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STUDIUM PRZYPADKU
CASE STUDY

An unusual manifestation of clear cell carcinoma – case report

Niezwykły objaw raka jasnokomórkowego – opis przypadku

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ABSTRACT

The metabolism of neoplastic cells is perceived as the cause of atherothrombotic incidents in cancers since the 19th century. Those incidents occur in 1–11% cancer cases. In clear cell carcinoma, accounting for 5% of ovarian cancers, atherothrombotic incidents tend to occur 2.5 times more frequently. Clear cell carcinoma is diagnosed earlier and at a younger age compared to other ovarian cancers. The cancer is also characterized by drug resistance to standard treatment.

A 47-year-old patient was admitted to the Department of Gynaecology and Obstetrics of School of Medicine in Katowice to treat a tumor of the right ovary. The tumor was detected a month before during the diagnostics of an ischemic stroke which occurred despite no risk factors being present. A laparotomy was performed and the tumor, left adnexa and uterus were removed, according to ovarian cancer protocol. Histopathological examination confirmed the diagnosis of *adenocarcinoma clarocellulare* (clear cell carcinoma – CCC). The patient was referred for further oncological treatment on 5th day after surgery.

Oncological alertness needs to be maintained in cases of unexplained atherothrombotic incidents. An interdisciplinary approach can improve patients' prognosis by diagnosing the cancer earlier.

KEY WORDS
ovarian cancer, clear cell carcinoma, atherothrombotic incident, stroke

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STRESZCZENIE

Choroba nowotworowa już od dawna uznawana jest za przyczynę incydentów zakrzepowo-zatorowych. Incydenty te występują w 1–11% przypadków raków. W raku jasnokomórkowym, który stanowi około 5% nowotworów złośliwych jajnika, incydenty zakrzepowo-zatorowe występują 2,5 razy częściej niż w innych typach histologicznych. Rak jasnokomórkowy jest rozpoznawany u młodszych kobiet i we wcześniejszym stadium. Nowotwór cechuje też chemiooporność na standardowe leczenie.

Kobieta 47-letnia została przyjęta do Kliniki Ginekologii i Położnictwa Wydziału Lekarskiego w Katowicach w celu leczenia guza (raka) przydatków prawych, którego wykryto miesiąc wcześniej w trakcie diagnostyki udaru niedokrwiennego. Udar wystąpił mimo braku czynników obciążających. Wykonano laparotomię według protokołu raka jajnika. Badanie histopatologiczne potwierdziło rozpoznanie: rak jasnokomórkowy (*clear cell carcinoma* – CCC). Pacjentkę w 5 dobie po operacji wypisano ze szpitala i skierowano do dalszego leczenia onkologicznego. Interdyscyplinarne podejście zespołu lekarskiego może poprawić rokowanie pacjentek przez wcześniejsze wykrycie nowotworu. Należy zachować czujność onkologiczną w przypadku niewyjaśnionego incydentu zakrzepowo-zatorowego.

SŁOWA KLUCZOWE

rak jajnika, rak jasnokomórkowy jajnika, incydent zakrzepowo-zatorowy, udar

INTRODUCTION

The link between thromboembolic incidents and malignant tumors is well established. It was first described by Trousseau in 1865. The occurrence of the mentioned incidents in cancer patients ranges between 1 and 11% [1]. In gynecological oncology thromboembolic incidents can indicate an ongoing oncological process. They are most commonly observed in ovarian cancer patients.

Clear cell ovarian cancer (CCC) when compared to other types of ovarian cancers has a different clinical impact. It is distinguished by a poor prognosis and higher drug resistance. Moreover this type of cancer is more often related to endometriosis, hypercalcemia and thromboembolic incidents when compared to other types of ovarian cancer [2,3].

A case study of a woman diagnosed with clear cell ovarian cancer, with the first symptom being an ischemic stroke is presented.

CASE STUDY

A 47-year-old woman was admitted to Department of Gynaecology and Obstetrics of School of Medicine in Katowice to treat a tumor of the right ovary. About a month earlier she was diagnosed with ischemic stroke of the right brain and cerebellum hemisphere. In the diagnostic process a right ovary tumor was revealed. It is worth mentioning that the patient did not have any previous predisposition to thrombosis and embolisms.

Upon admission the patient was in good condition with diminishing left-side hemiparesis, she had a medical history of iron deficiency anemia, nephrocalcinosis and a stomach polyp.

Physical examination revealed a tender tumor located in the right half of the abdominal cavity. The tumor was connected to the uterus and the perimetrium was shortened.

The gynecological examination showed the body of the uterus in a connection with a hard solid tumor, most probably originating in right adnexa, descending into the rectouterine excavation. The tumor was 15 cm in diameter, mobile, the left adnexa was without visible abnormalities. A digital rectal exam did not reveal any changes, the perimetria were unchanged.

Ultrasound confirmed the presence of a cystic-solid tumor with an irregular outline, size of 127 x 115 x 115 mm, few hypogenic spaces and thickened, irregular septa. The tumor was placed in right adnexa and filled the rectouterine excavation. Moreover the examination revealed a 19 mm myoma of the back uterine wall. The endometrium was 11 mm thick. The lab results: CA125 – 1057 UI/ml, CRP – 57.5 mg/l other parameters (including the coagulation parameters) were in order.

The patient was qualified for a laparotomy. During the surgery a neoplastic lesion was exposed – a tumor 15 cm in diameter expanding from right ovary. The anatomical structure of the ovary was not presented. The left ovary was not macroscopically changed. Visible metastases on the urinary bladder, visceral and parietal pleura as well as greater omentum were presented. The lesser pelvis was filled with a serosanguineous fluid. In the first stage of the surgery the fluid was collected for cytological examination. The

rest, around 2500 ml, was removed by suction. The tumor and right adnexa were removed as well as the uterus, greater omentum and appendix. The appendix was not visibly metastatic. In the next stage of surgery a systemic pelvic lymphadenectomy was performed – lymph nodes with macroscopically visible metastases. The specimens were sent for histopathological examination: the tumor of right ovary, left adnexa, uterus, greater omentum, appendix, lymph nodes and smears from phrenic domes and supracystic area.

After the surgery the patient remained cardiovascularly and respiratory stable. Due to the large postoperative blood loss (Hb 6.1%) stabilization was needed and on the fifth day after the procedure the patient was discharged with a referral to an oncological clinic for further treatment. The hemoglobin level on discharge was 10.2%. The histological examination result was adenocarcinoma clarocellulare (G3). The right adnexa – a tumor 14 x 8 x 5 cm, white and grey in sections with focal blood lesions, partially mucous, making up about 10% of cystic spaces. Neoplastic growth was also stated in the right uterine tube, greater omentum, parietal peritoneum, and lymph nodes from the right obturator fossa. Cancer cells were also detected in smears from the phrenic domes, supracystic area and from the pleural cavity fluid. Additionally endometriosis, adenomiosis and intramural myomas with diameters up to 1.5 cm were discovered.

The radicalization of the procedure was assessed as R1 and the disease was advanced at level III C on the FIGO scale.

DISCUSSION

Ovarian carcinoma is difficult to diagnose in the early stages which contributes to the high mortality rate. It is the leading cause of death from gynaecologic cancer.

The comparison between carcinoma clarocellulare (CCC) and planoepithelial carcinoma shows that CCC is usually diagnosed in younger patients (55 vs. 64 years; median age) and at an early stage (57–81% of CCC were diagnosed as stage I/II). These factors may affect the prognosis which is better at earlier stage. Nevertheless, at every stage of the International Federation of Gynecology and Obstetrics (FIGO) staging system the CCC five-year survival rate is lower than other epithelial ovarian cancer patients. The higher the FIGO stage the poorer the prognosis [4].

Clear cell carcinoma has a higher incidence in Asian populations, different than other types of epithelial carcinoma that usually occur in European populations. Clear cell carcinoma tumors are more likely to be platinum-resistant and have lower rates of BRCA1/2 mutation [3]. Clear cell carcinomas with a solid or papillary structure in the section are usually detected when they have grown over 15 cm in diameter [5]. These tumors are more often associated with malignant hypercalcemia, endometriosis, thromboembolic events and are bilateral. CA125 level is typically lower [3].

Thromboembolic events occur two and a half times more often in CCC than in other ovarian carcinomas. The most commonly reported events are venous thrombosis and pulmonary embolism [6,7]. 26–40% strokes are of unknown etiology [8]. In case of a female patient, we should pay particular attention to symptoms of ovarian cancer because it is associated with a 1.5 times higher risk of stroke. Independent risk factors for ischemic stroke include age ≥ 50, hypertension, diabetes mellitus and chemotherapy treatment (especially platinum-based therapy) [7]. Clear cell carcinoma should be considered especially in younger women without conventional stroke risk factors, with disseminated intravascular coagulation (DIC) [9] and infarction in multiple vascular territories or focal lesions on MRI [10]. In these patients, cancer should be excluded by expanded medical history, physical examination, tumor and serum markers (such as D-dimer) and imaging [8]. D-dimer levels are higher in patients with both ischemic stroke and cancer than in patients with stroke without the latter [9].

Most thromboembolic events occur during relapse, less often before cancer diagnosis [1]. Nevertheless, in stroke patients without a conventional mechanism, cancer should be always considered [9,10].

Cancer leads to stroke via multiple mechanisms: hypercoagulability, non-bacterial thrombotic endocarditis (NBTE), treatment-related effects and others [8]. Adenocarcinomas increase the risk of stroke via the production of mucin CA-125, a tissue factor-activated coagulation cascade, and the release of pro-coagulant cytokines [8].

There is no consensus about the prognosis in patients with thromboembolic events. Some specialists suggest that such incidents worsen the prognosis (five-year survival rate in patients with atherothrombotic complications vs. those without such complications – 0 to 38%). Other authors claim it does not affect the prognosis [11,12]. Further clinical studies of the association between thromboembolic events and poorer prognosis are needed.

Up to 50% of cancer patients have thromboembolic events soon after operation despite pharmacological prevention [6].

CONCLUSION

An oncological alertness must be kept with an unexplained atherothrombotic incident as it can be the first manifestation of ovarian cancer along with other

neoplastic processes – tumors of the pancreas, lung or liver. Earlier discovery equals a better prognosis in female patients.

Undoubtedly, one can reach a conclusion that female patients with an unexplained atherothrombotic incident should be consulted gynecologically to exclude an active neoplastic process, especially ovarian cancer. An interdisciplinary medical approach and oncological alertness can increase the chances of diagnosis at an early stage.

Author's contribution

Study design – A. Buczek-Kutermak (40%), W.M. Szanecki (40%), A. Witek (20%)
Data collection – A. Buczek-Kutermak (40%), W.M. Szanecki (40%), A. Witek (20%)
Data interpretation – A. Buczek-Kutermak (20%), W.M. Szanecki (20%), A. Jabłońska (20%), A.M. Witkowska (20%), M. Palowski (20%)
Statistical analysis – Not applicable
Manuscript preparation – A. Buczek-Kutermak (20%), W.M. Szanecki (20%), A. Jabłońska (20%), A.M. Witkowska (20%), M. Palowski (20%)
Literature research – A. Buczek-Kutermak (20%), W.M. Szanecki (20%), A. Jabłońska (20%), A.M. Witkowska (20%), M. Palowski (20%)

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