CASE OF **OVARIAN CANCER AFTER IN-VITRO FERTILIZATION.**
FORENSIC MEDICAL MALPRACTICE. CLINICAL CASE AND DATA REVIEW

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Ovarian cancer is a **leading cause of death amongst women**.

It accounts for more deaths than any other cancer of the female reproductive system.

Source: Pintas & Mullins, Available Types of Treatment for Ovarian Cancer
RISK FACTORS FOR OVARIAN CANCER

✓ Extreme hormonal stimulation;
✓ In-vitro fertilization (IVF);
✓ Family history of cancer;
✓ Genetic mutations (BRCA-1 & BRCA-2 genes);
✓ Pregnancy after 35 years;
✓ Lack of pregnancy;
✓ Early menarche;
✓ Late onset of menopause;
✓ Oral contraceptives;
✓ Hormone therapy after menopause;
✓ Obesity, etc.
<p>OVARIAN CANCER STAGING</p>

**Stage 1**<br>Cancer is found in one or both ovaries.<br><br>**Stage 2**<br>Cancerous cells have spread from the ovaries to other parts of the pelvis, such as the fallopian tubes or uterus.<br><br>**Stage 3**<br>Cancerous cells have spread outside the pelvis to the nearby lymph nodes, diaphragm, intestines, or liver.<br><br>**Stage 4**<br>The cancer has spread beyond the abdomen, such as to the lungs or spleen.<br><br>Source: Weill Cornell Medical Center
In-vitro fertilization procedures (IVF) are a part of the assisted reproductive technologies (ART). IVF includes:

1. Stimulation of the ovaries to obtain several eggs;
2. Follicular puncture to retrieve the eggs;
3. Fertilization of the eggs outside the body;
4. Implanting the eggs in the woman’s body.

IVF is used to treat infertility in women with different health conditions.
IN-VITRO FERTILIZATION (IVF) PROCEDURE

1. OVARIAN HYPERSTIMULATION
2. EGG RETRIEVAL
3. SPERM PREPARATION
4. CO-INCUBATION
5. EMBRYO TRANSFER
6. PREGNANCY

Source: In Vitro Fertilization (IVF): Side Effects and Risks, Laurel Fertility Care
There are known cases of **cystic and malignant formations in the ovaries**, as well as **Ovarian hyper stimulation syndrome**, after IVF procedures due to the usage of **ovulation stimulating drugs** such as gonadotropins, SERM (Selective estrogen receptor modulators), Clomiphene Citrate, etc.

There is a theory that **hyper stimulation with the purpose of provoking repeated ovulations lead to malignant transformation of the ovarian parenchyma.**
A 45-year-old woman with no family history of cancer, with almost diminished ovarian reserve started IVF procedures with the first two attempts being unsuccessful.

The subsequent IVF attempt was successful and embryo transfer was completed. The patient had a normal pregnancy and delivery at 39 weeks of gestation of a healthy fetus via Cesarean section.

The doses of the hormone medications that were used – Merional (highly purified Human Menopausal Gonadotrophin (HMG) and Cetrotide (Cetorelix Acetate), do not exceed the recommended values.
Three months later, during a gynecological ultrasound examination, formations were found (unilocular cysts) as follows:

✓ 30.5 mm in the right ovary & 20.0 mm in the left ovary.

Tumor markers testing:

- ROMA (Risk of Ovarian Malignancy Algorithm) – 12.36% (ref. <11.4%);
- Ca-125 – 37.34 (ref. <35);
- HE4 – 61.8 (ref. <70).
CASE REPORT

Therapy with *Dufaston (Dydrogesterone)* 2x1 tab. was prescribed with the assumption that the ovarian cysts indicate Luteinized unruptured follicle (LUF) syndrome.

After another 3 months, during a gynecological ultrasound examination it was established that the formations persisted:

✓ 49.0 mm in the right ovary & 15.0 mm in the left ovary.

*Regulon (Ethinylestradiol/ Desogestrel)* 1x1 tab. was included in the therapy.
Half a year later, the patient was hospitalized because of a sudden bloating and pain in the lower abdomen.

Ultrasound diagnostics revealed a formation measuring 25 cm/15 cm, with heterogeneous echogenic content, occupying almost the entire abdominal cavity.

The tumor markers indicated as follows:

- Ca-125 – 38.54 (ref. <35);
- HE4 – 106.3 (ref. <70).
A total hysterectomy with bilateral tumor adnexectomy was performed.

During the surgery two formations were found:

✓ A solid formation from the right ovary with dimensions 25 cm/25 cm;
✓ a solid formation from the left ovary with dimensions 5 cm/5 cm.

Histological examination confirmed the diagnosis:

➤ Malignant Mixed Müllerian Tumor, FIGO IB, pT1bNxMx.
**CASE REPORT**

**Adjuvant chemotherapy** was prescribed: *six courses of Carboplatin AUC 6 + Paclitaxel 175 mg/m²* with an interval of 21 days between the courses.

With the disease progression after first-line chemotherapy *Ifosfamide 1,500mg/m² + Etoposide 100mg/m³* 1-3 days was prescribed.

A BRCA-1 and BRCA-2 genetic mutation test was performed, and the result was negative.
In this particular clinical case, in addition to the development of ovarian cancer, an object of interest is *the delayed diagnosis of the malignant process (ovarian cancer)*, respectively its untimely staging and treatment.

Lack of regular ultrasound and tumor markers examinations as well as the neglected data from the already performed ones are an omission of the physician.
Each IVF procedure needs to be tailored to the individual patient with regards to the specific health conditions.

It is a necessity for a detailed medical history of inherited oncological diseases to be established, as well as for genetic testing of BRCA-1 and BRCA-2 mutations to be performed.

The strict and regular disease control is important if pathological changes are confirmed. It is a mandatory condition for implementing a good clinical practice.
IVF procedures should be performed by physicians who are highly qualified in the field.

Each clinical case should be managed particularly and in considering to the patient's individual needs and preferences. This ensures reliability for the absence of medical malpractice and an unfavorable outcome for the patients.
REFERENCES


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