal hysterectomy with bilatereal salpigo-oopherectomy, radical nephrectomy and resection of sigmoid colon with end-to-end anastomosis were performed. The resection was described as radical with no macroscopic residual tumor, and her postoperative course was uncomplicated, she was discharged from the hospital on 8th post-operative day. The histopathology report described tumor as carcinosarcoma of the left ovary, FIGO stage IV.

She was referred to oncologist for adjuvant chemotherapy, however before starting the systemic treatment she was urgently admitted to our department for abdominal pain. A CT scan confirmed several metastatic lesions in the abdomen and lungs. Since she was in good performance status, she started treatment with carboplatin and paclitaxel. She received 4 cycles, the last one only with carboplatin, since profound anemia and neutropenia during the chemotherapy. After that the rapid deterioration of health was noticed with malignant ileus occurring. She died on 12th of January 2017. At autopsy the final pathological report changed the diagnosis to undifferentiated endometrial stromal sarcoma with osteoclasts mimicking gigantic cells.

Retroperitoneal primary malignant tumors are very rare, among them sarcomas are the most frequent. Preoperative differential diagnosis is challenging for nonspecific symptoms, clinical signs and characteristics on different imaging. As well core needle biopsy and intraoperative frozen section shows low specificity. The pathological examination was hard to interpret for poor differentiation of the tumor. Due to the rarity of these tumors and the complexity of treatment, evaluation and management should be carried out in a center with multidisciplinary expertise in the treatment of sarcomas.

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Clinical case of ovarian cancer in pregnancy

Sebastjan Merlo (Ljubljana, Slovenia)

A 37 years old woman was pregnant for the fourth time. She had one spontaneous normal vaginal delivery. In her medical history she was operated at age 33 because of appendicitis (during procedure it was found she had endometriosis) and at age 34 for varicose vein of lower extremities. Her family history revealed that one grandparent had colon cancer and two aunts had breast cancer.

An early transvaginal ultrasound in first trimester did not report any adnexal masses.
The pregnancy was normal till 21 weeks of pregnancy, when she was presented for investigation from one week lasting pelvic pain, lower extremities pain and urinary frequency. The imaging examinations done showed a large ovarian mass, and tumorous changes of the omentum majus.
Examination of tumor markers revealed Ca-125 of 483 IU/L (normal range: <35 IU/mL), and HE4 of 179 pmol/L (normal range: <140 pmol/L).

Diagnostic laparoscopy was carried out at 28 weeks of gestation. The biopsies of parietal peritoneum metastasis were taken and showed high grade serous ovarian cancer, stage IIIC.
Tumor markers were higher: Ca-125 was 801 IU/L (normal range: <35 IU/mL), HE4 was 1457 pmol/L (normal range: <140 pmol/L).

The tumor - pediatric board decided to wait until 30 weeks of gestation and then to terminate the pregnancy with cesarean section and to do maximal cytoreduction surgery with intraperitoneal chemotherapy.

The patient underwent the operative procedure at 31 weeks of gestation. The procedure started with a cesarean section and

continued with complete cytoreductive surgery. A hysterectomy with bilateral salpingo-oophorectomy, complete omentectomy, resection of rectosigmoid colon with anastomosis and pelvic peritonectomy was performed.
At last there was performed intraperitoneal chemotherapy with Cisplatin for 24 hours.

Definitive histopathological diagnosis of the tumor confirmed high grade serous ovarian carcinoma. Both ovaries were overgrown with tumor. There were many metastasis of high grade serous ovarian carcinoma in the uterus, in the omentum, on peritoneum, rectosigmoid and cekum. The placenta was normal with no tumor infiltrates.
The baby weighed 1360 g and suffered a respiratory distress syndome after birth and needed intubation (before delivery mother received standard dose of dexamethasone). The baby was extubated 7 days after delivery. Ultrasound examinations of the baby at 1 month showed normal brain, heart and kidneys. The baby was discharged 2 months after delivery with the weight of 2760 grams and the need of support of oxygen therapy at home.
The recovery of mother after surgery was good and after 15 days she was discharged in good condition with tumor markers Ca-125 of 74 and HE4 of 154.
4 weeks after surgery the patient received first cycle of standard adjuvant chemotherapy with Paclitaxel and Carboplatin with total of 6 cycles every 3 weeks. After first cycle of chemotherapy tumor markers Ca-125 and HE4 dropped to normal levels.
The patient has been followed up by gynecological exams, gynecological and abdominal ultrasounds.
She is currently without evidence of disease 19 months after diagnosis and 13 months after the end of treatment. The baby is now 19-months old with normal physical and neurological development.

Recurrent cervical carcinoma

Barbara Šegedin (Ljubljana, Slovenia)

A 28 - years old women was referred to our institute for treatment of recurrent cervical carcinoma. She was primarily treated with radical histerectomy, bilateral tubectomy and pelvic lymphadenectomy for FIGO IB2 cervical carcinoma at the age of 27. Preoperative staging, including PET-CT and MRI of the pelvis and liver, showed no extracervical disease. Histology showed poorly differentiated adenocarcinoma of the cervix, 5 cm in the largest diameter, with negative lymph nodes. She received no adjuvant treatment.

Half year after surgery an exophytic tumour mass in the vaginal vault was visible at gynaecological examination, infiltration of the left paracolpium to the pelvic side wall was palpable. The biopsy proved poorly differentiated adenocarcinoma with necrosis. MRI showed tumour masses above the vaginal stump, 3.5x3x3.7cm on the left and 2.7x1.7x1.1cm on the right side. Additionally, there were pathological lymph nodes at the level of the left internal iliac vessels and by the right ovary, inguinal lymph nodes were suspicious, however, they were negative on aspirational biopsy.

The patient was treated with external beam radiotherapy (EBRT) with 45 Gy in 25 fractions to the pelvis and 57,5Gy in 25 fractions with the simultaneous integrated boost technique to the pathological lymph nodes. She received concomitant chemotherapy with cisplatin 40mg/m2. EBRT was followed by two applications of interstitial brachytherapy, using an individually modelled 3D printed applicator to ensure adequate target coverage, while respecting dose constraints for the organs at risk.

At the first follow up 3 months after treatment, no macroscopic tumour was visible or palpable at the gynaecological examination, PAP smear showed only non-neoplastic changes

due to radiotherapy. An MRI was performed 4 months after the treatment, showing complete remission of the disease locoregionally with no evidence of new metastases in the pelvis.

At the last follow up 16 months after treatment there is still no evidence of recurrent disease. The patient reported mild lymphoedema of the lower limbs with no other late side effects.

An unusual case of peritoneal endosalpingiosis

Katja Bricelj (Ljubljana, Slovenia)

Branko Cvjetičanin (Ljubljana, Slovenia)

Špela Smrkolj (Ljubljana, Slovenia)

Snežana Frković Grazio (Ljubljana, Slovenia)

A 26-year-old woman presented with a history of occasional cramps in the lower abdomen of 1 month duration. She was a nullipara, with history of 1 induced abortion and had been taking oral contraceptives. General examination was normal; on pelvic examination, her uterus was normal in size, however a movable elastic circular mass of 4-5 cm could be palpated in the left adnexal region.

An ultrasound of the pelvis was performed in which the uterus and the right ovary were normal while a 6 cm formation of mixed echogenicity with multiple septations and projections, with no pathologic blood flow patterns was observed in the left adnexal area. Minimal free fluid was present in the pouch of Douglas. Her blood level of CA 125 was raised (401 U/mL), with normal levels of CA 15-3, CA 19-9 and CEA. ROMA index (30.8) was elevated, sideropenic anaemia was present.

On laparoscopic examination, pelvic adhesions and bilateral sactosalpinx were present (consistent with pelvic inflammatory disease) and numerous 2 mm whitish lesions on the parietal peritoneum and pouch of Douglas were observed. Extensive bilateral adnexal adhesions were resolved and multiple peritoneal biopsies were taken for histopathological examination. Peritoneal washing was sent for cytological and microbiological examination. Mantoux test excluded tuberculosis infection. Microbiological test of peritoneal washing was negative, as was the cytology for malignant cells.

Microscopically, the specimens showed a florid reactive lymphoid and mesothelial proliferation and, in addition, many glandular structures, which were mostly simple, tubular, focally dilated and cystic. In some places they were showing a more complex cribriform pattern. Occasional psammoma bodies were

present. There was no atypia or mitotic activity. There were no granulomas and no clefting surrounding the epithelial islands. The immunophenotype was in keeping with a low grade serous proliferation with diffuse positive staining for ER, PR, WT1 and EMA. p53 showed wild type immunoreactivity, but in some areas quite a lot of the nuclei were p53 positive. We believed that the features were mostly consistent with florid endosalpingiosis and reactive lymphoid proliferation, so in the report we suggested wait and see policy but as the case was morphologicaly very peculiar and we were not confident about the diagnosis we sought the consultation of professor Glenn McCluggage (Belfast, United Kingdom)

He agreed that the case was most interesting and difficult. He thought that it represented a low grade serous proliferation, possibly representing a benign lesion such as endosalpingiosis and a reaction to the inflammation, but he was worried about the solid and cribriform arrangements, which are not typically seen in endosalpingiosis. That is why he thought that this proliferation could represent a primary extraovarian low grade serous neoplasm. He said that he would be reluctant to make a diagnosis of a low grade serous carcinoma but cannot exclude this or extraovarian serous borderline proliferation. Ultimately he said ”it is likely that the true nature of this lesion will reveal itself over the course of time”. So he advised careful clinical follow-up with second look laparoscopy in 6 months.

During follow-up the patient had no complaints, clinical and pelvic exams were normal, transvaginal ultrasound showed no pathology and her blood level of CA125 was in normal range (12 U/mL).

8 months later, a second laparoscopy was performed. Persistency

of lesions with no sign of progression was found. Excision of some lesions and coagulation of the remaining ones was performed. Pelvic adhesions were resolved. Minimal free fluid in cavum of Douglas was sent for cytological analysis. Peritoneal washing cytology was negative for malignant cells.

Histopathological features in second biopsy were in general similar to the first one but the epithelial proliferation and lymphoid infiltrate were less prominent. However, we were still unable to come up with a definite diagnosis. There were no signs of high-grade carcinoma or mesothelioma.

In regard to lack of a definitive diagnosis, the interdisciplinary tumour board suggested regular follow-up visits with the surgeon, consisting of clinical examination, transvaginal ultrasound and monitoring of Ca125.

On her next follow up visits at 2, 6 and 12 months following the second laparoscopy, the patient was free of disease (two years after the first laparoscopy).

Conclusion

We believe that the features of the presented case are most consistent with florid endosalpingiosis and reactive lymphoid proliferation.

The clinical presentation of endosalpingiosis is not specific. Patients may be asymptomatic or show symptoms of pelvic pain, dysmenorrhoea, menorrhagia and infertility. Imaging and operative findings can reveal cystic lesions, that may resemble gynaecological malignancies, which can lead surgeons to overtreat the patient.

Case report: chemotherapy treatment for advanced cervical cancer

Chiara Macchi (Turin, Italy)

On March 2016 a 50 years woman went to the hospital for a persistent abdominal pain and menstrual irregularities. A pelvic US showed some fluid in the pelvis, not regressed after antibiotics therapy.

In further pelvic US, the fluid increased and a pelvic MRI showed bulky lumbo-aortic lymph nodes and endometrial thickness of 30 mm. Cytologic sample of pelvic fluid was negative.
A CT scan confirmed multiple lymphadenopathy (iliac, aorto-caval and left inguinal lymph nodes) and found a solid node in the liver (S4).

We performed a VABRA sample (poorly differentiated adenocarcinoma with areas of squamous infiltration, probably derived from the cervical canal) and we removed a left inguinal lymph node (metastasis of poorly differentiated adenosquamous carcinoma). We found the same histological result from a pap smear and endocervical curettage and from a vulvar biopsy on the left inner labia. A PET/CT scan showed high level of metabolic activity on uterus, on liver (S4), on supraclavicular, subcarinal, bilateral lung hilum, celiac, bilateral lombo-aortic, bilateral iliac and left inguinal lymph nodes.

Based on these results, we supposed a diagnosis of cervix adenosquamous adenocarcinoma (stage IV).

The patient started a chemotherapy based on cisplatin 50 mg/mq + paclitaxel 175 mg/mq + bevacizumab 15 mg/mq every 21 days. She did it for 6 cycles and then she continued only with bevacizumab as maintenance for 24 cycles globally.

After 3 and 6 cycles of CT a CT scans showed a partial response of the disease. A PET/CT scan after 12 cycles of bevacizumab

showed a complete metabolic response, that was confirmed to another PET/CT after 22 cycles.

The last visit was on 21 of November and we organized a PET/CT evaluation and the first follow up visit on February 2018.

Clinical case of a large abdominal tumor mass in a 27 year old nuliparous woman

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A 27 years old woman was referred to our institution bacause of a large tumor mass, that was seen on a regular gynecological examination. The patient did not report any symptoms despite the size of the pelvic mass and the look of 30. weeks gestation.

The patient was a healthy, 27 year old nuliparous woman. She did not have any chronical illness and did not take any medications regularly. She did not have any operation till the referral to our institution. She had common child diseases and had no allergies. She also did not have any problems with defecation and urine voiding. There were no known malignancies in her family.

She had regualar gynecological exams. She had the first menstruation when she was 12 years old. She had regular cycles, every 28 days, with 3 days of menstrual bleeding. She did not have any abortion. She told us that she has a steady partner and that they are trying to concieve for about 9 months, but unsuccesfully. Our exam showed a distended abdomen, estimated size of 30 weeks of gestation. The palpable mass was hard and allowed very little movement. On VUS examination there was a normal uterus, with thin endometrium and homogeneus myometrium. There was a large solid tumor mass of at least 10x15 cm above the uterus. On the left side there was an enlarged ovary with a multilocular cyst, 8x6 cm in size with more solid inclusions of 0.5 to 1 cm in diameter. There was no free fluid in the Douglas cavity. There was no marked vascularisation of the left ovary but there was a pronounced vascularisation of the right tumor mass. We performed the IOTA adnexal index. It showed a 90% possibility for malignancy of the large ovarian tumor and a 75% possibility for the malignancy of the left ovary.

Blood was taken for laboratory exams. The values revealed Ca-125 of 170 IU/L (normal range: <35 IU/mL), and HE4 of 44

pmol/L (normal range: <140 pmol/L). Other tumor markers were normal.

A CT scan of the abdomen was performed. It showed a large tumor mass of 22x11x22cm. The tumor mass had a solid consistence, with some cystic areas. It seemed to belong to the right ovary and was compressing the sigmoid colon and vesical bladder. On the left side there was an enlarged ovary with multiple cysts with some small solid inclusions.

The patient underwent the surgical procedure. We performed a median laparotomy, right side adnexectomy, left side tubectomy and left side ovarian cysts enucleation. We also took some omental and peritoneal biopsies. A washing of the abdomen for cytological review was also taken. The patient recovered well after the surgical procedure in a few days. She was discharged on the 3rd postoperative day.

MANEC of the appendix presenting as a Krukenberg tumor: a case report

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Mixded adeno–neuroendocrine carcinoma (MANEC) is a rare pathological diagnosis defined by the WHO in 2010. Prior to the definition by the WHO , tumors with both adenocarcinoma and neuroendocrine components were given multiple pathological designations making it dificult to characterize the disease.

We are reporting a case of a 68 year old woman who presented to our clinic with postmenopausal vaginal bleeding. Dilatation and curettage was done and patohystology revealed prolierative endometrium. At a 3 month checkup after the procedure a left adnexal mass 8x6 cm was found.

After preoperative diagnostics, abdominal hysterectomy and bilateral salpingoophorectomy was done. Intraoperative patohystological diagnosis was: Tumor mixtum appendicis vermiformis; MANEC, goblet cell, carcinoid and signet cell adenocarcinoma pTNM pT3, pNx, pM1b. Appendectomy and omentectomy was performed in the same act, carcinosis of the peritoneum was found. After informed consent patient was scheduled for the second operation 32 days later in which cholecystectomy, splenectomy, subtotal colectomy, and peritonectomy with HIPEC were performed.

This case shows the importance of teamwork and raises questions on management of rare findings.

Parasitic myoma after morcellation

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We present an interesting case of a female patient in her mid 40s with parasitic fibroid probably developed from a morcellation remnant following laparoscopic myomectomy. The patient presented with growing pelvic mass in 2010. She underwent laparascopic myomectomy of a subserous myoma which was growing from left fundal tubal corner. She subsequently presented with another incidental finding of a 9 cm pelvic mass in 2017, found with ultrasound examination. She underwent laparoscopic operation but was converted to open abdominal surgery because of poor visualization of the tumor. We detected that mass was growing from anterior pelvic wall with his own blood supply. Histopathology of the mass confirmed it to be consistent with leiomyoma. This mass could probably be a morcellation remnant that has grown to this size taking blood supply from anterior pelvic wall. We report this case to emphasize that all tissue pieces that are morcellated should be diligently removed. Even small bits displaced into the abdomen can result in parasitic fibroids. Therefore, it can be concluded that parasitic myomas can arise from morcellated remnants and grow depending on the blood supply.

Smooth muscle tumor of uncertain malignant potential (STUMP) and hereditary leiomyomatosis: a case report

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25-year-old female was referred to our reproductive medicine department in november 2012, because of primary sterility and uterine myomas. At first presentation she was asymptmomatic. However, she already had laparoscopic myomectomy of multiple myomas 4 years ago and removal of skin leiomyoma from her left arm 3 years ago. Her family history revealed having more female relatives with leiomyomas, and her mother's sister was diagnosed with ovarian cancer in childhood.

Ultrasound examination confirmed recurrence of 2 leiomyomas of uterine wall, the largest measuring 7 cm. In april 2013, we did laparotomy and removed multiple miomas from uterus, the tumors were presented and removed from sigmoid colon and greater omentum as well.

Because of primary infertility (4 years of exposition) and recurrent myomas, we did in vitro fertilization 6 months later; 2 embryos were obtained, but embryo transfer was unsuccessful.

At the follow up visit in March 2015, the leiomyomas appeared again and new soft tissue tumors appeared inside the abdominal cavity. She started with 3-months uripristal acetate therapy as preoperative treatment. However in November 2015 MR imaging confirmed several uterine and extrauterine lying solid tumors with leiomyomatic features and their growth (the biggest tumor measuring 15 cm).

Another laparotomy was performed in January 2016 at the department for reproductive medicine. Multiple uterine leiomyomas were removed together with removal of tumors from peritoneum and greater omentum. The biggest tumor (640g in weight) was removed from Douglas cavity, which didn`t have direct communication with uterus. Two small tumors lying

deeply at Douglas cavity remained. The surgery was associated with almost 3 L of blood loss. All tumors were histologically leiomyomas except for the largest, extrauterine tumor, which after pathological consultation confirmed to be smooth muscle tumor of uncertain malignant potential.

Because of thrombocytosis, which appeared after surgery and was transient, she was referred to transfusiologist, who advised therapy with acetylsalicylic acid.

She started with uripristal acetate therapy again. There was no regression of remaining leiomyomas after 3 months of therapy and we changed it to GnRH analogue therapy, which she received for 3 months. On her wish, the therapy was extended to 1 year. We did bone density test, which was normal. Remaining tumors showed signs of regress 1 year after surgery. She was referred to genetic tests and counseling, where mutation in FH gene was discovered, which is connected to autosomal dominant hereditary leiomyomatosis. Several family members were confirmed to have the same mutation. Besides regression of abdominal leimyomas when using GnRH analogs, her skin leimyomas also disappeared.

We performed several consultations with the patient. She had recurrent hereditary leiomyomatosis, several procedures on the uterine wall, her disease was hormonally dependent. Disadvantages of prolonged GnRH analog therapy were explained. After more than 1 year of GnRH analog therapy the patient wished to stop it since symptoms of depression and sleep disorder. After discontinuation of the therapy, her symptoms improved, however the leiomyomas lying in Douglas cavity started to grow again.

After consultation with the patient and at the tumor board, the patient decided for total abdominal hysterectomy with bilateral

adnexectomy, although the later was not suggested by the tumor board. The patient decided for the adoption. The surgery was performed; the removal of tumors in Douglas cavity was feasible and there were no macroscopic residual of the disease in the abdominal cavity. The histological examination confirmed several uterine leiomyomas and benign extrauterine leiomyomas; besides that, the epithelial hyperplasia in fallopian tube was accidentally found.

Smooth muscle tumors of uncertain malignant potential (STUMP) have some characteristics of sarcomas, but do not meet the full diagnostic criteria. Among uterine leiomyoma variants, these are the most concerning in terms of progression or missed diagnosis of sarcomas. These tumors are very rare and there is a lack of data regarding their behavior, recurrence, association with hereditary diseases, their hormonal dependency and recommendation of best treatment approach. According to recent meta-analysis the recurrence rate was estimated to be 17 %, but this rate may vary depending on histological criteria used. The tumor may metastasize as well. It would be probably best for patients with STUMP, to be treated at centre with the expertise of gynecologic oncology and cooperation with rare tumors associations would be recommended. As for our patient, we will recommend her, to follow up her with pelvic ultrasound and MR imaging although the uterus was removed, since she had several extrauterine tumors.

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Paraneoplatic syndrome at first presentation in patient with advanced endometrial cancer (FIGO stage IIIA)

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A 60-year old woman was referred to our department because of abdominal pain and large abdominal mass. She had a complaint of tiredness, nausea, and loss of appetite that lasted one month. One week ago, she started to experience pain in the suprapubic, paraumbilical and epigastric area, with the feeling of fullness in the upper abdomen. She was febrile and noticed an increased vaginal discharge. Besides arterial hypertension, she had no other accompanying illnesses. Her last period was 2 years ago, she had one vaginal delivery. Her last visit at the gynaecologist was 35 years ago.

At the initial examination, a large palpable and painful mass was present in the lower abdomen. Gynaecological ultrasound revealed thickened endometrium with tumorous formation above and behind of the uterus. CA-125 and inflammatory markers were elevated. CT of the abdomen showed that the tumorous mass most likely originated from the right ovary, there were also signs of extensive ascites and omental carcinomatosis but no signs of perforation, ileus or abscess. CT of the thorax showed no signs of metastatic disease or inflammatory process. Since presentation with fever, profound sweating, vaginal discharge, abdominal tenderness and elevated inflammatory markers we empirically introduced broad spectrum antibiotic. Introducing the NSAID improved the symptoms.

Diagnostic laparoscopy with tumour biopsy and ascitic fluid sampling as well as diagnostic curettage was performed. Ascitic fluid sample revealed peritoneal adenocarcinosis, and endometroid type endometrial carcinoma was confirmed from the curettage sample. The process was assessed as operable. After histopathologic diagnosis was confirmed, the patient was presented at a gynaecologic-oncologic tumor board, a radical surgery was recommended.

However, while waiting for the surgery, the clinical signs of acute abdomen developed, the fever and elevated inflammatory markers persisted despite antibiotic therapy, the levels of haemoglobin was dropping. So the semi-urgent surgery was performed. Total abdominal hysterectomy with bilateral adnexectomy, adhesiolysis, omentectomy, ascites evacuation and removal of enlarged pelvic lymph nodes were performed. The procedure was uneventful and macroscopic radical. Inflammatory markers began to drop after the procedure, the clinical presentation of the patient markedly and quickly improved after removal of tumor mass. She was discharged on the fourth post-operative day. Histopathologic examination confirmed endometroid type endometrial carcinoma, FIGO IIIA with a metastasis in the right ovary, G2. Adjuvant chemotherapy was advised for the continuation of her treatment.

Paraneoplastic syndromes are rare disorders that are triggered by an altered immune system response to a neoplasm. They are defined as clinical syndromes involving nonmetastatic systemic effects that accompany malignant disease, the most frequent symptom being fever. In a broad sense, these syndromes are collections of symptoms that result from substances produced by the tumor, and they occur remotely from the tumor itself. The symptoms may be endocrine, neuromuscular or musculoskeletal, cardiovascular, cutaneous, hematologic, gastrointestinal, renal, or miscellaneous in nature. Paraneoplastic syndrome associated with endometrial cancer is extremely rare; there are only few case reports available at the literature search.

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Acute abdomen in older comorbid patient with newly diagnosed ovarian tumor: a case report

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86-year-old patient with a newly discovered 14 cm large tumour mass in the left adnexal region was admitted to our gynaecological department for further diagnostic evaluation. She was transferred from the department of haematology where she had been treated for a recent pulmonary embolism and signs of acute renal failure. At admittance, she was haemodynamically stable and well responsive. The therapy at transfer consisted of antihypertensive drugs and thyroid hormone, as well as therapeutic doses of LMWH for pulmonary embolism. The patient had a history of hypertension and hypothyroidism. She also had mild dementia.
The patient's cooperation at vaginal examination was poor. There were no signs of vaginal bleeding, the adnexal mass of 14 cm was poorly palpable vaginally, but obvious at abdominal palpation. Vaginal ultrasound showed no major discrepancies, the adnexal mass was not reachable with the vaginal probe. The abdominal ultrasound scan revealed a large multicystic mass with abundant vascularity and intracystic proliferation, there were no signs of ascites, and the tumor was according to IOTA simple rules malignant.

We began routine diagnostic procedures of the abdominal mass; the patient was firstly presented to an anaesthesiologist for evaluation of safety and risks associated with major abdominal surgery.

However, patient became suddenly poorly responsive; hemodinamical instability with major drop of blood pressure and levels of haemoglobin were observed (from 114 g/l to 42 g/l), a rise in inflammatory markes occured. The patient was firstly haemodynamically stabilized with blood transfusion.

An urgent abdominal CT scan was performed. Initial urgent consultation with the radiologist via telephone revealed two

masses in the abdomen. The first was ovarian tumor, already seen on US. The second one was a new mostly solid mass (8×6 cm), with a central liquid inclusion (5×4 cm), suspected of growing into the abdominal wall, it was located on the lower right side of the abdomen. No signs of abdominal carcinomatosis were observed.

Because of the rapidly deteriorating general condition of the patient, incidence of growing abdominal pain with signs of abdominal rigidity the decision was made to perform an urgent explorative laparotomy. A major bleeding into the tumour was suspected.

Upon inspection of the abdomen we saw the initial tumour in the left adnexal region, which had a smooth surface, was completely mobile, without signs of inflammation, necrosis or bleeding. Adnexectomy was performed. There were no signs of diffuse peritoneal carcinomatosis and any blood or ascites in the abdominal cavity. However, there was a mass in the lower right part of the abdominal wall. It was smooth, had a blueish tint and had all the characteristics of a haematoma. After consulting with the abdominal surgeon, the decision was made not to surgically open the haematoma because of the huge risk of major bleeding since the patient had been on high doses of LMWH.

The patient died 5 days after the surgery. Laboratory results after the surgery were improving, but clinically the patient had deteriorated and ultimately passed away. Histology findings are still pending.

In our opinion, this case is an interesting example of a difficult therapeutic decision in an older, comorbid patient, newly diagnosed with probably early ovarian cancer and with an acute

deterioration of health that followed acute major bleeding. The decision between urgent surgery or Liverpool palliative clinical pathway in such circumstances is always demanding, not only for physicians, but also for the relatives. Especially when we have to deal with a patient who was previously capable of independent living and caring for herself despite having mild dementia.

In order to make the decision easier and more objective, for physicians and relatives, there are scores to help evaluate fragility of the older patients and for the patients with malignant disease. One of them is a ''Comprehensive geriatric assessment (CGA)", defined to detect vulnerability in elderly patients so that treatment can be adjusted accordingly; it has been used for cancer patients as well. However, this process is time-consuming and pre-screening is often used to identify fit patients who are able to receive standard treatment versus those in whom a full CGA should be done (i.e. Vulnerable Elders Survey-13, Geriatric 8, Triage Risk Screening Tool, Groningen Frailty Index (GFI), etc.). But unfortunately, the recent results show, for now, it might be beneficial for all elderly patients with cancer to receive a complete geriatric assessment, since available frailty screening methods have insufficient discriminative power to select patients for further assessment.

The scores are not routinely used currently at our institution; their use should be encouraged and implemented. And multidisciplinary approach should always be performed in such circumstances.

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Missed metastatic high grade endometrial stromal sarcoma: a case report

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A 54 years old patient was referred to general gynecologic department for supposed uterine leiomyoma. Her main symptom was a postmenopausal bleeding of 1 month with occasional mild abdominal pain.

Her history revealed a known leiomyoma of 3 cm, already seen one year ago, normal cervical cytology so far, her last period was in 2011. She underwent several surgical procedures in the past: appendectomy (1985), removal of the right ovarian cyst (1996), sterilization and urinary incontinence surgery in 2016. Her mother was diagnosed with laryngeal cancer. The patient was a breast cancer survival, primary treatment with surgery, chemotherapy and radiotherapy was performed in 2010, currently she was receiving hormonal treatment with letrozol. In 2016 the patient survived a mild stroke and was at the time of presentation with postmenopausal bleeding fully rehabilitated. However in June 2017 the stenosis of the left carotid arteries was confirmed. She also had a known arterial hypertension.

The gynecological examination at her presentation in June 2017 showed enlarged uterus spreading up to the umbilicus and it was sensitive to palpation. There was medium to heavy bleeding from the uterus. Transvaginal sonography showed enlarged uterus of size 170x110 mm, uterine cavity was partially opened with the endometrial thickness of size 26 mm. There was a round non-homogenous structure in fundus and on the back wall of the uterus of size 140x100 mm. Next to the cervix was located another round non-homogenous structure of size 54x40 mm. She underwent the therapeutic dilatation and curettage, but the histology results were not useful because the pathologist could not interpret the sample.

One month later the postmenopausal bleeding recurred and she was referred to the general gynecologic department to tertiary centre. As a part of preoperative examinations she had a chest X-ray, which did not show any abnormality. Abdominal CT scan showed enlarged uterus with tumorous formation showing central necrosis; the radiological differential diagnosis was leiomyoma or sarcoma of the uterus. The basal parts of the lung, seen on CT scan, were described as having several small nodular changes. No further diagnostic procedures were performed. The neurologists, vascular surgeons and internal medicine specialists suggested the surgery could be performed safely regarding associated comorbidity.

Patient underwent a total abdominal hysterectomy with bilateral adnexectomy. The operation proceeded with no complications, no abnormalities were seen on other organs in abdomen. Histology results showed high grade endometrial stromal sarcoma with invasion into the cervix and deep invasion into the myometrium without hormone receptors. After the surgery the patient was presented at the gynecologic-oncology tumor board. The lung CT scan was recommended and performed, it confirmed several metastases in the lungs. Since she was a breast cancer survival, the biopsy of the metastases was suggested; the high grade endometrial stromal sarcoma spread was confirmed. The patient is currently receiving a systemic chemotherapy.

Endometrial stromal tumors are very rare uterine neoplasms, accounting about 1 % of all uterine malignancies. High grade endometrial sarcoma is a subset of them, showing high grade nuclear atypia, lack of hormonal dependency and poor prognosis. The preoperative diagnosis is hard, usually endometrial sampling and imaging are not specific and sensitive enough. Since the rarity of the disease there are no high quality data on the best treatment

approach; however some data show better overall survival with complete cytoreduction, when the disease is resectable. The metastastic disease with extra abdominal spread is currently recommended to be treated with chemotherapy. The patients however might benefit from treatment at gynecologic oncology departments.

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A colon metastasis to the ovary mimicking advanced ovarian cancer: a case report

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A 72-year old patient was referred to gynecologic oncology department for incidentally found pelvic tumor on CT scan and MR scan performed during the follow up after treatment of the cecum cancer in 2015. She was surgically treated and received adjuvant chemotherapy. The CT scan revealed pelvic tumor, the carcinomatosis of the peritoneum, omentum and mesentery of the bowel, ascites and suspected retroperitoneal lymph nodes. MR scan confirmed ovarian tumor, up to 12 cm large, multilocular with solid areas. The radiological opinion suggested primary ovarian pathology.

At the presentation at gynecologic oncology office she was completely asymptomatic. The pelvic US examination was performed, showing multilocular tumor of the right ovary, up to 12 cm large in the greatest dimension, with solid proliferations and high vascularity (according to IOTA simple rules it was assessed as malignant tumor). Some ascites was seen in the pouch of Douglas (5 cm) with suspected peritoneal carcinomatosis. The tumor markers CA 125 and CEA were elevated.

Although the imaging suggested the primary ovarian pathology the cecum cancer progression was possible. Since the treatment modalities are completely different preoperative histological conformation was recommended by the tumor board. The diagnostic laparoscopy was associated with higher risk for perioperative complications (previous surgery and chemotherapy for malignant abdominal tumor, current spread of the disease); that is why the transabdominal US guided core needle biopsy was performed.

The histological review confirmed the cecum cancer metastasis to the ovary. And the patient was referred to the medical oncologist for further treatment.

Colorectal cancer is the most common cancer metastatic to ovaries. Metastatic ovarian tumor is usually discovered as adnexal mass in a patient with prior history of colon cancer. It has been reported that approximately 2 % of the patients with primary colorectal cancer develop metachronous ovarian metastases within 2 years after primary resection. When presented with pelvic mass after the treatment of colorectal cancer it is more likely that the metastasis to the ovary is accurately diagnosed before the surgery; otherwise colorectal cancer with ovarian metastasis are often discovered at the time of surgery presumably for advanced ovarian cancer. However the recommended treatment modality for advanced ovarian cancer (with the aim of complete cytoreduction) is markedly different to recommended treatment of advanced colorectal cancer (medical treatment with different chemotherapy regiments as for ovarian cancer). Our experience with transabdominal US guided core biopsy of ovarian tumors shows the method to be feasible and safe.

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Cervical fibroid in pregnancy: a case report

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We present a 37-old multigravida who had cervical fibroid diagnosed and hystologically confirmed in another hospital before her second pregnancy, measuring 3 cm in the largest diameter at that time. She had consultation before trying to concieve in another institution reagrding the removal of the myoma. The tumor board at that time suggested not to remove it before pregnancy.

She presented at our divison for gynecology and perinatology in the 8th week of her second pregnancy with vaginal bleeding. An ultrasound scan demonstrated a single viable intrauterine pregnancy corresponding to dates and an intracervical fibroid measuring 36x37 mm. She was admitted multiple times durig the first and second trimester of pregnancy due to vaginal bleeding from the surface of the fibroid. A conservative approach was chosen with observation, compression, hemostatic patch use if needed, and rest. An operative procedure was advised only in case of unstoppable heavy bleeding. In the 20th week, electrocoagulation of a bleeding spot was performed on the cervical myoma surface for bleeding management. In the 28th week, bleeding was stopped with tamponade and a hemostatic patch was used; in other cases, bleeding was mild and resolved spontaneously. Haemoglobin levels were followed frequently, the lowest level was 99 g/L. Peroral iron therapy was prescribed. The fibroid doubled in size during the pregnancy, measuring 68x65 mm in the 36th week. The pregnancy was additionaly complicated by a suspicious of preterm premature rupture of membranes in 28th week, but the cervical canal was closed, and the pregnancy was succesfully continued until completed 37th week of gestation. Frequent ultrasound scans of fetal wellbeing and growth were performed, following the amount of amniotic fluid, along with antibiotic prophylaxis and steroid administration for fetal lung maturation. Indicators of inflammation were negative.

An elective caesarian section was performed at 37 weeks and 1 day of pregnancy, and a healthy male infant was delivered. The cervical fibroid was left in situ. The operation and postoperative period passed without complication. She was discharged home with the infant on postpartum day 5.

Cervical fibroids in pregnancy are rare and present a unique management challenge. Although succesful myomectomy during pregnancy has been reported, in most cases, surgery was performed postdelivery and conservative management was chosen during pregnancy. Antenatal and postnatal complications can arise depending on the size and type of the fibroid. Complications include degeneration of the fibroid, spontaneus misscarriage, preterm labor, fetal malpresentation, antepartum and postpartum haemorrhage and puerperal sepsis.

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