OVARIAN CANCER

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PRESENTATION OUTLINE

- Introduction
- Anatomy overview
- Practice essentials
- Epidemiology
- Etiology
- histopathology
- Clinical presentation
- screening
- Investigations
- Pattern of spread
- Staging
- Management
- Prognosis

INTRODUCTION

- Fifth most common cancer in women
- Fifth most frequent cause of cancer death
- 1 in 70 newborn girls will develop cancer during her lifetim
- Disease of postmenopausal women and all ages
- The ovary is home to many types of pre-malignant and malignant tumors
- The origins include:
  - Peritoneal covering of the ovary - epithelial malignancies
  - Primordial germ cells - germ cell tumors
  - Hormone producing cells in the stroma - specialized stromal tumors
  - Non specific tissues of origin - non specific mesenchymal tumors
  - Primary tumors elsewhere - metastatic tumors

ANATOMY OVERVIEW

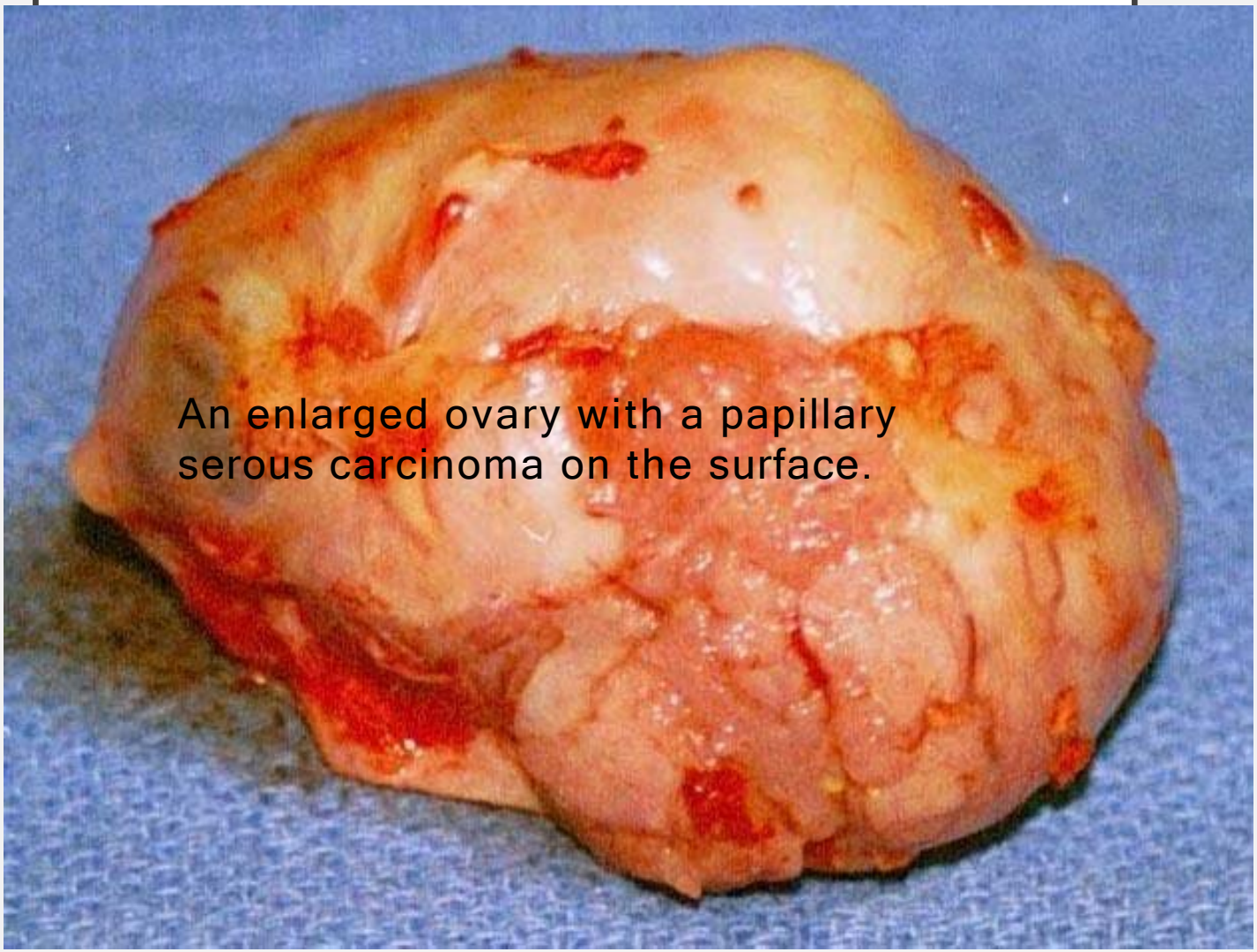
- Blood supply: ovarian artery - descending aorta
- Venous drainage: left ovarian - left renal vein, right ovarian vein - inferior vena cava
- Nerve supply - ovarian, hypogastric and aortic plexuses
- Lymphatic drainage - lateral aortic nodes, sometimes iliac nodes

PRACTICE ESSENTIAL

- Ovarian cancer is the most common cause of cancer death from gynecologic tumors in the United States. Malignant ovarian lesions include primary lesions arising from normal structures within the ovary and secondary lesions from cancers arising elsewhere in the body. Primary lesions include epithelial ovarian carcinoma (70% of all ovarian malignancies). Current research suggests that the majority of these originate from the fallopian tubes.

EPIDEMIOLOGY

- More in western countries – 15-20% of all genital malignancies
- Mostly affects menopausal women
- Peak incidence in 6th decade
- Risk of developing it – 2/100,000 in the 20's and 56/100,000 in the 70's
- Runs in families
- Nulliparity predisposes – frequent ovulatory trauma, repeated pregnancies, contraceptives are protective
- Use of coffee, tobacco, alcohol, fats been implicated, + exposure to talc, asbestos
- High mortality rate due to late presentation – initially asymptomatic or non-specific symptoms


An enlarged ovary with a papillary
serous carcinoma on the surface.

ETIOLOGY

- Cause is unknown
- Genetics (10%): BRCA 1, BRCA 2, HNPCC
- Predisposing factors
  - Repeated ovulation
  - Infertility treatment
  - PCO 2.5 fold increase
  - Unopposed estrogen therapy

ETIOLOGY

- **Increase risk by**
  - High diet in saturated animal fats
  - Alcohol and milk (never confirmed)
  - Exposure to talk powder

ETIOLOGY

- **Protective factors**
  - Chronic anovulation
  - Multiparty
  - Breast feeding
  - Pregnancy -reduction 13-19% per pregnancy
  - COC Pills decrease by 50% for 5 years and more of use

HEREDITARY

- In two forms
  - Breast and ovarian syndrome (BOC)
    - Germline mutation in BRCA1 gene on chromosome 17(28-44%)
    - Less common BRCA2 on chromosome 13 (1/800)
  - Lynch syndrome (hereditary nonpolyposis colorectal cancer syndrome)HNPCC

HISTOPATHOLOGY

- Divided to three categories according to cell type of origin
  - Epithelial neoplasms
  - Germ cell neoplasms
  - Sex cord and stromal neoplasms
- May be the site of metastatic disease
  - Neoplasms metastatic to the ovary

I-EPITHELIA NEOPLASMS

- Tend to occur in the sixth decade of life
- Derived from the ovarian surface mesothelial cells , six types:
  - Serous
  - Mucinous
  - endometroid
  - clear cell
  - Transitional cell
  - undifferentiated
- Account for over 60% of all ovarian neoplasms
- More than 90% of malignant ovarian tumors

OVARIAN SEROUS CYSTADENOCARCINOMA

- Most common 35-50% of all epithelial tumors
- Bilateral in 40-60%
- 85% with extra ovarian spread at diagnosis
- Over 50% exceeds 15 cm, solid areas, hemorrhage, cyst wall invasion
- Mostly poorly differentiated

MUCINOUS NEOPLASMS

- 10-20% of epithelial ovarian tumor
- Second most common type of epithelial ovarian carcinoma
- Bilateral in less than 10% Average size is 16-17 cm (large)
- multilocular ,viscous mucus

CLEAR CELL CARCINOMA

- Called mesonephroid carcinoma
- 5% of epithelial ovarian cancer
- Small size
- Aggressive ,hypercalcemia ,hyperpyrexia
- Cystic and solid

2-GERM CELL NEOPLASMS

- Tend to occur in second and third decade of life
- Better prognosis
- Many produce biological markers
- Types:
  - Dysgerminoma
    - Young females (Seminoma in male)
    - 30-40% of germ cell tumors
    - Unilateral in 85-90%
    - Solid

ENDOMETRIAL SINUS TUMOR

- Was called yolk sac tumor
- Second most common germ cell tumor
- Occurs in 20% of cases
- Bilateral in less than 5%
- Commonly present with acute abdomen
- Produces AFP

Immature teratomas

- Malignant counterpart of mature cystic teratoma

- 20% of germ cell neoplasms
- Bilateral in less than 5%
- Elevated serum AFP
- Three germ layers
- Immature neuroectodermal element

3-SEX CORD-STROMAL

-
  - 1-2% of all ovarian neoplasms
  - Most common malignant tumor of sex cord-sromal
  - Associated with hyperestrogenism
  - May cause precocious puberty(girls) ,adenomatous hyperplasia and vaginal bleeding(postmenopausal women)
- **Ovarian thecoma**
  - Associated with hyperesrogenism
  - Benign tumor
- **Ovarian fibroma**
  - Benign tumor
  - Associated with Meig's syndrome
- **Sertoli-stromal cell tumors**
  - Rare
  - consist of testicular structures
  - Occur during third decade

4-NEOPLASMS METASTATIC TO THE OVARY

- Accounts for 25% of all ovarian malignancy
- Mimic primary ovarian cancer
- Present as bilateral adnexal masses
- 25% unilateral
- Common primary cancers
  - Breast (40%)
  - Stomach (Krukenberg tumors)
  - Colon
  - endometrium

SIGNS AND SYMPTOMS

- Bloating; abdominal distention or discomfort
- Pressure effects on the bladder and rectum
- Constipation
- Vaginal bleeding
- Indigestion and acid reflux
- Shortness of breath
- Tiredness
- Weight loss
- Early satiety
- Ascites

CLINICAL PRESENTATION

- Dependent on stage of disease – early, late, advanced
- **Early disease** – usually symptomless.
- Symptoms when present include:
  - Dyspareunia
    Constipation
  - Urinary frequency Pelvic
    fullness
  - Large tumors may present as abdominal mass or cause pain from torsion or rupture

CLINICAL PRESENTATION 2

- **Late disease** – usually metastatic. Symptoms include those due to metastases i.e.
  - Vague abdominal pain
  - Abdominal swelling – mass or ascites
  - Anorexia, dyspepsia, indigestion, constipation, nausea, vomiting
  - Early satiety
  - Uterine bleeding if hormone producing

CLINICAL PRESENTATION 3

- Advanced disease - presents with complications:
  - Intestinal obstruction

    Pleural effusion

    Respiratory distress

  - Supra-clavicular or inguinal lymphadenopathy

    Extreme weight loss = cachexia

PHYSICAL EXAMINATION

- Comprehensive examination
  - Lymph node , Sister Mary Joseph's nodule
  - Abdomen examination
  - Pelvic examination
- Physical findings are uncommon in patients with early disease. Patients with more advanced disease may present with any of the following

- Ovarian or pelvic mass
- Ascites
- Pleural effusion
- Abdominal mass or bowel obstruction

SCREENING

- Routine pelvic examination
- Ultrasound examination
- Tumor markers
  - CA-125 antigen from fetal amniotic and coelomic epithelium
  -

INVESTIGATIONS

- **Laboratory Evaluation**
  - CBC
  - Serum electrolytes
  - hCG (pregnancy)
  - AFP ,LDH lactate dehydrogenase (young girls)
  - Serum CA-125 antigen levels - elevated in 80% of cases of advanced disease
  - Renal function tests, liver function tests - dependent on signs/symptoms or as pretreatment evaluation

RADIOGRAPHIC EVALUATION

- Computed tomography (CT)-Pelvic organs and Retroperitoneal structures
- Magnetic resonance imaging (MRI)-Nature of ovarian neoplasm
- X ray chest
- Barium enema
- mammogram

PATTERN OF SPREAD

- Direct extension – through capsule to adjacent pelvic structures including uterus, tubes, pelvic peritoneum
- Transcoelomic spread – most common, follows clockwise flow of peritoneal fluid – Right paracolic gutter, sub-diaphragmatic space, liver capsule, mesenteric surfaces. Omentum may form omental cakes
- Lymphatic - pelvic /para-aortic lymph nodes – in 50% of those with advanced disease
- Hematogenous – late, grave prognostic significance

STAGING

- FIGO staging used - largely surgical but with cytological aspects
- 1 - Growth limited to the ovaries
  - 1a - 1 ovary involved, not reaching capsule
  - 1b - both ovaries, not reaching capsule
  - 1c - either Ia or Ib but with evidence of tumor on surface, ruptured capsule or malignant cells in peritoneal fluid/ascites

STAGING CONTD.

2 – Extension to other pelvic structures

- 2a – extension to uterus or tubes
- 2b - extension to other pelvic structures
- 2c – IIa or IIb with evidence of tumor on ovarian surface or malignant cells in peritoneal fluid

3 – Extension to abdominal cavity

- 3a – abdominal peritoneal surfaces involved- microscopic
- 3b – metastatic tumor lesions bigger but < 2cm
- 3c – Tumor masses >2cm or inguinal, pelvic or para-aortic node involvement

STAGING CONTD.

- 4 - Distant metastases:
  - Pleural effusion with malignant cells
  - Lung metastases
  - Liver/spleen - parenchymal metastases
  - Supraclavicular nodes or skin involvement

PROCEDURE OF STAGING

- Done at laparotomy
- Ascites or peritoneal washings sampled
- Complete abdominal exploration
- Hysterectomy + infracolic omentectomy
- Biopsy of peritoneal implants
- Biopsy of pelvic or para-aortic nodes
- Cytoreductive surgery - target to remove all visible tumor tissue
- Histology done to confirm tumor and type
- Complete staging only after cytology/histology

MANAGEMENT

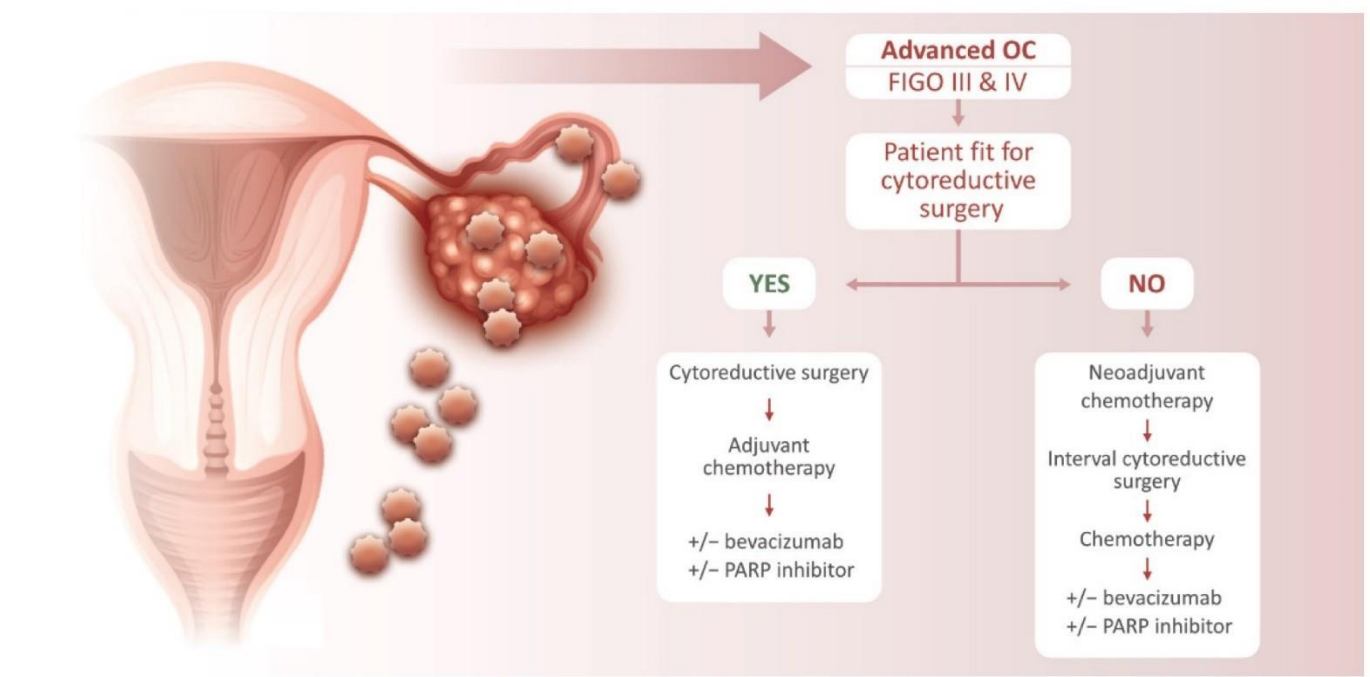
- Surgery is the corner stone of therapy
- Surgical staging to
  - Reduce amount of disease
  - Evaluate the extent of spread
- Debulking or cytoreductive surgery is removal
  - Primary tumor
  - Associated metastasis disease.
- Begins with cyto-reductive surgery and histology
- Epithelial tumors: - 80-90% of all tumors, serous 60%, mucinous 20%, endometrioid 2%
  - 70-80% beyond pelvis at diagnosis
  - Chemotherapy - If there is evidence of metastasis. Drugs used - Cisplatin, Carboplatin, Cytoxan, Taxol, Doxorubicin, Vincristine, Ifosphamide Paclitaxel
  - Commonest regime - Cisplatin + Cytoxan every 3-4 weeks for 6-8 courses
  - Paclitaxel +Carboplatin -best survival rate in stage 3,4
  - CA-125 levels, size of palpable masses used to assess response (monthly history, physical exam)

MANAGEMENT CT.

- Whole abdomen irradiation (phophorus 32 colloid) for stage 3 and 4
- Salvage therapy for recurrence, inadequate response to primary treatment
- Palliative care

- Germ cell tumors (10-20%)
  - Most often, surgery alone is sufficient - occurs at younger age, tends to be symptomatic early
- Dysgerminomas
  - Respond best to both radiotherapy and chemotherapy (offered primarily or after surgery). Chemotherapy preferred where fertility is to be preserved

TREATMENT FLOW CHAT



PROGNOSIS

- Related to
  - Response to chemotherapy
  - Differentiation of tumor
  - Germ cell better than epithelial
  - Stage of the disease -5 year survival rate (epithelial)
    - Stage I -75-93%
    - Stage II- 65-74%
    - Stage III- 23-41%
    - Stage IV- 11%

END