Clinical Evaluation Of A Patient With Suspected Epithelial Ovarian Cancer

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The presentation of Epithelial Ovarian Cancer (EOC) can be to the gynaecologist; the physician with ascites, dyspepsia and loss of appetite; or to the general surgeon with abdominal mass and symptoms of intestinal obstruction .It is important for not only the gynaecologist but also the other specialists to keep this disease in mind.

The presentation can be with symptoms due to the primary disease or those due to metastases. 75-85% of women are diagnosed only when the disease has spread throught the peritoneal cavity ie with stage III or IV disease.

Evaluation of a patient includes:

1. A detailed history
2. Complete general examination
3. Pelvic examination

History: The points to be noted in the history are:

1. **Age:** EOC is rare before the age of 35 years. The incidence increases with age and peaks at 54 years. BRCA 1 gene cancers can present in their forties or earlier. Secondary malignant transformation in a benign epithelial tumor peaks at an older age.

2. **Presenting Symptoms:**

Abdominal Pain & Discomfort: Most common presenting symptom seen in about 47% of patients.More than half of the tumors are painless.

- **Abdominal Swelling:** Can be due to the primary tumor, epigastric omental plaque or due to ascites and is seen in about 57% of patients.
- **GI Symptoms:** Dypepsia seen in 10%, vomiting due to UGI obstruction seen in 10% and alteration of bowel habit is seen in about 16% of patients. These symptoms could also be due to a GI primary causing secondaries in both ovaries(Krukenberg tumor).
- **Urinary Symptoms:** Seen in about 13% of patients .These include frequency or retention of urine due to pressure effects of the tumor.
- **Incidental finding:** 3% of ovarian cancers are unsuspected and noted only during an examination or operation for some unrelated cause.
- **Pleural Effusion:** Respiratory sumptoms may dominate the clinical scene with an occult ovarian primary. Pleural effusion is seen in about 5% of patients, only half of them are clinically detectable.
- **Enlarged Cervical/Inguinal lymph nodes:** due to nodal metastases from the primary.
- **Unilateral/ Bilateral Deep Vein Thrombosis or Unilateral Varicose Veins** could be the initial presentation. This could be due to pressure effects from the primary tumor. Venous thrombosis could be due to polycythemia secondary to the paraneoplastic effect of an mucinous cystadenocarcinoma.
- **Post-menopausal Bleeding:** Seen in 20% of patients with EOC ; could be due to endometrial hyperplasia, associated endometrial carcinoma or spread to the endometrium
- **Symptoms due to para-neoplastic syndromes:**
- Hypercalcemia-seen with mucinous cystadenocarcinoma
- Zollinger-Ellison Syndrome: seen with mucinous cystadenocarcinoma due to increased gastrin production
- Scleroderma, Dermatomyositis, Palmar fasciitis (Dupuytren's Contracture) seen in association with endometroid ovarian cancer
- Acanthosis nigricans: patchy keratosis and hyperpigmentation at odd sites including axilla

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- Neuropathy,necrotising mylopathy,lower motor neurone paralysis and limbic encephalitis are rare but have been reported
- Retroperitoneal fibrosis-seen in recurrent ovarian cancer due to spread to retroperitoneal lymphatics causing fibrosis.

3. **Parity:** Pregnancy provides a protective effect due to cessation of ovulation, hence its rarity in parous women.The risk decreases with increasing number of pregnancies. Involuntary infertility increases the risk.
4. **Breast-feeding**: decreases the risk due to ovulation suppression during lactation
5. **Previous Infertility Treatment:** A pooled analysis of various studies indicates a small increased risk in women treated with prolonged ovulation inducing agents.
6. **Previous Contraceptive Usage:** Oral contraceptives decrease the risk of ovarian cancer as they suppress ovulation, the risk decreases approximately 11% per year of usage to a maximum of 46% after 5 years of use.
7. **Previous history of tubal ligation and hysterectomy:** decreases the risk due failure of potential carcinogens reaching the ovaries.
8. **Family History:** Family history of ovarian, breast, colorectal and endometrial cancer needs to be taken.

   Family history of ovarian cancer is significant as inheritance plays a role in 5-10% of of epithelial ovarian cancers (usually serous adenocarcinomas). Women who are below 45 years & have one affected relative have a life-time risk of 4%; if the affected relative is her mother, the risk increases to 7%. If there is more than one relative with ovarian cancer, the increases to 14%.

   Familial Ovarian Cancer Syndromes: Three syndromes have been described:

1. Hereditary breast ovarian cancer syndrome-most common, characterised by multiple cases of early onset (<50 years) of breast & ovarian cancer.Accounts for 75-90% of hereditary ovarian cancers.
2. Hereditary site specific ovarian cancer syndrome-increase in cases of early onset ovarian cancer. These patients are younger & more commonly have tumors of serous histology
3. Lynch-syndrome-characterised by early onset proximal colon cancer in association with cancer of the endometrium and ovary These familial caner syndromes are inherited by autosomal dominant transmission, hence children of an affected parent have a 50% risk of inheriting the genetic abnormality.

   Gene Positivity: Germline mutations of BRCA1 & 2 genes account for most hereditary ovarian cancers. BRCA1 is a tumor suppressor gene located on the short arm of chromosome 17 & BRCA2 is localised on the short arm of chromosome 13.

9. **Duration of Symptoms:** Long duration (upto 12 months) indicates a well-differentiated tumor; short duration (upto 6 months) indicates an undifferentiated tumor.

The aims of clinical examination and investigation are:

- To assess whether the tumor is likely to be benign or malignant
- To detrmine the clinical stage of the disease
- To assess it's operability
- To assess the ability of the patient to tolerate extensive surgery

EXAMINATION: A thorough general and pelvic examination needs to be carried out.

General Examination: The points to be noted are general condition of the patient: A patient with poor general condition has a poor performance status and will have a poor response to surgery and chemotherapy

Anaemia and icterus is to be noted- icterus indicates the possibility of liver metastases.

Presence of cervical or axillary lymphadenopathy- indicates the possibility of metastases

Examination of the chest-for any evidence of pleural effusion

Examination of the legs-for any edema, varicose veins or deep vein thrombosis

Examination of the Abdomen: The abdomen is examined for any evidence of ascites, cutaneous nodules (Sister Marie Joseph's nodules) due to cu-

taneous lymphatic spread, hepatomegaly due secondaries in the liver.

Pelvic Examination: A rectovaginal examination is carried out to note the presence/absence of any adnexal mass, it's size, consistency, mobility & to note the presence of any nodules in the pouch of Douglas.

INVESTIGATIONS: These include general and specific investigations.

General Investigations:

- Haemogram with platelet count,
- Random blood sugar,
- Liver and renal function tests,
- Serum proteins,
- Chest x-ray (erect posture) for any evidence of pleural effusion and evidence of enlarged mediastinal lymph nodes.

Specific Investigations:

1. **Tumor Markers: S.CA125, CEA,**

   S.CA-125: This is a secretory product of uterine and tubal fluids,breast milk and amniotic fluid of healthy women. Normal ovarian epithelium does not express CA 125. A level of <35 u/l is considered normal. This cut-off represents the 97.5 percentile in healthy female blood donors. The level is increased in about 50% of EOC.

   CEA: A level of >20ng/ml suggests an ovarian tumor, the level is increased in mucinous cystadenocarcinoma.

2. **Ultrasound:** Ultrasonography of the abdomen and pelvis helps in knowing the origin & nature of the pelvic mass & differentiating it form a uterine mass. It can also detect the presence of free fluid, bilaterality of the tumor and the presence of liver metastasis. Doppler blood flow in the ovarian vessels helps in differentiating beningn from malignant ovarian tumors, as malignant tumors are associated with increased diastolic blood flow.

Assessment of Risk of Malignancy in Ovarian Tumors:

Menopausal status-10-15% of ovarian tumors in pre-menopausal women and 40% of tumors in post-menopausal women are malignant

Tumor morphology on ultrasound-three variables are to be noted, tumor volume, wall structure and septal structure. Unilocular cystic tumors of <5cm have an extremely low risk of malignancy; complex ovarian tumors with solid or papillary projections have a higher risk

CA 125 levels:Patients with increased levels in the presence of abnormal ovarian morphology have an increased risk

Color flow Doppler-vessels supplying ovarian malignancy are characterised by a central location, decreased medial thickness and increased diastolic flow

3. **Contrast Enhanced CT Scan of the abdomen & pelvis:**

   It is indicated in patients with ascites in the presence/absence of a palpable pelvic mass to know the presence or absence of omental caking, the presence of metastasis in the liver and para-aortic lymph nodes.

4. **Ascitic fluid cytology:**

   In a patient presenting with ascites alone, presence of cells from an adenocarcinoma indicate the possibility of carcinoma ovary.

5. **UGI endoscopy & Barium meal follow-through:**

   indicated in patients with haematemesis and suggestive of UGI obstruction as the ovarian tumor could be a secondary from a primary tumor in the GI tract.

6. **Colonoscopy:** indicated in patients >45 years and having occult blood in the stools

7. **Mammography:** indicated in women >40 years as a screening test and those with a palpable mass.

8. **Pap Smear:** Should be done if not performed in the last 3 years.

9. **Dilatation & Curettage:** indicated in women with a history of vaginal bleeding to detect the presence of a co-existing primary in the endometrium or to detect spread to the endometrium.

A thorough work-up helps in assessing the status of the patient and decide the optimum mode of management.