

BACKGROUND INFORMATION FOR MEDICAL TRADE MEDIA

Ovarian Cancer

In 90 % of all cases malignant ovarian tumors originate in cells of the surface epithelium, however, it has to be distinguished between invasive ovarian cancer and borderline tumors (tumors of low malignant potential).

Histologically these tumors are further classified into serous, mucinous, endometrioid, clear cell, transitional cell and mixed type tumors.

In industrial countries, ovarian cancer is the second most common form of gynecological cancer after uterine cancer (Corpus Uteri) whereby the incidence has hardly changed over the last decades (Globocan 2002). The risk of developing ovarian cancer rises with age and reaches its peak between the ages of 60 and 75. As the tumor rapidly metastasizes and is only diagnosed in the late phases III and IV in more than two thirds of cases, the prognosis is generally unfavorable. With an overall 5 year survival rate of approximately 45 %, ovarian cancer has the highest mortality rate of all gynecological tumors.

The exact causes of ovarian cancer are yet unknown, however, in 5 % of cases there is a genetic predisposition which leads to a high familial occurrence. This is caused by a mutation of the genes BRCA-1 and 2. Approximately every second woman with a defect BRCA-1 gene develops ovarian cancer, whereas the risk from a BRCA-2 mutation is lower. Also hormonal factors such as menopause and childlessness seem to be connected to a higher cancer risk. Factors reducing the risk to develop ovarian cancer include a higher number of pregnancies and the duration of the intake of ovulation inhibitors.

Diagnosis

Ovarian cancer can remain undetected for a long time as it is able to spread uncontrolled in the abdominal cavity. The condition first becomes symptomatic when the tumor causes pressure onto other organs or a peritoneal spread of malignant cells leads to an ascites. Possible warning signs of ovarian cancer are bleedings outside of the normal menstruation cycle or after the

menopause, abdominal pain or digestion problems without discernible causes or an inexplicable loss of weight combined with an increased girth.

Indications for the presence of ovarian cancer and metastases can be found using abdominal sonography, intravaginal sonography, CT and MRI. The diagnosis can be confirmed by a laparoscopy or during the actual surgery, where biopsy samples are taken for histological analysis.

The prognosis for ovarian cancer depends heavily upon the tumor stage. In stage I the five year survival rate is between 80 and 90%. The prognosis for stages III and IV correlates strongly with the residual tumor mass after the primary surgery. The 5 year survival rate in these stages is ranging between 60% (R0-resection) and 20% (residual tumor > 2cm).

Therapy

A significant factor for the successful treatment of ovarian cancer is - if possible - the complete removal of the tumor tissue (R0-resection). This is carried out by means of a laparotomy, in which both ovaries, the fallopian tubes, the uterus, the greater omentum, parts of the peritoneum and if necessary the lymph nodes of the larger vessels are removed. Depending upon the extent to which the tumor has spread it may also be necessary to do a partial resection of the intestine.

To reduce the risk of relapse for most patients the surgery is followed up with a systemic chemotherapy, using a combination of Carboplatin and Paclitaxel. In addition the intraperitoneal chemotherapy is also being investigated at present. The first clinical trials report improvements in progression free survival and overall survival. Adverse effects were recorded due to the high toxicity of this treatment, which, due to high intraperitoneal concentration levels of chemotherapeutic agents can lead to damage of the abdominal tissue, intestinal obstruction or perforation.

The intraperitoneal administration of the trifunctional antibody catumaxomab, which is currently being investigated in clinical trials, could prove to be a more effective and comfortable option for an intraperitoneal therapy. catumaxomab binds to the over-expressed cell adhesion molecule (EpCAM) on ovarian cancer cells. Pre-clinical data has shown that catumaxomab is capable of recruiting T-lymphocytes and accessory cells, which via their mutual stimulation could lead to a more effective immune reaction against the tumor

cells. The current US Phase II study IP-CAT-OC-01 is examining the effectiveness and safety of catumaxomab in patients suffering from advanced ovarian cancer, who after tumor resection and 1st line standard chemotherapy achieved a complete remission. In an already concluded phase II/III study of patients with malignant ascites caused by ovarian cancer it could be shown that catumaxomab was well tolerated and at the same time led to a significantly extended puncture free survival period and puncture free time.

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