OVARIAN CANCER

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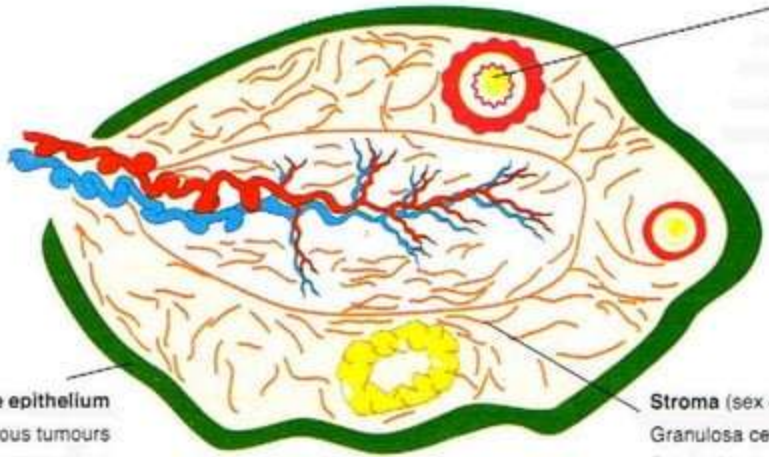
INTRODUCTION

- Fourth most common cause of death in women
- 30% of genital malignancies in the developed countries
- 5% of all gynecological cancers in India.
- Lifetime risk of having ovarian cancer 1.7%
- Majority (70%) of cases are diagnosed in advanced stage .

HISTOLOGICAL CLASSIFICATION OF OVARIAN TUMORS



Diagrammatic representation of origin of ovarian tumours. The epithelial tumours arise from the surface epithelium, germ cell tumours from the germ cells in the ovarian follicles and the sex cord-stromal tumours from the stroma of the ovary. (SCST, sex cord-stromal tumours.)

EPITHELIAL CANCER

- Most common ovarian cancer- 90% .
- 80% are primary in ovary
- 20% -metastatic from breast ,GIT , and colon
- Mean age at diagnosis - 60 years.
- Effect of menopausal status In menopausal women- 30% of ovarian neoplasm are malignant In premenopausal women- 7% are malignant.

ETIOLOGY

Various theories

Etiology not well known

Hereditary or familial ovarian cancer

1) BRCA 1&2 mutations
2) Ras oncogenes,
3) p53 mutations

RISK MODIFIERS

Risk factors

- Nulliparity
- Infertility
- Early menarche
- Late menopause
- Endometriosis
- Family history
- Talc use
- Prolonged use of ovulation inducing drugs
- HRT

Protective factors

- Oral contraceptive
- Pregnancy
- Breast feeding
- Tubal –ligation
- Hysterectomy
- Prophylactic salpingo-oophorectomy.

WHO CLASSIFICATION OF EPITHELIAL TUMOURS (2003)

Serous adenocarcinoma

Mucinous tumours

- Adenocarcinoma
- Pseudamyxoma peritonei

Endometroid tumours

- Adenocarcinoma
- Mixed mullerian tumour

Clear cell adenocarcinoma

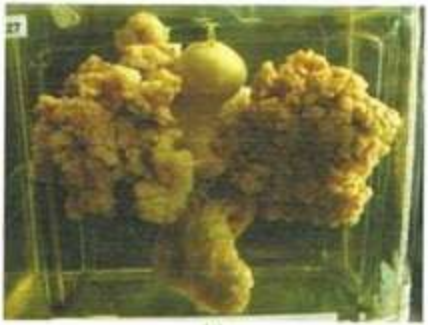
Transitional cell tumours

- Brenner tumour
- Transitional cell carcinoma

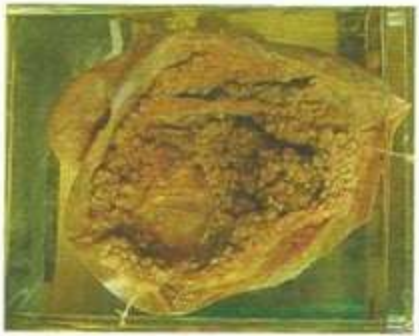
Rare tumours

- Mixed carcinoma
- Squamous cell carcinoma
- Undifferentiated
- Small cell carcinoma

PATHOLOGY



(a)



(b)

(a) Specimen of uterus and ovaries covered with papillary excrescences. (b) Papillary projections within the cyst on cut section.

Large mucinous tumour. Blood vessels are seen on the surface indicating a vascular tumour.

Histological features and frequency of Epithelial tumors

	Cellular type	Other features	Frequency
Serous	Fallopian tube	Psammoma bodies	80%
Mucinous	Endocervical	Mucin-secreting cells	10%
Endometroid	Endometrial	Majority well differentiated	10%
Clear cell	Mullerian	Clear and hobnail cell	<1 %
Transitional cell	Transitional cell	Dense, abundant fibrous stroma	<1%

DISTINCT CLINICAL BEHAVIOR

Irrespective of histology

- Low grade tumors-
  usually serous or mucinous, asstd
  pseudomyxoma peritonei, responsive to CT,
  B raf and K raf
  mutations, longer progression free
  survival
- High grade (Invasive cancer)-
  invasive(G2&3),
  p53 mutations,
  Poor prognosis
- Borderline tumors —15%, more in
  premenopausal, only 20% of
  these are metastatic

Ovarian cancer screening

Methods

1. Annual pelvic examination
2. Pelvic ultrasound
3. CA 125
4. Serum proteomic screening.
5. Multimodal screening

None is reliable and cost effective in general population

Indicated in familial ovarian cancers only

BRCA1 & 2 gene mutations- if positive (82% risk) screen from 35yrs or prophylactic OCP or RR salpingooophorectomy

CLINICAL FEATURES

Symptoms	Sign
Asymptomatic	Ascites
Anorexia, wt loss	Lower abdominal/ pelvic mass
Abdominal –pain/ distension/bloating	Omental cake
Irregular mass	Nodules in pouch of douglas
Dyspnoea	
Nausea/constipation	
Urinary frequency	Rectal examination

DIAGNOSTIC CRITERIA OF OVARIAN CANCER

- **Ultrasonography**
1. Ovarian volume>10cm3
2. Solid/complex(solid and cystic)
3. Multiloculated
4. Thickness of cyst wall>3mm
5. Septal thickness>2mm
6. Bilaterality
7. Papillary excrescences

- **Doppler flow studies**
1. Increase in vascularity
2. RI<0.04
3. PI<1
- **CA-125**
- HE 4, S. Inhibin

OTHER DIAGNOSTIC METHODS

- CT scan -Detects disease 1.5-2 cm
- MRI - Detects disease >1cm
- PET Scan- for distant disease

Confirmed by Cytology or tissue diagnosis

- Paracentesis
- FNAC

- Surgical specimen

ASSESSING RISK OF MALIGNANCY IN OVARIAN TUMOUR

1. Morphological index
2. Risk of malignancy index
3. Serum biomarker levels
4. Colour flow doppler
5. Serum proteomics.

RMI (RISK OF MALIGNANCY INDEX)

- RCOG guidelines
- **RMI=U X M X CA125**

  USG score(0, 1,3)

  Multilocular cyst, solid areas, metastasis, ascites, bilateral lesions

  M score (premenop=1, postmenop=3)
- RMI <25-low risk,

  25-250-mod risk,

  >250-high risk

FIGO STAGING OF OVARIAN CANCER 1ST JAN 2014

Stage I	Growth limited to the ovaries
IA	Growth limited to one ovary, No tumor on surface, negative washings
IB	Growth in both ovaries else same as IA,
IC	Tumor limited to one or both ovaries
IC1	Surgical spill
IC2	Tumor rupture before surgery or tumor on surface
IC3	Malignant cells in ascites or peritoneal washings

STAGE II GROWTH INVOLVING ONE OR BOTH OVARIES WITH PELVIC EXTENSION

IIA	Extension and/or metastases to the uterus and/ or fallopian tubes
IIB	Extension to other pelvic tissues- bladder , rectum, sigmoid colon

Stage III A	Positive retroperitoneal lymph nodes and/or microscopic metastasis beyond pelvis
IIIA1	i--- metastasis<10mm ii—metastasis> 10mm
IIIA2	Microscopic extrapelvic peritoneal involvement with or without RP LN
IIIB	Macroscopic extrapelvic peritoneal metastasis, none exceeding 2 cm in diameter with or without RPLN Includes capsule of liver or spleen
IIIC	Macroscopic, extrapelvic, peritoneal implant >2 cm with or without positive retroperitoneal nodes.
Stage IV A	Pleural effusion with positive cytology .
IV B	Hepatic and/or splenic parenchymal metastasis Metastasis to extra abdominal organs (inguinal nodes)

MANAGEMENT

Early ovarian cancer (Stage I and II)
Surgical staging and debulking

- Ascitic fluid cytology or peritoneal washings
- Total abdominal hysterectomy
- Bilateral salpingo-oophorectomy
- Omentectomy
- Pelvic and para-aortic lymphadenectomy
- Multiple peritoneal biopsies

ADJUVANT THERAPY

Early stage disease

- Stage IA G1/2 (low risk)
  No adjuvant therapy
- Stage IA G3, IB-II (high risk)
  3 cycles of chemotherapy

Advanced stage disease

- Stage III & IV
  3-6 cycles of chemotherapy

- Carboplatin and Paclitaxel- Standard combination

MANAGEMENT OF ADVANCED-STAGE EPITHELIAL OVARIAN CANCER

- Staging laparotomy and primary cytoreductive surgery followed by
- Postoperative adjuvant chemotherapy.
- Best results with Nil residual disease
- Debulk to microscopic level

- For inoperable tumors or high surgical risk cases

Neoadjuvant Chemotherapy (NACT) followed by surgery and post operative chemotherapy .

SUBSEQUENT MANAGEMENT

- Complete response Follow-up
- Partial response Continue same chemotherapy or switch to second line chemotherapy
- Stable disease switch to second line chemotherapy
- Progression of d/s switch to second line chemotherapy

Second line chemotherapy and other modalities

- Docetaxel
- Topotecan
- Doxorubcin
- Gemcitabine
- Etoposide
- Ifosfamide
- Tamoxifen

- Immunotherapy
- Hormone therapy
- Gene therapy
- Radiation therapy
- High dose chemotherapy and autologus bone marrow transplantation

Follow up

- 3 monthly for 2yrs
- 4-6monthly for 3-5 yrs
- Annually after 5 yrs

- **Methods**– clinical, CA 125 (optional)
- CA 125 and CT for suspected recurrence

Q1

Which is the most common type of ovarian cancer?

a) Epithelial
b) Germ cell
c) Sex cord stromal
d) Undifferentiated

Q2 All are risk factors for ovarian cancer EXCEPT

- Nulliparity
- Early menarche
- Endometriosis
- Tubal ligation

Q3

Screening for ovarian cancer is recommended for

a) Women above 40 years
b) Women above 60 years
c) All women
d) Women at high risk for familial ovarian cancer

Q4
FIGO stage III of ovarian cancer includes

a) Tumor limited to one ovary
b) Tumor involving both ovaries
c) Tumor extending to pelvic organs
d) Tumor extending to abdominal cavity

Q5 Ovarian cancer is primarily managed by

a) Chemotherapy
b) Radiotherapy
c) Immunotherapy
d) Staging Laparotomy

What is the position of prevalence of ovarian cancer among genital cancers

- 1
- 2
- 3
- 4

Which other cancer is Associated with hereditory ovarian cancer

- GB
- Lung
- Breast
- cervix

Borderline ovarian tumors are also known as

- Tumors of low malignant potential
- Tumors of high malignant potential
- Hereditory ovarian tumors
- Seccondary ovarian tumors
-

Spread to RP LN is seen in

- Stage1&2
- Stage 2&3
- Stage3&4
- Stage4 only

5YR SURVIVAL RATE OF STAGEI OVARIAN CA IS

- 30%
- 50%
- 70%
- 90%