

Ovarian Carcinoma: A Deadly Disease

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Ovarian carcinoma is one of the deadly diseases which can affect the females in their lifetime. Worldwide, ovarian cancer is diagnosed in a quarter million females annually. This deadly cancer is responsible for 140,000 deaths per year. Ovarian cancer is the most lethal of the gynaecological malignancies and 4th most common cause of death in females.

It is associated with high mortality when diagnosed at advanced stage. It is because of lack of reliable screening tests. Cancer antigen 125 (CA 125) and transvaginal ultrasound are only available screening modalities available at present. These are not well authenticated in screening as their sensitivity and specificity is questionable. Diagnostic potential of CA 125 is poor as it is raised in other conditions like endometriosis, pelvic inflammatory disease and menstruation. Poor sensitivity and specificity of screening tests lead to late diagnosis of the disease. Now, new tumour markers such as human epididymis protein 4 (HE4), mesothelin, macrophage colony-stimulating factor (M-CSF), osteopontin, kallikrein, soluble epidermal growth factor (EGF) are available but not yet worldwide applicable.¹

The incidence of ovarian cancer varies around the world, with the lowest rate recorded in Japan (3/100,000 women) and some of the highest rates recorded in the Nordic countries (20/100,000 women). In UK, approximately 7000 cases are reported each year, with upto 4500 mortalities.

Risk factors which are responsible for ovarian cancer include age, history of infertility, use of ovulation induction agents (clomiphene citrate), endometriosis and family history of ovarian cancer. Hereditary factors play an important role in ovarian cancer pathophysiology in 10% of population. Two mutations of breast cancer (BRCA) 1 and BRCA 2 are responsible.² These mutations will affect the efficiency of P53 gene and lead to the progression of the

malignant disease. BRCA1 mutation is associated with a lifetime risk of 40% of ovarian cancer and 80% risk of breast cancer, while with BRCA2 mutation, the risk of developing ovarian cancer is 20-25%. Prophylactic oophorectomy before forty years of age can be considered in the patients with these mutations or with positive family history of ovarian cancer.

Lynch type 2 syndrome is a combination of ovarian, colorectal and endometrial carcinoma. This syndrome has a mutation at chromosome 5 and risk of developing ovarian cancer is 12% with this syndrome as compared to the risk of developing ovarian cancer up to 2% in general population.³ These patients need regular colonoscopic examination and prophylactic hysterectomy.

Presentation of patients is with abdominal pain, bloating, postmenopausal bleeding, weight loss and loss of appetite.

World Health Organisation classifies ovarian cancer on the basis of origin.⁴ Tumour can be classified into epithelial, sex cord, stromal and germ cell tumours. Epithelial tumours are further classified into serous, mucinous, endometrioid, clear, transitional and squamous carcinoma.⁵ They account for 50-55% of ovarian tumours. In the western world, these epithelial tumours are responsible for 90% of malignant form of the tumour.

Borderline ovarian tumours are the type of epithelial tumour which has varying degree of nuclear atypia and increase in the mitotic activity, but no stromal invasion. They account for 10% of all ovarian tumours and carry a better prognosis.⁶

Five year survival is 70% in cases of early stages of the disease but it decreases to 30% if the disease is advanced and metastatic.⁷

In symptomatic patients, initial investigation includes abdomino-pelvic ultrasound with Doppler, computed tomography (CT) scan of abdomen and pelvis and in certain cases magnetic resonance imaging (MRI) may be needed. Risk of malignancy index is calculated that is based on the menopausal status, sonographic findings and CA 125 levels.⁷ CA 125 is a tumour marker for epithelial ovarian tumour which has more prognostic value in the follow-up of the patients after surgery or chemotherapy. Tumour marker for germ cell tumours are beta human chorionic gonadotropin (B-HCG) and alpha fetoprotein. Carcinoembryonic antigen is used

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when there is doubt about the primary origin of the disease. Chest X-ray is helpful if the disease is metastatic.

Most of the patients present at an advanced stage of the disease, so surgery is mainly aimed on debulking the tumour, to stage the disease, to get a histopathological diagnosis and for symptomatic relief. Staging laparotomy is performed which includes total abdominal hysterectomy, bilateral salpingo oophorectomy, omentectomy, retroperitoneal lymph node sampling, sampling of peritoneal fluid and other biopsies if needed.⁸ Fertility sparing surgery is performed in cases of germ cell tumours which are confined to the ovaries. Optimum debulking is considered when the residual tumour is < 2cm. Interventional debulking surgery can be performed in selected patients; it is done in those cases when optimum debulking is not achieved at the time of primary operation.

Chemotherapy is given before or after surgery. The main aim of giving chemotherapy is to regress the residual tumour. Combination chemotherapy in the form of cisplatin and paclitaxil are used effectively as first line agents.⁹⁻¹¹

Neoadjuvant chemotherapy is a novel approach used for ovarian cancer.¹² More exciting approaches relate to using a greater number of molecular targets and developing studies which are more tumour specific. The main molecular targets of therapy are polymerase inhibitors, used in BRCA mutational tumours such as breast and ovarian cancer.¹³ The results of large trials targeting vascular and endothelial growth factors are awaited with interest and should hopefully add another approach to therapy.

In conclusion, the diagnosis of ovarian cancer is usually made at advanced stage, this is because of lack of adequate screening tests and non specific nature of symptoms. Ovarian cancer management is mainly surgical followed by adjuvant chemotherapy in most cases. Combination chemotherapy in the form of cisplatin and paclitaxil is done. Each patient should be individualised according to the clinical condition of the patient.

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